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Rethinking Assessment: OSPEs Provide Authentic Alternatives in the Generative AI Era

Dr Nilushi Karunaratne

Oral presentations 1: Education & Gillian Shenfield Early Educator Award, Hall E1, December 10, 2025

Biography:

Nilushi Karunaratne is a dynamic Education-focused academic specialising in skill-based instruction and innovative teaching practices in physiology and pharmacology. Her education research spans building core pharmacology knowledge and essential skills, as well as exploring teamwork and resilience skill-based instruction to support students in contemporary educational landscapes.

Rethinking Assessment: OSPEs Provide Authentic Alternatives in the Generative AI Era

Nilushi Karunaratne[1], Edris Chan[1], Karen Gregory[1], Lauren May[1], Angelina Lim[1], Betty Exintaris. Faculty of Pharmacy and Pharmaceutical Sciences Education Research, Monash University[1], Melbourne, VIC, Australia

Introduction. Generative AI has disrupted traditional approaches to assessment, challenging the validity of tasks that rely heavily on written responses. This raises the central question: *does the task genuinely measure student learning?*
Aims. To design and implement an OSPE in a 2nd-year pharmacology unit as an authentic alternative to written examinations, with the aim of promoting deep learning and assessing applied reasoning and judgement.
Methods. A three-station OSPE was developed to assess both hands-on and cognitive skills. The first station focused on practical laboratory tasks including safety, experiment planning, calculations, pipetting technique, and data interpretation. The second station was a verbal consult requiring students to defend experimental decisions by interpreting data, justifying methodology, and articulating reasoning. The third station required students to explain a key laboratory concept or technique, assessing clarity of explanation and conceptual understanding. Students rotated through stations under timed conditions. Feedback was gathered through student surveys and examiner reflections.
Results. Evaluation indicated that the OSPE effectively assessed both technical skills and higher-order reasoning. Students valued the authenticity of demonstrating practical techniques and explaining their thinking aloud, noting this better reflected real-world expectations than a written exam. Examiners reported that the format revealed differences in depth of understanding and communication that traditional exams often overlook.
Discussion. OSPEs provide an assessment structure aligned with authentic, transferable skills. In contrast to traditional exams vulnerable to AI assistance, OSPEs assess reasoning, judgement, and reflection - core human learning dimensions. While resource-intensive, they represent a powerful shift in assessment design, ensuring student learning outcomes are measured meaningfully in an AI-enhanced educational landscape.

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Are interactive oral interview assessments only useful as a secure AI assessment?

A/Prof Kellie Charles

Biography:

Kellie Charles is a passionate educator and education researcher from the Pharmacology Discipline in the Sydney Pharmacy School at the University of Sydney. She is a Senior Fellow of the Academy Higher Education in the UK and previous recipient of the ASCEPT Outstanding Teaching Excellence Award. Her recent Churchill Fellowship focused on the educator's experiences of integrating AI into education practice and assessment. She continues to explore changes to the higher education ecosystem through disruptive paradigms.

Are interactive oral interview assessments only useful as a secure AI assessment?

Kellie A. Charles[1]. Pharmacology Discipline, Sydney Pharmacy School, University of Sydney[1], Sydney, NSW, Australia.

Introduction. Interactive oral interview (IOI) assessments are becoming the *assessment du jour* with educators scrambling to find ways to evaluate the student's own knowledge and application without the use of AI. Introduced by educators at Griffith University, IOI assessments are not viva voce or oral presentations. They are instead professionally focused, educator-guided conversations that allow students to reflect on their performance (usually within another submitted assessment) and be able think creatively when challenged with an alternative piece of evidence. While this format is being sought primarily to evaluate student performance, I pose the perspective that the IOI format also supports student development and assessment of skills that are very difficult to assess with traditional forms of assessment and greater alignment with educator's teaching philosophies.

Aims. To provide a reflective account of my own experience implementing and examining science students' reflective thinking of their professional growth using the IOI assessment.

Methods. Three IOI assessments were conducted individually with final year science students completing PCOL3888, an inter-disciplinary research capstone unit (25-30% of final mark). Each 10-minute interview posed a specific professionally focused discussion on identification of strengths and weaknesses, setting developmental goals, challenges in teamwork, influence and leadership, which were skills students developed in this semester-long, team-based project. Autoethnography was used to explore and critically reflect on my perspective as an educator, curriculum designer and examiner of the IOI assessments.

Results. While it does allow for a secure non-AI allowed assessment, IOI allowed me to direct a fluid, free-flowing conversation that facilitated the student's development as a future leader, make connections with emotional intelligence and empathy and enabled an assessment of the process of learning authentically. The two-way dialogue caused a switch in my teaching roles from examiner to feedback partner. Due to the natural alignment with my teaching philosophy of wayfinding and supportive developmental learning, IOI also proved an unanticipated reward.

Discussion. The assessment of the student learning process is challenging within traditional science assessments. IOI provide an exciting form of assessment that supports learner professional growth and educator satisfaction.

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How does generative AI impact student motivation and academic self-efficacy?

Assoc Prof Tina Hinton

Biography:

Tina Hinton (BSc Hons, PhD, Grad Dip Sci Psych) is an Associate Professor of Pharmacology (Education Focussed) and Director of Pharmacology Education in the Sydney Pharmacy School, Faculty of Medicine and Health, at The University of Sydney, Australia. Tina's research focuses on complex learning environments for biomedical sciences and healthcare students and the influences of physical and virtual design, instructional design and social design on learner experience, engagement and participation in valued practices. Tina is also involved in national and international projects on pharmacology curriculum. Tina currently leads projects investigating the impact of technology-enhanced learning strategies and online education practices on student motivation and engagement from both students' and educators' perspectives.

How does generative AI impact student motivation and academic self-efficacy?

Tina Hinton[1,2], Amber Perkins[1], Benedict Tsang[1], Grace Xu[3], Jessica Pace[1], Rania Salama[3]. Sydney Pharmacy School, The University of Sydney[1], Sydney, NSW, Australia. Charles Perkins Centre, The University of Sydney[2], Sydney, NSW, Australia. Department of Health Sciences, Macquarie University[3], Macquarie Park, NSW, Australia.

Introduction. Understanding the influence of artificial intelligence (AI) on student motivation and academic self-efficacy in higher education is necessary for optimising educational strategies and policies. Current literature focuses on the role of AI in completing academic tasks yet overlooks its impact on students' psychological needs. Self Determination Theory[1] and Self Efficacy theory[2] provide theoretical frameworks to understand psychological needs of intrinsic motivation and academic self-efficacy, respectively, in an education context.

Aims. To examine the impacts of AI on psychological needs of intrinsic motivation and academic self-efficacy of biomedical sciences and healthcare students at two universities in Australia.

Methods. A convergent parallel mixed-methods approach was used. A questionnaire including Likert-scale and open-ended questions aligning with the Intrinsic Motivation Inventory and University Academic Self-Efficacy Scale was conducted with students. Semi-structured interviews of students and staff further explored attitudes toward AI in learning, teaching, and assessment, aligning with Self Determination and Self Efficacy theories. Quantitative and qualitative data were analysed statistically and thematically. (HREC Approval No. 2023/HE000432).

Results. Analysis of 113 questionnaire and 58 interview responses revealed AI platforms had a moderately positive impact upon students' intrinsic motivation and academic self-efficacy, with different AI platforms reinforcing different psychological needs to varying degrees. Positive attitudes emerged around curiosity, equity, and the role of AI in enhancing writing, summarisation, and content adaptation. Negative attitudes focused on the impact of AI on critical thinking and ethical concerns. Strong support for AI integration into education was conveyed.

Discussion. This study provides evidence-based recommendations that highlight effective strategies for promoting student engagement and success. AI use supports individualised learning and increases equity and access to educational resources. These insights should inform the development of curricula and teaching practices that better align with the contemporary students' needs.

[1]Ryan and Deci (2000). *Am. Psychol*., 55(1), 68-78; [2]Bandura (1977). *Psychol. Rev.* 84(2), 191–215.

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Sustainable organ bath pharmacology experiments for continued experiential learning in Science

Dr Brent Mcparland

Biography:

Brent McParland (BSc, MSc(Hons), PhD) is a Senior Lecturer of Pharmacology in the Sydney Pharmacy School, Faculty of Medicine and Health, at The University of Sydney. Dr McParland's research focuses on mechanisms that cause exaggerated narrowing of the airways in asthma and COPD. He coordinates foundational pharmacology units of study in Science programs and contributes his teaching expertise to Pharmacy, Medicine, Science, Medical Sciences, Oral Health and other programs of study. Dr McParland has been instrumental to the development of numerous practical learning activities for the teaching of pharmacology in the laboratory setting. These include cell-based assays, 3D printing, organ bath experimentation, and the reimagination and redevelopment of experiments to replace, reduce and refine the use of animals in pharmacology teaching.

Introduction of sustainable organ bath pharmacology experiments for continued experiential learning in Science.

Brent McParland[1,2], Tina Hinton[1,2], Nehan Munasinghe[2]. Sydney Pharmacy School, The University of Sydney[1], Sydney, NSW, Australia. Charles Perkins Centre, The University of Sydney[2], Sydney, NSW, Australia.

Introduction. Dose/concentration-response relationships are one of the fundamental core concepts that all students of pharmacology must learn. Traditionally, animal tissue-based organ bath experiments have been used at universities globally to demonstrate the concentration-response relationship of agonists and the function of antagonists. Increasing difficulty in obtaining ethical approval for the use of small animals for teaching purposes has led to abandonment of this experiential education practice across many pharmacology schools. Considering the 3R principles, cryopreservation of secondary use organ tissues may provide a sustainable alternative.

Aims. To develop a sustainable approach to animal organ bath pharmacology experiments using cryopreserved tissues obtained from meat industry cattle for use in foundational pharmacology practical laboratory teaching.

Methods. Tracheae were collected within 30 minutes of euthanasia from cattle used in the meat industry. Ethical approval was not required from the University. Tracheae were placed in ice-cold HEPES (10 mM)-buffered saline for the 1.5-hour transit back to the laboratory. Smooth muscle was dissected from the tracheae, cut into ~15x3 mm strips then cryopreserved in 10% DMSO containing M199-based freezing media at -80C for up to 12 weeks. ~170 tracheal strips could be dissected from two tracheae. Tissues were rapidly defrosted in prewarmed (37°C), carbogenated (5% CO_2 in O_2) Krebs-Henseleit medium prior to set up in organ baths (Danish Myo Technology). Cumulative physiological responses to acetylcholine alone and in the presence of atropine were used to generate concentration-response curves.

Results. Pharmacodynamic testing by students using acetylcholine (0.01-1000 µM) showed reproducible EC_{50} values of ~17 µM (95% CI:15-19 µM). 3, 10 or 30 nM atropine caused concentration-dependent rightward shifts of the acetylcholine concentration-response curves. The experiment has been effectively implemented within the MEDS2002 and PCOL2021 Foundations of Pharmacology second year units of study (500-600 students) for past 6 years.

Discussion. Approaches to preserving essential educational experiences should be carefully considered in curriculum decision-making. Animal-based organ bath experiments using cryopreserved tissues remain a viable, scalable and valuable tool for teaching core concepts, experimental design, analysis and ethical practice within pharmacology.

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Health professional co-teaching teams enhance clinical pharmacology learning and teaching in optometry

Dr Tori Llewelyn

Biography:

Dr Tori Llewelyn is a pharmacist, teaching specialist academic, and Associate Dean Learning and Teaching (Student Success and Engagement) in the College of Nursing and Health Sciences at Flinders University. Tori has over 15 years' teaching and learning experience in the higher education (medical and allied health) sector in Australia. She joined Flinders University in 2019, with her teaching focusing on pharmacology, quality use of medicines, and research and study skills.

Tori is passionate about creating authentic and practical learning experiences for students, most recently instituting interprofessional co-teaching teams in foundational and clinical pharmacology to ensure optimal authenticity and relevance for clinical allied health students.

Health professional co-teaching teams enhance clinical pharmacology learning and teaching in optometry

Tori Llewelyn[1], Gemma Wewegama[2], Sara Carrison[2]. Health Sciences, Flinders Unviersity[1], Adelaide, SA, Australia; Optometry and Vision Science, Flinders University[2], Adelaide, SA, Australia.

Introduction. Co-teaching, where two or more professionals with complementary skills deliver content simultaneously, has demonstrated positive impacts on learner engagement and success in primary and secondary education for over five decades. However, limited research exists on co-teaching outcomes in pre-clinical healthcare education, where foundational theoretical knowledge integration with clinical context is essential for student success.

Aims. To investigate whether co-teaching in an undergraduate ocular pharmacology unit would improve student understanding and preparedness for clinical training.

Methods. A co-teaching model was adopted in an undergraduate ocular pharmacology unit. Health professional academics (optometrists and a pharmacist) collaborated to develop and deliver case-based learning materials in weekly workshops over the semester. Students in the unit completed validated surveys (Dhar, 2019) to evaluate their confidence in theoretical content, perceived effectiveness of the co-teaching model, and preparedness for advanced studies. Students who had completed the unit prior to the change in teaching were also surveyed.

Results. Responses (N=54) showed favorable perceptions of co-teaching effectiveness. 78.4% reported improved understanding of the relationship between pharmacology and optometry practice, and 72.8% felt better-prepared for clinical expectations.

Discussion. These findings suggest that co-teaching enhances student engagement and contextual understanding in pre-clinical pharmacology education. Reported improved preparedness for clinical training highlights the potential of co-teaching to support transition to advanced study. Further research could explore long-term impacts on clinical performance and interdisciplinary collaboration.

Dhar A (2019) *Co-teaching in health sciences in higher education* [Curtin University]. https://espace.curtin.edu.au/bitstream/handle/20.500.11937/79580/Dhar%20A%202019.pdf?sequence=1

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Strategies for effective teamwork in the pharmacology practical class (Gillian Shenfield Early Educator Award)

Dr Makhala Khammy

Biography:

Dr Makhala Khammy started out as a cardiovascular pharmacologist, obtaining her PhD at the University of Melbourne. Her postdoctoral research investigated the complex and integrated mechanisms that regulate vascular tone and contribute to blood pressure elevation. Driven by an interest in teaching, she returned to the University of Melbourne to take on a Teaching and Research role in the Department of Pharmacology. As of 2021, she is a Teaching Focused Academic in the Department of Biochemistry and Pharmacology. She is passionate about improving student engagement and the student learning experience and believes this can be aided in part by including experiential learning opportunities that encourage student agency within teaching programs, and fostering inclusive and collaborative learning environments that nurture a culture of inquiry and curiosity. A curiosity with emerging pedagogical approaches and technologies motivates her to explore, develop, and implement new strategies to enhance teaching and learning in pharmacology education.

Strategies for effective teamwork in the pharmacology practical class

Makhala M Khammy, Department of Biochemistry and Pharmacology, The University of Melbourne, Parkville, VIC, Australia

Introduction. The ability to work effectively in teams to address a shared goal is a critical employability skill. However, while collaborative learning is known to promote deep learning, this can be impeded by negative perception of group work, interpersonal conflicts, inequitable contributions, and communication and trust issues. Anecdotally, these issues have been observed in a level 3 undergraduate pharmacology practical class subject core to the pharmacology major at The University of Melbourne. These issues were observed even when team tasks were designed to be authentic and sufficiently challenging – factors that are known to contribute to effective collaboration.

Aims. Therefore, the aim was to introduce interventions that support effective teamwork.

Methods. Teamwork agreements can help student teams identify individual and shared motivations, establish behavioural norms and clear working conditions. We provided class time for student teams to complete a teamwork agreement with four domains: communication, participation and contribution to group work, professional conduct, and conflict resolution. To encourage meaningful engagement with the task, a workshop preceding the practical was used emphasise the importance of teamwork skills to future employment. During weeks 3, 6, 9, and 12 of the semester, students performed a self-reflection and evaluated each member against the expectations outlined in their teamwork agreement. A small completion mark was allocated to peer assessments 2-4. To evaluate students' perception of the teamwork agreement and peer assessment process, a survey comprising Likert-type items (5-point scale) was deployed.

Results. Self-reported survey data indicated that while the peer assessment encouraged respondents to take accountability for their own contribution to team tasks, they were less assured that it promoted accountability among their teammates. Notably, approximately 50% of respondents indicated that they did not provide critical feedback out of concern that it would negatively impact team dynamics.

Discussion. Students have mixed perceptions about the value of the teamwork agreement and peer assessment process for effective collaboration. Further studies are required to ascertain whether students engaged meaningfully in the teamwork agreement.

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Prescription sequence symmetry analysis of glucagon-like peptide-1 receptor agonist and neuropsychiatric conditions

Dr George Tan

Biography:

George is a Research Fellow in Pharmacoepidemiology and Real-world Evidence at the Centre for Medicine Use and Safety, Monash University. His research focuses on generating real-world evidence on medication use patterns and outcomes. George has a specific interest in generating and validating drug repurposing hypotheses using real-world data. George currently serves as the Deputy Chair of the ASCEPT Pharmacoepidemiology SIG. George also teaches undergraduate and postgraduate topics such as Medication Safety, Evidence-based Practice, as well as coordinating the Objective Structured Clinical Examinations (OSCEs). He is also a practising pharmacist, with experience in both community and hospital pharmacy.

Prescription sequence symmetry analysis of glucagon-like peptide-1 receptor agonist and neuropsychiatric conditions

Maria J Alfonso Arvez,[1] Sam Wade,[1] Darshna Goordeen,[1] Jenni Ilomäki,[1] Amanda J Cross,[1] George SQ Tan[1].
Centre for Medicine Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences, Monash Univ[1], Parkville, VIC.

Introduction. Glucagon-like peptide-1 receptor agonist (GLP1Ra) use has surged since its expanded use for weight management, beyond the original indication of type 2 diabetes. Recent preclinical evidence suggests GLP1Ra may have neuroprotective, antidepressant, and anxiolytic properties through direct effects on the CNS and indirect effects on the gut-brain axis, thereby opening the possibility of using GLP1Ra to treat neuropsychiatric conditions.
Aim. To examine the association between GLP1Ra initiation and a range of neuropsychiatric conditions using prescription sequence symmetry analysis (PSSA) on prescription claim records.
Methods. Prescription claims data (Jul 2013 – Dec 2024) from a 10% sample of the Australian Pharmaceutical Benefits Scheme were analysed to determine whether GLP1Ra initiation was associated with initiation of marker medications for depression, substance use disorder, schizophrenia, attention-deficient hyperactivity disorder, epilepsy, migraine, Alzheimer's, and Parkinson's disease. The PSSA was used to estimate adjusted sequence ratios (aSRs), accounting for underlying temporal trends in medication use. The aSRs compared the number of initiators of GLP1RA followed by marker medications to those initiating in the reverse order within a one-year exposure window, excluding those who initiated both within a 14-day blackout period. Sensitivity analyses varied the exposure and blackout windows.
Results. 32,429 individuals initiated GLP1Ra and one of the marker medications within one year. An inverse association between GLP1Ra and antidepressants (aSR: 0.85, 95%CI 0.76 - 0.94), and medications for substance use disorders (aSR: 0.70, 95%CI 0.51 - 0.88) was observed. No associations were observed for other marker medications. Using a longer two-year exposure window, we additionally observed inverse associations for antipsychotics (aSR: 0.76, 95%CI 0.60–0.92), antiepileptics (aSR: 0.83, 95%CI 0.70–0.96), and antimigraine agents (aSR: 0.83, 95%CI 0.70–0.96).
Discussion. Initiation of medications for depression and substance use disorder was less likely in the year after GLP1Ra initiation, suggesting a protective association. This finding is consistent with preclinical evidence that GLP1RAs may modulate reward pathways and related behaviours. Future well-designed cohort studies and randomised trials are needed to confirm causality.

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Drug Burden Index–guided stewardship intervention to deprescribe in Older Acute Inpatients

Dr Kenji Fujita

Biography:

Dr. Kenji Fujita is a Postdoctoral Research Fellow at the Laboratory of Ageing and Pharmacology, Kolling Institute, University of Sydney. His research focuses on evaluating interventions for deprescribing inappropriate polypharmacy in older inpatients, developing a multidomain frailty index using routinely collected clinical data, and investigating the impact of deprescribing on physical functions in older mice with polypharmacy using neural network models. Since 2020, he has served as the working group co-lead on guidelines and indicators within the Pharmaceutical Care Network Europe (PCNE). With expertise in big data analysis, epidemiology, statistical modelling, and web application development, he has co-led a Japanese government funded project developing and validating quality indicators for community pharmacies (2024-2026).

Drug Burden Index-guided stewardship intervention to facilitate deprescribing anticholinergic and sedative drugs in older acute inpatients: A stepped wedge multi-site cluster randomised trial

Kenji Fujita[1], Nashwa Masnoon[1], Sarah N Hilmer[1] for the *Optimising Quality Use of Medicines in Hospital to Improve Outcomes in Frail Older People* investigators. Kolling Institute[1], The University of Sydney and Northern Sydney Local Health District, Sydney, NSW, Australia.

Introduction. The Drug Burden Index (DBI), a measure of a person's total exposure to medications with anticholinergic and sedative effects, may be useful as a clinical risk assessment tool to facilitate deprescribing in hospital patients.

Aims. To evaluate how a comprehensive intervention bundle using the DBI impacts on the proportions of older inpatients with at least one DBI-contributing medication (DBI drug) prescribed on admission, in whom a DBI drug is (i) dose-reduced or ceased on discharge and (ii) recommended for deprescribing in the discharge summary.

Methods. A stepped wedge cluster randomised trial was conducted in up to 4 services/hospital in six NSW hospitals (4/1/2022-3/7/2023). Participants were adults aged ≥65 years with DBI >0 at admission and hospital stay ≥48 hours. In pre-trial phase, the DBI Calculator was switched on in the electronic medical record (eMR) without visibility to clinicians to collect baseline data. In eMR phase, a report on each patient's DBI was automatically displayed in the eMR with links to guidance. In stewardship phase, a stewardship pharmacist facilitated deprescribing using the eMR intervention providing patient level advice and supporting co-design integrating its use in usual care. In sustainability phase, the stewardship pharmacist prompted use of the intervention 1-2 times per month per site.

Results. A total of 5,733 patients were included. There were no statistically significant differences in any outcomes between the pre-trial and eMR phases. The proportion of patients with ≥1 DBI drugs deprescribed on discharge increased significantly from 37.1% in eMR phase to 42.4% in stewardship phase (average treatment effect (ATE) with 95% CI: +5.3% [0.1, 10.6], p<0.05). However, it declined to 37.1% in sustainability phase (ATE: −5.3% [−10.9, 0.3]). Deprescribing recommendations for DBI drugs documented in discharge summaries increased from 7.9% in eMR phase to 14.5% in stewardship phase (ATE: +6.6% [2.7, 10.5], p<0.05). Frailty subgroup analysis revealed that the greatest impact was observed in the least frail group, with intervention effects diminishing as frailty levels increased.

Discussion. The DBI intervention with pharmacist stewardship significantly increased deprescribing of anticholinergic and sedative medications in older inpatients, but was not sustained when intensive stewardship was withdrawn. Intervention effects extended beyond hospital to support post-discharge deprescribing with GP recommendations.

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Clusters of psychotropic and health service use in people with dementia

Mr Edward Chun Yin Lau

Biography:

Edward is a community pharmacist in Australia and PhD student at the University of Sydney with a research interest in pharmacoepidemiology in older people, especially people living with dementia in community settings in Australia. He is particularly interested in the prevalence, risk factors and outcomes of high-risk prescribing in this population. His research is aimed at improving the safety and effectiveness of medication use in people living with dementia.

Clusters of psychotropic and health service use in people with dementia living

Edward C.Y. Lau[1], Sarah Hilmer[2], Yun-Hee Jeon[3], Christine Y. Lu[1,2], Chin Hang Yiu[1,2], Edwin C.K. Tan[1]. Sydney Pharmacy School, The University of Sydney[1], Sydney, NSW, Australia; Kolling Institute, The University of Sydney [2], Sydney, NSW, Australia, Susan Wakil School of Nursing and Midwifery, The University of Sydney [3], Sydney, NSW, Australia.

Introduction. Psychotropics are commonly used in people with dementia. Health service utilisation is important in managing both dementia-related symptoms and multimorbidity. However, patterns and clusters of psychotropic and health service utilisation among people with dementia remain poorly understood in the Australian context.

Aims. To identify prevalence of and factors associated with different clusters of psychotropic and health service use, and assess their association with mortality in Australians with dementia.

Methods. This cohort study utilised linked 2021 Census, death registration, Pharmaceutical Benefits Scheme (PBS) and Medicare Benefits Schedule data. People with dementia aged ≥65 years in Australia in 2021 were included in the study. Latent class analysis involving 16 variables, including different classes of psychotropics (antipsychotics, opioids, antidepressants, antiepileptics and benzodiazepines), chronic health service use (such as chronic disease management plans and medication review), mental and physical healthcare (such as allied health and psychiatrist visits). Logistic regression was used to identify factors associated with class assignment. Association with 12-month mortality was assessed using inverse probability of treatment weighting adjusted Kaplan-Meier curves and Cox regression.

Results. Overall, 165,655 people with dementia were included. A five-class model was selected using data-driven approach. Groups were described as (1) low-risk psychotropic & high chronic disease management use (35.3%); (2) low-risk psychotropic & low health services use (36.0%); (3) high-risk psychotropic & high chronic disease management use (12.6%); (4) high-risk psychotropic & low health service use (13.2%); and (5) moderate-risk psychotropic & high mental health service use (2.8%). People with dementia residing in remote/regional areas were less likely to be in high health service utilisation classes. Compared to those in the low-risk psychotropic use group, mortality risk was higher among those in high-risk psychotropic use groups (adjusted hazard ratio [aHR]: 1.35, 95% confidence interval [CI] 1.30-1.40). In contrast, those with high mental health services use had a lower mortality risk (aHR: 0.84, 95% CI 0.72-0.97).

Discussion. Health services may mitigate mortality risk in individuals with dementia but disparities in access to these services highlight the need for more equitable service delivery across Australia.

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Mapping multimorbidity clusters in older Australians using linked administrative health data

Dr Edwin Tan

Biography:

Dr Edwin Tan is a Dementia Australia Mid-Career Research Fellow and Senior Lecturer at the School of Pharmacy, Faculty of Medicine and Health, University of Sydney. He is a registered pharmacist with clinical experience in both Australia and the UK. He chairs the ASCEPT Pharmacoepidemiology Special Interest Group, co-chairs the ADNeT EMCR Accelerator Group and co-leads the Pharmaceutical Policy Node, Charles Perkins Centre. His research interests include geriatric pharmacy, pharmacoepidemiology, medication safety and personalised medicine.

Mapping multimorbidity clusters in older Australians using linked administrative health data

Edwin CK Tan[1,2], Weisi Chen[1], Christine Y Lu[1,2], Sarah N Hilmer[2]. Sydney Pharmacy School, The University of Sydney[1], Camperdown, NSW, Australia; Kolling Institute, The University of Sydney[2], St. Leonards, NSW, Australia

Introduction. Multimorbidity is common in older adults and contributes to increased healthcare use, poorer quality of life, and higher mortality. Understanding how chronic conditions co-occur can inform more effective, person-centred care. However, national data on multimorbidity patterns in Australia remain limited, particularly across diverse sociodemographic groups. Mapping these patterns can inform strategies to optimise polypharmacy management and reduce medication-related harm in older adults.

Aims. To (i) estimate the national prevalence of multimorbidity and (ii) examine sociodemographic variation in the prevalence of disease clusters among older adults.

Methods. We conducted a nationwide cross-sectional study using linked Pharmaceutical Benefits Scheme (PBS) and Medicare Benefits Scheme (MBS) data. The study included adults aged ≥65 years with at least one PBS and/or MBS claim between 1 July 2022 and 30 June 2023. Fifty-two chronic conditions were identified using the Rx-Risk index, based on ATC codes. Prevalence was defined as ≥2 dispensings for a given condition. Networks of co-occurring conditions were constructed using odds ratios from pairwise logistic regression as the primary similarity measure, and clusters were identified via Louvain modularity optimisation. Robustness was assessed using Yule's Q and Jaccard coefficients. Cluster composition and prevalence were examined by age, sex, remoteness, and area-level disadvantage (SEIFA).

Results. A total of 4,435,784 individuals (mean age 74.8 years; 53.2% female) were included. Multimorbidity (≥2 conditions) was present in 76.1% of the cohort. The most common dyad was hypertension and hyperlipidaemia (40.6%). Three major clusters emerged: (1) cardiovascular-metabolic, (2) mental health-neuropsychiatric; and (3) musculoskeletal-pain-cancer. Cluster structures were stable, but prevalence of conditions within clusters varied across sociodemographic groups, with higher multimorbidity in socioeconomically disadvantaged and regional populations.

Discussion. Multimorbidity is highly prevalent among older Australians, with disease clusters showing marked sociodemographic variation in prevalence. These findings highlight the need for integrated, tailored care models and can inform health policy and service planning to address geographic and socioeconomic disparities.

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Age-stratified trends in Australian prescribing of controlled ovarian hyperstimulation medications between 2016-2024

Ms Toni Michael

Biography:

Toni is a PhD student from the School of Pharmacy at the University of Sydney. Her research is on understanding the pharmacodynamic, pharmacokinetic, and pharmacogenomic properties of commonly prescribed fertility mediations to inform optimal use of medications in practice.

Age-stratified trends in Australian prescribing of controlled ovarian hyperstimulation medications between 2016-2024
Toni Michael[1], Mohammed Ali[1,2], Vinayak Smith[3,4], Beverley Vollenhoven[1,4,5,6], Christine Lu[1,2,7], Sophie Stocker[1,3,8], Sch. Pharm., Univ. Sydney[1], Sydney, NSW; Kolling Institute, Univ. Sydney[2], Sydney, NSW; Virtus Health Pty Ltd[3], Melbourne, VIC; Dept. Ob. & Gyn., Monash Univ.[4], Melbourne, VIC; Monash IVF[5], Melbourne, VIC; Monash Health[6], Melbourne, VIC; Dept. Pharm., RNS Hosp.[7], Sydney, NSW; Dept. Clin. Pharmacol. & Toxicol., St. Vincent's Hosp.[8], Sydney, NSW.

Introduction. While controlled ovarian hyperstimulation (COH) medications are used by most women undergoing fertility procedures, there has been no research into their prescribing trends. With older women recommended different COH medications than younger women, consideration of age within prescribing trends is warranted.
Aims. Identify the use of COH medications by Australian women between 2016-2024, focused on age-specific trends.
Methods. A population-wide retrospective observational study using the Pharmaceutical Benefits Scheme and the Census 2021 data was conducted, assessing COH medication prescribing data between January 1, 2014 and December 31, 2024. Data from women was stratified into three age categories: <35, 35-39, ≥40 years. Annual prescription rates for women <35 versus ≥40 years per medication were compared by Wilcoxon matched-pairs signed rank tests.
Results. There were 825,785 prescriptions for COH medications, with the highest counts occurring in 2023 and 2024. Prescribing of all COH medications increased in 2021. Follitropin alfa was most commonly prescribed (~50% each year) irrespective of age. Highly-purified human menopausal gonadotropin was the second most prescribed medication in 2021 and 2022, with women ≥40 years 2.24 times (2.12 to 2.37, p=0.0039) more likely to be prescribed the medication compared to women <35 years. Combination therapy of follitropin alfa and lutropin alfa was the second most prescribed medication in 2023 and 2024, with women ≥40 years 2.02 times (1.73 to 2.38, p=0.0039) more likely to be prescribed this combination compared to women <35 years.
Discussion. Prescribing of COH medications is increasing, and older women are more commonly prescribed a combination of hormones compared to younger women. Older age reduces response to COH, requiring multiple follicular pathways to be stimulated to enable adequate ovarian response, which may explain this prescribing trend. Future clinical trials should consider including older women, particularly when evaluating combination therapy, to ensure findings inform clinical practice.

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Incidence and profiles of poisonings in older people with dementia in Sweden

Ms Ilsa Wojt

Biography:

Ilsa Wojt is a hospital pharmacist and PhD candidate at the University of Sydney, focusing on pharmacoepidemiology and medication safety in older adults. Her research focuses on dementia, real world data, and poisoning risk, using large-scale registry data to describe real-world evidence that helps inform best practice. Alongside her academic work, as a hospital pharmacist, she has a strong interest in the societal dimensions of medication safety, including how health systems, caregiving structures, and social contexts shape risks and outcomes for older adult and behavioural health outcomes. Her broader research aim is to advance safe, effective, and person-centred medication use in vulnerable populations.

Incidence and profiles of poisonings in older people with dementia in Sweden: a matched registry-based cohort study

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Introduction. Poisonings are a significant global public health challenge, especially for older adults with dementia. However, few studies have examined poisonings in this vulnerable group. This study aims to explore the incidence, types, and substances involved in poisonings among older people with and without dementia in Sweden.
Aims. This study aims to estimate and describe: (i) the incidence rate, (ii) the types, (iii) the drug utilisation patterns and (iv) risk factors of poisonings in older people with dementia compared to those without dementia in Sweden.
Methods. This matched cohort study utilized linked Swedish national registries to examine poisonings. Participants aged 65 and over, with an initial dementia diagnosis between 2014 and 2018 were matched to controls by age and sex in a 1:3 ratio and followed until December 31, 2019. Poisoning cases were identified using ICD-10 codes, and incidence rates (IR) and hazard ratios (HR) with 95% confidence intervals (CI) for poisonings were calculated using Kaplan-Meier and survival regression models.
Results. Overall, 415,016 people (103,943 with dementia and 311,073 without dementia) were included. The incidence of any kind of poisoning was higher in people with dementia than those without dementia (IR: 100.3 per 100,000 person-months, 95%CI, 96.7–104.0 vs 76.4 per 100,000 person-months, 95%CI 74.8-78.1). Dementia was associated with a higher risk of any poisoning (HR: 1.48, 95%CI 1.39-1.58), particularly from unintentional poisonings (HR: 2.48, 95%CI 1.96-3.13) and adverse drug reactions (HR: 1.46, 95%CI 1.37-1.57) in the six months following diagnosis. Psychotropics, anti-thrombotics and cardiovascular medications were most associated with poisonings.
Discussion. Older adults with dementia are at an increased risk of poisonings, especially immediately following a dementia diagnosis. Judicious prescribing of high-risk medications and appropriate management strategies should be prioritised during this time.

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Pharmacokinetics, and efficacy/safety, of thioguanine suppositories in patients with refractory proctitis

Prof Murray Barclay

Biography:

Murray Barclay is a Clinical Pharmacologist and Gastroenterologist at Christchurch Hospital and Clinical Professor with the University of Otago. His research areas of interest include pharmacokinetics, therapeutic drug monitoring, pharmacogenetics, various aspects of inflammatory bowel disease, thiopurines, and biologic drugs.

Pharmacokinetics, and efficacy/safety, of thioguanine suppositories in patients with refractory proctitis

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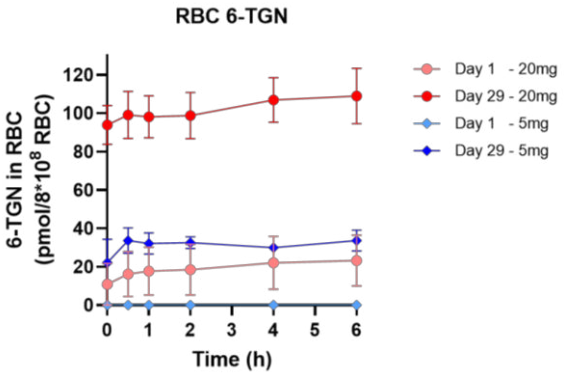
Introduction. Refractory proctitis can be difficult to manage even with newer inflammatory bowel disease treatments. A case series showed that rectal thioguanine appears to have a high rate of response. Thioguanine suppositories have been developed in NZ (Douglas Pharmaceuticals).

Aims. To assess the pharmacokinetics of thioguanine (TG) and its metabolite 6-thioguanine nucleotides (TGN), and assess for efficacy and safety signals, following rectal administration of thioguanine suppositories.



Methods. Eight patients with refractory ulcerative proctitis were prescribed either 20mg (n=6) or 5mg (n=2) thioguanine suppositories at night for 4 weeks. The pharmacokinetics of TG and TGN was assessed over 6h on days 1 and 29. Efficacy was assessed using weekly disease activity, and endoscopy scores before treatment and on day 29. Safety was assessed by weekly questionnaire and blood testing.

Results. RBC TGN concentrations on days 1 and 29 are shown in Figure 1. Clinical response at 4 weeks (SCCAI ≥3 point reduction) occurred in 8/8 patients (100%) and remission (SCCAI<3) in 3/8 (38%). Endoscopic remission (Mayo score 0 or 1) occurred in 6/8 patients (75%). UCEIS improved in 7/8 patients (88%) with remission in 4/8 (50%). No adverse effects were reported.

Discussion. In this phase IIa study, the efficacy at 4 weeks has high, without toxicity, with thioguanine 20mg or 5mg suppositories. TGN concentrations observed in RBCs were ~10-fold lower than seen with similar doses given orally.

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Is one-dose-for-all suitable for low dose colchicine in patients with gout?

Associate Professor Daniel Wright

Biography:

Dan Wright is an Associate Professor in Clinical Pharmacy at the University of Sydney. His research interests span clinical pharmacology, pharmacometrics, and medication adherence. He has expertise in modelling and simulation and the quantitative analysis of medication adherence data. His research platform aims to enhance the quantitative understanding of how drug treatments impact human biology and to explore the sources of variability in drug response between individuals. He uses this information to improve outcomes for patients through individualised dosing. Dan conducts research across several therapeutic areas notably cardiology, nephrology, transplant medicine and rheumatology.

Is one-dose-for-all suitable for low dose colchicine in patients with gout?

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Aims. Colchicine is commonly prescribed at a fixed dose of 0.5mg daily for the management of gout and has recently been approved for the secondary prevention of cardiovascular disease. The aim of this study was to determine the probability of achieving steady-state plasma concentrations within the safe and effective range using low dose therapy.

Methods. Colchicine plasma concentrations from 78 people with gout and 13 healthy volunteers were analyzed using non-linear mixed effects modelling [1]. Body size, kidney function, concomitant drugs, ethnicity, sex, and age were tested as covariates in the model. Stochastic simulations were conducted to determine the probability of achieving colchicine $C_{av,ss}$ values within the proposed therapeutic range of 0.5-3 ng/mL at doses of 0.5-1mg daily and for different patient characteristics. Reduced kidney function was simulated using a fractional effect on colchicine CL/F [2]. Doses that produced $C_{av,ss}$ concentrations >0.5 or < 3ng/mL more than 80% of the time were assumed to be efficacious and safe. Observed gout flare rates at 3 months were compared to the probability of subtherapeutic concentrations.

Results. Body weight, sex, and statin use predicted colchicine pharmacokinetics. Colchicine 0.5mg daily achieved $C_{av,ss}$ > 0.5 ng/mL 65% of the time. When stratified by body weight quartiles, $C_{av,ss}$ values were > 0.5 ng/mL in 87% (Q1), 72% (Q2), 61% (Q3) and 42%(Q4) of simulates while mean gout flares increased numerically for the same quartiles from 0.7- 2.20 flares after 3 months of therapy. An increased dose of 0.5mg twice daily resulted in $C_{av,ss}$ concentrations between 0.5-3ng/mL in >80% of simulates with body weight above 95kg, regardless of kidney function and statin use.

Discussion. Our simulation study suggests that colchicine 0.5mg daily will not consistently achieve therapeutic concentrations in gout patients > 95kg. Increasing the dose to 0.5mg twice daily is expected to achieve therapeutic concentrations in patients >95kg without exceeding the proposed upper limit of the therapeutic range. Further work to validate the colchicine therapeutic range and to explore individualised dosing needs for some patients is needed.

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Is it time to replace the 'prescription' with the medication management plan?

A/Prof Matt Doogue

Biography:

Matt Doogue is a clinical pharmacologist passionate about clinical pharmacology in patient care. He has clinical and academic roles in clinical pharmacology and as a physician in a busy acute general medicine service. His interests include quality use of medicines, adverse drug reactions, clinical decision support, and therapeutic drug monitoring.

Is it time to replace the 'prescription' with the medication management plan?

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Introduction. A prescription is legally defined and regulated as a single task. This was valid in the mid 20th century for a patient 'problem' treated with a short course of a single medicine determined in a single patient-doctor appointment. The plan to use and order to dispense were recorded in the three lines of text in a prescription. In the 21st century the patients we care for have one or more chronic conditions each managed with one or more medicines.

Aims. To question the existing definition of 'prescription' and propose a set of tasks to manage medicines.

Methods. Lessons from: 1. Iterative review and updating of teaching prescribing to medical students in a clinical pharmacology course over 12 years. 2. Implementation and management of electronic prescribing and administration systems. 3. Both informed from prescribing medicines to complex patients in acute inpatient general medicine.

Results. The WHO guide to good prescribing was initially used to teach students. We found the six steps did not capture the clinical tasks and iteratively developed an alternative framework. Lectures, workshops and tutorials were developed and used to evolve the framework. A medication management plan spans many health encounters across a health system, needing common definitions and standards. The plan with the patient to treat a new 'problem' is an update to the existing treatment plan. In addition to ordering supply of product this includes: specifying monitoring of disease response and adverse effects at specified times; and scheduling review. These include criteria for dose titration and/or criteria to continue, cease or change treatment. Orders to renew product supply only sometimes coincide with clinical review. Definitions and standards for the tasks of medication management are lacking.

Discussion. Regulatory reform in Australia and New Zealand is redefining scopes of practice of health professionals. The tasks to manage each patient's medicines have not had similar attention. Prescribing defined by the supply order from a single health professional is insufficient to manage use of medicines by patients. Is it time for medication management plans for us as patients taking several long-term medicines. In addition to the tasks of product supply and dose administration, let's specify the goals of treatment and the tasks of assessing responses and reviewing and modifying regimens based on responses. My medical treatment is more likely to be effective if my goals and criteria for success (benefit) and failure (harm or lack of response) are part of the plan.

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Therapeutic benefits of megadose sodium ascorbate for blood pressure management in sepsis

Ms Maya Bishop

Biography:

Maya Bishop is a first-year PhD candidate at the Florey Institute of Neuroscience and Mental Health, University of Melbourne, under the supervision of Professor Yugeesh Lankadeva. Her doctoral research investigates megadose sodium ascorbate as a novel therapy to improve blood pressure regulation and brain function in sepsis, a life-threatening condition with high mortality and limited treatment options. This work is embedded within the Translational Cardiovascular and Renal Research Group and contributes to therapies that are already progressing to multi-centre clinical trials across Australia. Maya holds a Bachelor's degree (Honours) specialising in Biomedical Science and a Master's in Cancer Research. She has also worked as a sessional academic and junior anatomist, contributing to teaching and student learning in the field of biomedical science. With over ten years of combined research and academic experience, she is dedicated to advancing translational therapies that improve survival and long-term recovery for critically ill patients.

Therapeutic benefits of megadose sodium ascorbate for improving blood pressure management in sepsis

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Introduction. Sepsis is characterised by life-threatening falls in blood pressure that can lead to multi-organ dysfunction. Noradrenaline is the primary clinical vasopressor to restore blood pressure in sepsis. A major unresolved clinical complication is patients becoming unresponsive to noradrenaline, which can lead to catecholamine-refractory shock and death. Sodium ascorbate may be beneficial for restoring responsiveness to noradrenaline during sepsis.
Aims. To determine the ability of intravenous megadose sodium ascorbate to reverse vascular hypo-responsiveness to noradrenaline in non-anesthetised sheep with established live Gram-negative sepsis.
Methods. Fourteen adult Merino ewes were surgically implanted with a catheter in the carotid artery to assess mean arterial pressure and facilitate blood sampling for lactate measurements. The jugular vein was cannulated for infusion of *Escherichia coli* and drugs. Sepsis was induced by an intravenous bolus (2.8×10^9 CFU/ml) followed by a continuous infusion (1.26×10^9 CFU/ml/h) of live *Escherichia coli* for 32h. Sheep were randomised to receive either sodium ascorbate (3 g/kg; n=7) or fluid-matched placebo (n=7; 5% glucose) from 24 to 32-h of sepsis. Pressor responsiveness to increasing doses of noradrenaline (0.2, 0.3, 0.4, 0.5 µg/min/kg) was assessed at pre-morbid baseline, at 23-h of untreated sepsis, and then at 28 and 32-h of sepsis following sodium ascorbate or placebo treatment.
Results. At 23-h of *Escherichia coli* infusion, sepsis was characterised by reductions in mean arterial pressure (84.0 ± 2.6 to 74.0 ± 3.1 mmHg; *P*=0.0003) and increases in arterial blood lactate levels (0.58 ± 0.05 to 1.44 ± 0.27 mmol/L; *P*=0.005). Pressor responsiveness to noradrenaline was significantly blunted from baseline to 23-h of untreated sepsis (*P*=0.004). In placebo-treated septic sheep, pressor responsiveness to noradrenaline remained suppressed by 32-h of sepsis (*P*=0.003). In contrast, there was a restoration of noradrenaline pressor responsiveness in sheep treated with sodium ascorbate such that there was no significant difference from pre-morbid levels (P=0.9).

Discussion. Megadose sodium ascorbate restored vascular sensitivity to noradrenaline in a clinically relevant sheep model of sepsis. These findings provide the scientific rationale to design a multi-centre clinical trial using megadose sodium ascorbate to reduce noradrenaline requirements for blood pressure management in patients with sepsis.

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Predictors of non-cardiovascular readmissions in multimorbid adults with heart failure

Dr Joshua Inglis

Biography:

Joshua Inglis is a Clinical Pharmacologist working across digital health, medication safety and hospital medicine. He is currently completing his PhD on improving medication-related outcomes for older adults living with multimorbidity.

Predictors of non-cardiovascular readmissions in multimorbid adults with heart failure

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School of Biomedicine, Faculty of Health Sciences, University of Adelaide[1], Department of Clinical Pharmacology, Flinders Medical Centre and Flinders University[2], Registry of Senior Australians Research Centre, South Australian Health and Medical Research Institute[3], Caring Futures Institute, Flinders University[4] Northern Adelaide Local Health Network[5], Faculty of Health, Medicine and Behavioural Sciences, University of Queensland[6]

Introduction. Heart failure is common in hospitalised adults who have high rates of polypharmacy. Two-thirds of readmissions are for non-cardiovascular reasons where medications and comorbidities may be contributing factors.

Aims. To examine the association between long term medicines or comorbidities and time to non-cardiovascular readmission among multimorbid adults with heart failure.

Methods. We conducted a retrospective cohort study of multimorbid adults aged ≥45 years with heart failure who were discharged from four metropolitan hospitals in Adelaide between August 2016 and June 2023. Long term medications at discharge were extracted from the electronic medical record. Non-cardiovascular polypharmacy was defined as the use of five or more non-cardiovascular medications. Comorbidities were identified using hospital coding data and the RxRisk comorbidity index. Non-cardiovascular readmissions were defined as primary diagnosis admissions for non-cardiovascular conditions. Fine and Grey regression was used to assess the factors associated with time to non-cardiovascular readmission accounting for the competing risk of death. Covariates included age, gender, medications and comorbidities. Analyses were performed using R Statistical Software (version 4.1.2).

Results. 8,532 patients were included in the study with 57% (n=4,848) having non-cardiovascular polypharmacy. 39.5% of patients had a non-cardiovascular readmission within 12 months following discharge. Non-cardiovascular polypharmacy (sHR 1.11 95% CI 1.03-1.19), chronic kidney disease (sHR 1.50 95% CI 1.40-1.61), cancer (sHR 1.46 95% CI 1.34-1.59), anxiety disorders (sHR 1.44 95% CI 1.30-1.60), chronic obstructive pulmonary disease (sHR 1.18 95% CI 1.10-1.27) and dementia (sHR 1.14 95% CI 1.04-1.25) were associated with reduced time to readmission.

Discussion. Non-cardiovascular readmissions are common in multimorbid adults with heart failure. Non-cardiovascular polypharmacy and select comorbidities were associated with a 11-50% reduced time to readmission. These findings identify targets for medication optimisation and chronic disease management to potentially prevent non-cardiovascular readmissions in multimorbid adults with heart failure.

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Co-design of medication management resources for people with dementia in the community

Miss Xenia Nastatos

Biography:

I am a registered pharmacist currently working as a research assistant for the School of Pharmacy at the University of Sydney. Our current research project is focused on co-designing medication management resources for people with dementia and carers in both community and aged care setting. My research interests/experience span across aged care, dementia, health economics and oncology.

Co-design of medication management resources for people with dementia in the community

Joanne Lo[1], Shoohb Alassadi[1], Dr Jacqueline Wesson[2], Dr Amanda J Cross[3], Dr Karen Watson[4], Dr Natali Jokanovic[5], Xenia L Nastatos[1], Dr Mouna J Sawan[1]. Sydney Pharmacy School, Univ. of Sydney[1]; School of Health Sciences, Univ. of Sydney[2]; Centre for Medicine Use and Safety, Monash Univ.[3], Parkville, VIC, Australia; Sydney Nursing School, Univ. of Sydney[4], Camperdown, NSW, Australia; The Alfred Hospital and Monash Univ.[5], Melbourne, VIC, Australia.

Introduction. People living with dementia (PLWD) and their carers often receive insufficient information and support to facilitate safe medication management in the community. This increases their risk of medication-related harm. Existing medication management resources for PLWD and carers lack comprehensiveness in content. Moreover, efforts to collaboratively design tools with this population are scarce.

Aims. This study aimed to co-design and develop medication management guidance resources for PLWD and carers in the community.

Methods. This multi-methods study had two sequential phases. During Phase 1, focus groups, interviews and a modified-Delphi study with PLWD, carers and healthcare professionals in Australia were conducted. Phase 1 informed the content and generated two resource prototypes – one for PLWD and another for carers. During Phase 2, additional focus groups, two with carers and two with PLWD, were conducted to evaluate the prototypes. Feedback was provided on content and design, and resources were updated accordingly.

Results. In phase 1, four key content areas were identified: 1) questions to ask health professionals for medication management; 2) informed consent and active participation in shared decision-making; 3) risk and benefits of common medications; 4) strategies to address complexities in medication management. In Phase 2, both PLWD and carers noted that the resource was informative, easy to understand and would be useful when given at the time of dementia diagnosis. According to PLWD, the resource gave them a greater understanding of their rights and the concept of shared-decision making in medication management. Participants also recommended making the resources more user-friendly by reducing text, increasing font size and adding infographics.

Discussion. This study addresses gaps in medication related health literacy tools for PLWD in the community using a robust co-design approach. The inclusion of question prompts and shared decision-making information in the resources will help support PLWD and carers to be actively involved in decision making regarding safer medication use.

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Safety and efficacy of RDN post-stroke: results from the Global SYMPLICITY Registry

Mr Gianni Sesa-ashton

Biography:

Gianni is a research assistant in the Cardiometabolic Health and Exercise Physiology laboratory exploring the role of the sympathetic nervous system in health and disease. Overactivity of this system contributes strongly to the development and maintenance of cardiovascular diseases such as hypertension and heart failure.

Gianni's work has looked at therapies that target this system in the form of renal denervation — a surgical approach to lowering blood pressure by 'silencing' the nerves which control the kidneys and consequently drive-up blood pressure. They continue to work on projects investigating the role of the microbiome in the development of a hyperactive sympathetic nervous system in patients with hypertension and understanding which brain regions controls blood pressure.

Safety and efficacy of RDN after stroke: results from the Global SYMPLICITY-Registry

Gianni Sesa-Ashton[1], Felix Mahfoud[2], Roland Schmieder[3], Krzysztof Narkiewicz[4], Bryan Williams[5], Michael Böhm[6]. Markus P Schlaich[7,8]. Baker Heart and Diabetes Institute[1], Melbourne, VIC, Australia; Department of Cardiology, University Hospital Basel[2], Basel, Switzerland; University Hospital Erlangen[3], Erlangen, Germany; Medical University of Gdansk[4], Gdansk, Poland; University College London[5], London, United Kingdom; Saarland University Hospital[6], Homburg, Germany Dobney Hypertension Centre, Medical School, The University of Western Australia[7] and Departments of Cardiology and Nephrology, Royal Perth Hospital[8], Perth, WA, Australia.

Introduction. Radiofrequency (RF) renal denervation (RDN) is a guideline-recommended therapy for patients with hypertension (HTN), especially those with higher risk of cardiovascular (CV) events such as stroke. Moreover, prior stroke predicts increased risk for future CV events.

Aims. We assessed outcomes in stroke patients from the Global SYMPLICITY Registry (GSR) through 3-years after RDN.

Methods. Blood pressure (BP) and adverse events were evaluated for high-risk stroke patients in GSR, the largest international registry in patients with HTN. Measures were compared with baseline values using paired t-test.

Results. A total of 299 patients enrolled in GSR had a stroke prior to undergoing RDN. Stroke patients had a mean age of 62±11 years, 42% of whom were female, with 57% having a history of cardiac disease, 15% with atrial fibrillation, 44% with type II diabetes mellitus, 30% with chronic kidney disease (eGFR<60mL/min/1.73m^2), and 12% were current smokers. Mean baseline office systolic BP was 168±28mmHg and mean 24-h ambulatory systolic BP was 159±22 mmHg. Patients with stroke history were prescribed an average of 4.9±1.5 antihypertensive medications at baseline. At 3 years after RDN, stroke patients had a 21.4 mmHg and 11.7 mmHg reduction in office systolic and 24-h ambulatory systolic BP, respectively (both p<0.001 from baseline). The mean number of medications at 3 years was unchanged (4.6±1.6). At 3-years after RDN, the rate of death in stroke patients was 9%, with a CV death rate of 6%. The rate of recurrent stroke was 12%, and the rate for hospitalization due to hypertensive crisis/emergency was 7%.

Discussion. Stroke patients from GSR had sustained long-term BP reductions through 3 years after RF RDN. Rates of death, cerebro- and cardiovascular event rates in GSR compare favorably to those reported in contemporary population-based studies. RDN was overall safe in stroke patients and may be a suitable treatment option for high-cardiovascular risk patients with HTN in the management of high BP.

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Pre-existing Heart Failure Exacerbates Neuroinflammation After Cardiopulmonary Bypass

Dr Lindsea Booth

Biography:

Dr. Lindsea Booth is an Allan and Maria Myers Senior Research Fellow and head of the Neurocardiovascular Physiology Group at the Florey Institute. Her laboratory is focused on understanding how the brain communicates with other vital organs (heart and kidneys) via autonomic nerves in disease and, using state-of-art genetic engineering techniques, investigating how modifying activity within these nerves can improve outcome. Her research group is embedded within Florey's Stroke and Critical Care Research Priority area.

Pre-existing Heart Failure Exacerbates Neuroinflammation After Cardiopulmonary Bypass

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Introduction. Postoperative neurocognitive dysfunction is a major complication of cardiac surgery, particularly in patients with pre-existing heart failure (HF). No treatments exist, and mechanistic insight has been limited by the lack of clinically relevant models.

Aims. To determine how pre-existing HF influences cerebral oxygenation, neuroinflammation and blood biomarkers of neuronal injury after cardiopulmonary bypass (CPB).

Methods. Female sheep were instrumented under isoflurane anaesthesia (2.0–2.5% in oxygen–air) for continuous monitoring of systemic haemodynamics and cerebral tissue oxygenation (PO_2) across pre-CPB (conscious), CPB (anaesthetised), and recovery (conscious). At 48 h post-CPB, frontal lobe brain tissue was collected for immunohistochemistry and microglial morphology quantified. HF was induced by progressive coronary ligation and defined by a ≥25% reduction in ejection fraction. HF (n=8) and control (n=8) animals underwent 2 h CPB with aortic cross-clamp and 48 h recovery.

Results. CPB caused marked reductions in systemic oxygen delivery and mean arterial pressure in both groups (both $P_{time} < 0.001$), which were more pronounced in HF animals (both $P_{group} < 0.05$). Despite these systemic changes, cerebral PO_2 was relatively preserved during the transition to CPB, though it declined progressively while on bypass ($P_{time} = 0.002$), with a trend toward hypoxia in HF animals during the final 30 min (17 ± 2 vs 36 ± 10 mmHg, $P = 0.065$). Over the 48 h postoperative period, cerebral PO_2 remained near baseline in both groups, and plasma neurofilament light chain increased to ~1.5-fold baseline ($P_{time} = 0.008$), with no group differences. The most striking finding was exaggerated microglial activation in HF animals, evidenced by shorter branches (588 ± 49 vs 903 ± 63 µm, $P = 0.005$), fewer segments (129 ± 12 vs 211 ± 20, $P = 0.005$), and fewer terminal points (71 ± 7 vs 114 ± 10, $P = 0.006$) compared with controls.

Discussion. Heart failure exacerbates postoperative neuroinflammation, potentially due to lower cerebral oxygenation at the end of CPB, identifying neuroinflammation as a potential therapeutic target in cardiac surgery.

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Cardiovascular mechanobiomarkers relate to poorer cognition in older Australians. The Mind-Your-Heart Study

Dr Louise Goodall

Biography:

I'm an endocrinologist and PhD candidate at the Garvan Institute, where my research focuses on cardiometabolic contributors to cognitive ageing.

Cardiovascular mechanobiomarkers relate to poorer cognition in older Australians. The Mind-Your-Heart Study.

Louise Goodall[1], Audrey Adji[2,3], Perminder S. Sachdev[4], Nicole A. Kochan[4], Katya Numbers[4], Henry Brodaty[4], Jason Kovacic[2], Katherine Samaras[1,4,5]

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Arterial disease and heart failure cause vascular dementia and progress all dementia subtypes. The heart-brain nexus warrants investigation to determine cardiovascular mechanobiomarker associations with cognition.
Aims. To examine relationships between cardiac and arterial function and cognitive performance in older people without dementia.
Methods. Sydney Memory and Aging Study 2 is a longitudinal study of community-dwelling individuals. Mind-Your-Heart, a substudy (n=128), measured pulse wave velocity (PWV, applanation tonometry) and echocardiography (systolic function [left ventricular ejection fraction, global longitudinal strain, GLS; diastolic dysfunction [mitral E/A, E/E]; and left atrial size). Cognitive performance by neuropsychological testing of (i) executive function (Trail Making Test [TMT} A & B); (ii) memory (Logical Memory Story immediate- & delayed-recall, Rey Auditory Verbal Learning Test (RAVLT), Benton Visual Retention Test); (iii) attention-processing speed (Digit Symbol-Coding test [DSCT]; (iv) language (Boston Naming Test, oral word association (FAS), Semantic Fluency [animals]); (v) visuospatial function (Block Design) and (vi) global performance (Montreal Cognitive Assessment-MoCA, with mild cognitive impairment [MCI]: 19-25/30). Data were analysed by logistic regression (covariates: age, blood pressure).
Results. The mean age was 76±4y (51%F); 31% had mild cognitive impairment Mean PWV was 7.5±2.1 m/sec. Higher PWV related to lower executive function, memory and language (DSCT [β=-0.21, p=0.048], Logical Memory Immediate Recall [β=-0.26, p=0.016], FAS [β=-0.19, p=0.042]). GLS was associated with poorer memory and language (Logical Memory Story Delayed Recall [β=-0.24, p=0.011], RAVLT [β=-0.24, p=0.013, FAS [β=0.19, p=0.044], Animals [β=-0.28, p=0.002]). Diastolic dysfunction (mitral E/A) associated with poorer memory (RAVLT delayed recall [β=-0.26, p=0.007]).
Discussion. Mechanobiomarkers of GLS, diastolic dysfunction and arterial stiffness relate to poorer cognitive performance in older Australians. Longitudinal studies determining their impact on cognition are planned.

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Associations of blood pressure parameters with cognitive decline and dementia: umbrella review

Dr Sultana Shajahan

Biography:

Dr Sultana Shajahan is a Sydney, Australia-based dementia and cardiovascular researcher with a background in clinical medicine, public health, and epidemiology. After completing her medical degree, she earned a Master's degree in Public Health Research with High Distinction, followed by several years of research in stroke, women's health, dementia, and cardiovascular disease at The George Institute for Global Health. She is completing her PhD on blood pressure parameters and dementia at The George Institute and the University of New South Wales (UNSW). She has expertise in systematic reviews and statistical analysis of large clinical trials and cohort studies. She was the recipient of the Young Investigator Award at the European Stroke Organisation Conference in 2023. She also brings experience in building local and international research networks through her work at The George Institute and an invited research exchange program (2024) at Linköping University in Sweden.

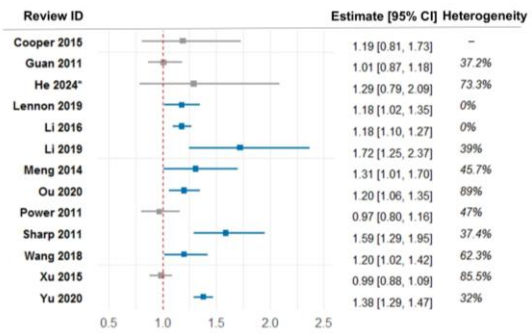
Associations of blood pressure parameters with cognitive decline and dementia: umbrella review

Sultana Shajahan[1], Megan Heffernan[1], Katie Harris[1], Cheryl Carcel[1], Mark Woodward[1,2], Craig S. Anderson[1,3], Ruth Peters[1]. The George Institute for Global Health, UNSW[1], Sydney, NSW, Australia; TGI UK, Imperial College London[2], Sydney, NSW, Australia; Institute of Sci and Tech for Brain-inspired Intelligence, Fudan University[3], Shanghai, China.

Introduction. Evidence syntheses on the associations between blood pressure (BP) parameters and cognitive decline and/or dementia have taken different methodological approaches and targeted different BP parameters and outcomes.

Aims. The aim of this umbrella review was to provide a high-level synthesis of published systematic reviews with meta-analyses on these associations.

Methods. PubMed, Embase, PsycINFO, and Cochrane were searched up to April 2025 for eligible reviews. Risk of bias was assessed using the AMSTAR-2 tool and overlap of constituent studies between reviews was explored.



Results. Among 31 included reviews, eight reported positive associations between higher BP and greater incidence of cognitive decline or dementia, five drew neutral conclusions, and one reported an inverse relationship. Greater mid-life BP was associated with greater risk of all-cause dementia, whereas late-life hypertension might have a mixed or overall neutral association. Three reviews reported associations between higher BP variability and all-cause dementia, and two for cognitive decline. Reviews also reported associations between higher pulse wave velocity and orthostatic hypotension and poorer outcomes. No reviews examined pulse pressure, mean-arterial pressure or cumulative BP load. Most reviews were of low quality, with considerable heterogeneity in BP parameter definitions and outcome criteria. Overlap of constituent studies for each BP parameter was low.

Discussion. In addition to high BP, incorporating variability, pulse wave velocity and orthostatic hypertension into risk assessments of cognitive decline or dementia and adopting standardized definitions for BP parameters and cognitive outcomes may improve comparability across future studies and strengthen clinical guidance.

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Association between Arterial Stiffness and Cognitive Decline in an Older Chinese Population

Dr Audrey Adji

Biography:

Dr. Audrey Adji is a research scientist at the Victor Chang Cardiac Research Institute and a research fellow at St Vincent's Hospital, Sydney. Her work explores pulsatile function in cardiovascular and pulmonary diseases, including mechanical circulatory support devices in heart failure. She has authored >80 peer-reviewed publications, presented at international conferences, and fostered collaborative research networks. Dr. Adji has received multiple scientific awards and serves on editorial boards of hypertension journals. She mentors postdoctoral fellows and supervises higher degree students across medicine and engineering. As Chair of the Women in Hypertension (Research) Committee at Hypertension Australia and the Early Career Research Network of Pulse of Asia, she advocates for equity and emerging researchers. She is a member of the Hypertension Australia Taskforce and a Fellow of both the International Society of Hypertension and the Cardiac Society of Australia and New Zealand. Dr. Adji actively cultivates national and global research partnerships.

Association between Arterial Stiffness and Cognitive Decline in an Older Chinese Population

Huijuan Chao[1], Qian Wang[1], Biwen Tang[1], Yue Hu[1], Hong Zhang[1], Junli Zuo[1,2], Ning Song[3], Audrey Adji[2,3,4] 1. Department of Geriatrics, Ruijin Hospital, Jiao Tong University, Shanghai, China; 2. Macquarie Medical School, Sydney, NSW; 3. St Vincent's Hospital, Sydney, NSW; 4. Victor Chang Cardiac Research Institute, Sydney, NSW

Introduction. Age-associated arterial stiffening is associated with end-organ damage in microvascular beds. The amplified pulse pressure transmission to the cerebral microvasculature may result in accelerated cognitive decline.
Aims. To explore the association between end-organ microvascular damage, including cognitive decline, with markers of arterial stiffness.
Methods. Older adult inpatients (≥50 years) at Northern Shanghai Ruijin Hospital were enrolled from Dec 2020 to Sep 2024. Arterial stiffness was assessed using carotid-femoral pulse wave velocity (cf-PWV) and carotid intima media thickness (CIMT), and markers of end-organ damage were assessed using estimated glomerular filtration rate (eGFR) and left ventricular mass index (LVMI). Cognition was assessed using the Mini-Mental State Examination (MMSE), with mild cognitive impairment (MCI) defined as an MMSE score <27.
Results. A total of 224 patients were enrolled, with the MCI group (n=102, 44F) being significantly older (74.2±8.7years, p<0.001) than the normal group (66.6±9.5years). The eGFR was comparable between the two groups (MCI 95.2±23.1, normal 95.3±27.4 ml/min/1.73m^2, p=0.972). The MCI group had higher cf-PWV (9.1±2.0m/s, p=0.011, vs 8.2±2.1m/s), and elevated CIMT (0.99±0.32mm, p=0.024, vs. 0.67±0.24mm). Significant inverse associations between MMSE scores and age (r=−0.465, p<0.001), LVMI (r=−0.147, p=0.038), and cf-PWV (r=−0.151, p=0.056) was observed. Multivariate logistic regression identified age (OR=0.874, 95% CI: 0.806–0.949), diabetes mellitus (OR=0.141, 95% CI: 0.037–0.529), and cf-PWV (OR=0.703, 95% CI: 0.520–0.950) as independent risk factors for cognitive impairment (p<0.05).
Discussion. In older Chinese populations, arterial stiffening and related microvascular end-organ damage may be associated with MMSE-assessed cognitive dysfunction. In addition to age, diabetes mellitus and cf-PWV may represent risk factors for cognitive impairment. Further assessment of the usefulness of arterial stiffness measured by cf-PWV and CIMT as biomarkers for detecting early cognitive dysfunction in an age-matched cohort may prove beneficial.

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Seizure-induced cardiovascular dysregulation: a clinically relevant sheep model for SUDEP therapeutics development

Dr Ruslan Pustovit

Biography:

Dr Ruslan Pustovit completed a PhD in Veterinary Surgery (2006) in Ukraine and spent more than 10 years in private veterinary surgical practice and lecturing the Veterinary Surgery.
From 2013–2023, Dr Pustovit worked with Professor John Furness on establishing the neural pathways that control bowel function. Ruslan made the striking discovery that defecation is dependent on ghrelin receptors, but not ghrelin (PMID:28801520).
From 2023 onwards, Dr Pustovit was recruited to The Florey's Translational Cardiovascular and Renal Research Group led by Professor Yugeesh Lankadeva. Dr Pustovit's current research focuses on understanding the impact of seizures on cardiac sympathetic nerve activity and heart dysfunction. His aim is to develop new therapies to mitigate sudden unexpected death in epilepsy (SUDEP). This collaborative research program across The Florey's Epilepsy Mission and Systems Neuroscience Theme is supported by a MRFF grant [2022–2025].

Seizure-induced cardiovascular dysregulation: a clinically relevant sheep model for SUDEP therapeutics development

Ruslan V Pustovit[1], Yugeesh R Lankadeva[1], Lindsea C Booth[1], Sally G Hood[1], Ming Soh[1], Sam F Berkovic[2], Terase F Lancefield[3], Chis A Reid[1] and Clive N May[1]

[1] The Florey Institute of Neuroscience and Mental Health, University of Melbourne, Parkville, VIC, Australia
[2] Epilepsy Research Centre, Department of Medicine, Austin Health, Heidelberg, VIC, Australia
[3] Department of Cardiology, Austin Health, Heidelberg, VIC, Australia

Introduction. Generalised convulsive seizures is the biggest risk factor for premature death in patients with epilepsy. The mechanism by which seizures can trigger terminal events remain unclear. Some studies have shown that seizure-induced cardiac functional defects, mediated by autonomic dysfunction, are frequently observed and may be the leading cause of death in a significant proportion of people with epilepsy.
Aims. To establish and characterise haemodynamic changes in an unanaesthetised sheep model of convulsive seizure.
Methods. Twelve adult female merino sheep were surgically instrumented to record mean arterial pressure (MAP), heart rate (HR), cardiac output (CO), electrocardiogram (ECG) and electroencephalogram (EEG), cardiac sympathetic nerve activity (CSNA) and renal SNA (RSNA). The effect of seizures induced by intravenous administration of pentylenetetrazol (PTZ) (5.0 mg/kg/min, 4 minutes) was compared with baseline measurements before the seizures.
Results. Generalised convulsive seizures induced in unanaesthetised sheep by intravenous administration of PTZ led to a rapid increase in the first 10 minutes in MAP (79 ± 5 to 129 ± 6 mmHg, P<0.0001), CO (4.1 ± 0.2 to 7.9 ± 0.5 L/min, P<0.0001) and HR (80 ± 2 to 124 ± 2 beats/min, P<0.0001). Similar abrupt changes were observed in heart rate variability (4826 ± 1766 to 211 ± 98 ms, P = 0.0155) and corrected QT interval at 30 minutes (12.6 ± 0.2 to 14.2 ± 0.4 ms, P = 0.0245). These changes remained significantly elevated for 60 minutes postictally. CSNA (n=4) was significantly elevated during the seizure (15.6 ± 1.2 to 76.8 ± 27.9 bursts/minute, P = 0.03), meanwhile RSNA (n=5) kept reducing and was almost completely abolished by 10 minutes post-seizure (63.8 ± 9.8 to 19.8 ± 3.1 bursts/minute, P = 0.0012).
Discussion. PTZ-induced seizures in unanaesthetised sheep caused cardiovascular dysfunction driven by elevated sympathetic outflow to the heart and reduced renal sympathetic nerve activity. Therapies that mitigate these cardiac effects may hold promise in reducing the risk of sudden premature death in people with epilepsy.

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Climatoxicology: ACTRA warns that climate change is impacting the toxicology and risk assessment of chemical exposures

Prof Paul Wright

Biography:

Paul Wright is the Toxicologist in the School of Health and Biomedical Sciences at RMIT University and an Adjunct of the School of Chemistry at Monash University, Melbourne, Australia. He is the previous president of the Australasian College of Toxicology and Risk Assessment (ACTRA, 2019-23), and a Fellow of both ACTRA and the International Union of Pure and Applied Chemistry (IUPAC), and a former elected Director of the International Union of Toxicology (IUTOX). Paul is a researcher in toxicology, nanotoxicology/nanosafety, natural product development and the safety of Australian native foods, supported by external government and industry grants, and is an appointed toxicology expert on various government and university panels. Paul teaches toxicology at several universities and institutions while based at RMIT University for over 3 decades, including for the Masters of Green Chemistry and Sustainable Technologies since it commenced in 2022 at Monash University. He received an ACTRA Award of Merit in 2023 in Recognition of Excellence in Toxicology Education and contributed to Edith Cowan University's new short course in Applied Toxicology.

Climatoxicology: ACTRA warns that climate change is impacting the toxicology and risk assessment of chemical exposures

Paul F A Wright. School of Health and Biomedical Sciences, RMIT University, Bundoora, VIC, Australia

There are growing concerns about the impacts of climate change on the toxicology and risk assessment of chemical exposures in both humans and the environment – these issues were raised by the Australasian College of Toxicology and Risk Assessment (ACTRA, https://actra.org.au) at its 16th Annual Scientific Meeting in 2024, on the theme of "Climatoxicology: Assessing risk in a time of rapid change" (ACTRA, 2024). Most atmospheric CO_2 has a lifetime of several centuries – its slow environmental toxicokinetics is driving global warming. Emissions of this main greenhouse gas from our industrialized society are causing global temperatures to progressively increase and extreme weather events to worsen. However, Australia's land temperature has increased even more rapidly, coupled with disrupted rainfall patterns, more droughts and longer fire seasons. This climate change causes environmental conditions with many knock-on effects, e.g.: increased volatilization of certain Chemicals of Potential Concern (COPCs) and their exposures; increased humidity favouring mycotoxin contamination in crops and skin absorption of some pesticides; more frequent and harmful algal blooms that affect fishing and seafood safety; reduced rainfall leading to decreased water quality and flow, more concentrated effluents from wastewater systems, and massive fish kills. More frequent heatwaves also require higher individual water consumption, have a greater effect on the elderly and those with cardiovascular disease, and interact with ozone levels to increase mortality rates. More extreme wildfire events on the wildland-urban interface produce a more toxic smoke than from remote wildfires, with more persistent health effects. Pesticide practices and risk assessments need to change in response to global climate change, which has also increased mercury exposure from enhanced environmental toxicokinetics. In conclusion, climate change stressors can alter chemical toxicity and all parts of risk assessment process, requiring a more holistic approach to environmental risk assessment. Urgent implementation of green chemistry practices within a true circular economy is important in helping to achieve net-negative CO_2 emissions, and the sustainable use of natural resources and recyclables, in order to decrease the impact of industries on human and environmental health.

ACTRA (2024) 16th Annual Scientific Meeting, "Climatoxicology". Canberra, Australia, August 2024.

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Toxicology challenges of emerging pharmaceutical modalities

Dr Sharleen Menezes PhD

Biography:

Sharleen is a Senior Regulatory Toxicologist at a global clinical research organisation (CRO), Novotech and works in drug development. She is involved in providing technical toxicology advice and product development strategy for clinical trial entry and testing of therapeutics in humans. As a toxicologist, she is involved in interpreting toxicity data conducted by clients and assisting in nonclinical study design, as well as writing and reviewing regulatory submission documents and packages for new medicinal drug products across ANZ, Asia, the US, and Europe. Sharleen received her PhD from the University of Sydney and previously worked at the university as a Post-Doc in molecular biology and oncology.

Toxicology challenges of emerging pharmaceutical modalities

Sharleen V Menezes[1]. Drug Development Consulting, Novotech-CRO[1], Sydney, NSW, Australia.

Emerging pharmaceutical modalities such as gene therapies, mRNA and siRNA drugs, and cell therapies, introduce novel mechanisms of action, biodistribution profiles, and pharmacokinetics that challenge traditional toxicology designs. Due to their complex, long-lasting, and often irreversible biological activity, these drug modalities differ fundamentally from traditional small molecules or biologics. Key challenges often include the selection of pharmacologically relevant animal models, evaluation of off-target effects, managing immune responses, and uncertainties in biodistribution, persistence, and clearance, as well as the lack of formal regulatory guidance. In many cases, conventional toxicology study designs are insufficient, requiring the adaptation of protocols, extended study durations, or the use of surrogate vectors, humanized models, or transgenic animals to generate meaningful safety data. For cell therapies, additional complexities arise from product heterogeneity, viability, and potential for uncontrolled proliferation or differentiation. Regulatory expectations for these modalities continue to evolve, with increasing emphasis on case-by-case justification and risk-based safety strategies. Early scientific engagement with regulatory agencies and tailored development plans are critical to navigating these challenges. Ultimately, the safe and efficient advancement of next-generation therapies demands a multidisciplinary approach that integrates pharmacology, toxicology, and regulatory expertise.

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Thought for food: assessing agricultural risks from PFAS in the current regulatory environment

Tarah Hagen MSc DABT FACTRA

Biography:

Tarah is a certified toxicologist and fellow of the Australasian College of Toxicology and Risk Assessment (ACTRA) who has over 15 years' experience in conducting screening and detailed human health and ecological risk assessments for a variety of industries and government. Included are industrial emissions, contaminated land and water, consumer goods and food. She has written and co-written numerous major reports, which have been influential in shaping Australian health risk assessment methodology and policy decisions in relation to environmental issues. Included are guidance documents for undertaking risk assessments, complicated risk assessments dealing with a variety of emissions to the environment, deriving the scientific basis for workplace exposure standards, interpretation of biological monitoring results for chemical exposures, toxicological reviews on various chemicals in relation to work and public health and safety, as well as research into clearance and distribution of per- and poly-fluorinated alkylated substances (PFAS) in livestock. She has also acted as an expert witness in a number of legal cases involving chemical emissions. She is currently President of ACTRA and has been actively involved with ACTRA for over 12 years. She is a ministerial appointed member of the Industrial Chemical Environmental Management Standard (IChEMS) advisory committee and regularly teaches University Masters students in the fields of toxicology and epidemiology. She has also acted as an independent expert in the fields of toxicology and human health risk assessment in several court cases.

Thought for food: assessing agricultural risks from PFAS in the current regulatory environment

Tarah G Hagen[1]. SLR Consulting Australia Pty Ltd[1], Melbourne, VIC, Australia

Per- and polyfluoroalkyl substances (PFAS), used widely in consumer and industrial products over many decades, are now ubiquitous environmental contaminants. Certain PFAS are highly persistent, mobile, and bioaccumulative, making them globally important environmental pollutants. Dietary PFAS exposure is typically the major route of exposure and while it is still generally low for most people, higher exposures can occur near contaminated sites - particularly through consumption of local seafood, market garden produce, or meat and milk from livestock raised on affected soil or water.

Sustainable farming practices, such as using biosolids or recycled water, may inadvertently increase PFAS concentrations in soils and consequently also in food products grown or raised on such farms (HEPA 2025). Estimating exposure in these settings requires considering the fraction of affected food, consumption rates, and PFAS concentrations. When measured data are unavailable, modelling of PFAS concentrations can be undertaken using literature information for plant uptake and tissue distribution / clearance in livestock.

Health risk assessment involves comparing estimated exposures with toxicity reference values (TRVs). However, differing TRVs across jurisdictions, even within Australia (FSANZ 2017, NHMRC and NRMMC 2025), complicate interpretation. This presentation outlines strategies for navigating these regulatory challenges, while effectively assessing potential health risks from PFAS in agricultural food production.

FSANZ (2017) Perfluorinated chemicals in food, Food Standards Australia New Zealand. April 2017.
HEPA (2025) PFAS National Environmental Management Plan 3.0. National Chemicals Working Group of the Heads of EPA Australia and New Zealand
NHMRC and NRMMC (2025). Australian Drinking Water Guidelines 6 2011; Version 4.0 updated June 2025, National Health and Medical Research Council and Natural Resource Management Ministerial Council.

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Non-animal models: Current status for toxicology and specific challenges including virtual control groups, in silico modelling, AI predictive tools, organ on a chip/organoids

Dr Slade Matthews

Biography:

Slade Matthews is a researcher and educator whose career has been marked by his dedication to the intersection of biomedical science and machine learning. He is committed to fostering mathematical literacy among students and has made contributions to both research and education in the field. He holds two teaching awards for university teaching. Recognizing the importance of effective pedagogy, Slade completed a Graduate Certificate in Higher Education in 2011. He has a Bachelor of Medical Science, Honours (1995) which included an investigation into the venom of the Australian copperhead snake using classical pharmacological bioassays, chromatography, and electrophysiology. His doctoral research (PhD 2007) focussed on the integration of machine learning techniques for cell classification tasks and modelling relationships in clinical data. Slade's primary research focus centres on the fusion of experimental design, statistical analysis, and machine learning to investigate biomedical problems, especially in toxicology. He has published 43 publications in peer-reviewed journals and has been cited 1275 times.

Current status for toxicology and specific challenges including virtual control groups, in silico modelling, AI predictive tools, organ on a chip/organoids

Slade Matthews. Sydney Pharmacy School, The University of Sydney, Sydney, NSW, Australia.

In “Weapons of Math Destruction” author Cathy O’Neil highlights the dangers of allowing algorithms to make high stakes decisions such as those in criminal justice, hiring, and education. Similarly, Dr Miles Dyson in Terminator 2: Judgment Day said, “The thing that terrified me most was the thing that I created”. And we all know how that turned out. AI has the potential to be of enormous benefit to humankind, but so-called guardrails and other checks and balances are essential to prevent harm.

In this talk I will present some of the advances that have been made in the development of machine learning approaches to in silico prediction of toxic substances as well as some of the rules and guidelines that have been developed to ensure high quality predictions with well established points of departure.

The OECD has developed a set of principles for the validation of quantitative structure activity relationship (QSAR) models for regulatory purposes as well as standardised formats for QSAR model reporting and development. Meanwhile, the USA has introduced the FDA Modernization Act 3.0, (April 2025) aimed at reducing unnecessary animal testing in drug development by establishing a qualification process for nonclinical testing methods that improve predictivity and reduce development time. Specifically, the FDA has announced plans to phase out animal testing requirements for monoclonal antibody therapies.

At the University of Sydney, we have developed several toxicological quantitative structure activity relationship (QSAR) models for predicting “Ames mutagenicity” for new chemical entities. Our latest models come in the wake of the seminal transformer paper, Vaswani 2017, which introduced transformers and has changed the world of artificial intelligence. I will present our latest Ames mutagenicity graph transformer model and compare its performance to that of a host of models competing in the latest global Ames predication challenge run by the National Institute of Health Sciences, Japan.

Vaswani A et al (2017) arXiv. https://arxiv.org/abs/1706.03762

Furahama, A. et al (2023) SAR and QSAR in Environmental Research. 34(12) 983-1001.

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Novel precision medicine approaches to target neoepitopes in myelofibrosis

A/Prof Daniel Thomas

Biography:

Dr Daniel Thomas, clinical haematologist, pathologist, and cancer scientist, trained at Stanford University School of Medicine. He leads the Myeloid Metabolism Lab at SAHMRI, focusing on the interplay between cancer, metabolism, and epigenetics to develop new drugs for rare and hard-to-treat cancers. His lab values creativity, compassion, and generosity, and has pioneered mutation-specific drug targets, repurposed medicines, and clinical trials, including Australia's first precision medicine trial for CMML using an anti-GM-CSF antibody and high-dose Vitamin C.

Dr Thomas has co-led discoveries now in clinical use, such as therapies for myelofibrosis, JAK2 mutations, and IDH1-mutated cancers. He directs major conferences including New Directions in Leukaemia Research and the National Cancer & Metabolism Meeting. Awarded the CSL Centenary Fellowship and multiple NHMRC and MRFF grants, his goal is to deliver mutation-targeted treatments with global impact. Prospective students passionate about innovative cancer research are encouraged to contact him for internship opportunities.

Novel precision medicine approaches to target neoepitopes in myelofibrosis

Daniel Thomas[1,2], [1]Precision Medicine, South Australian Health and Medical Research Institute, SA, Australia, [2]Adelaide Medical School, University of Adelaide, Adelaide, SA, Australia

Introduction. Calreticulin is recurrently mutated in primary myelofibrosis via a frameshift that removes an endoplasmic reticulum retention signal, exposing a neoepitope potentially targetable by immunotherapeutic approaches.

Aims. We wished to test whether cancer-encoded somatic neoepitopes are susceptible to targeting with monoclonal antibodies.

Methods. We developed a high affinity monoclonal IgG2 antibody, 4D7, directed against the common neoepitope peptide sequence encoded by both insertion and deletion frameshift mutations. 4D7 blocked JAK-STAT signalling, thrombopoietin-independent proliferation and megakaryocyte differentiation of CALR mutated myelofibrosis progenitors but not JAK2 mutated cells. Importantly, 4D7 showed inhibition of both insertion and deletion CALR mutations in myelofibrosis patients (62% decrease progenitors, P = 0.0001; 46% decrease megakaryocyte colonies, P = 0.0001).

Results. Strikingly, 4D7 exhibited activity against ruxolitinib-resistant cells without inhibiting normal hematopoiesis. We mapped the 4D7 binding epitope to an N-terminal arginine-rich segment of the neo-peptide and show that 4D7 functions by increased shedding of mutant CALR protein to the extracellular space, consistent with antibody-mediated disruption of the calreticulin-thrombopoietin receptor cell surface complex.

Discussion. Together, our data demonstrate a novel approach to target a problematic disease driven by a recurrent somatic mutation that would normally be considered "undruggable". New approaches to targeting neoepitopes are also presented.

Thompson-Peach, C, Foßelteder, J, Reinisch, A*, Thomas, D* (2023) Thrombopoietin-independent megakaryocyte differentiation of hematopoietic progenitor cells from patients with myeloproliferative neoplasms. Bio-protocol, Jan 20, 13:2, DOI: 10.21769/BioProtoc.4592.

Foßelteder, J, Schlacher, A, Pabst, G, Auinger, L, Kashofer, K, Christine Beham-Schmid, C, Trajanoski, S, Waskow, C, Sill, H, Wölfler, A, Zebisch, A, Thomas, D, Reinisch,A. (2022) Human gene-engineered calreticulin mutant stem cells recapitulate MPN hallmarks and identify targetable vulnerabilities." Leukemia Feb 22. doi: 10.1038/s41375-023-01848-6.Tvorogov, D, Thompson-Peach, C, Foßelteder, J, Dottore, M, Stomski, F, Lim, K, Onnesha, S, Moretti, P. Pitson, S, Ross, D, Reinisch, A, Thomas,D#, Lopez, A #(2022) Selective targeting of human CALR+ myelofibrosis with a neoepitope-directed monoclonal antibody. EMBO Reports Apr 5;23(4):e52904. #Equal contribution

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Development of radiotracers for TSPO polymorphisms

Miss Grace Cumbers

Biography:

Grace Cumbers is a PhD candidate at the University of Sydney, conducting her research in the Kassiou Drug Discovery Lab as part of the Danon Group. Her work focuses on investigating the functional effects of the A147T single nucleotide polymorphism in the translocator protein (TSPO) on neurosteroid production, and on developing PET radiotracers to image TSPO as a biomarker of neuroinflammation.

Grace has a background in complementary medicine and is a qualified, practicing Naturopath. After several years in clinical practice, she transitioned into research by completing a Master of Brain and Mind Sciences at the University of Sydney. She then joined the Kassiou Lab as a research assistant, where she developed a strong interest in neuroscience and drug discovery.

Now in the second year of her PhD, Grace is applying CRISPR gene editing technologies to develop drug-testing platforms using iPSC-derived brain cells. She is a recipient of the John A. Lamberton Scholarship and has participated in the SPARK commercialisation program, which supports the translation of academic research into real-world applications.

Drawing on her clinical experience, Grace is passionate about bridging the gap between laboratory research and patient care. She has a strong interest in the development and operation of clinical trials and is particularly focused on the integration of plant-based compounds into evidence-based neuropharmacological therapies.

Development of radiotracers for TSPO polymorphisms

Grace A. Cumbers[1], Eryn L. Werry[1,2], Michael Kassiou[1], Albert D. Windhorst[3,4], Wissam Beaino[3,4], Jonathan J. Danon[1], School of Chemistry[1], Central Clinical School[2], The University of Sydney, Sydney, NSW, Australia. Department Radiology & Nuclear Medicine, Amsterdam UMC Location Vrije Universiteit Amsterdam, De Boelelaan 1117, Amsterdam 1081 HV, The Netherlands[3], Amsterdam Neuroscience, Brain Imaging, Amsterdam, The Netherlands[4]

Introduction: The translocator protein (TSPO) is a key PET imaging target for visualizing neuroinflammation across a broad range of CNS diseases. The clinical utility of TSPO-PET has been hindered by genotype-dependent radiotracer binding discrepancies related to the rs6971 polymorphism (A147T). These binding variations compromise radiotracer reliability across patient populations.

Aims: To develop a pan-TSPO radiotracer that enables specific, accurate imaging of microglial-mediated neuroinflammation.

Methods: We employed a validated HEK293T cellular model overexpressing either wild-type or A147T variant TSPO to screen compounds. These candidates were assessed for high-affinity, genotype-independent binding using a competition radioligand binding assay. Our lead candidate was radiolabelled and progressed to small animal pharmacokinetic studies, as well as *in situ* autoradiography on diseased human brain tissue from patients homozygous for wild type or A147T TSPO as well as heterozygous patients.

Results: Structure-affinity relationships identified a lead radiotracer candidate with robust, genotype-insensitive binding. Our lead tracer was able to image all genotypes of TSPO tissue in the *ex vivo* study, in contrast to another TSPO radiotracer widely used in human studies, which loses affinity at the A147T TSPO polymorphism.

Discussion. Current radiotracers are limited by genotype-dependent variability. Our work addresses the barrier of genotype-dependent variability seen in past TSPO PET tracers which have held back the field. By identifying a genotype-independent candidate TSPO-PET ligand, this work advances a new generation of TSPO PET tracers suitable for broader clinical application.

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Patients carrying epilepsy-causing variants in GABAA receptors require treatments based on a precision medicine approach

Prof Mary Chebib

Biography:

Professor Mary Collins Chebib is a distinguished senior academic leader at the University of Sydney, currently serving as Associate Dean (Research) for the Faculty of Medicine and Health, following her tenure as Head of the School of Medical Sciences. Her leadership portfolio encompasses strategic research development, academic mentorship, and fostering cross-disciplinary collaboration across multiple STEM faculties, and commitment to nurturing the next generation of biomedical researchers. Renowned for her pioneering work in neuropharmacology, Professor Chebib's research centres on Cys-loop ligand-gated ion channels, with a particular focus on GABAA and nicotinic acetylcholine receptors. She is nationally and internationally recognized as a leading GABAA receptor pharmacologist, evidenced by her editorial appointments with high-impact international journals and frequent invitations to present at major scientific conferences.

Professor Chebib has authored over 150 peer-reviewed publications in top-tier journals, collectively cited more than 5,500 times. Her research excellence has been supported by competitive funding from the National Health and Medical Research Council, the Australian Research Council, and industry partners, with total grant income exceeding $12 million.

A dedicated mentor and educator, she has successfully supervised 16 PhD candidates and 2 Master's students, many of whom have gone on to prominent roles in academia, international research institutions, and the pharmaceutical and biotechnology sectors. Among her 41 Honours students, 7 have received the prestigious University Medal, and 34 graduated with First Class Honours.

Patients carrying epilepsy-causing variants in $GABA_A$ receptors require treatments based on a precision medicine approach.

Mary Chebib. [1] School of Medical Sciences, Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia

Introduction: γ-amino butyric acid type A ($GABA_A$) receptors are ligand-gated ion channels that mediate fast synaptic inhibition in the brain. Among the nineteen identified subunits (α1-6, β1-3, γ1-3, δ, ε, θ, π, and ρ1-3), 11 subunits significantly contribute to severe developmental and epileptic encephalopathies (DEEs), intellectual disability (ID) with or without seizures, and, in some cases, no symptoms at all.

Aims: In this presentation, I will focus on the α3 subunit, encoded by *GABRA3*, as it stands out for several reasons. Firstly, *GABRA3* is the only epilepsy-associated $GABA_A$ receptor gene that is located on the X chromosome. Secondly, compared to more common receptor types, α3-containing receptors exhibit restricted spatial expression in the brain, with high levels in regions important for epilepsy, such as the cerebral cortex, amygdala, hippocampus, and thalamus (Hörtnagl et al, 2013). Thirdly, α3 subunit-containing receptors mediate synaptic neurotransmission with prolonged synaptic currents (Syed et al, 2020). Together, these unique features separate α3-containing receptors from e.g., the more ubiquitous α1-containing receptors.

Methods: We assessed a cohort of 43 individuals with presumed pathogenic *GABRA3* variants and conducted detailed genotype-phenotype analyses. A novel mouse model carrying a recurrent variant was developed and assessed.

Results: Our findings revealed that pathogenic *GABRA3* variants can cause either dominant or recessive X-linked disorders, each associated with distinct functional impact: GOF variants caused severe phenotypes and followed X-linked dominant inheritance, while LOF variants resulted in milder phenotypes and followed an X-linked recessive pattern. Key aspects of

the human condition, including epilepsy and increased severity in males, were recapitulated in a novel mouse model carrying a recurrent GOF variant.
Conclusions: Treatment options must consider the functional phenotype of patients to avoid severe adverse effects.

Hörtnagl, H. *et al. Neuroscience* **236**, 345-372 (2013).
Syed, P., Durisic, N., Harvey, R. J., Sah, P. & Lynch, J. W. *Front Mol Neurosci* **13**, 602559 (2020).

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Novel GRM1 mutations in juvenile ataxia

Dr Shane Hellyer

Biography:

Dr Hellyer is an EMCR researcher at the Monash Institute of Pharmaceutical Sciences, and it Deputy lab head of the Neuropharmacology lab within Drug Discovery Biology. His works focuses on the molecular pharmacology of GPCRs involved in neurophysiology and neuropathophysiology. In particular, Dr Hellyer is interested in the impact of single nucleotide variants found in patients populations, how they contribute to disease aetiology and how they potentially affect drug action on through changing receptor function. Dr Hellyer has published 21 peer reviewed journal articles and 1 book chapter, acting as a Chief Investigator on competitive grants worth $1.4 million.

Novel GRM1 mutations in juvenile ataxia

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Introduction. Metabotropic glutamate receptor 1 ($mGlu_1$) is a class C GPCR that plays a critical role in cerebellar development, neuronal architecture and function. Single nucleotide polymorphisms in the gene coding for $mGlu_1$ (GRM1) are associated with rare forms of spinocerebellar ataxias (SCAs), with both gain and loss of function mutations causing ataxic syndromes. Here we describe two novel GRM1 mutations, K918R and P1068H, found in juvenile patients presenting with ataxic syndromes at the Children's hospital at Westmead.

Aims. To functionally characterise the K918R and P1068H $mGlu_1$ variants

Methods. Wildtype and mutant $mGlu_1$ with an N-terminal FLAG tag were stably expressed with inducible expression in FlpIn Trex HEK293A cells. Cell surface expression was determined using FACS with anti-FLAG antibody. Orthosteric agonists and positive allosteric modulators (PAMs) were assessed for pharmacological activation across two functional endpoints (iCa^{2+} mobilisation and IP_1 accumulation). Operational models of agonism were used to derive potency, efficacy and affinity estimates from concentration-response curves, which were compared using one-way ANOVA.

Results. Mutation prediction algorithms had conflicting predictions of the pathogenicity of both mutations. P1068H, but not K918R, significantly reduced cell surface expression compared to wild-type. Both mutations had effects on glutamate affinity and efficacy in calcium mobilisation assays. P1068H significantly reduced agonist-induced IP_1 accumulation compared to WT, while paradoxically enhancing baseline IP_1 accumulation

Discussion. Both K918R and P1068H are loss-of-function $mGlu_1$ mutations, but act through divergent mechanisms to cause aberrant signalling. Given the amenability of $mGlu_1$ to positive modulation by small molecule, drug like compounds, targeting $mGlu_1$ with allosteric activators may represent a therapeutic approach for such mutations.

Wang et al (2024) BJP 181(22): 4514-4530

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Environmental Exposures on the Cardiorespiratory system: New Models, Drug Targets and Treatment Approaches

Dr Richard Kim

Biography:

Dr Richard Kim is a respiratory immunologist and leader in pulmonary research. Since completing his PhD in 2015 (Immunology and Microbiology, The University of Newcastle), he has established a dynamic research and leadership portfolio as Senior Lecturer at the University of Technology Sydney (UTS), Laboratory Head of the UTS ImmunoPharmacology Research Group, and research leader at the Woolcock Institute of Medical Research. He also serves as the National Convenor of the Asthma and Allergy Special Interest Group within the Thoracic Society of Australia and New Zealand (TSANZ), driving collaborative research and clinical translation across the respiratory health sector. During his postdoctoral training, he was awarded a Lung Foundation Australia & Boehringer Ingelheim research fellowship (2018-2020) and was recruited to a tenured Faculty position at UTS in 2019. In 2022, he established a multi-institutional severe asthma research initiative with UTS, The University of Newcastle, and the Woolcock Institute to advance discovery-to-translation research through cross-sector partnerships.

Dr Kim leads an internationally recognised research program aimed at advancing our understanding of, and developing new treatments for, chronic lung diseases including severe asthma and chronic obstructive pulmonary disease. His work is also providing critical insights into the health impacts of emerging environmental threats such as e-cigarettes and bushfire smoke. Dr Kim specialises in developing and interrogating novel mouse models of human lung disease that are highly representative of the human scenario. These models are used to investigate disease-causing mechanisms and assess the effects of new therapies on respiratory immunology and function, and are cited in European Respiratory Society Practice Guidelines as crucial tools for research and drug testing. He has received over 25 awards and prizes recognising his research excellence, and his work is routinely published in leading respiratory and general interest journals such as Science Translational Medicine, American Journal of Respiratory and Critical Care Medicine, Cell Metabolism, Lancet Respiratory Medicine, and Nature Communications.

Environmental exposures on the cardiorespiratory system: new models, drug targets and treatment approaches.

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Introduction. Environmental exposures are major risk factors for cardiorespiratory diseases. Despite convincing epidemiological links between different emerging exposures and increased morbidity and mortality, the mechanisms that drive these associations remain incompletely understood. Progress in this area has been, in part, limited by the lack of representative experimental models.

Aims. To investigate the effects of emerging environmental exposures on cardiorespiratory health using novel, clinically relevant mouse models that replicate real-world exposure scenarios in humans.

Methods. We examined the effects of key environmental exposures, including air pollution, third-hand e-cigarette vapour, and bushfire/landscape fire smoke on the cardiovascular and respiratory systems. We sought to develop several murine and cell culture models that allow for mechanistic investigations of these interactions and identified potential molecular targets for therapeutic intervention.

Results. We developed novel and clinically relevant models of air pollution, third-hand e-cigarette vapour, and bushfire/landscape fire exposure, and showed that these exposures have detrimental effects on cardiorespiratory health and function. We also showed that these exposures increase the severity of, and exacerbate pre-existing, respiratory conditions, including asthma and chronic obstructive pulmonary disease (COPD).

Discussion. Innovative and translational models of environmental exposures are essential for uncovering disease mechanisms and accelerating the development of targeted therapies for cardiorespiratory conditions.

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Advancing Strategies in Cardiopulmonary Disease: Pioneering Pathways to Therapeutic Innovation

Dr Helena Qin

Biography:

Dr Chengxue Helena Qin is Laboratory Head in Cardiovascular Pharmacology at Monash University, where she leads a pioneering research program focused on developing next-generation pro-resolving medicines for cardiopulmonary diseases. Her work bridges the gap between fundamental pharmacology and clinical translation, addressing one of the most pressing global health challenges. Recognized as an Australian Research Council Future Leader, Dr Qin is among Australia's most accomplished mid-career researchers. She earned her PhD in Pharmacology & Therapeutics/Chemistry from the University of Melbourne, completed postdoctoral training at the Baker Heart and Diabetes Institute, and has led her independent research group at the Monash Institute of Pharmaceutical Sciences since 2019. Her research has been published in leading journals, including Nature Communications, Cardiovascular Research, Circulation, British Journal of Pharmacology, and Pharmacology & Therapeutics.

Dr Qin's leadership and scientific excellence have been acknowledged through more than 20 prestigious awards, including the Hypertension Australia Mid-Career Award, American Heart Association International Scholar Award. For more information, please visit: https://www.monash.edu/mips/themes/drug-discovery-biology/labs/cardiovascular-pharmacology.

Advancing Strategies in Cardiopulmonary Disease: Pioneering Pathways to Therapeutic Innovation

Chengxue Qin, Drug Discovery Biology, Monash Institute of Pharmaceutical Science

Pulmonary arterial hypertension (PAH) remains a devastating condition marked by elevated pulmonary arterial pressure, progressive vascular remodelling, and persistent inflammation, ultimately leading to right ventricular failure. Despite decades of progress, current therapies primarily target vasoconstriction and offer symptomatic relief without halting disease progression. This gap underscores an urgent need for strategies that address the underlying biology of cardiopulmonary disease. Our work explores innovative therapeutic pathways that integrate vascular, inflammatory, and resolution biology. Using complementary ex vivo human lung models and in vivo disease systems, we reveal that PAH is characterised by disrupted pro-resolving signalling and sustained inflammatory activation, alongside structural changes in the pulmonary vasculature. Lipid mediator profiling and receptor analyses highlight resolution pathways as untapped targets for restoring vascular homeostasis. Novel agents tested in these models demonstrated effects beyond haemodynamic improvement—reducing vascular remodelling, modulating inflammatory gene expression, and preserving right ventricular function. These findings point toward a paradigm shift: therapies that combine vasodilation with anti-remodelling and immunomodulatory benefits, moving beyond symptom management to disease modification. By leveraging insights into resolution biology and vascular signalling, this research provides foundational knowledge for precision medicine in PAH and broader cardiopulmonary conditions. These strategies represent an innovative approach to improving patient outcomes and redefining therapeutic innovation in cardiovascular and pulmonary health.

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Thinking Outside the Box: Immune-Modifying Methods to Reduce Lung Infections on the Cardiovascular System

Dr Madison Coward-Smith

Biography:

Dr. Coward-Smith is a young early career researcher at The University of Technology Sydney. She is focused on understanding the complex interplay between the respiratory and cardiovascular systems in models of respiratory disease and infection, which comprise major clinical comorbidities in Australia and worldwide. Dr. Coward-Smith's research has highlighted the significant potential of aspirin as a novel treatment to target viral escape during pregnancy and also spans other models of disease such as chronic obstructive pulmonary disease and atherosclerotic cardiovascular disease.

Thinking Outside the Box: Immune-Modifying Methods to Reduce Lung Infections on the Cardiovascular System

Madison Coward-Smith[1,2].School of Life Sciences, University of Technology Sydney1, Sydney, NSW, Australia. Woolcock Institute of Medical Research, Macquarie University2, Sydney, NSW, Australia.

Introduction. Respiratory infections are a major contributor to cardiovascular complications, particularly in vulnerable populations and those with underlying chronic disease. While traditional therapeutics primarily target pathogens, emerging evidence suggests that modifying the host immune response may offer a novel therapeutic opportunity. This approach may help to mitigate the systemic consequences of respiratory infections and improve long term cardiovascular complications.
Aims. To investigate innovative immune-modifying strategies to reduce the impact of lung infections on the cardiovascular system in mouse models of respiratory infection.
Methods. Using influenza infection as a model, we investigated how modifying the immune response could reduce downstream cardiovascular health by assessing vascular function, systemic inflammation and immune signalling. Vascular function was assessed via myography and inflammation was assessed via RT-qPCR.
Results. Immune modulating strategies showed reductions in vascular inflammation and improved vascular function. Modulation of key inflammatory pathways was associated with preserved endothelial integrity and function as well as reductions in markers of systemic inflammation. These findings support the potential of host targeted therapies to reduce complications beyond the primary site of infection.
Discussion. Our findings suggest that reprogramming the immune response during lung infections can reduce the burden on the cardiovascular system.

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Endogenous TGF-β immune suppression in chronic inflammatory lung disease

Dr Belinda Thomas

Biography:

Dr Belinda Thomas is a senior postdoctoral scientist in the Respiratory Research Laboratory based at the Hudson Institute of Medical Research in Melbourne. Her research interest is viral-induced exacerbations of chronic lung disease, investigating the effects of current and repurposed therapeutic agents on disease severity. Her work utilises a panel of respiratory pathogens including influenza A virus, in vitro primary cell cultures and in vivo mouse models, and more recently, precision-cut lung slice models.

Endogneous TGF-β immune suppression in chronic inflammatory lung disease

Belinda J Thomas. Centre for Innate Immunity and Infectious Diseases, Hudson Institute of Medical Research, Melbourne, VIC, Australia

Introduction. Viral infections in patients with pre-existing lung inflammation such as asthma and chronic obstructive pulmonary disease (COPD) often have devastating and prolonged consequences. In these diseases, transforming growth factor-beta (TGF-β) levels are elevated and due to its immunosuppressive properties, may increase the vulnerability of patients. Current standard-of-care glucocorticosteroids help to control excessive inflammation associated with infection, however they also have detrimental immunosuppressive properties, thus resulting in more severe outcomes.

Aims. This study investigated the potential repurposing of pirfenidone, an anti-fibrotic and anti-inflammatory small molecule used to slow the progression of pulmonary fibrosis, as a non-steroidal anti-inflammatory treatment for viral-induced exacerbations of COPD.

Methods. A transgenic mouse model of lung-specific TGF-β over-expression was utilised. Following influenza A virus (IAV) infection, tissue and bronchoalveolar lavage (BAL) fluid were assessed for virus replication, disease severity, inflammation and immune responses. Treatment with pirfenidone was given by oral gavage and outcomes compared.

Results. Mice with elevated TGF-β developed more severe inflammation ($p<0.05$), IAV replication was increased ($p<0.001$) and innate immune responses were blunted ($p<0.001$). Administration of pirfenidone significantly reduced disease severity by dampening inflammatory responses ($p<0.05$) and reducing IAV replication ($p<0.05$).

Discussion. During viral infections, detrimental effects of TGF-β enhance airway inflammation and amplify the extent of infection. We provide proof-of-concept evidence that repurposing pirfenidone can oppose TGF-β activities and attenuate virus infections. This may be of benefit in susceptible populations.

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Emerging therapies for treatment resistant hypertension

Professor Markus Schlaich

Biography:

Prof Markus Schlaich is a renal physician and a European Society of Hypertension (ESH) accredited hypertension specialist. Markus is Chair of Hypertension Australia and Co-Chair of the National Hypertension Taskforce. He has a strong background in clinical research with a focus on the pathophysiology of hypertension, the role of the sympathetic nervous system, involvement of the kidneys, and hypertension mediated organ damage. He has a specific interest in treatment modalities targeting the sympathetic nervous system and has been a pioneer of renal denervation and other interventional approaches. He has authored more than 475 articles in peer reviewed journals and serves on the Editorial Board of Hypertension, Journal of Hypertension, and Hypertension Research.

Emerging therapies for treatment resistant hypertension

Markus P Schlaich[1,2]. Dobney Hypertension Centre, University of Western Australia and Royal Perth Hospital Research Foundation, Perth, WA, Australia[1]; Department of Cardiology and Department of Nephrology, Royal Perth Hospital, Perth, WA, Australia[2].

Introduction. Hypertension affects one third of the adult population in Australia. Resistant hypertension, defined as uncontrolled blood pressure despite the use of 3 or more antihypertensive agents at maximally tolerated doses is increasingly common with an estimated prevalence of 10% amongst patients with hypertension. Resistant hypertensin is associated with a fourfold increase in CV events and death. Novel therapeutic approaches are required to curb the significant burden of resistant hypertension.

Aims. To explore the safety and utility of novel lifestyle, pharmacologic, and device-based therapies for hypertension in an Australian context.

Methods. Review of recent randomized controlled trials and observational cohort studies in patient populations living with difficult-to-control and resistant hypertension.

Results. Lifestyle modification remains a cornerstone of management. Non-adherence with prescribed medication remains a significant problem. Novel pharmacologic approaches have been shown to result in significant and clinically meaningful BP lowering. These include dual endothelin receptor antagonists (aprocitentan), aldosterone synthase inhibitors (baxdrostat, lorundrostat), and siRNA therapies targeting angiotensinogen (zilebesiran). Other promising agents targeting natriuretic peptides are in development. Device-based approaches such a catheter-based renal denervation is now recommended by all international guidelines as an adjunct therapy.

Discussion. Several promising new therapeutic approaches are available or on the horizon. Potassium-enriched salt supplements have been shown to improve BP control and reduce the risk of stroke. More frequent use of single pill combinations may help to improve adherence. Endothelin receptor antagonists have been approved in the US and Europe and should be available soon in Australia. Regulatory approval for novel aldosterone synthase inhibitors is expected for 2026. Silencing RNA therapies targeting angiotensinogen may only require 6-monthly injections to improve BP control. Renal denervation is now a guideline recommended therapy.

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New Australian Guideline for Children and Adolescents - when, why and how to manage BP in children

Dr Nicholas Larkins

Biography:

Dr Larkins is paediatric nephrologist at Perth Children's Hospital and Senior Research Fellow at the ECU Nutrition & Health Innovation Research Institute. He is an active researcher whose PhD studied hypertension and albuminuria among Australian Children. His current research includes efforts to better define and identify hypertension among children, along with a focus on early-life risk factors among Australian Aboriginal children. Dr Larkins is the Chair of the Clinical Advisory Panel for the BPOzKids Network creating the first Australian Guideline for the Investigation and Management of Hypertension in Children collaborating with diverse interdisciplinary healthcare professionals and consumers to fill an important gap and promote a lifecourse approach to blood pressure and cardiovascular risk.

New Australian Guideline for Children and Adolescents - when, why and how to manage BP in children
Nicholas G Larkins.[1,2] Department of Nephrology and Hypertension, Perth Children's Hospital[1], Nedlands, WA, Australia; Nutrition and Health Innovation Research Institute, Edith Cowan University[2], Joondalup, WA, Australia.

Introduction. A lack of guidelines specific to the Australian healthcare context may imply that hypertension in childhood is rare or inconsequential, despite evidence to the contrary.
Aims. The BPOzKids initiative, supported by Hypertension Australia, sought to produce an Australian guideline that was trustworthy and pragmatic.
Methods. An ADAPTE process was followed and the American Academy of Paediatrics (AAP) 2017 Guideline Key Action Statements selected as the framework for a modified Delphi process undertaken by a 12-person inter-disciplinary Clinical Advisory Panel. A 13-person Guideline Steering Committee that included 2 consumers oversaw the process, endorsements and will help to guide forthcoming implementation. Public consultation and targeted consumer review was also undertaken, including from Elders, and children with kidney disease.
Results. Of 35 AAP Key Action Statements, 20 were adopted, 12 were adapted, and 3 removed or combined with other items. Simplified thresholds for screening were adopted based on those from Hypertension Canada, with continuous diagnostic thresholds adjusted for growth and development taken from the European Society of Hypertension being more congruent with the 140/90 mmHg threshold applicable from 18 years of age according to the National Heart Foundation of Australia. Screening was recommended but at a substantially reduced frequency compared to international guidelines acknowledging limitations within current models for preventative healthcare in Australia.
Discussion. The first Australian Guideline for the Identification and Management of Hypertension in Children and Adolescents represents broad collaboration between consumers, clinicians, and researchers with specific expertise in hypertension and guideline development. Endorsement is being sought from relevant stakeholders and the guideline will be accompanied by concurrent publications highlighting practical implications for primary healthcare providers and paediatricians.

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DASH diet resource to support lifestyle intervention for paediatric hypertension

Arielle Hyland

Biography:

Arielle Hyland is a Senior Paediatric Dietitian at Perth Children's Hospital, specialising in nephrology, familial hypercholesterolaemia, and ketogenic diets for epilepsy. Over the past 10 years she has worked across various hospital and community settings in Western Australia and recently worked in nephrology at BC Children's Hospital in Vancouver. Arielle is focused on translating evidence into practical, family-centred strategies to improve growth, feeding development, and prevention of cardiovascular disease. She has co-designed an Australian paediatric DASH diet resource to support the new Australian paediatric hypertension guidelines. Arielle is currently leading the development of education resources for both dietitians and consumers on familial hypercholesterolaemia, in response to increasing diagnoses identified via cascade screening.

DASH diet resource to support lifestyle intervention for paediatric hypertension

Arielle Hyland[1], Kristy Bolton[2], Carley Grimes[2], Sherly Li[3].
Department of Nutrition and Dietetics, Perth Children's Hospital[1], Perth, WA, Australia; Institute for Physical Activity and Nutrition, School of Exercise and Nutrition Sciences, Deakin University[2], Geelong, VIC, Australia; Heart Research, Murdoch Children's Research Institute[3], Melbourne, VIC, Australia.

Introduction. High blood pressure in childhood is a growing concern, yet few dietary resources exist to support its management in Australian children. The Dietary Approaches to Stop Hypertension (DASH) eating plan has proven effective in lowering blood pressure, but available materials are primarily adult-focused and not suited to the Australian context.
Aims. To develop a brief, evidence-based DASH dietary resource suitable for use by Australian families and health professionals to support dietary management of high blood pressure in children.
Methods. A working group of paediatric dietitians and nutrition researchers conducted a scoping review of existing DASH resources via grey literature searches, professional databases, and DASH-related smartphone apps. Resources were assessed for relevance, child-specific content, and cultural applicability to the Australian context. Findings guided the development of a printable, consumer-focused resource for families, with secondary use by general practitioners and dietitians.
Results. No existing DASH resources specific to children in the Australian setting were identified. Most materials targeted adults or were U.S. based with limited cultural relevance. No suitable apps for children were found. In response, a concise educational resource was developed, focusing on three key dietary areas—fruit, low-fat dairy, and nuts/seeds—along with sodium reduction. Behavioural strategies, including goal setting, were incorporated to support dietary change. The resource aligns with national blood pressure screening checkpoints at ages 7–9 and 13–15.
Discussion. This new resource fills a key gap in paediatric hypertension management by providing family-friendly dietary guidance for the Australian context. It simplifies DASH principles with a focus on behaviour change strategies. Designed for distribution by health professionals, it offers consistent, practical dietary advice for families. Future work may explore digital adaptation and evaluate its effectiveness in clinical practice.

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Emerging treatments for obesity in children, and impact on blood pressure

Dr Danielle Longmore

Biography:

Danielle Longmore is a senior paediatric endocrinology clinician researcher. She works in the Department of Endocrinology and Diabetes at the Royal Children's Hospital, Melbourne and in the Paediatric Department at Western Health. She has a particular clinical and research interest in youth-onset type 2 diabetes and management of complex obesity. She co-leads the Youth Type 2 Diabetes Clinic and Complex Obesity Assessment Service at RCH.

She is a post-doctoral researcher at the Murdoch Children's Research Institute, with a Clinician Scientist Fellowship to evaluate the complex drivers of obesity and youth-onset type 2 diabetes. Her PhD evaluating modifiable factors to prevent childhood obesity and youth-onset type 2 diabetes was undertaken on the PANDORA birth cohort in the Northern Territory, among First Nation Australians in remote Australia.

Emerging treatments for obesity in children, and impact on blood pressure

Danielle K Longmore. Murdoch Children's Research Institute, Royal Children's Hospital, Melbourne, VIC, Australia

Introduction. Management and treatments for obesity are rapidly evolving. Among children, new agents are increasingly being used off label to manage obesity. There is very limited long-term data on medications including glucagon-like-peptide 1 receptor agonists (GLP1RA) and glucose-dependent insulinotropic polypeptide (GIP) receptor agonists which is particularly relevant for children who may be on these medications long term. Children living with obesity are more likely to have hypertension and long term adverse cardiometabolic health outcomes.

Aims. This presentation will discuss the effects of new treatments for obesity among children (those aged <18 years) and explore the impact of new obesity treatments on blood pressure/hypertension.

Methods. Review of clinical trials of obesity treatments among those aged <18 years, presentation of reported findings relevant to blood pressure.

Discussion. Understanding the cardiovascular effects, including on blood pressure, of obesity treatments among children is vital to understanding how these agents may affect long term health outcomes and will help clinicians to determine the risk/benefit of using these medications among those aged under 18 years.

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Active Learning with Thompson Sampling for hERG Risk Modelling in Drug Development

Dr Slade Matthews

Biography:

Dr. Slade Matthews is a Senior Lecturer specializing in computational pharmacology and toxicology. His research focuses on predicting chemical properties and bioactivity using Python-based QSAR models and cheminformatic techniques such as molecular fingerprinting, quantum molecular calculations, clustering, and substructure analysis. He earned his PhD in 2007 on machine learning in biomedical data and has published 48 peer-reviewed papers (Scopus h-index: 18). In 2025 Slade published a state-of-the-art graph transformer-based QSAR model for Ames mutagenicity prediction. He serves on the TGA Medical and Scientific Evaluation Services Panel and the NSW Poisons Advisory Committee both since 2010. In 2024, he was elected to the ASCEPT Board and awarded Fellowship of ACTRA in 2025. Based at the University of Sydney, Slade collaborates with academic and regulatory partners to advance public safety through application of in silico toxicology and is passionate about mentoring students and interdisciplinary research bridging chemistry, biology, and data science.

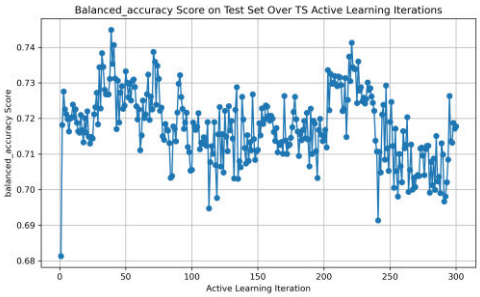
Active Learning with Thompson Sampling for hERG Risk Modelling in Drug Development

Slade Matthews, CPT Lab, Sydney Pharmacy School, The University of Sydney, Sydney, NSW, Australia

Introduction. The human Ether-à-go-go-Related Gene (hERG) encodes a potassium channel critical for cardiac repolarization. Making hERG binding a key component of the standard preclinical safety assay battery. Traditional machine learning approaches train over an entire dataset, potentially limiting efficiency when data are scarce, or labelling is costly.

Aims. To improve hERG prediction with active learning approaches.

Methods. This work builds on previous active learning experiments with the addition of Thompson sampling (TS). TS is an active learning approach where epistemic uncertainty is within the model itself rather than in the training loop (prediction outputs) presented at ASCEPT 2024. To approximate Bayesian inference a Bayesian neural network with Monte Carlo (MC) dropout is used. MC Dropout is applied during inference creating a predictive posterior distribution consisting of several possible models arising from the stochastic dropout mask. Data (pCI50 >6) from Konda et al., 2019 and Pytorch for model generation was used.



Results. Preliminary results generated using 300 queries for code development. The balanced accuracy on the training data reached over 74% (Figure 1) and on hold-out test set 71.8% with precision and recall of 0.559, and 0.535 respectively. Performance is anticipated to improve when the final model is presented with 3000 queries.

Discussion. The significance of development of active learning models, including Thompson sampling, is that they typically require fewer data points than traditional approaches. Data availability remains a challenge in the development of in silico toxicity models making the efficient use of existing data a high global priority. The move away from animal-based toxicity assessments positions in silico toxicity assay models at the forefront of toxicology in the 21st century.

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Novel informatics approaches for the regulatory management of UVCB substances

Ms Hannah Gerstmyer

Biography:
Hannah Gerstmyer is an undergraduate student at the University of Sydney, currently pursuing a Bachelor of Science and Advanced Studies majoring in Chemistry and Pharmacology. Her academic interests include span materials chemistry, drug design, and cheminformatics.
Hannah's current research focuses on the cheminformatics challenges posed by substances of unknown or variable composition, complex reaction products, and biological materials (UVCBs). This work aims to assist regulatory bodies such as AICIS in linking chemical structure to bioactivity.
Hannah has previously contributed to the University of Sydney's Education Innovation program, aiding in the development and implementation of a chemical biology laboratory activity designed to foster collaborative learning and student engagement. She is passionate about bridging supramolecular chemistry, data science and drug discovery and hopes to continue exploring these areas in postgraduate research.

Novel informatics approaches for the regulatory management of UVCB substances
Hannah Gerstmyer[1], Raymond Lui[2], Slade Matthews[1]. Computational Pharmacology and Toxicology Laboratory, Sydney Pharmacy School, The University of Sydney[1], Sydney, NSW, Australia; Australian Industrial Chemicals Introduction Scheme, Department of Health, Disability and Ageing, Australian Government[2], Sydney, NSW, Australia.

Introduction. Common chemical entities such as petroleum products, botanical extracts, and resins frequently have large numbers of constituents whose identities and concentrations fluctuate with source material and manufacturing processes. These entities, 'substances of unknown or variable composition, complex reaction products and biological materials' (UVCBs) evade precise structural representation [1]. This poses an ongoing cheminformatics challenge for federal regulators like AICIS who rely on accurate substance characterisation to manage hazard data for public safety.
Aims. This project aims to establish a new *uvcbfile* format to encode UVCB constituent data in a manner that: (1) accounts for structural variability and (2) facilitates the transformation of structural data for modelling and analysis.
Methods. A literature review of international regulatory requirements for UVCB nomenclature and current methods of encoding UVCB substance data was completed. Potential UVCB datasets were investigated and will be used to populate *uvcbfiles* with constituent information collated by semi-automated data-scraping. Markush structures and associated fingerprints that capture structural variability will be generated from *uvcbfiles.* Structure-based clustering of fingerprints will be performed and compared with manufacturing and hazard classifications.
Results. The *uvcbfile* format has been developed using a JSON-based structure to encode five levels of constituent structural representation [2]. A new dataset of *uvcbfiles* is being generated for 141 petroleum UVCBs [3] and a workflow for augmenting structural information from PubChem has been developed.
Discussion. It is expected that further chemical structure-based clustering of this petroleum dataset will align with existing manufacturing and bioactivity-based groupings, thereby linking structure and hazard classification, and aiding AICIS in its management of UVCB data. Once finalised, this methodology should also be applicable to other UVCBs.

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Isolated compounds from ginseng and green tea increase oxidative stress in spermatozoa

Dr Tayler Catherine Kent

Biography:

Tayler is an Associate Lecturer in Human Pharmacology in the School of Medical, Molecular and Forensic Sciences at Murdoch University in Perth, WA. She coordinates the school's two pharmacology units, as well as contributing to Forensic Toxicology, Veterinary Reproduction and first-year Biomedical Science units. Tayler submitted her PhD thesis earlier this year, which investigated the functional and metabolic changes that occur in male reproductive cells exposed to common herbal medicines. Her current research focuses include oocyte metabolism, and further investigation into changes in male reproductive cells exposed to herbal fertility supplements.

Isolated compounds from ginseng and green tea increase oxidative stress in spermatozoa

T. Kent[1,2], K. Pool[3], M. Tree[1], G. Maker[2], G. Rossi[1], A. Barnes[1] School of Vet. Med[1]., MU, Perth, WA Australia. School of Med., Mol. and Forensic Sciences[2], Murdoch University, Perth, WA, Australia. School of Ag. and Env[3]., UWA, Perth, WA, Australia.

Introduction. The use of herbal medicines and supplements is prevalent, and these products are typically easy to obtain without consultation with a medical practitioner, pharmacist or herbalist. A popular category of supplements in Australia and abroad are those that are marketed for improving fertility. *Panax ginseng* and *Camellia sinesis* (green tea) extract are common ingredients, despite limited and conflicting data regarding their safety and efficacy.

Aims. We have previously demonstrated an increase in oxidative stress and DNA fragmentation in ram spermatozoa exposed to ginseng and green tea extract (GTE). Therefore, this study aimed to measure changes in spermatozoa exposed to specific active compounds isolated from ginseng and GTE.

Methods. Ram spermatozoa was exposed to ginsenosides (100 mM) and catechins (80 mM) and analysed at 0.5, 3 and 6 h. Flow cytometry was used to assess changes to viability, oxidative stress, DNA fragmentation, membrane fluidity and the acrosome reaction.

Results. The proportion of acrosome-reacted spermatozoa was increased with some ginsenoside treatments, and almost all catechin treatments. In some cases, this was accompanied by an increase in membrane fluidity. Notably, several treatments increased either mitochondrial or cytoplasmic oxidative stress, but not both.

Discussion. The increased frequency of acrosome reaction and membrane fluidity suggests changes consistent with capacitation, a process preceding fertilization, despite no oocyte being present. The oxidative stress observed is particularly interesting, as many compounds assessed increased either mitochondrial or cytoplasmic reactive oxygen species (ROS), indicating different mechanisms; given the presence of multiple compounds in herbal supplements, it is likely that both mitochondrial and cytoplasmic ROS may increase with their use. These observations suggest that exposure to these compounds may impact the fertilising capacity of spermatozoa, potentially due to disrupted metabolism or cellular signalling processes. We recommend caution regarding the use of ginseng or GTE-containing supplements until these results can be further elucidated.

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Assessing the impact of Phenazopyridine on the efficacy of BCG-immunotherapy

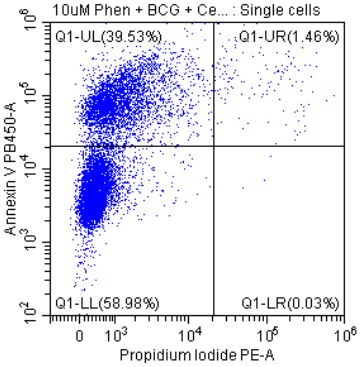
Miss Georgia Bourlotos

Biography:

Georgia Bourlotos is a currently in her third year of her PhD at Flinders University in the Neurourology Research Group. She graduated with a Bachelor of Medical Science and Honours in Medical Science from Flinders University. Her research focuses on bladder cancer and improving patient outcomes and their wellbeing. Georgia has previously published a review titled "BCG induced lower urinary tract symptoms during treatment for NMIBC - Mechanisms and management strategies" (DOI: 10.3389/fnins.2023.1327053) in Frontiers in Neuroscience. She was awarded the Flinders Health and Medical Research Institute PhD Scholarship and the Australian Governement Research Training Program Scholarship. Georgia is passionate in exploring potential pathways to reduce pain in patients suffering from superficial bladder cancer.

Assessing the impact of Phenazopyridine on the efficacy of BCG-immunotherapy

Georgia Bourlotos[1], Meera Elmasri[1], Tanvi Narke[1], Steven Taylor[2], Alana White[1], Luke Selth[1], Giles Best[1], Luke Grundy[1]. FHMRI, Flinders University[1], Adelaide, SA, Aus; SAHMRI[2], Adelaide, SA, Aus.



Introduction. Non-muscle invasive bladder cancer (NMIBC) is typically treated by Intravesical Bacillus Calmette-Guerin (BCG) immunotherapy. However, up to 70% of patients experience lower urinary tract symptoms (LUTS) including bladder pain, urinary urgency, and urinary frequency that significantly reduce quality of life during BCG treatment that can lead up to 20% of patients to cease therapy. Phenazopyridine (PAP) is urinary tract analgesic that is clinically effective in relieving LUTS during urinary tract infection. PAP could be effective in treating BCG-induced LUTS, however, whether it impacts with the efficacy of BCG needs to be established.

Aims. To determine whether PAP interferes with the therapeutic mechanism of action of BCG.

Methods. Urothelial cancer cell lines (MB49, T24 and UMUC3) were exposed to BCG (2hrs - $6.64x10^5$ CFU) in the absence and presence of PAP (10, 30, 100μM). Changes in BCG induced apoptosis and cytotoxicity were assessed by flow cytometry (Figure). Changes in BCG internalisation were quantified via qPCR, and immunohistochemistry (IHC). Mice (N=10) were treated with BCG ($1.2x10^7$CFU) or BCG + PAP (300μM) once-weekly for six weeks. Mouse bladders were excised, and flow cytometry was used to characterise immune cell infiltration.

Results. BCG induces early and late apoptosis *in vitro* in urothelial cells ($p<0.001$) that is unaffected by PAP ($p>0.05$). qPCR and IHC reveals BCG urothelial cell internalisation is unaffected by PAP. Flow cytometry of BCG treated bladders shows PAP had no significant impact on infiltration of immune cell subtypes, including Neutrophils, Natural Killer cells and Dendritic cells

Discussion. This study shows that PAP, a urinary tract analgesic, does not significantly impact the apoptotic, internalisation, or immunogenic effects of BCG *in vitro* or *in vivo*. The results of this study indicate that PAP maybe be useful as an adjunct therapeutic to relieve LUTS associated with BCG therapy for NMIBC without impacting the mechanisms necessary for the efficacy of BCG.

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Towards Safer Medication Practices: A Retrospective Analysis of Adverse Drug Reactions

Ms Jing Xin Goh

Biography:

Jing Xin has recently completed her MPhil at the University of Sydney, where she conducted research on "The Impact of Medication Regimen Complexity on Patient-Centred Outcomes in Kidney Failure." Her passion for clinical pharmacy was ignited during her previous work experience in hospital and health clinic settings. Jing is dedicated to advancing the field of nephrology and improving the care of patients with renal diseases. She is eager to contribute her knowledge and skills to make a meaningful impact in this critical area of healthcare.

Towards Safer Medication Practices: A Retrospective Analysis of Adverse Drug Reactions

Jing Xin Goh[1], Fatima Small[2], Ronald L Castelino[1,2]. School of Pharmacy, Faculty of Medicine and Health, University of Sydney[1], Sydney, NSW; Pharmacy Department, Blacktown Hospital[2], Blacktown, NSW.

Introduction. Adverse drug reactions (ADRs) remain a significant challenge in modern healthcare, raising concerns among clinicians and healthcare systems worldwide. Despite advances in medical research and pharmacology, ADR reporting rates among healthcare providers remain low, primarily due to barriers such as limited time and insufficient knowledge.

Aims. This study aims to examine the patterns and impact of ADR reporting to the Therapeutic Goods Administration (TGA) using an automated reporting tool embedded within the electronic medical records (eMR).

Methods. This retrospective study was conducted at Blacktown Hospital, where an automated ADR reporting tool was integrated into the eMR in 2022. The tool captured all the necessary information for regulated TGA reporting. Monthly ADR reports were compiled by the hospital's medication safety committee and submitted to the TGA. ADRs were categorised using the Medical Dictionary for Regulatory Activities (MedDRA), and causality was assessed using the World Health Organization-Uppsala Monitoring Centre (WHO-UMC) criteria.

Results. In contrast to the 13 reports submitted in 2021, over 1,500 ADR reports were submitted to the TGA from Blacktown and Mt Druitt Hospitals between March 2022 and June 2025 using the automated tool. Analysis of 1,181 reports revealed that 11% of patients experienced two or more distinct ADRs. Anti-infectives (39%) and nervous system drugs (17%) were the most frequently implicated drug classes. Dermatological reactions accounted for the highest proportion of ADRs at 33%.

Discussion. The findings demonstrate that embedding an automated ADR reporting tool within clinical workflows significantly enhances reporting rates. This digital health solution effectively addresses key barriers faced by healthcare professionals, promoting safer medication practices and improved patient outcomes.

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A novel GPCR heteromer demonstrates unique pharmacology revealed with live cell biosensors

Mr Henry Purbrick

Biography:

Henry Purbrick is a CSIRO Industry PhD candidate at the University of Western Australia. His project is linked with Dimerix Bioscience, a Melbourne-based biopharmaceutical company, to investigate the molecular pharmacology of novel G protein-coupled receptor (GPCR) heteromers. Henry is investigating these heteromers in the context of complex inflammatory and fibrotic indications, where current therapeutics are inadequate in controlling progression. He is using live-cell biosensors, predominantly bioluminescence resonance energy transfer, to comprehensively profile the pharmacology of these heteromers. As his project is commercially orientated consideration must be made in how his research may be viably translated through to the clinic.

A novel GPCR heteromer demonstrates unique pharmacology revealed with live cell biosensors.

Henry G Purbrick[1,2,3,4], Elizabeth KM Johnstone[1,2], Carl W White[4], Robert Shepherd[4], Kevin DG Pfleger[1,4]. Molecular Endocrinology and Pharmacology, Harry Perkins Institute of Medical Research[1], Nedlands, WA, Australia. School of Biomedical Sciences, The University of Western Australia[2], Nedlands, WA, Australia. Health & Biosecurity, CSIRO[3], Kensington, WA, Australia. Dimerix Biosciences Pty Ltd[4], Fitzroy, VIC, Australia.

Introduction. Chronic inflammation and organ fibrosis underpins much of the morbidity and mortality of many common diseases, such as chronic obstructive pulmonary disease, stroke, cirrhosis, diabetes and chronic kidney disease. There is clearly an unmet need in controlling the complex pathophysiological inflammatory axes of these diseases effectively. G protein-coupled receptors (GPCRs) are prominent drug targets, due to their cell membrane expression, and ability to modulate physiology. Some GPCRs are shown to form receptor heteromers, complexes composed of two different GPCRs with distinct pharmacology from the component protomers. Given the molecular complexity of these diseases, GPCR heteromer discovery may yield effective targets with profound pharmacology distinct from monomers. This project, linked with an industry partner, aims to discover and profile heteromers with a strong scientific rationale and commercial potential.

Aims. To identify novel GPCR heteromers and elucidate their unique molecular pharmacology.

Methods. Receptor-Heteromer Investigation Technology (HIT) identifies receptor-receptor proximity. The β-arrestin2 recruitment bioluminescence resonance energy transfer (BRET) Receptor-HIT assay was conducted to screen for proximity of GPCR combinations of interest. Positive 'hits' proceeded toward pharmacological characterisation with BRET sensors for intracellular trafficking, G protein activation and second messenger generation.

Results. Receptor-HIT identified multiple novel heteromer candidates, with a selected candidate proceeded toward comprehensive pharmacological profiling. The intracellular trafficking sensor revealed an asymmetrical perturbance to the internalisation of protomers upon their coactivation. The G protein and second messenger sensors revealed complementary effects upon protomer coactivation, observing an asymmetrical loss of agonist potency. A selective antagonist for one protomer rescued the loss of potency induced by protomer coactivation.

Discussion. We have identified a novel candidate, Het-3X, demonstrating pharmacology that satisfies the criteria in classifying a putative GPCR heteromer. This candidate will undergo further scientific and commercial validation.

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Bi-specific diabodies targeting β-amyloid to microglial phagocytic proteins for treating neurodegenerative diseases

Dr Emma Van der Westhuizen

Biography:

Dr. Emma van der Westhuizen is a Senior Research Officer at St Vincent's Institute of Medical Research. She received her BSc (Hons) degree from the University of Melbourne (Australia) and her PhD from Monash University (Australia). She has completed post-doctoral research at the University of Montreal (Canada) and at Monash University (Australia), as an independently funded post-doctoral scholar (NHMRC, Australia; CIHR, Canada; FRSQ, Canada). Emma designs novel therapeutics to treat neurodegenerative diseases, within a collaborative multidisciplinary team. Emma strives to bridge the gap between research capabilities and clinical possibilities, by translating lead compounds from the developmental and experimental phases through to pre-clinical and clinical use.

Bi-specific diabodies targeting β-amyloid to microglial phagocytic proteins for treating neurodegenerative diseases.

Emma T van der Westhuizen[1,2], Gabriela AN Crespi[1,2], Stefan J Hermans[1,2], Nancy C Hancock[1,2], Tracy L Nero[2], Juliet M Taylor[3], Peter J Crack[3], Michael W Parker[1,2]. [1]Structural Biology Lab, St Vincent's Institute, Fitzroy 3065, VIC, Australia; [2]Bio21 Molecular Science and Biotechnology Institute, The University of Melbourne[2], Parkville 3052, VIC, Australia. [3]Neuropharmacology Lab, Department of Biochemistry and Pharmacology, University of Melbourne, Parkville, Australia.

Introduction. Bi-specific diabodies are composed of two short chain variable fragments (scFv) with the variable domains (V_H-V_L) bonded together (Hollinger et al., 1993). They can join two different proteins together and are currently used therapeutically to treat acute myeloid leukaemia and haemophilia. We hypothesised that diabodies could clear toxic β-amyloid peptides (Aβ) from the brain by directly coupling Aβ to microglial proteins involved in Aβ phagocytosis.
Aims. To develop high affinity bi-specific diabodies against Aβ and microglial proteins involved in Aβ phagocytosis. Then to test these diabodies in Aβ phagocytosis and neuroinflammation assays and for blood-brain-barrier permeability.
Methods. Bi-specific diabodies (δ) were designed to bind to Aβ and either "triggering receptor expressed on myeloid cells 2" (TREM2) or "cluster of differentiation 33" (CD33). Diabodies were expressed in Expi293F cells and purified using standard protein chromatography. Binding affinities (pK_D) for the diabodies were determined for Aβ and microglial proteins by microscale thermophoresis (MST) or surface plasmon resonance (SPR). pHrodo-red-Aβ phagocytosis was measured by flow cytometry. Neuroinflammation was measured by qPCR, Western blots and ELISA. Diabodies were administered to mice by tail vein injection (10mg/kg) and the amount crossing into the brain was determined by Western blots.
Results. The bi-specific diabodies bound to Aβ with micromolar affinity (pK_D = 5.9±0.1; n=3), to TREM2 (pK_D = 8.8; n=2) and CD33 (pK_D = 8.8; n=2) with nanomolar affinities. δTREM2 (ΔMFI = 195) and δCD33 (ΔMFI = 9764) diabodies increased Aβ phagocytosis. δTREM2 triggered neuroinflammation but δCD33 did not. δCD33 successfully crossed into the brain.
Discussion. Bi-specific diabodies can directly couple Aβ to microglial proteins involved Aβ phagocytosis. Our results suggest that δCD33 increases microglial phagocytosis of Aβ without triggering neuroinflammation. δCD33 successfully crossed the blood-brain-barrier in mice. Together these results suggest that directly coupling Aβ to microglial proteins involved Aβ phagocytosis is a feasible strategy for novel neurodegenerative disease treatments.
Reference: Hollinger et al., 1993, PNAS 90(14):6444–6448

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Applying Artificial Intelligence to develop high-affinity antagonists of the relaxin receptor, RXFP1

Prof Ross Bathgate

Biography:

Professor Ross Bathgate is a group leader at the Florey Institute and is an Honorary Professorial Fellow in the Department of Biochemistry and Pharmacology at the University of Melbourne, Australia. He is a molecular pharmacologist with broad expertise in bioactive peptides and their G protein-coupled receptors (GPCRs). He has authored over 300 publications, is an inventor on 15 patents and was listed in the 2019 and 2020 world's most highly cited researchers for Pharmacology and Toxicology (Web of Science). He works closely with a number of pharmaceutical companies interested in the clinical development of GPCR-targeted therapeutics.

Applying Artificial Intelligence to develop high-affinity antagonists of the relaxin receptor, RXFP1.

Ross AD Bathgate[1,2], Janik Clement[2], Brad Hoare[1], Tselmeg Lkhagvajargal[1], Tiffany Myint[1,2], Gavin Knott[3], Rhys Grinter[2]. Florey Institute[1], and Department of Biochemistry and Pharmacology[2], University of Melbourne, Parkville; Monash Biomedicine Discovery Institute[3], Monash University, VIC, Australia.

Introduction. Within the past three years, machine-learning-based artificial intelligence (AI) tools capable of accurately designing new-to-nature proteins with high affinity for protein targets, including RFDiffusion, ProteinMPNN, and BindCraft, have been developed. These binders are small (5-15 kDa), single-domain proteins, with an affinity for their target comparable to antibodies and impressive stability and protease resistance.

Aims. We have utilized this technology to design and test protein binders to the relaxin receptor, RXFP1. High affinity full antagonists of this novel G protein-coupled receptor, and important target for the treatment of heart failure, are not currently available.

Methods. Both RFDiffusion/ProteinMPNN and Bindcraft were utilized to design novel binders to the RXFP1 ectodomain. Binder design was rationalized based on the known binding mode of the native ligand H2 relaxin to RXFP1 and our unpublished cryo-EM structural information on the RXFP1 ectodomain. 48 and 96 potential binders from RFDiffusion and Bindcraft, respectively, were cloned into bacterial expression plasmids for small-scale expression and His-tag mediated purification. Binding and signalling were tested in validated assays in RXFP1 expressing cells.

Results. Putative binders were expressed in high yield and partially purified for initial screening based on RXFP1 competition binding assays using Europium-labelled H2 relaxin. Screening identified a successful binding hit rate of 60% for Bindcraft and 40% for RFDiffusion. Binders showed no agonist activity but were able to antagonise H2 relaxin mediated cAMP activation in HEK cells expressing RXFP1. The top 4 hits from both methods were produced in higher yield and purified to homogeneity using FPLC. Detailed functional testing demonstrated nanomolar binding affinity for RXFP1 and potent full antagonist activity. The best binders had affinities similar to H2 relaxin (~1 nM).

Discussion. Both RFDiffusion and Bindcraft were successfully used to develop nanomolar affinity RXFP1 binders which are the first ever full antagonists of RXFP1. These studies highlight the potential utility of these methods for designing high-affinity binders for GPCRs. Importantly, binder generation is rapid and cost-effective, producing high-affinity binders in weeks, significantly faster and cheaper than antibody or nanobody technologies.

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Development of P2Y2 receptor antagonists with improved physicochemical properties for drug discovery

Dr Natasha Dale

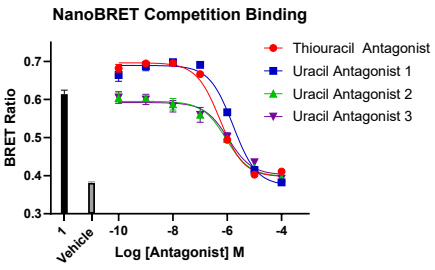
Biography:

Following completion of her PhD research at the Harry Perkins Institute of Medical Research, Dr Natasha Dale joined the Cell Signalling Institute at the University of Nottingham as a Postdoctoral Research Fellow. In this role, Dr Dale works alongside medicinal chemists to use structure-activity-relationship-informed drug design to develop novel molecular scaffolds to antagonise the purinergic P2Y2 receptor. Dr Dale was previously the ASCEPT Drug Discovery Special Interest Group student representative throughout her PhD as well as Chair of the Harry Perkins Institute Student Committee.

Development of $P2Y_2$ receptor antagonists with improved physicochemical properties for drug discovery

Natasha C Dale[1,2], Mahesh Puthanveedu[3], Laura E Kilpatrick[2,3], Michael J Stocks[3], Stephen J Hill[1,2]. School of Life Sciences, University of Nottingham[1], Nottingham, UK; Centre of Membrane Proteins and Receptors, University of Nottingham[2], Nottingham, UK; School of Pharmacy, University of Nottingham[3], Nottingham, UK

Introduction. Antagonism of the purinergic $P2Y_2$ receptor ($P2Y_2R$) presents an attractive aim for drug discovery. The receptors' role in inflammation gives potential clinical applications in chronic inflammatory disease, neurodegenerative disorders and cancer metastasis. Despite this, unfavourable physicochemical properties of existing antagonists, including the presence of a reactive thiouracil moiety have hampered preclinical progress.



Aims. Investigate $P2Y_2R$ structure-activity relationship to inform development of uracil moiety-based $P2Y_2R$ antagonists with similar affinity and efficacy to existing thiouracil moiety-based antagonists through bioisosteric replacement.

Methods. Based on the chemical structure of known literature $P2Y_2R$ antagonists, match-paired thiouracil and uracil-based analogues were synthesized. Ligands were screened for binding to Nluc-$P2Y_2R$ using NanoBRET ligand binding (Conroy et al, 2018). Antagonist activity was investigated using a Fluo-4 calcium accumulation assay.

Results. Pyrimidine containing aminothiazole tricyclic compounds retained affinity for binding to $P2Y_2R$ upon isosteric replacement of the 4-thiouracil fragment with a uracil. These compounds displayed comparable affinity for receptor binding and efficacy in stimulating calcium release as previously disclosed thiouracil based antagonists. In addition, uracil-containing compounds displayed lower cLogP values (lipophilicity) than their thiouracil counterparts.

Discussion. A series of new $P2Y_2R$ antagonists with favourable physicochemical properties for drug discovery have been described. The aminothiazole-containing tricyclic ring structure was vital to the retention of affinity when substituting the thiouracil moiety for a uracil moiety. These compounds open new directions for the development of clinically viable $P2Y_2R$-targeted antagonists.

Conroy S, Kindon N, Glenn J et al. (2018) J Med Chem 61(7) 3089-3113.

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Structure-Guided Design of Allosteric Modulators at the Delta Opioid Receptor

Dr Arisbel Batista Gondin

Biography:

Dr Arisbel B. Gondin is a DECRA Fellow and NHMRC EL1 Investigator at the Monash Institute of Pharmaceutical Sciences, with expertise in drug discovery and the structural biology of G protein-coupled receptors (GPCRs).

Her research program focuses on the molecular pharmacology of opioid receptors, with a particular interest in developing safer therapeutic strategies for pain management through allosteric modulation. By integrating cryo-EM structural analysis, and pharmacological profiling, Dr Gondin aims to uncover the mechanistic basis of receptor modulation and guide rational drug design.

Structure-Guided Design of Allosteric Modulators at the Delta Opioid Receptor

Arisbel B Gondin[1], Jesse I Mobbs[1,2], Mai Nguyen[1], Owindeep Deo[1], Peter J Scammells[1], Celine Valant[1], David M Thal[1,2]
Monash Institute of Pharmaceutical Sciences[1], Parkville, VIC, Australia
ARC Centre for Cryo-Electron Microscopy of Membrane Proteins[2], Parkville, VIC, Australia

Introduction. Positive allosteric modulators (PAMs) represent a promising pharmacological approach to enhance opioid receptor signalling with improved selectivity and reduced side effects. However, the structural basis for allosteric modulation at the delta opioid receptor (DOR) remains poorly understood.
Aims. This study aimed to elucidate the structural basis of DOR allosteric modulation by a novel small-molecule PAM and to use this information to guide structure–activity relationship (SAR) efforts.
Methods. We determined a high-resolution cryo-EM structure of DOR bound to the PAM, combined with structure-guided mutagenesis and pharmacological profiling in heterologous cell systems and ex vivo neuronal tissues.
Results. The structure revealed a previously uncharacterised allosteric site involving a conserved sodium binding residue. Key interactions within this site were identified and validated through mutagenesis. The PAM selectively enhanced agonist-induced DOR signalling, and SAR guided by the structure led to analogues with improved affinity.
Discussion. This study integrates structural biology, mutagenesis, and pharmacological profiling to advance our mechanistic understanding of delta opioid receptor allosteric modulation. The identification of a novel binding site overlapping the sodium pocket, along with validated interactions critical for PAM activity, provides a foundation for future structure-guided design. These findings represent an important step toward rational development of allosteric modulators with improved pharmacological profiles.

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Co-trimoxazole-induced SCAR is globally defined by HLA-B alleles with shared peptide-binding specificities

Assoc Prof Andrew Gibson

Biography:

Since relocation from the UK's dedicated MRC Center for Drug Safety Science in 2019, Associate Professor Andrew Gibson leads the drug hypersensitivity focussed research group at the Personalised Medicine Center at Murdoch University, Western Australia. He was awarded an NHMRC ideas grant in 2023, an Ian Potter Infrastructure award in 2024, and published the first single-cell atlas of skin during Stevens Johnson Syndrome in 2024 to elucidate shared cell signatures towards the development of the first targeted treatments. His work continues to focus on the use of advanced genomic tools to define genetic, cellular, and structural risk factors predisposing patients to severe cutaneous adverse drug reactions.

Co-trimoxazole-induced SCAR is globally defined by HLA-B alleles with shared peptide-binding specificities.

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Introduction. Co-trimoxazole is a front-line antibiotic but also a leading cause of severe cutaneous adverse drug reactions (SCAR) including drug reaction with eosinophilia and systemic symptoms (DRESS) and Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN). Human leukocyte antigen (HLA) class I alleles including HLA-B*13:01 and HLA-B*38:02 are associated with co-trimoxazole-induced SCAR in Southeast Asian (SEA) populations. However, the global generalizability of these associations remains unknown but critical for population-appropriate risk stratification.

Aims. To determine the HLA risk factors associated with co-trimoxazole-induced SCAR in the US and South Africa using prospectively collected and geographically matched SCAR patients and survivors and population-based controls.

Methods. High-resolution HLA-typing was performed on co-trimoxazole-induced SCAR patients from the US (n=63 SCAR, n=54) and South Africa (n=26 SCAR) compared to population controls. Shared peptide binding analyses were performed using MHCcluster2.0 and drug and HLA allele docking simulations using AutoDock Vina and CB-Dock2.

Results. HLA-B*44:03 (Pc<0.001, OR: 4.08), HLA-B*38:01 (Pc<0.001, OR: 5.66), and HLA-C*04:01 (Pc=0.003, OR: 2.50) were independently associated with co-trimoxazole-induced SJS/TEN in the US. HLA-B*44:03 was also associated with co-trimoxazole-induced DRESS in SA (Pc=0.019, OR: 10.69). HLA-B variants with shared peptide binding specificities (SPBS) to HLA-B*44:03 overlapped with the B44 supertype and were significantly associated with co-trimoxazole SJS/TEN (Pc<0.001, OR: 2.70) and DRESS (Pc=<0.001, OR: 12.84) in the US population. HLA-B variants with SPBS to HLA-B*44:03 or HLA-B*38:01 but also HLA-C*04:01 identified 94% and 78% of co-trimoxazole-induced SJS/TEN and DRESS in the US, respectively. The SEA risk allele HLA-B*13:01 was identified in just 1/63 US SCAR patients.

Discussion. HLA alleles with SPBS to SEA-related risk alleles including HLA-B*44:03 (SPBS with HLA-B*13:01) and HLA-B*38:01 (SPBS with HLA-B*38:02) but also HLA-C*04:01 predisposed to co-trimoxazole-induced SCAR in the US and South Africa. These findings provide biological plausibility linking primary risk alleles across populations and strategies for global population risk prediction and diagnosis of co-trimoxazole-induced DRESS and SJS/TEN.

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Implementation of a pharmacogenomic testing service in residential aged care: Preliminary findings

Miss Eman Wehbe

Biography:

A higher degree by research student at the University of Sydney under the supervision of A/Prof Sophie Stocker (School of Pharmacy). My work focuses on the implementation of pharmacogenomics into clinical practice.

Implementation of a pharmacogenomic testing service in residential aged care: Preliminary findings

Eman Wehbe[1], Jennifer Hewitt[2], Michael Scalley[3], Alyson Jarrett[2], Zanfina Ademi[4], Stephen Hughes[1], Sam Mostafa[1,4,5], Carl Kirkpatrick[4], Sophie L Stocker[1]. Sch of Pharm, Univ of Sydney[1], Sydney, NSW; Whiddon[2], Glenfield, NSW; Choice Aged Care[3], Sydney, NSW; Cent for Med Use & Safety, Monash Uni[4], Parkville, VIC; myDNA Life[5], South Yarra, VIC.

Introduction. Pharmacogenomics (PGx) as an emerging tool for precision medicine is particularly relevant for older adults at risk of medication-related harm due to polypharmacy. Despite its potential, PGx-guided medication management has not yet been implemented in Australian residential aged care, and its feasibility remains uncertain.

Aims. To evaluate the feasibility, clinical utility and value for money of implementing PGx-guided medication management in Australian residential aged care.

Methods. An observational study was conducted across five NSW aged care homes, where clinical staff collected buccal swabs from residents for analysis using an 11-gene PGx panel (myDNA, NATA-accredited laboratory; CYP1A2, CYP2B6, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, OPRM1, SLCO1B1, VKORC1, ABCG2). Pharmacists reviewed PGx reports and made prescribing recommendations during routine residential medication management reviews. Service evaluation was guided by the RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) framework.

Results. Three of five aged care homes have completed recruitment, with 76 of 168 residents (45%) consenting to participate; 74% self-consented and 26% via their Registered Supporter. Fourteen residents were excluded due to palliative care or behavioural concerns. Common reasons for refusal to participate included satisfaction with current medications or lack of interest. Of the 63 PGx reports generated to date, 22 identified major prescribing considerations (dose change or alternative medication recommended), and 49 identified minor ones (possible altered medication response but no specific dose change).

Discussion. Preliminary data demonstrates the feasibility of implementing a PGx testing service in residential aged care, with moderate resident participation and successful integration into existing workflows. The PGx reports revealed clinically relevant prescribing considerations, supporting the potential utility of PGx-guided medication management in this population. While prescribing adjustments and economic impact data are pending, early findings suggest potential value; however, challenges with Registered Supporter consent and inclusion of residents with cognitive impairment may limit broader reach and sustainability.

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Microbial Metabolite Receptor FFA2 Improves Post-Ischaemic Reperfusion

Dr Kristen Bubb

Biography:

Dr Kristen Bubb is Lead of the Translational Vascular Therapeutics Group in the Biomedicine Discovery Institute at Monash University. Kristen obtained her PhD at Monash University, before completing a post-doctoral fellowship at the William Harvey Research Institute in London, supported by the British Pharmacological Society. She then co-led a research program to investigate novel therapeutics and signalling pathways applicable to vascular diseases at the University of Sydney, before being recruited to Monash University in 2019 to establish the founding laboratory in the Victorian Heart Institute. Her main research interests are to investigate inflammatory and redox signalling in vascular diseases, with the aim of developing novel therapeutics for atherosclerosis, pulmonary hypertension and pre-eclampsia.

Microbial Metabolite Receptor FFA2 Improves Post-Ischaemic Reperfusion

Alex Pokrassen[2], Nasrin Nazari[1,2], Swarn Saxena[1], Jordyn Thomas[1,2], Thi Kim Dao[1,2], Stephen J Nicholls[2], Rikeish R. Muralitharan[1,2], Francine Z. Marques[1,2], Kristen J Bubb[1,2]. Biomedicine Discovery Institute[1] and Victorian Heart Institute[2], Clayton, VIC, Australia.

Introduction. Short-chain fatty acids (SCFA) are gut microbiome metabolites derived from fibre fermentation, activating free fatty acid (FFA) receptors. FFA2-mediated signalling deficiency increases the risk of cardiovascular diseases, including hypertension, potentially via angiogenesis. We hypothesised that FFA2 receptor activation may enhance neovascularisation and improve recovery in response to ischaemic vascular injury.
Aims. To examine the effect of FFA2 receptor activation on post-ischaemic reperfusion and endothelial cell function.
Methods. Male and female C57BL6/J wildtype (WT) and FFA2 receptor knockout (KO) mice (n=7-8/group) underwent isoflurane anaesthesia to induce hind limb ischaemia via femoral vascular ligation, and laser speckle contrast imaging to measure reperfusion over 15 days. Mice were treated with either vehicle (VEH, 50% DMSO) or FFA2 receptor agonist, TUG1375 (TUG, 1 mg/kg/day, s.c via osmotic minipump). Human umbilical vein endothelial cells (<passage 3, n=5/group) underwent scratch migration, proliferation and tubule formation assays, in the presence of FFA2 receptor activator, AZ1729 (AZ; 0.03-3 μmol/L) or vehicle (0.02% DMSO). Statistical analysis was by 1-way or 2-way ANOVA.
Results. Post-ischemic reperfusion was faster across the treatment period in WT mice treated with the FFA2 receptor agonist vs. control (p=0.03), with the maximal difference at day 7 (ischaemic : non-ischaemic limb: VEH 0.60±0.02, TUG 0.68±0.01, p=0.01). In KO mice, the initial response to ischemia was similar to WT controls but the reperfusion was impaired by day 15 post-ischemia (ischaemic : non-ischaemic limb: WT 0.77±0.03, KO 0.63±0.04, P=0.02). FFA2 receptor activation resulted in increased tubule number (VEH 175.2±3.5 vs. AZ 310.8±3.9, p<0.001) and proliferation (fold change from baseline: VEH 2.07±0.03, AZ 2.8±0.15, p<0.001) and accelerated migration of endothelial cells over 24-hours (p=0.01 VEH vs. AZ), suggesting angiogenesis might be improved.
Discussion. Activation of the FFA2 receptor led to accelerated recovery from vascular ischaemia; consistently, FFA2 receptor deficiency impaired reperfusion. Exogenous upregulation of FFA2 ligands, including short-chain fatty acids or small molecules, might provide a new strategy to stimulate collateral vessel development in ischaemic conditions.

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Bromodomain extra-terminal inhibitors prevent inflammation-induced stromal cell signalling & cardiac dysfunction

Associate Professor Simon Foster

Biography:

A/Prof Simon Foster is a Bellberry-Viertel Senior Medical Research Fellow, Heart Foundation Future Leader Fellow and head of the Cardiac Drug Discovery lab at QIMR Berghofer. A/Prof Foster's research focusses on novel aspects of cell signalling and receptor biology, with recent publications in Cell, Brit J Pharmacol, Cell Reports and Nat Cardiovasc Res. He was awarded the ASCEPT/BPS Outstanding Young Investigator Prize and Certara New Investigator Award in 2019. After his BA/BSc (Hons) degrees (University of Melbourne) and PhD (University of Queensland), Simon led a large project on orphan GPCRs in Denmark, supported by consecutive fellowships from Lundbeck Foundation and Danish Council for Independent Research. He returned to Australia in 2018 to Monash University, and was recruited to QIMR Berghofer in late 2020. A/Prof Foster is now combining his expertise in cardiovascular biology, inflammation and cell signalling to discover new avenues to target cardiac fibrosis and heart failure.

Bromodomain extra-terminal inhibitors prevent inflammation-induced stromal cell signalling & cardiac dysfunction

Janice D Reid[1,2], Christopher R Hunter[1,2], Isabelle Haddon[1], Lynn AC Devilée[1], Harley R Robinson[1], Rebecca L Fitzsimmons[1], Mary Lor[1], Simon R. Foster[1,2,3]*, James E. Hudson[1,2]*. QIMR Berghofer[1], Brisbane, QLD. Sch of Biomedical Sciences[2], Univ of Queensland, St Lucia, QLD. Dept of Pharmacol[3], Biomedicine Discovery Institute, Monash University, Clayton, VIC.

Introduction. Bromodomain and extra-terminal domain (BET) proteins represent attractive therapeutic targets and BET inhibition can prevent acute inflammation-induced cardiac dysfunction in human cardiac organoids (hCO) and in vivo (Mills R et al, 2021). However, a more detailed understanding of transcriptional control and mechanisms of the different BET family members and domains are required to improve BET inhibitor efficacy in cardiovascular disease.
Aims. To characterise the cell type-specific transcriptional responses during inflammation-induced dysfunction in hCO.
Methods. Multi-cellular hCO were exposed to an inflammatory 'cytokine storm' cocktail (24 h, 10 ng/mL IL-1β, 100 ng/mL IFNγ, and 10 µg/mL poly(I:C); CS) to induce dysfunction (increased relaxation time, Tr50). We then used single nuclei RNA-sequencing (snRNA-seq) to identify paracrine mechanisms of CS-induced dysfunction, AAV-mediated knockdown to discern the role of BET family members, and cardiac function and RNA-sequencing following BET inhibition to determine the role of different bromodomains in inflammation-induced dysfunction.
Results. snRNA-seq data showed that fibroblasts and endothelial cells were primary contributors to the CS-induced transcriptional response in hCO (60% of genes; $log_2FC>0.5$, adj. p-value <0.05). These included multiple paracrine factors, including leukemia inhibitory factor and neuregulin-1, which both induced dysfunction individually (20 and 30% increase in Tr50, respectively). AAV6-shRNA knockdown of BET proteins in CS-treated hCOs showed BRD2 + BRD4 were key mediators of cardiac dysfunction. Phenotypic screening and RNA-seq of CS-treated hCO with multiple BETi revealed differential efficacy on Tr50 and regulation of a core gene set, linked to bromodomain 2 specificity.
Discussion. We identify that inflammatory medaitors activate stromal cells to produce multiple paracrine factors that drive cardiac dysfunction in a BD2 domain and BRD2+4 dependent manner. This approach integrating phenotypic drug responses together with omics in multicellular organoids could form a powerful approach for translational programs.

Mills R et al (2021) Cell. 184(8):2167-2182.e22.

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Marginal Zone B cells: potential drivers of inflammation associated with hypertension

Dr Hericka Figueiredo Galvao

Biography:

Dr Figueiredo Galvao is a post-doctoral research officer at the Center for Cardiovascular Biology and Disease Research at La Trobe University. Her work investigates the role of immune-mediated inflammation in the development of hypertension. She uses a range of pharmacological interventions, genetically modified mice and next generation single-cell transcriptomic and proteomic sequencing to expand the current knowledge in her field.

Marginal Zone B cells: potential drivers of inflammation associated with hypertension

Hericka B. Figueiredo Galvao[1,2], Maria Jelinic[1,2], Vivian Tran[1,2], Buddhila Wickramasinghe[1,2], Jake N. Robertson[1,2], Tayla A. Gibson Hughes[1,2], Henry Diep[3], Asha Haslem[4], Mathew Lewsey[4], Alexander Bobik[5], Christopher G. Sobey[1,2], Grant R. Drummond[1,2], Antony Vinh[1,2]. Cent for CV Bio & Disease Res, La Trobe Inst of Med Sci[1], Melbourne, VIC, Australia; Dept of Micro, Anat, Phys & Pharmacol, La Trobe Univ[2], Melbourne, VIC, Australia; Vic Heart Inst, Monash Univ[3], Clayton, VIC, Australia; Genom Plat, La Trobe Univ[4], Melbourne, VIC, Australia; Baker Heart & Diabetes Inst[5], Prahran, VIC, Australia;

Introduction. Experimental hypertension is associated with inflammation and B cell activation. Moreover, global B cell depletion blunts increases in BP, inflammation, cardiac and vascular remodelling. However, it remains unclear which B cell populations mediate pro-hypertensive responses and if B cell activation involves classical antigen recognition.
Aims. To characterise B cell populations and determine the nature of B cell activation in experimental hypertension.
Methods. Hypertension was induced in male and female C57BL6 mice via angiotensin II infusion (0.7 mg/kg/day, s.c., 28 days). Control mice received vehicle (veh; saline). Systolic BP was measured by tail-cuff plethysmography. The impact of hypertension on B cell populations was characterised by single-cell RNA sequencing (scRNAseq) of spleens. The expression of specific immunoglobulin heavy chains (IGHVs) that form B cell receptors (BCRs) are increased in antigen-driven activation. IGHV expression was assessed by single-cell BCR sequencing (scVDJseq) to determine if B cell activation is antigen-driven. Multi-organ flow cytometry was used to validate findings.
Results. Angiotensin II increased BP in both sexes by ~40mmHg compared to veh-infused mice (166±3 vs 124±2 mmHg veh), although pressor responses in females developed at a slower rate. Marginal zone (MZ) B cells were significantly expanded in spleens from hypertensive mice in scRNAseq (7% vs 4% veh) and flow cytometry ($P<0.01$) datasets. scVDJseq revealed increased IGHV1 expression in MZBs ([0.01, 0.08] 95% CI, $q<0.02$) from hypertensive mice, suggesting antigen-driven activation. Flow cytometry showed angiotensin II increased the proportion of splenic MZBs bearing the antigen-specific activation marker Nur77 ($P<0.02$). In hypertensive mice, renal flow cytometry revealed infiltration ($P<0.02$), antigen-specific activation ($P<0.02$) and accumulation of MZB-like memory cells ($P<0.01$).
Discussion. Hypertension is associated with antigenic activation of MZB cells expressing unique BCRs that recognise pro-hypertensive (auto)antigens that may drive local and/or systemic inflammation associated with hypertension.

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Retinal capillary rarefaction is associated with systemic immune-inflammatory index in hypertensive patients

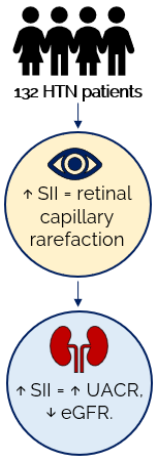
Dr Louise Woodhams

Biography:

Louise is a registered pharmacist who has worked in a variety of pharmacy sectors including community pharmacy, hospital pharmacy, research, and academia. She is an experienced compounding pharmacist and clinical trials pharmacist, with extensive experience in pharmacy clinical practice. She has a special interest in cardiovascular disease, diabetes and its associated microvascular complications, deprescribing, and more recently, applications of retinal imaging in hypertension. Her passion for helping others and reducing the risks of cardiovascular disease saw Louise successfully implement a Heart Foundation Walking Group through the community pharmacy she worked at in Albany. Louise authored several articles in peer reviewed journals and presented research outputs at national pharmacy conferences before being awarded her PhD in 2024.

Retinal capillary rarefaction is associated with systemic immune-inflammatory index (SII) in hypertensive patients.

Louise Woodhams[1], Revathy Carnagarin[1], Shaun Frost[1,2], Eve Martin[1,2], Janis M Nolde[1], Lakshini Y Herat[1], Justine Chan[1], Anu Joyson[1], Dennis Kannenkeril[1], Marcio G Kiuchi[1], Leslie Marisol Lugo-Gavidia[1], Markus P. Schlaich[1,3,4]. [1]Dobney Hypertension Centre, Medical School - Royal Perth Hospital Unit / RPH Medical Research Foundation, University of Western Australia, Perth, WA, Australia; [2]Commonwealth Scientific and Industrial Research Organisation (CSIRO), Kensington, WA, Australia; [3]Departments of Cardiology and Nephrology and Transplantation, Royal Perth Hospital, Perth, WA, Australia; [4]Neurovascular Hypertension & Kidney Disease Laboratory, Baker Heart and Diabetes Institute, Melbourne, VIC, Australia.



Introduction. Retinal capillary rarefaction is a hallmark of microvascular damage in hypertension (HTN). The severity of retinal blood vessel damage parallels blood pressure increases. HTN and HTN-mediated organ-damage are increasingly understood as immune-mediated inflammatory processes. As such, inflammatory markers may be useful in predicting adverse outcomes associated in HTN.

Aims. Study the association between systemic immune-inflammation index (SII), and retinal capillary density, as well as other indicators of microvascular damage in hypertension.

Methods. We conducted a cross-sectional analysis of data from 132 hypertensive patients. All patients underwent retinal imaging to assess retinal capillary density and blood sampling for inflammatory markers. We examined the association of SII and its individual components with retinal capillary rarefaction and other markers of microvascular damage, such as the urinary albumin-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR).

Results. Retinal capillary rarefaction was associated with increased white cell count, particularly neutrophils, and the SII. Through predictive margin analysis, an optimal cut-off value of 600 x 109/L for SII was determined for median CDF of 34.1 mm². The analysis showed a reduction in CDF of 1.3 mm² for every 250 x 109/L increase in SII. Additionally, higher SII levels (≥ 600 x 109/L) were associated with elevated high-sensitivity C-reactive protein (hs-CRP) levels and markers of microvascular damage, such as increased UACR and reduced eGFR.

Discussion. In patients with primary hypertension, SII and related inflammatory markers were associated with retinal rarefaction and renal indices of microvascular damage. SII may serve as a useful clinical marker of microvascular damage in the retinal and renal vascular bed in clinical settings where advanced imaging is unavailable.

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Low-dose Australian air pollution promotes neutrophilic, steroid-insensitive, experimental asthma

Mr Hudson Taylor-Blair

Biography:

Hudson is an emerging researcher who is currently an Honours student at the University of Technology Sydney under the supervision of Distinguished Professor Brian Oliver.

Low-dose Australian air pollution promotes neutrophilic, steroid-insensitive, experimental asthma

Hudson C. Taylor-Blair[1,2], Chantal Donovan[1,2], Madison Coward-Smith[1,2], Jessica Tolentino[1,2], William Dewar[1], Cory Butlin[1], Meng Wang[1,2], Alexia Defrancesco[1], Andrew E. Thorpe[1,2], Hongdan Wang[2], Baoming Wang[1,2], David D. Cohen[3], Armand Atanacio[3], Richard Y. Kim[1,2], Brian G. Oliver[1,2]. School of Life Sciences, UTS[1], Sydney, NSW, Australia; Woolcock Institute of Medical Research[2], Sydney, NSW, Australia. ANSTO[3], Menai, NSW, Australia.

Introduction. Particulate matter <2.5 µm ($PM_{2.5}$) is an airborne pollutant and a critical global health threat. Epidemiological studies show that $PM_{2.5}$ exposure is associated with the development and increased severity (including reduced symptom control with corticosteroids) of asthma. However, the pathobiology of $PM_{2.5}$ exposure at levels present in Australia is relatively unexplored.

Aims. To investigate how chronic Sydney $PM_{2.5}$ exposure influences the phenotype of experimental asthma and response to corticosteroids.

Methods. Mice (*n*=12/group) were exposed daily to $PM_{2.5}$ (i.n.; 10 µg) or Sham (PBS) control. In some groups, experimental asthma was superimposed by sensitising with ovalbumin, (Ova; i.p.; 50 µg; day 21) or saline, followed by challenge (i.n; 20 µg Ova; days 33, 34, 54, 55) and corticosteroid treatment (i.n.; 2 mg/kg dexamethasone; days 53-55) or vehicle control. At endpoint (day 56), we measured lung function and airway hyperresponsiveness (AHR), airway inflammation (bronchoalveolar lavage fluid), and lung leukocytes (flow cytometry).

Results. In Ova-sensitised mice, PM exposure resulted in an 18% reduction in inspiratory pulmonary capacity compared to sham (*n*=8/group; *p*<0.05), although no changes in the magnitude of AHR or total airway leukocyte numbers occurred. Analysis of bronchoalveolar lavage fluid revealed that Ova-sensitised, sham-exposed mice had airway eosinophilia; however, Ova-sensitisation with PM exposure caused a significant shift to airway neutrophilia (*n*=12/group; *p*<0.001), but a >40% and >70% increase in both eosinophils and neutrophils in lung tissue (*n*=8/group; *p*<0.01). In Ova-sensitised mice, PM-exposure reduced the ability of corticosteroid treatment to suppress AHR and inflammation back down to baseline levels observed in corticosteroid-treated, sham-exposed groups, indicating steroid insensitive disease.

Discussion. Our data show that PM exposure promotes a neutrophilic inflammatory phenotype and reduced responsiveness to corticosteroid treatment in experimental asthma. Next, characterising cytokine, chemokine, and histopathological changes will help elucidate our findings and determine the potential relevance to other diseases.

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Targeting C-C motif chemokine receptor 6 with PF-07054894 in COPD

Mr William Dewar

Biography:

William Dewar is a Bachelor of Medical Science (Honours) student at the University of Technology Sydney under the primary supervision of Dr Richard Kim and co-supervision of Dr Chantal Donovan.

Targeting C-C motif chemokine receptor 6 with PF-07054894 in COPD

William F Dewar[1], Chantal Donovan[1,2], Madison L Coward-Smith[1,2], Cory Butlin[1], Jessica R Tolentino[1], Hudson C Taylor-Blair[1], Brian GG Oliver[1,2], Richard Y Kim[1,2]. School of Life Sciences, Univ of Technology Sydney[1], Sydney, NSW, Australia; Respiratory Cellular and Molecular Biology, Woolcock Institute of Medical Research[2], Sydney, NSW, Australia.

Introduction. Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death globally with approximately 480 million reported cases in 2020. Current COPD therapies fail to reduce airway obstruction in most patients and cause adverse effects, necessitating the need for better therapies. C-C motif chemokine receptor 6 (CCR6) is implicated in several inflammatory diseases and is detected in the airways of COPD patients. However, no *in vivo* studies of CCR6 in COPD have assessed changes in lung function or explored the potential for therapeutic targeting of CCR6 in COPD.

Aims. To determine the effects of administering the novel CCR6 inhibitor, PF-07054894, to the lungs in a porcine pancreatic elastase (PPE)-induced model of COPD, and to characterise the roles of CCR6 in inflammation and airway obstruction.

Methods. Six-week-old, male, wild type, BALB/c mice (*n*=8/group) were treated with 50µL of PPE (0.25IU) or PBS intranasally. Mice were treated with PF-07054894 (5mg/kg) or vehicle (PBS [2% dimethyl sulfoxide]) intranasally from day 7, 3 times per week, for 2 weeks. Intranasal treatments were administered under isoflurane anaesthesia (3% isoflurane, 2.0L/min O^2). At the endpoint (day 21), several lung function parameters were measured using a FlexiVent FX1 apparatus (SCIREQ), airway inflammation assessed in bronchoalveolar lavage fluid, and immune cells analysed in lung and bone marrow cell suspensions by flow cytometry.

Results. Treatment with PF-07054894 had no effects on airway and tissue inflammation, however, it robustly reduced PPE-induced increases in hysteresis (P = 0.0019) back to baseline levels. PF-07054894 treatment also resulted in close to statistically significant reductions in Newtonian resistance (P = 0.0813), respiratory system resistance (P = 0.0693) and elastance (P = 0.0723).

Discussion. Targeting CCR6 with PF-07054894 improved lung function in PPE-induced COPD but had no effects on inflammation in the airways, lungs, and bone marrow. These data highlight the need for greater exploration of the potential of CCR6 inhibition in the treatment of COPD.

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The effect of aprocitentan in patients with very high baseline blood pressure

Professor Markus Schlaich

Biography:

Prof Markus Schlaich is a renal physician and a European Society of Hypertension (ESH) accredited hypertension specialist. Markus is Chair of Hypertension Australia and Co-Chair of the National Hypertension Taskforce. He has a strong background in clinical research with a focus on the pathophysiology of hypertension, the role of the sympathetic nervous system, involvement of the kidneys, and hypertension mediated organ damage. He has a specific interest in treatment modalities targeting the sympathetic nervous system and has been a pioneer of renal denervation and other interventional and pharmacological approaches to treat hypertension. He has authored more than 500 articles in peer reviewed journals and serves on the Editorial Board of Hypertension, Journal of Hypertension, and Hypertension Research.

The effect of aprocitentan in patients with very high baseline blood pressure

Markus P Schlaich[1,2], Michael A Weber[3], Krzysztof Narkiewicz[4], Ji-Guang Wang[5], John M. Flack[6]. Dobney Hypertension Centre, University of Western Australia[1], and Departments of Cardiology and Nephrology, Royal Perth Hospital[2], Perth, WA, Australia; Downstate College of Medicine, State University of New York[3], Brooklyn, NY, USA; Department of Hypertension and Diabetology, Medical University of Gdańsk[4], Gdańsk, Poland; Department of Hypertension, The Shanghai Institute of Hypertension[5], Shanghai, China; Department of Medicine, Hypertension Section, Southern Illinois University School of Medicine[6], Springfield, IL, USA.

Introduction. Sustained elevated blood pressure (BP) markedly increases the risk of stroke, heart failure, kidney disease, and cardiovascular death, especially in patients with resistant hypertension (RHT). Aprocitentan, a newly approved dual endothelin receptor antagonist, offers a novel therapeutic option for these patients.

Aims. This post hoc analysis aimed to evaluate the effect of aprocitentan in patients with Grade 2 Hypertension (HTN) at baseline (160 to 179 mmHg).

Methods. In PRECISION, patients with office systolic BP (SBP) ≥140 and <180 mmHg despite standardized background therapy of 3 antihypertensive drugs were initially randomized to receive aprocitentan (12.5 mg or 25 mg daily) or placebo for 4 weeks in Part 1, followed by a 32-week single-blind Part 2. BP was measured at trough. Here patients from PRECISION with Grade 1 (BL SBP <160 mmHg) and Grade 2 HTN (BL SBP ≥160 mmHg and <180 mmHg) were evaluated. Of the 730 patients, 23.4% (n=171) had Grade 2 HTN.

Results. The baseline characteristics of both groups were similar. At Week 2, the Grade 2 HTN group showed a mean reduction (SD) in SBP of 22.3 (13.7) mmHg and 21.8 mmHg (15.1) in the aprocitentan 12.5mg and 25mg arms, respectively (Placebo: 14.3 mmHg (16.8)) with similar BP at week 4. This reduction was maintained at Week 36 and confirmed by 24-hour ambulatory BP monitoring. At week 4, a higher reduction in UACR (urine albumin-creatinine ratio) was observed in the Grade 2 HTN group, i.e. 32.3% and 44.1% in the aprocitentan 12.5 mg and 25 mg arms, respectively (compared to reduction in the Grade 1 HTN group: 26.3% and 26.8% in the aprocitentan 12.5 mg and 25 mg arms). At Week 36, the reduction in UACR was similar in both groups.

Discussion. This analysis suggests that aprocitentan is effective and well-tolerated in patients with very high blood pressure, with a rapid onset of action by Week 2 and potential reno-protective effects.

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Chronic hypertension in young women – are we adequately preparing for pregnancy?

Dr Madeleine Cosgrave

Biography:

Madeleine is a renal and obstetric medicine physician at Eastern Health, Melbourne. She is completing a PhD in hypertensive disorders of pregnancy. She is passionate about improving care for women with these disorders and has recently been involved in implementing a new postpartum hypertension surveillance program at Eastern Health.

Chronic hypertension in young women – are we adequately preparing for pregnancy?

Cosgrave M[1,2], C Brumby[1,2], LP McMahon[1,2]. Department of Renal Medicine and Obstetric Medicine[1], Box Hill Hospital, Box Hill, VIC, Australia; Eastern Health Clinical School[2], Monash University, Box Hill, VIC, Australia

Introduction. Obstetric risk is higher in women with chronic hypertension (CHTN), and control of blood pressure (BP) preconception is associated with better outcomes. Both hypertension and obstetric guidelines support preconception optimisation, including screening for causes of secondary hypertension (2HTN), though this does not often occur. Furthermore, data accuracy is limited.

Aim. To investigate preconception and early-pregnancy hypertension management and associated pregnancy outcomes in women with CHTN.

Methods. We conducted a cohort study of pregnancies in women with CHTN at two obstetric centres in Melbourne from 2008-2024. Clinical data were collected on maternal demographics, anti-hypertensive use, CHTN duration, secondary hypertension (2HTN) screening, and obstetric and perinatal outcomes.

Results. Among 82,083 deliveries, 492 pregnancies were affected by CHTN. 67 women (14%) were first identified as having CHTN at the beginning of their pregnancy, suggesting poor preconception care. Overall, blood pressure control at pregnancy booking visit was suboptimal, with 148 women (30%) having a systolic BP (SBP) >135mmHg. Every 1mmHg increase in SBP corresponded to a 2% increase in odds of preeclampsia (p=0.009). 265 women (54%) were on antihypertensive medication at conception and were more likely to have a SBP under target (73% vs 54%, p<0.001). Of these women, 76 (29%) were on an ACE inhibitor/angiotensin receptor blocker and, while 46 (61%) ceased these before 8 weeks' gestation, 6 (8%) were not stopped until the second trimester. Screening for 2HTN became more common over time, however in 273 pregnancies (55%), an underlying cause was not considered. A partial or full 2HTN screen was undertaken in 188 pregnancies (38%) with renal disease the most common cause (34 pregnancies, 18%).

Discussion. Opportunity to optimise pregnancy outcomes was missed in many pregnancies, despite 76% being planned. This study demonstrates missed preconception and early-pregnancy opportunities for improving pregnancy outcomes in women with CHTN. As highlighted in this study, preconception care and planning should focus on improving blood pressure control, use of pregnancy-safe medications and screening for secondary causes of CHTN.

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Australia lacks a high-quality national database system on blood pressure

Dr Alexandra Gallagher

Biography:

Dr Alexandra Gallagher is a Staff Specialist Nephrologist at St George Hospital and PhD candidate at the NHMRC Clinical Trials Centre at the University of Sydney. Her PhD is exploring the efficacy and safety of cardioprotective strategies in high risk patients, including inpatient blood pressure measurement. She is a member of the National Hypertension Taskforce, working group 4 and medical lead for the NSW Ministry of Health's renal Net Zero hub.

Australia lacks a high-quality national database system on blood pressure

Alexandra Gallagher[1]*, Lachlan L. Dalli[2]*, Heidi Dietz,[3] Amirul Islam,[4] Markus Schlaich,[5] Nelson Wang,[6] Xiaoyue Xu[7], James E. Sharman[8] on behalf of the National Hypertension Taskforce Working Group 4. NHMRC Clinical Trials Centre, University of Sydney, Camperdown, NSW, Australia[1]; School of Clinical Sciences, Monash University, Clayton, VIC, Australia[2]; Cardiovascular, Diabetes and Kidney Unit, AIHW, Australia;[3] Swinburne University of Technology, Hawthorn, VIC, Australia;[4] University of Western Australia, Perth, WA, Australia;[5] Brigham and Women's Hospital, Boston, MA, USA;[6] School of Population Health, University of NSW, Sydney, NSW, Australia;[7] Menzies Institute for Medical Research, University of Tasmania, Hobart, TAS, Australia.[8] **AG and LD are co first authors*

Introduction. Raised blood pressure (BP) in Australia remains underdiagnosed and undertreated, leaving many people at risk of preventable complications. A high-quality national database will inform health care providers and policy makers on the incidence, prevalence and complications of raised BP. It is unclear if any such databases currently exist.

Aims. To conduct a review of existing national databases in Australia that collect BP and cardiovascular disease data and (1) evaluate their quality, and (2) identify gaps to inform future needs for a national BP database.

Methods. A comprehensive environmental scan was conducted to identify Australian national databases containing BP and cardiovascular disease data. This involved systematic searches of Google and PubMed and targeted searches of government websites and research institution repositories, in addition to contacting key stakeholders from relevant organisations. A standardised data extraction and analysis framework was used to evaluate database quality, features, map overlap, and identify gaps.

Results. There were 12 national databases identified containing BP and/or cardiovascular disease data. The database with highest quality BP data was the National Health Survey—the only source with standardised BP measurement and representative data collection. Notable gaps were found in the quality of BP measurements and inclusion of non-representative rather than probability sampling. None of the databases had real-time monitoring capabilities and there were no standardised BP measurement protocols within and across databases.

Discussion. Current BP databases have inconsistent data standards, which limit their utility to estimate the prevalence and control of hypertension in Australia. Action now is necessary to develop a coordinated national surveillance framework to help increase hypertension control rates and lower Australia's burden of cardiovascular disease.

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Improved cardiovascular disease risk management via pathology services: a randomised clinical trial

Prof James Sharman

Biography:

James Sharman is a professor of medical research at the Menzies Institute for Medical Research. He heads the Blood Pressure Research Group and is former Deputy Director of the Institute.

Improved cardiovascular disease risk management via pathology services: a randomised clinical trial
James E Sharman[1], Katherine Chappell[1], Julie A. Campbell[1], Niamh Chapman PhD[1,2], Alison J. Venn[1], Petr Otahal[1], Christopher M Reid[3], Paul Scuffham[4], Mark R. Nelson[1] on behalf of the IDEAL Study investigators. Menzies Institute for Medical Research, University of Tasmania, Hobart, TAS, Australia.[1] School of Health Sciences, University of Sydney, Sydney, NSW, Australia.[2] School of Population Health, Curtin University, Perth, WA, Australia.[3] School of Medicine & Dentistry, Griffith University, Gold Coast, QLD, Australia.[4]

Introduction. Cardiovascular disease (CVD) prevention guidelines recommend clinical management based on CVD risk stratification. People at high CVD risk are recommended to be treated with both cholesterol-lowering and antihypertensive therapies, but this does not routinely occur in primary care, and solutions are needed.
Aims. To determine whether CVD risk assessment conducted in a pathology service and reported to general practitioners (GPs) will improve clinical management of people at high CVD risk.
Methods. This was a cluster, randomized controlled trial among adults from 60 general practice clinics eligible for CVD risk assessment and having routine cholesterol testing ordered by their GP. The trial was conducted at 14 pathology services sites across Tasmania, with 12-months follow-up. All participants had blood pressure and CVD risk factors measured at pathology sites for calculation (Framingham) of 5-year absolute CVD risk. Intervention participants had blood cholesterol, plus additional information on absolute CVD risk and recommended treatment strategies reported to their referring GP, whereas control participants followed usual care with only cholesterol results reported. Primary outcome was difference in adherence to guideline-recommended treatment (dispensing of both cholesterol-lowering and antihypertensive medications) in people at high CVD risk. Secondary outcome was a health economics analysis.
Results. Baseline characteristics were similar between intervention (n=1,380) and control (n=1,360) groups. Intention-to-treat analysis showed intervention was associated with a significantly higher proportion of people at high CVD risk receiving both cholesterol-lowering and antihypertensive medications within 12-months (0.11 [95%CI 0.08, 0.14] vs 0.22 [0.16,0.29]; relative risk 2.02 [1.36, 3.02]; p=0.001). Expanding the intervention across Australia would save $1.9 billion per annum from CVD events averted.
Discussion. Absolute CVD risk assessment conducted in pathology services and reported to GPs improves clinical management of people at high CVD risk and would generate significant cost savings to Australian society.

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What attributes influence antihypertensive prescribing to older adults? A discrete choice experiment

Dr Edel O'hagan

Biography:

Edel is a postdoctoral researcher focused on improving blood pressure control in older and underserved populations through innovative digital health approaches.

What attributes influence antihypertensive prescribing to older adults? A discrete choice experiment.

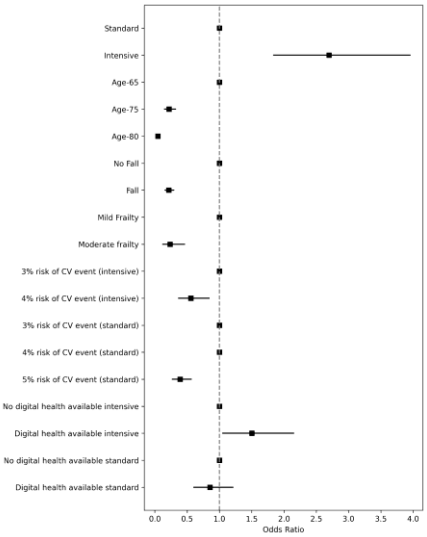
Edel O'Hagan[1], Ann Livingstone[2], Thomas Gadsden[3], Timothy Usherwood[1,3], Tu Nguyen[3,4], Aletta E Schutte[3,5], Anne Tiedemann[4,6], Richard I Lindley[1], Anthony Rodgers[3], Stephen Jan[3], Clara K Chow[1,7].Westmead Applied Research Centre, USyd[1], NSW; Institute for Health Transformation, Deakin Uni[2], VIC; The George Institute for Global Health, UNSW[3], NSW; Sydney School of Public Health, USyd[4], NSW; School of Population Health, USyd[5], NSW; Institute for MSK Health, USyd[6], NSW; Dept of Cardiology, Westmead Hosp[7], NSW, Australia.

Introduction. Clinical inertia in managing high BP among older adults contributes to preventable cardiovascular events. Understanding prescribing preferences can inform strategies to support appropriate treatment intensification.

Aims. To explore how clinicians weigh patient characteristics and contextual factors when deciding whether to intensify antihypertensive treatment in adults aged ≥65 years.

Methods. An online discrete choice experiment surveyed Australian doctors who prescribe BP-lowering medications. Respondents chose between intensive (≤130 mmHg) and standard (131–150 mmHg) systolic BP targets across hypothetical patient scenarios varying by age, frailty, fall history, cardiovascular risk, and access to digital health data. Mixed logit models and latent class analysis were used.

Results. Clinicians favored intensive targets overall, but were less likely to do so for patients aged ≥80, with recent falls or moderate frailty. Higher cardiovascular risk and access to digital health data increased the likelihood of intensive prescribing. Two clinician subgroups emerged: digital health adopters and hesitant users.



Discussion. Prescribing decisions are shaped by clinical risk, patient vulnerability, and digital data availability. Digital health tools may support more intensive treatment decisions and help address clinical inertia.

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Impact of packaging aids on medication errors: a systematic scoping review

Miss Ngoc Tran

Biography:

Ngoc Tran is an honours student in the Bachelor of Pharmacy program at the University of Sydney. Her current research focuses on the role of dose administration aids in improving medication safety, particularly for vulnerable patient groups. Her broader research interests include pharmacoepidemiology and the quality use of medicines. She aims to pursue a PhD to build on her research in medication safety, with the goal of improving patient outcomes.

Impact of packaging aids on medication errors: a systematic scoping review

Ngoc P A Tran[1], Rose Cairns[1,2], Ricki Ng[1], Nicholas Buckley[1,2]. School of Pharmacy, Univ of Sydney[1], Camperdown, NSW, Australia; NSW Poisons Information Centre, Children's Hosp at Westmead[2], Westmead, NSW, Australia.

Introduction. Medication errors pose a significant threat to public health, especially in outpatient settings, where close monitoring is often not feasible. Packaging aids, which organise doses by date and/or time, are widely used to improve adherence (Conn et al, 2015). However, evidence regarding their impact on medication errors remains limited in the literature.

Aims. To assess the effect of packaging aids on medication errors, compared to original packaging, in outpatient care.

Methods. We searched the Cochrane Central Register of Controlled Trials, Medline, CINAHL, Embase, and Scopus from inception to 17 April 2025. We also searched the reference lists from relevant articles. We selected studies that met the following criteria: (1) conducted in outpatient settings, (2) measured medication errors, (3) involved a packaging aid, such as an automated medication dispensing system, monitored dosage system, or daily dose reminder, for medications in solid oral dosage form, and (4) contained an English title and abstract. Full texts not published in English were translated using Google Translate.

Results. Four studies were identified from 2206 titles/abstracts and 45 full text articles. All were non-randomized, observational studies, with quality rated as moderate to good using the Newcastle-Ottawa Scale. Three studies were conducted in long-term residential care facilities, whereas one was undertaken in a youth camp. Outcomes included medication administration errors and discrepancies between general practitioners and home care records. The use of packaging aids resulted in a statistically significant reduction in risks of medication errors, relative risk = 0.42 (95% CI 0.25 to 0.71). Notable heterogeneity was observed among these studies I^2 = 72.8%.

Discussion. Packaging aids may provide a simple and convenient approach to improving medication safety in the outpatient settings. Further methodologically robust trials are warranted to evaluate the impact of different types of packaging aids and their respective fillers (e.g., pharmacists, patients, carers, or automated systems) on various categories of medication errors.

Conn VS et al (2015) Curr Med Res Opin 31:145-160

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Psilocybin-assisted psychotherapy: A trans-diagnostic therapy?

Dr Jonathan Brett

Biography:

Dr Jonathan Brett is a senior staff specialist in clinical toxicology and addiction medicine at St. Vincent's Hospital, Sydney, clinical director of the Psychiatry and Non-Prescription Drug and Alcohol Unit and a clinical toxicologist with the NSW Poison's Information Centre. He has fellowships with the Royal Australian College of Physicians in clinical pharmacology, toxicology and addiction medicine. He is a conjoint Professor with St. Vincent's Clinical School, UNSW and a Senior NHMRC Research Fellow with the Medicines Policy Unit of Centre for Big Data Research in Health, UNSW. He is president elect of the Royal Australian College of Physicians Chapter of Addiction Medicine. He completed his PhD in biostatistics in 2018 with a focus on the use of big data measure the quality use of psychotropics in mental health and has a research interest in psychopharmacology.

Psilocybin-assisted psychotherapy: A trans-diagnostic therapy?

St. Vincent's Clinical School, University of New South Wales

Methamphetamine (MA) use disorder is a growing global health concern with no approved pharmacotherapies and limited efficacy of existing psychosocial treatments. Psilocybin-assisted psychotherapy (PAT) has emerged as a promising intervention for substance use disorders. The **Psi-MA pilot program,** conducted at St Vincent's Hospital Sydney, represents the world's first clinical evaluation of PAT in people with MA use disorder. 15 participants received preparatory psychotherapy, a single 25 mg oral psilocybin dose in a supportive therapeutic setting, and integration sessions. Safety and feasibility were established, with no serious adverse events. Quantitative findings demonstrated reduced frequency of MA use, cravings, depression, anxiety, and stress over 90 days post-treatment. Neuroimaging sub-studies revealed reorganisation of large-scale functional networks, including increased connectivity between attentional, salience, and executive circuits, and reduced synchrony in reward-related regions, correlating with improvements in clinical outcomes. Complementary qualitative analysis highlighted participant narratives of confronting and resolving "psychological obstacles," leading to reduced salience of MA use and new insights into self and relationships.

In parallel, the **TRIP-D study** investigates PAT for treatment-resistant depression (TRD) in patients maintained on concurrent antidepressants, addressing an important translational gap given that most prior psilocybin trials have excluded participants on psychotropic medications. TRIP-D is an open-label, single-centre pilot study with dose-titration (15–45 mg) followed by a final therapeutic dose, combined with structured psychotherapy. Primary outcomes assess feasibility, safety, and acceptability; secondary outcomes examine mood, quality of life, cognition, and connectedness. TRIP-D provides the first evidence on safety, tolerability, and efficacy of psilocybin in real-world clinical contexts where medication discontinuation is impractical or unsafe.

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Characterising a rat model of polycystic kidney disease to identify therapeutic targets

Dr Quynh Dinh

Biography:

Dr Quynh Dinh is a lecturer in Pharmaceutical Sciences at RMIT University. Dr Dinh's research focuses on understanding inflammatory pathways that contribute to the development of cognitive impairment in cardiovascular disease and dementia.

Characterising a rat model of polycystic kidney disease to identify therapeutic targets Quynh Nhu Dinh1,2, Emily Major2, Jemma Gasperoni2, Chris Sobey2, Grant Drummond2, Avril Robertson3, Jacqueline Phillips4, Brooke Huuskes2. School of Health and Biomedical Sciences, RMIT University1, VIC; Centre for Cardiovascular Biology and Disease Research, La Trobe University2, VIC; School of Chemistry and Molecular Biosciences, University of Queensland3 QLD; Department of Biomedical Science, Macquarie University4, NSW.

Introduction. Polycystic kidney disease (PKD) is the most common genetic form of chronic kidney disease and a major risk factor for dementia. PKD and dementia are leading causes of death as there are no disease modifying drugs available. It is not clear how PKD may promote cognitive impairment and dementia, however, systemic inflammation is emerging as a key driver of kidney cyst formation and the development of cognitive impairment. The NLRP3 inflammasome has been implicated in the pathophysiology of other forms of kidney disease but it's contributions in PKD is unknown.
Aims. In a rat model of PKD we aimed to 1) establish the first rat model of PKD-induced cognitive impairment, 2) characterise the inflammatory profile and 3) determine if inhibiting NLRP3 can reduce end-organ damage.
Methods. In the characterisation study, male and female Lewis wild-type (WT) and Lewis polycystic kidney (LPK) rats were studied at 6, 12 and 18 weeks of age. In the intervention study, male and female WT and LPK rats began daily IP injections with the NLRP3 inflammasome inhibitor, MCC950, from 6 weeks of age for 10 weeks.
Results. LPKs had higher BP compared to WT from 6 weeks of age (n=10, $P<0.05$). LPKs had intact recognition memory (n=5-9) but spatial working memory was impaired at 12 and 18 weeks ($P<0.05$). Kidney T cells and macrophages were increased at 6 and 12 weeks but decreased at 18 weeks in LPKs (n=8-10, $P<0.05$). Expression of inflammasomes; NLRP3, NLRC4, AIM2, and components; caspase 1, IL-18 and IL-1b were elevated in LPK kidneys. Inhibition of NLRP3 reduced expression of kidney collagen (n=6-8, $P<0.05$) but overall did not decrease BP, number of kidney cysts or improve kidney function in LPKs.
Discussion. Cognitive impairment was observed in a rat model of PKD from 12 weeks of age which was associated with hypertension and kidney inflammation. Inhibition of NLRP3 inflammasome reduced kidney fibrosis but did not affect blood pressure, cyst growth or kidney function suggesting potential involvement of other inflammasomes in the pathophysiology of PKD.

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Understanding sex-based cardiometabolic responses to contemporary diabetes therapies

Dr Abhipree Sharma

Biography:

Dr. Abhipree Sharma received her PhD in 2024 at Monash University in the Heart Failure Pharmacology laboratory. Since completing her PhD, she has continued as a postdoctoral fellow in the same laboratory. Her research focuses on investigating the potential sex-specific cardiac and systemic effects of newer classes of glucose-lowering therapies in patients with type 2 diabetes and in animal models of obesity and diabetes.

Understanding sex-based cardiometabolic responses to contemporary diabetes therapies

Abhipree Sharma1, Minh Deo1, Tayla Bishop1, Abdullah Mamun1, Timothy Roberts1, Alex Parker1, Anida Velagic1, Dovile Anderson2, David Shackleford3, Miles De Blasio1, Rebecca Ritchie1. Drug Discovery Biology1, Monash Proteomics and Metabolomics Platform2, Centre for Drug Candidate Optimisation3, Monash University, Parkville, Australia

Introduction. The impact of sex is often overlooked in presentation and treatment of cardiometabolic disease. We have demonstrated that contemporary therapies, such as sodium glucose co-transporter 2 inhibitors (SGLT2i), may exert sex- and comorbidity-specific cardioprotection in patients with type 2 diabetes (T2D) when compared to glucagon-like peptide 1 receptor agonists (GLP-1RAs) (Sharma et al., 2023), with the underlying mechanisms unknown.
Aims. To investigate sex differences in phenotype and the effects of SGLT2i and GLP-1RAs in mouse models of metabolic syndrome or type 2 diabetes (T2D).
Methods. The cardiometabolic effects of the SGLT2i, dapagliflozin (moderate dose: 2.5 mg/kg/day; high dose: 5 mg/kg/day, s.c. osmotic mini-pumps), and the GLP-1RA, liraglutide (1 mg/kg, thrice-weekly s.c. injections), were assessed in male and female high fat diet (HFD) mice (n=8-12 per treatment group), or in female T2D db/db mice (n=59 per treatment group).
Results. HFD-induced impairment in body composition was more evident in female mice, with dapagliflozin treatment improving glucose tolerance only in male HFD mice. In female T2D mice, both dapagliflozin and liraglutide improved glucose homeostasis with no impact on body weight or composition. However, only SGLT2i treatment improved cardiac function (E/e' ratio, global longitudinal strain) and pathological remodelling (cardiomyocyte hypertrophy).
Discussion. In HFD mice, modest sex differences in disease phenotype and dapagliflozin-mediated improvements in glucose homeostasis were observed. Consistent with our previous report, greater improvements in cardiometabolic phenotype were observed with dapagliflozin treatment in female T2D mice. Our findings highlight the importance of continuing to interrogate sex-based differences in cardiometabolic disease and efficacy of contemporary therapeutics. This allows for the development of more targeted treatment approaches, which is especially important for women, as they are often underdiagnosed and undertreated for cardiometabolic diseases.

Sharma A et al (2023) Lancet Reg Health West Pac 33:100692

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Novel in vivo and ex vivo applications utilising transgenic TGFβ overexpressing mice

Dr Julia Chitty

Biography:

Julia is a dedicated pharmacologist specialising in lung diseases, focusing on COPD and viral AECOPD, with a special interest in the cytokine Transforming Growth Factor Beta. Julia is currently a Research Fellow at Monash University, where her research aims to develop a novel mouse model of COPD to assess therapeutic strategies for viral-induced inflammation and lung damage. I utilise cutting-edge ex vivo models, including precision-cut lung slices (PCLS), to test drug efficacy and improve treatments for COPD.

Novel in vivo and ex vivo applications utilising transgenic TGFβ overexpressing mice

Julia Chitty[1,2], Maggie Lam[2], Simon Royce[1], Paris Papagianis[1], Zifra Kuijper[1], Philip Bardin[2,3], Jane Bourke[1,2], Belinda Thomas[2]. Pharmacology, Biomedicine Discovery Institute, Monash University[1]; Centre for Innate Immunity and Infectious Diseases, Hudson Institute of Medical Research, VIC, Australia[2]; Monash Lung, Sleep, Allergy and Immunology, Monash Health, VIC, Australia[3].

Introduction. TGFβ is elevated in the lung in chronic respiratory diseases, driving fibrosis, inflammation and immune dysregulation, leading to enhanced viral infections during acute exacerbations. We have utilised a transgenic mouse model of inducible, lung-specific TGFβ overexpression to study the impacts of increased TGFβ *in vivo.* We extended our assessment to precision-cut lung slices (PCLS), in which lung architecture and resident cells are preserved *ex vivo*.

Aims. To investigate the effects of chronic endogenous TGFβ overexpression on (1) lung structure and function *in vivo*, (2) influenza A virus (IAV) infection *in vivo*, and (3) whether *ex vivo* activation of the transgene in PCLS recapitulates these *in vivo* responses, to support their use for high-throughput novel drug screening.

Methods. Transgenic mice received doxycycline (dox: 0.25 mg/ml) to induce TGFβ or control (water) for 8 weeks; (1) *in vivo* plethysmography was performed, and lungs and BALF were collected (Chitty et al, 2025). (2) Dox and control mice were infected with IAV (10^2 PFU, HKx31) and culled 3 days post-infection for fibrotic, inflammatory, and viral analysis. (1 & 2) PCLS were prepared from the *in vivo* model for assessment of intrapulmonary airway reactivity to methacholine. (3) PCLS from naïve transgenic mice were treated with dox *ex vivo* in the media (0.025 mg/ml) for up to 5 days, and assessed for markers of viability, inflammation, and fibrosis (Lui et al, 2025).

Results. (1) Chronic TGFβ overexpression caused airway fibrosis in the absence of inflammation, resulting in airway hyperresponsiveness both *in vivo* and in PCLS. (2) TGFβ overexpression amplified viral loads and inflammation, while IAV enhanced TGFβ-induced fibrosis. Both TGFβ and IAV independently increased airway contraction in PCLS. (3) *Ex vivo* treatment of PCLS with dox induced TGFβ secretion and alterations in collagen consistent with *in vivo* findings.

Discussion. Chronic TGFβ overexpression *in vivo* exerts detrimental impacts on lung structure, function, and host antiviral responses. Induction of TGFβ can be achieved *ex vivo* in transgenic mice PCLS to mimic these pathologies, providing a high-throughput model to assess novel therapeutics targeting TGFβ. This body of work offers innovative approaches for modelling viral-induced acute exacerbations to address the unmet need for novel therapeutics.

Chitty (2025) Am J Physiol Lung Cell Mol Physiol 329:L255-L265; Lui (2025) Am J Physiol Cell Physiol 329:C611-C623.

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Reimagining Hypertension Care: Feasibility and Acceptability of Remote Wearable Blood Pressure Monitoring

Miss Heshmiha Christy

Biography:

Heshmiha is a fourth year medical student (honours) at the University of New South Wales (UNSW), co-supervised by A/Prof Hueiming Liu and Dr Isabella Tan. Her research interests lie at the intersection of digital health, cardiology, and implementation science. She is involved in the NEXTGEN-BP study, focusing on the process evaluation of cuffless BP monitoring devices and their integration into routine general practice workflows across primary care settings.

Reimagining hypertension care: Can wearable blood pressure monitoring with remote care be feasible and acceptable in practice?

Heshmiha Christy[1], Isabella Tan[1,2], Aletta E Schutte*[1,2], Hueiming Liu*[1,2] University of New South Wales[1], Sydney, NSW, Australia; The George Institute for Global Health[2], Sydney, NSW, Australia; Joint senior authors*

Introduction. Clinic blood pressure (BP) monitoring often provides limited data which fails to capture circadian BP variations and can be influenced by white-coat hypertension. Wearable BP devices with the ability to monitor continual BP can overcome these challenges to provide comprehensive and personalised BP profiles.

Aims. This ongoing study aims to evaluate within a randomised control trial (RCT) whether a wearable BP monitoring strategy coupled with remote care is acceptable and feasible from the perspectives of patients, general practitioners (GPs), practice staff and clinical trial coordinators (CTCs) for hypertension management and further implementation.

Methods. Process evaluation informed by the implementation science non-adoption, abandonment, scale-up, spread, and sustainability framework, was integrated in a RCT (the NEXTGEN-BP trial). Clinical decision support for remote care was based on proportion of BP readings below treatment target of 135/85mmHg (%BP at target) – as opposed to average BP - provided by a wearable BP monitoring device (Hilo, Aktiia SA, Switzerland). Semi-structured interviews were conducted with a purposive sampling of 14 patients (7 intervention, 7 control; 6 females; 8 males; mean age 67 ± 7 years), 2 GPs, 2 CTCs and 1 practice staff. Interview transcripts were analysed using thematic analysis.

Results. There was high acceptability of the wearable BP device among patients, who cited convenience, ease of use and minimal disruption to routines. Patients in the intervention arm also reported increased engagement with BP that resulted in changed behaviours (e.g. exercise). GPs valued the potential for increased number of BP readings and %BP at target from the device to support clinical decisions, but a preference for BP values in addition to %BP at target was identified for more nuanced patient-centred decision-making. Practice staff and CTCs emphasised the importance of workflow adjustments, technical support and patient education for future implementation of the novel strategy.

Discussion. Findings suggest that wearable BP monitoring with remote care is feasible and acceptable across stakeholder groups with strong potential to enhance hypertension management though not yet guideline-recommended. To optimise implementation patient training, ongoing technical support and workflow integrations should be prioritised ensure engagement and clinical value.

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Hypertensive response to exercise, fitness, left ventricular hypertrophy and cardiovascular outcomes

Ms. Catalina Silva Ruiz

Biography:

Catalina Silva Ruiz is a PhD student at the Menzies Institute for Medical Research at the University of Tasmania in Australia. She holds a degree in physiotherapy from the University of Desarrollo in Santiago, Chile, and a Master's in Exercise Physiology from the Norwegian University of Science and Technology in Trondheim, Norway. Her PhD research focuses on understanding how fitness influences the relationship between exercise blood pressure, hypertension, and cardiovascular disease. She is committed to identifying new strategies for improving the screening of hypertension and assessing cardiovascular disease risk within the community.

Hypertensive response to exercise, fitness, left ventricular hypertrophy and cardiovascular outcomes.

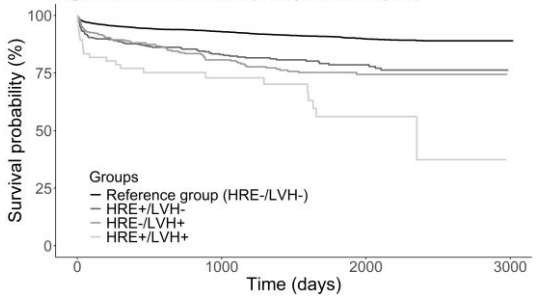
Catalina P Silva-Ruiz[1], James E Sharman[1], Petr Otahal[1], Tony Staton[2], Alison J Venn[1], Thomas H Marwick[1,3], Martin G Schultz[1]. Menzies Institute for Medical Research, University of Tasmania[1], Hobart, TAS, Australia; Sunshine Coast University Hospital[2], Birtinya, QLD, Australia; Royal Hobart Hospital[3], Hobart, TAS, Australia.

Introduction. A hypertensive response to exercise (HRE) is associated with left ventricular hypertrophy (LVH), both increasing cardiovascular disease (CVD) risk. However, aerobic capacity (fitness) may confound these associations.

Aims. To investigate the association of an HRE relative-to-fitness and LVH with risk of fatal and non-fatal CV events.

Methods. Data from 5,086 individuals (aged 57.9±12.7 years, 53.1% male) who underwent exercise stress echocardiography were linked to hospital records and death registers to assess CV events. An HRE relative-to-fitness was defined as peak systolic (SBP) divided by peak metabolic equivalents (MET) ≥90th percentile (30 mmHg/MET_{peak}). LVH was defined as LV mass indexed to body surface area ≥115 g/m^2 (men) and ≥95 g/m^2 (women). Cox-proportional hazard regression models, adjusted for age, sex, pre-exercise SBP, and CVD history, were used to evaluate CV event risk across groups defined by combinations of presence/absence of HRE (HRE+/HRE-) with LVH (LVH+/LVH-).

Figure 1. Survival curve (unadjusted analysis)



Results. A total of 543 CV events were observed over a mean follow-up of 46.7±27.3 months. There was a stepwise increased risk of CV events (Figure 1) across groups: HRE+/LVH- (adjusted HR:1.46, 95%CI:1.13,1.90), HRE-/LVH+ (adjusted HR:2.20, 95%CI:1.71,2.85), HRE+/LVH+ (adjusted HR:2.91, 95%CI:1.82,4.65) compared to reference (HRE-/LVH-). Results remained similar in those with pre-test BP <140/90 mmHg or without CVD history and were not apparent when an HRE was defined without consideration of fitness.

Discussion. Individuals with both HRE relative-to-fitness and LVH are at the highest risk of fatal and non-fatal CV events. These findings highlight the importance of evaluating an HRE relative-to-fitness in managing CVD risk, especially in individuals with LVH.

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Interleukin-18 signals via a non-canonical short IL-18 pathway during deoxycorticosterone/salt-induced hypertension

Miss Buddhila Wickramasinghe

Biography:

Buddhila Wickramasinghe is a final-year PhD candidate in the Hypertension and Diabetes division at the Centre for Cardiovascular Biology and Disease Research, La Trobe University, Melbourne, Australia. Her research focuses on understanding the role of the immune system in hypertension and chronic kidney disease by utilizing various animal models and in vitro methods. As she continues to develop her research profile, she has presented her work at both national and international conferences, including the High Blood Pressure Research Council of Australia ASM and International Society of Hypertension Scientific Sessions. In addition to her research, Buddhila advocates for HDR students as the student representative for the Cardiovascular SIG of ASCEPT. She is also dedicated to promoting STEM education and inspiring the next generation of scientists by engaging with primary and high school students.

Interleukin-18 signals via a non-canonical short IL-18 pathway during deoxycorticosterone/salt-induced hypertension

Buddhila Wickramasinghe[1,2], Vivian Tran[1,2], Tayla Hughes[1,2], Henry Diep[1,2], Maria Jelinic[1,2], Grant Drummond[1,2] and Antony Vinh[1,2]. Cent for Cardiovasc Biol & Disease Res, La Trobe Inst of Med Sci[1], Melbourne, VIC, Australia; Dept of Micro, Anat, Phys & Pharmacol, La Trobe Univ[2], Melbourne, VIC, Australia.

Introduction. The pro-inflammatory cytokine, interleukin-18 (IL-18), is elevated in patients with hypertension and chronic kidney disease. We have reported that genetic ablation of IL-18 prevents the development of experimental hypertension and renal inflammation. IL-18 signals via the IL-18 receptor that requires recruitment of the IL-18 receptor accessory protein (IL-18RAP) for canonical signalling. However, it was recently discovered that a truncated '*short*' IL-18 fragment, can activate downstream inflammation via an alternative interferon-stimulated gene-15 (ISG15) pathway.

Aim. To determine whether IL-18 drives deoxycorticosterone acetate (DOCA)/salt-induced hypertension and renal inflammation via its canonical receptor complex.

Methods. Male and female wild type (WT), *Il18*$^{-/-}$ and *Il18rap*$^{-/-}$ mice (n=10-12) were anaesthetised (5% isoflurane) and subjected to uninephrectomy. Mice were randomly assigned to receive either DOCA (2.4 mg/d, *s.c.* pellet) with high salt (0.9% in drinking water), or placebo with normal drinking water for 21 days. Systolic blood pressure (SBP) was measured weekly (tail-cuff plethysmography). At endpoint, the remaining kidney (right) was harvested to assess renal immune cell accumulation (flow cytometry) and renal inflammatory gene expression, including *Isg15* (qPCR).

Results. Baseline SBP was similar across sexes and genotypes (WT: 131±2 mmHg; *Il18*$^{-/-}$: 131±3 mmHg; *Il18rap*$^{-/-}$: 133±2 mmHg). In WT mice, DOCA/salt caused an increase in SBP compared to placebo controls (161±3 mmHg; $P<0.05$). Consistent with previous findings, *Il18*$^{-/-}$ mice exhibited a blunted pressor response to DOCA/salt (147±5 mmHg; $P<0.05$ vs WT). In contrast, *Il18rap*$^{-/-}$ mice were not protected from DOCA/salt-induced hypertension (167±3 mmHg) or renal leukocyte (CD45^{+}) accumulation. In both male and female WT mice, DOCA/salt-treatment caused a >2-fold increase in renal *Isg15* mRNA expression, which was completely abolished in *Il18*$^{-/-}$ mice, but unchanged in *Il18rap*$^{-/-}$ mice.

Discussion. *Il18rap* deficiency does not protect against DOCA/salt-induced hypertension and renal inflammation, suggesting that IL-18 may act via a non-canonical ISG15-dependent pathway to drive DOCA/salt-induced hypertension.

Shen J et al (2025) Nat Immunol 26(3): 416-428

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High-fibre diet intervention post-stroke is protective in male but not female mice

Miss Charlotte Barker

Biography:

Charlotte is a third year PhD candidate in the department of pharmacology at Monash University. Her project investigates the effect of dietary fibre intervention following stroke. She works under the guidance of A/Prof Brad Broughton, Prof Francine Marques and A/Prof Barbara Kemp-Harper.

High-fibre diet intervention post-stroke is protective in male but not female mice

Charlotte MO Barker[1], Chaoran Yang[1], Barbara K Kemp-Harper[1], Francine Z Marques[1], Brad RS Broughton[1]. Department of Pharmacology, Monash University[1], Clayton, VIC, Australia

Introduction. A lack of dietary fibre intake is associated with an increased risk of ischaemic stroke. However, the average person consumes only 40-50% of the recommended daily dietary fibre intake. The gut microbiota uses dietary fibre to generate short-chain fatty acids (SCFAs). We recently found that a high fibre diet or SCFA intake post-stroke improves functional outcomes, decreases neuroinflammation and promotes neurogenesis in male mice. However, whether a high fibre diet or SCFAs post-stroke have similar benefits in females remains undetermined.

Aims. To assess whether a lack of dietary fibre worsens stroke outcomes and if a post-stroke intervention with a high fibre diet or SCFAs improves outcomes in female mice.

Methods. Female and male C57BL6 mice (7-8 weeks old) were placed on a low or high fibre diet for 4 weeks before photothrombotic (PT) stroke or sham surgery (n=9-10/group, anaesthetic: inhaled 2% isoflurane). Following stroke, mice either continued on a low fibre diet, with or without SCFAs added to the drinking water (100mM Mg-Acetate and 100mM Na-Butyrate) or were switched to a high fibre diet. Female mice were assessed for motor function impairment pre-stroke and 1-7 days post-stroke. Magnetic resonance imaging and thionin staining were performed to evaluate infarct volume. Immunofluorescence was used to label immune cells and neuroblasts in the brain. RNA-sequencing was performed in the ischaemic and contralateral hemisphere of female and male mice (n=4-6/group).

Results. Neither dietary fibre nor SCFAs improved motor function or infarct volume following PT stroke in female mice. Additionally, neither treatment decreased neutrophil and macrophage numbers or promoted neurogenesis, which had been previously observed in male mice. However, a high fibre diet, but not SCFAs, decreased microglia within the ischaemic hemisphere by ~50% (0.15±0.02, n=9) compared to the low fibre group (0.28±0.02, n=9, $P<0.005$) in females. Genes associated with the resolution of ROS-induced DNA damage were uniquely upregulated in the ischaemic hemisphere of high fibre male, but not female mice ($P<0.05$).

Discussion. We observed sex-specific differences in the benefit of dietary fibre on functional outcomes, neuroinflammation and neurogenesis acutely following PT stroke in mice. This suggests post-stroke fibre interventions may be more beneficial for males.

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Exploring the role of steroid profiling in understanding the pathophysiology of hypertension

Dr Sonali Shah

Biography:

Dr Sonali Shah is a PhD candidate in the Endocrine Hypertension Research Group and an endocrinologist at Monash Health. Her research aims to gain insights into the prevalence and optimal management of low-renin hypertension, a common subtype of hypertension.

Exploring the role of steroid profiling in understanding the pathophysiology of hypertension

Sonali S Shah[1], Muhammad Akram[1], Morag J Young[1], Peter J Fuller[1], Graeme Eisenhofer[2] and Jun Yang[1]
[1]Centre of Endocrinology and Reproductive Health, Hudson Institute of Medical Research, Clayton, Vic, Australia. [2]Department of Medicine III, University Hospital Carl Gustav Carus, Dresden, Germany.

Introduction. Hypertension has multiple aetiologies. Around one in four individuals with hypertension have low renin concentration; however, the pathophysiology remains poorly understood. A recent meta-analysis suggests that mineralocorticoid receptor antagonists or epithelial sodium channel inhibitors may be particularly effective in lowering blood pressure in low-renin hypertension (LRH)[1]. This leads us to hypothesize that LRH may be caused by over-activation of the mineralocorticoid receptor or the epithelial sodium channel. Peripheral steroid profiling, with particular attention to steroids with mineralocorticoid activity, may help dissect the pathophysiology of LRH.
Aim. To explore the steroid profiles of participants with LRH and compare these to other hypertension subtypes.
Methods. Data were collected from the multicentre international PROSALDO study (2019-2024)[2]. Participants were classified as having primary hypertension, primary aldosteronism (positive saline suppression test), or LRH (direct renin concentration <10mU/L without a positive saline suppression test). Group comparisons were performed using linear regression in R 4.5.0 statistical software. The log-transformation was applied to non-normally distributed data.
Results. Of 860 participants, 185 had LRH. Participants with LRH were older, more likely to be female, and had a lower waist circumference than those with primary aldosteronism or primary hypertension ($p<0.05$). After adjusting for age and sex, multiple serum steroid hormones were lower in LRH ($p<0.05$): a) aldosterone, 18-hydroxycortisol, 18-hydroxycorticosterone, and 17-hydroxyprogesterone compared to primary aldosteronism and primary hypertension, b) 18-oxocortisol, 11-deoxycortisol, 11-deoxycorticosterone, 11-dehydrocorticosterone, corticosterone, and androstenedione compared to primary aldosteronism, and c) progesterone compared to primary hypertension.
Discussion. An overall decrease in steroidogenesis was observed in LRH, including steroids with mineralocorticoid activity. This suggests that LRH may be caused by renal sodium channel overactivity or aldosterone-independent activation of the mineralocorticoid receptor.

1. Shah et al. JHH. 2024;38:383-392.
2. Eisenhofer G et al. JCEM. 2022;107:e2027-e2036.

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Adverse drug withdrawal event identification and adjudication

Dr Emily Reeve

Biography:

Dr Emily Reeve is a Senior Research Fellow and NHMRC Emerging Leadership Fellow. She is Deputy Theme Lead of the Centre for Medicine Use and Safety at Monash University and Chair of the Australian Deprescribing Network (ADeN). Dr Reeve worked as a clinical pharmacist at the Royal Adelaide Hospital before completing a PhD at the University of South Australia.

Adverse drug withdrawal event identification and adjudication

Emily Reeve[1], Orla C Sheehan[2,3], Elizabeth A Bayliss[4,5], Cynthia M Boyd[3], Ariel R Green[3] on behalf of the GEODES Investigator Team. Fac Pharm Pharmaceutical Sci, Monash University[1], Melbourne, VIC, Aus; Dep Geriatric Med, RCSI Hospitals Group[2], Dublin, Ireland; Johns Hopkins University Sch Med[3], Baltimore, MD, USA; Inst Health Res, Kaiser Permanente Colorado[4], Aurora, CO, USA; Dep Fam Med, U Colorado Sch Med[5], Aurora, CO, USA.

Introduction. Deprescribing is an essential part of optimising medication use. However, lack of evidence on adverse drug withdrawal events (ADWEs) is a significant barrier to deprescribing in practice. New approaches utilising routinely collected data are required to generate evidence about ADWEs on a population scale.
Aims. To explore the challenges with adjudication of potential ADWEs identified in routinely collected data.
Methods. Likely discontinuations and potential ADWE cases were identified through algorithmic approaches which combined text string searches of clinical documentation, medication order data, diagnosis and procedure codes and clinical parameters. Approaches were specific to drug groups and were tested within unique samples of older adults (age 65+): oral hypoglycemics, statins, antihypertensives, bladder antimuscarinics, and anticoagulants/anti-platelet agents. Identified records were then manually adjudicated to confirm discontinuations and ADWEs. Qualitative content analysis was applied to adjudication notes to identify challenges to ADWE identification.
Results. 294 potential ADWEs were adjudicated with 210 (71%) assessed as doubtful, 61 (21%) as possible, 21 (7%) as probable, and 2 (<1%) as definite. Five themes were identified which describe the challenges in adjudication of ADWEs: terminology (symptoms were also present before discontinuation, e.g. medication stopped due to inefficacy), intent (the event that occurred was the intent of discontinuation, e.g. increased blood pressure in an individual with hypotension), causal inference (multiple other factors could have caused or contributed to the event), timeframe (difficulties discerning between the event being due to discontinuation versus progression of disease) and acute contraindications (where the medication was temporarily held).
Discussion. Less than one third of identified events were determined to be possible, probable or definite ADWEs. While algorithmic approaches are able to be developed to support identification of ADWEs in routinely collected data, adjudication was extremely complex. Further research is needed to develop standardised adjudication methods and working definitions for ADWEs; these may need to differ based on specific drug groups.

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Beyond blood: feasibility of saliva-based assays for antiviral therapeutic drug monitoring

Miss Cassandra Lai

Biography:

Cassandra is an Honours student in the Bachelor of Pharmacy and Management program at the Sydney Pharmacy School, The University of Sydney. Her research in clinical pharmacology examines saliva as a non-invasive matrix for antiviral therapeutic drug monitoring, with the goal of improving dosing precision, ensuring quality use of medicines, and reducing toxicity risks in vulnerable patient populations such as transplant recipients. She is passionate about personalised medicine, improving patient outcomes through innovative monitoring strategies, and translating research into clinical practice.

Beyond blood: feasibility of saliva-based assays for antiviral therapeutic drug monitoring

Cassandra Weng-Yan Lai[1], Suzanne Wenker[2], Paul W. Groundwater[1], Ricky Hao Chen[1,3,4], Anne-Grete Märtson[2], Jan-Willem C. Alffenaar[1,3,4]. School of Pharmacy, University of Sydney[1], Sydney, NSW, Australia; Leiden Academic Centre for Drug Research, Leiden University[2], Leiden, South Holland, Netherlands; Westmead Hospital[3], Sydney, NSW, Australia; Sydney Institute for Infectious Diseases, University of Sydney[4], Sydney, NSW, Australia

Introduction. Transplant recipients are highly vulnerable to opportunistic viral infections, necessitating antiviral prophylaxis or treatment post-transplantation. Optimal therapy depends on maintaining appropriate drug exposure to prevent treatment failure or toxicity. Therapeutic drug monitoring (TDM) enables individualised dosing but currently relies on blood samples. Saliva is a non-invasive alternative matrix for antiviral TDM, but its feasibility remains uncertain.
Aims. This systematic review aims to assess the feasibility of saliva-based assays for antiviral TDM.
Methods. A systematic search of MEDLINE, EMBASE, clinicaltrials.gov, regulatory databases, and conference abstracts identified primary studies reporting both saliva and plasma concentrations of (val)acyclovir, amantadine, baloxavir, brivudine, cidofovir, famciclovir, favipiravir, foscarnet, (val)ganciclovir, letermovir, maribavir, molnupiravir, nirmatrelvir, oseltamivir, peramivir, remdesivir, ribavirin and rimantadine. Physicochemical properties were extracted from PubChem and DrugBank to predict salivary excretion. Feasibility was assessed using clinical data and physicochemical analyses, and classified as: (1) likely, (2) possible, (3) unlikely, (4) unclear but possible, or (5) unclear but unlikely.
Results. Nine studies were included in the review. (Val)acyclovir and favipiravir were considered possibly feasible for saliva-based TDM, whereas molnupiravir and oseltamivir were unclear but possible. Nirmatrelvir was deemed unclear but unlikely. For other antivirals, no primary studies were available, yet most physicochemical profiles suggested limited salivary penetration to facilitate antiviral TDM.
Discussion. Evidence for saliva-based antiviral TDM was limited. Inconsistencies between physicochemical predictions and clinical data suggest that factors such as drug transporters, saliva flow, pH, and interpatient variability can influence salivary drug penetration. Despite these challenges, preliminary studies demonstrating measurable antiviral concentrations in saliva and detectable correlations with plasma levels indicate promising potential for saliva as a non-invasive alternative to blood. Standardised collection methods, validated assays, and robust pharmacokinetic studies are needed to confirm the clinical feasibility of saliva-based antiviral TDM.

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Medication data collection in Frailty Intervention Through Specific Therapies (FITTEST) trial participants

Miss Temitope Esther Afolabi

Biography:

With a keen interest in geriatric medicine, research and education, I am currently undertaking my Doctor of Philosophy at The University of Sydney under main supervisor Professor Sarah Hilmer. My research centres round co-designing digital solutions for older people, that optimises medication management and promotes collaboration with health care practitioners.

Medication data collection in Frailty Intervention Through Specific Therapies (FITTEST) trial participants
Temitope E Afolabi[1], Lisa Kouladjian O'Donnell[1,2], Christopher Etherton-Beer[3], Sarah N Hilmer[1] for the FITTEST trial investigators. Laboratory of Ageing and Pharmacology, Kolling Institute of Research, Faculty of Medicine and Health, The Univ of Sydney[1], Sydney, NSW, Australia; School of Pharmacy, Faculty of Medicine and Health, The Univ of Sydney[2], Camperdown, NSW, Australia; School of Medicine, Univ of Western Australia[3], Crawley, WA, Australia.

Introduction. Ensuring the validity of remotely collected medication data from clinical trial participants' is essential for accurately translating research findings into clinical practice, particularly among older people with polypharmacy.
Aims. To assess feasibility and validity of a structured approach for remotely collecting medication data in older people.
Methods. Informed by literature and investigators' expertise, a data collection tool was developed using Microsoft Excel, to facilitate remote medication data collection for participants in the FITTEST trial. All participants engaged in structured telephone interviews with a clinical pharmacist. A subset also participated in follow-up video calls to validate the initial self-reported medication list against the 'brown bag' method for clinical trials. Data collected included medication name, dose, frequency, indication, interview duration, data completeness, call completion rate and number of call attempts per participant. Medication regimen complexity index (MRCI), frailty status, medication adherence (using Morisky Green Levine Scale (MGLS-4)) and Drug Burden Index (DBI) were calculated for participants.
Results. Preliminary findings focused on feasibility measures. Medication data from the first twelve FITTEST trial participants were included in this pilot. Mean participant age was 77 years, 67% (n=8) were female and 83% (n=10) were mildly frail (FI <0.2). Feasibility: 86% of scheduled calls were completed; 92% of participants were reached on the first call attempt; mean interview duration was 33mins. All medication data fields were completed during calls, except for certain generic and brand names (due to confusion between generic versus brand names) and strengths of certain over-the-counter medications. Medication measures: 83% (n=10) of participants were on ≥5 regular medications; 42% (n=5) had a DBI>0; MRCI scores ranged from 5 to 43.5; Majority (n=8, 67%) scored 1-2 on the MGLS-4 suggesting moderate levels of medication adherence. Remaining participants (n=4, 33%) scored 0 (high adherence) on the MGLS-4.
Discussion. Preliminary findings suggest a structured phone interview is feasible to remotely collect data and calculate medication-related metrics in older people. Analysis of the methodological validity against the gold standard for medication data collection in clinical trials, clinician-observed 'brown bag' is ongoing and will be reported in future work.

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Navigating Complexity: Developing a Regulatory Pathway for Advanced Therapeutics in Australia (Tony Smith QUM Prize finalist)

Ms Kerry Watts

Biography:

Kerry Watts is an expert consultant pharmacist in compounding and research, working in NSW Office for Health and Medical Research as senior officer in training, education and regulatory compliance for health system preparedness to deliver advanced therapeutics as standard of care. Kerry has recently embarked on a PhD with the University of Sydney to explore the impact of collaboration with government and academia to improve knowledge, understanding and compliance to regulation and improve patient access to advanced therapeutics.

Navigating Complexity: Developing a Regulatory Pathway for Advanced Therapeutics in Australia

Kerry Watts[1,2], Caitlin Guilfoyl[1], Christine Lu[2], Sophie Stocker[2], Julia Warning[1]. Office for Health and Med Res, NSW Min of Health[1], School of Pharm, Fac Med & Health, The Univ of Sydney[2], Sydney, NSW

Introduction. The translation of advanced therapeutics from research to clinical practice is complex because of regulatory requirements. While the Australian Clinical Trials Handbook provides general guidance, researchers must interpret multiple Commonwealth laws including the Therapeutic Goods Act 1989, and related regulations, alongside varying state legislation, without any regulatory training. Regulatory knowledge gaps can contribute to delays in product accessibility and delayed patient access to advanced therapeutics.

Aim. To develop a practical web-based regulatory pathway to support the translation of advanced therapeutics from research and development to clinical implementation and commercialisation.

Methods. National and state regulations were reviewed to identify regulatory requirements across therapeutic categories including medicines, biologicals, medical devices, and unclassified therapies such as bacteriophages. Semi-structured interviews with stakeholders at various stages of the regulatory process, and discussions with key regulatory bodies such as the Therapeutic Goods Administration were used to explore knowledge gaps in navigating the regulatory pathways.

Results. The regulatory review identified a gap in regulatory guidance, supporting the need for a practical regulatory framework to guide researchers and sponsors through the translational process. Preliminary stakeholder engagement highlighted revealed widespread regulatory knowledge gaps and identified the need for better support to navigate first-in-human trials, Good Manufacturing Practice (GMP) compliance, challenges in identifying qualified regulatory service providers, and clarity around specific requirements for novel therapeutics.

Discussion. Improved navigation of the regulatory system is essential to accelerate research translation. This initiative should provide researchers with an accessible, practical resource that is designed to clarify regulatory expectations, guide stakeholders through approval processes, support compliance, and reduce delays in delivering advanced therapeutics to patients.

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What support Healthcare Professionals need to deprescribe opioids at transitions of care (Tony Smith QUM Prize finalist)

Mr Jeffery Wang

Biography:

Jeffery Wang is a hospital pharmacist and early career researcher completing a Master of Philosophy at the University of Sydney, with his thesis titled 'Opioid deprescribing in patients at transitions of care'.

What support Healthcare Professionals need to deprescribe opioids at transitions of care

Jeffery Wang[1], Carl R Schneider[1], Aili V Langford[1,2], Chung-Wei Christine Lin[3,4], Mouna Sawan[1], Danijela Gnjidic[1]
Sydney Pharmacy School[1], The University of Sydney, Sydney, NSW, Australia; Centre for Medicine Use and Safety[2], Monash University, Parkville, Victoria, Australia; Sydney School of Public Health[3], The University of Sydney, Sydney Musculoskeletal Health, Sydney, NSW, Australia; Institute for Musculoskeletal Health[4], The University of Sydney, Sydney, NSW, Australia

Introduction: Transitions of care, such as discharge from hospital to the community, represent critical opportunities to review and reduce opioid use. Whether healthcare professionals (HCPs) feel adequately supported to implement opioid deprescribing plans at these junctures remains unclear.
Aims: To identify the support required by Australian HCPs to deprescribe opioids during transitions of care.
Methods: An anonymous, online survey was developed and pilot tested by the research team and a multidisciplinary group of clinicians to ensure relevance. The survey was disseminated from September 2024 to February 2025, targeting Australian HCPs practicing in any setting. Participants' confidence and perspectives on existing support to deprescribe opioids were explored. Quantitative data was analysed descriptively, and qualitative data thematically analysed using the Theoretical Domains Framework (TDF).
Results: Of 229 participants who started the survey, 46% (n=105) completed it, and 68.6% (n=72) were female. Participants were predominantly pharmacists (48.6%, n=51), followed by doctors (32.4%, n=34) and nurses (16.2%, n=17). Of the participants, 26% (n=27) stated their most preferred opioid deprescribing support was a locally approved opioid policy, followed by clinical guidelines 23% (n=24). While 76% (n=80) reported confidence to deprescribe opioids at transitions of care, 31.4% (n=33) were not satisfied with the existing support provided. The TDF analysis highlighted barriers including time constraints, inconsistent workflows, and knowledge gaps in implementing opioid deprescribing plans.
Discussion: While Australian HCPs demonstrate confidence to deprescribe opioids at transitions of care, current support needs may not align with clinical workflows to routinely deprescribe opioids in patients across different care settings.

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Patient Decision-Aids for Pain Medication Management: A Scoping Review (Tony Smith QUM Prize finalist)

Dr Aili Langford

Biography:

Dr Aili Langford is a pharmacist, Lecturer and National Health and Medical Research Council (NHRMRC) Emerging Leader Research Fellow at the Sydney Pharmacy School. Dr Langford's research focuses on reducing medication-related harm through deprescribing.

Patient Decision-Aids for Pain Medication Management: A Scoping Review

Yiwen Lu[1], Carl R Schneider[1], Mouna Sawan[1], Danijela Gnjidic[1], Emily Reeve[2], Joshua Zadro[3], Aili V Langford[1,2]. Sydney Pharmacy School, The University of Sydney[1], Sydney, NSW, Australia; Centre for Medicine Use and Safety, Monash University[2], Parkville, VIC, Australia; School of Health Sciences, The University of Sydney[3], Sydney, NSW, Australia

Introduction. Analgesics are commonly used to manage pain; however, patients may find it challenging to assess the potential benefits and risks within the context of their clinical circumstances, goals, and preferences. Patient Decision Aids (PtDAs) can improve knowledge and engagement in health decisions, yet the nature, content and quality of PtDAs for pain medication management have not been systematically evaluated.
Aims. To identify and appraise PtDAs for pain medication management and evidence of their evaluation.
Methods. A systematic search was conducted across four databases, eight decision aid repositories, and Google. Screening and data extraction were performed in duplicate, capturing target conditions, decision options, format, and outcomes. PtDAs were appraised using the International Patient Decision Aid Standards instrument (IPDASi) and evaluation studies with the Standards for UNiversal reporting of patient Decision Aid Evaluations (SUNDAE) checklist.
Results. Thirty-nine PtDAs and 17 evaluation studies were included. PtDAs most commonly addressed osteoarthritis (49%) and back pain (21%), with nonsteroidal anti-inflammatory drugs (77%), corticosteroid injections (74%), and paracetamol (56%) the most frequently included medications. Although all PtDAs included medication-related content (e.g., role in therapy), information on safety, effectiveness, and cost were often limited, with most PtDAs emphasising non-pharmacological strategies (e.g., exercise, surgery) as the primary decision. The majority of PtDAs met IPDASi qualifying criteria, however, few achieved higher certification standards due to inconsistent reporting of outcome probabilities and limited evidence transparency. Despite this, evaluation studies generally reported improved knowledge and reduced decisional conflict following PtDA use. Medication-related outcomes were rarely reported.
Discussion. There was substantial variability in PtDA content and format, though core principles of balanced information, transparency, and patient-centred functionality appeared universally important. PtDA certification rates could be strengthened through simple measures such as citing evidence and reporting publication dates. Future research should assess whether higher-quality PtDAs can better support shared decision-making in pain management and guide appropriate analgesic use, particularly for high-risk medicines, across the continuum of care.

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Residential aged care quality use of medicines indicators: a Delphi study

Dr Daria Gutteridge

Biography:

Dr. Daria Gutteridge is a postdoctoral Research Fellow at the University of South Australia (UniSA) where she focuses on the quality use of medicines in Australian aged care facilities, working on the MRFF-funded PHarmacists Actioning Rational use of Medicines in Aged Care (PHARMA-Care) project. At the end of 2023, Daria completed her PhD in the field of Psychology (Cognitive Neuroscience) at UniSA, at the Cognitive Ageing and Impairment Neuroscience Lab. Her PhD focused on the relationship between blood pressure variability, cognitive functioning and cerebrovascular health in older adults. Daria is an early career researcher who is passionate about improving cardiovascular health, cognitive functioning and aged care services to advance the quality of life and health outcomes in older adults.

Residential aged care quality use of medicines indicators: a Delphi study

Daria S Gutteridge[1], Sara Javanparast[1], Annabel H Calder[1], Gillian E Caughey[2], Andrew C Stafford[3], Gregory M Peterson[4], Maria C Inacio[2], Peter D Hibbert[5], Elizabeth Manias[6], Jodie B Hillen[7], Janet K Sluggett[1]. 1 Allied Health & Human Performance, Univ of SA, Adl, SA, Aust; 2. ROSA Research ctr, Caring Futures Inst, Col of Nursing & Health Sci, Flinders Univ, Bedford Park, SA; 3 Curtin Med Sch, Fac of Health Sci, Curtin Univ, Perth, WA, Aust; 4 Sch of Phar & Pharmacol, Univ of Tasmania, Hobart, TAS, Aust; 5 Aust Inst of health Innov, Macquarie Univ, Macquarie Park, NSW; 6 Monash Nurs & Midwif, Monash Univ, Clayton, Vic; 7 Col of Nursing & Health Sci, Flinders Univ, Bedford Park, SA.

Introduction. In 2024, Australia implemented an on-site pharmacist program in residential aged care homes (RACHs) to support quality use of medicines and person-centred care.

Aims. This Delphi study, conducted as part of the PHarmacists Actioning Rational Use of Medicines in Aged Care (PHARMA-Care) project, aimed to achieve subject matter expert (SMEs) agreement on quality indicators (QIs) for application at the population level, to support and monitor quality use of medicines and pharmacist services in RACHs.

Methods. An initial systematic review and pre-screening identified 58 QIs to progress to a Delphi study. We conducted a 2-round modified online Delphi study, with a panel of Australian SMEs. Panellists rated each QI on three criteria (importance, feasibility and amenability to change by an on-site pharmacist) using a 9-point Likert scale. A QI was selected if it reached agreement between panel members (defined as a disagreement index of ≤ 1) on a high median score (≥7 on the Likert scale) on all three criteria.

Results. Twenty-seven experts provided informed consent, 25 completed the first Delphi round and 24 completed the second Delphi round. The feasibility and amenability scores were typically lower than importance scores, with 45 QIs (77.6%) receiving a high score with agreement for importance, versus 27 QIs (46.6%) for feasibility and 25 QIs (43%) for amenability. Seventeen of the 58 QIs were selected, covering multidisciplinary clinical care (n=7), clinical governance (n=5), medication-specific issues (n=3) and end of life care (n=2).

Discussion. The identified QIs provide a valuable foundation for subsequent pharmacoepidemiological studies to monitor quality use of medicines and on-site pharmacist services in Australian RACHs to optimise medicines-related quality of care and improve outcomes for RACH residents.

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Psychotropic use in community-dwelling people with dementia: a systematic review and meta-analysis

Mr Edward Chun Yin Lau

Biography:

Edward is a community pharmacist in Australia and PhD student at the University of Sydney with a research interest in pharmacoepidemiology in older people, especially people living with dementia in community settings in Australia. He is particularly interested in the prevalence, risk factors and outcomes of high-risk prescribing in this population. His research is aimed at improving the safety and effectiveness of medication use in people living with dementia.

Psychotropic use in community-dwelling people with dementia: a systematic review and meta-analysis

Edward C.Y. Lau[1], Sarah Hilmer[2], Yun-Hee Jeon[3], Edwin C.K. Tan[1]. Sydney Pharmacy School, The University of Sydney[1], Sydney, NSW, Australia; Kolling Institute, The University of Sydney [2], Sydney, NSW, Australia, Susan Wakil School of Nursing and Midwifery, The University of Sydney [3], Sydney, NSW, Australia.

Introduction. Psychotropic medications are commonly prescribed for changed behaviours in people with dementia. While their use has been associated with increased risk of mortality and adverse drug events, the global prevalence of psychotropic use in community-dwelling people with dementia remains unclear.

Aims. To estimate the global prevalence of psychotropic use and identify associated factors in people with dementia living in the community.

Methods. In this systematic review and meta-analysis, five databases (Embase, Medline, PsycINFO, International Pharmaceutical Abstracts, and CINAHL) were searched in January 2025 using a combination of keywords and Medical Subject Heading (MeSH) terms related to dementia, older adults, psychotropics and community settings. Title and abstract screening, full text assessment, data extraction and quality assessment were performed independently by two authors, with conflicts resolved by consensus among all authors. Meta-analysis was performed with the R package *meta* to estimate pooled prevalence of psychotropic use and meta-regression was used to explore heterogeneity.

Results. From 3486 studies identified, 93 studies were included. Majority of studies included were conducted in Europe (n=49), followed by North America (n=38), Asia (n=3) and Oceania (n=3). The pooled prevalence of psychotropic use was 51% among community-dwelling people with dementia. Antidepressants were the most commonly used (29%) followed by benzodiazepines (19%), opioids (15%) and antipsychotics (14%). Temporal trends showed stable overall psychotropic use since 2005, with declining use of antipsychotics and benzodiazepines. Factors associated with lower psychotropic use included older age, higher socioeconomic status, fewer comorbidities, absence of mental health conditions, and higher education levels.

Discussion. Over half of community-dwelling individuals with dementia are prescribed psychotropic medications. Sociodemographic factors including education and socioeconomic status may influence prescribing patterns, highlighting future areas for targeted policy initiatives.

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Adverse Outcomes Associated with Risperidone in Dementia: An Individual Participant Data Meta-Analysis

Mr Harry Le

Biography:

Trong Hieu (Harry) Le is a recent Master of Philosophy graduate from the School of Pharmacy, The University of Sydney. His research focuses on pharmacoepidemiology, dementia, and the quality use of medicines. Harry has experience working with a range of large-scale datasets, including the Person Level Integrated Data Asset (PLIDA), The National Health Data Hub (NHDH), and individual participant data from clinical trials. His research applies advanced pharmacoepidemiological methods and machine learning approach to evaluate medicine use, safety, and treatment outcomes in older adults and people living with dementia."

Adverse Outcomes Associated with Risperidone in Dementia: An Individual Participant Data Meta-Analysis
Hieu T. Le[1], Edward C.Y. Lau[1], Sarah N Hilmer[2], Yun-Hee Jeon[1], Christine Y. Lu[1,2], Tuan A. Nguyen[3], Lee-Fay Low[1], and Edwin C.K. Tan[1,2]. Faculty of Medicine and Health, The University of Sydney, Sydney, NSW[1]; Kolling Institute, Royal North Shore Hospital, St Leonards, NSW[2]; National Aging Research Institute, Parkville, VIC[3].

Introduction. Risperidone has modest efficacy in managing behaviours and psychological symptoms of dementia but is associated with a range of adverse events. Individual participant data meta-analysis (IPD-MA) from multiple clinical trials offers enhanced statistical power to detect rare adverse outcomes, identify predictors and conduct robust subgroup analyses.
Aims. To evaluate the risks of multiple adverse outcomes associated with risperidone use in people with dementia across different time periods, identify key predictors, and characterise high-risk subgroups using IPD-MA.
Methods. A one-stage IPD-MA of six randomised controlled trials (risperidone: n=1009; placebo: n=712) was conducted. Mixed-effects models estimated treatment effects, predictors, and subgroup differences for multiple adverse outcomes over varying time periods.
Results. Risperidone was associated with increased risks of cerebrovascular events (hazard ratio [HR]: 4.11; 95% CI: 1.77–9.51; p = 0.001) and major cardiovascular events (HR: 2.00; 95% CI: 1.23–3.26; p = 0.006), with mean onset at 1.2 and 1.4 months, respectively. Somnolence occurred before and after week 4, while upper respiratory tract infections (OR: 2.31; 95% CI: 1.24–4.32; p = 0.009) and extrapyramidal symptoms (OR: 2.93; 95% CI: 1.68–5.08; p < 0.001) emerged after week 4. Compared to placebo, the risperidone group had lower MMSE scores after treatment (Mean difference [MD]: -0.66; 95% CI: -1.14 to -0.17; p = 0.008). Older age, male sex, and baseline cardiac pharmacotherapy use predicted serious adverse outcomes. Among baseline antidepressant users, risperidone use led to a greater reduction in serum sodium at endpoint compared to placebo (MD: –1.99mM; 95% CI: –3.46 to –0.52; p = 0.008).
Discussion. Risperidone use in people with dementia is linked to a range of adverse outcomes. These often occur with 1-2 months of treatment and risk varies with sociodemographics and comedications. Use of risperidone should be limited to the shortest duration possible, with careful assessment of baseline risk factors to minimise harm. Risk–benefit calculators may support individualised prescribing.

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Impact of medication management interventions on healthcare utilisation in dementia: Systematic review

Miss Jiefei Yu

Biography:

Jiefei Yu is a PhD student in clinical pharmacy and pharmacy practice at the University of Sydney studying under Professor Danijela Gnjidic and Dr Mouna Sawan. Jiefei completed her bachelor's degree in pharmacy and a master's degree in brain and mind science from the University of Sydney. Her research is focused on optimising medications in individuals living with dementia.

Impact of medication management interventions on healthcare utilisation in dementia: Systematic review

Jiefei Yu[1], Xenia Nastatos[1], Mouna Sawan[1], Danijela Gnjidic[1]. School of Pharmacy, The University of Sydney, Sydney, NSW, Australia[1]

Introduction. People with dementia often face challenges associated with managing multiple comorbidities and polypharmacy, which consequently may contribute to increased demand on healthcare services. Medication management interventions have demonstrated effectiveness in reducing medication-related problems; however, their impact on healthcare utilisation outcomes in dementia populations remains unclear.

Aims. To summarise the impact of medication management interventions on healthcare utilisation in people with dementia.

Methods. A systematic literature search was performed in Embase, MEDLINE, Web of Science, Cochrane CENTRAL Register of Controlled Trials, CINAHL, PsycINFO from database inception to April 2025. All interventional studies reported on medication management interventions for people with dementia were included. Interventions were categorised based on the global evidence guide of health system decision-making (Cochrane Effective Practice and Organisation of Care). A narrative synthesis was conducted to report study outcomes. Mixed Methods Appraisal Tool was used to assess the quality of all studies.

Results. A total of 13294 articles were identified with 12 studies eligible for inclusion. Interventions were categorised into interventions targeted at healthcare professionals (n=7), coordination of care (n=4), and technology-based intervention (n=1). Key components of medication management targeted across interventions were medication adherence, monitoring, review, reconciliation and deprescribing. Among these, significant reduction was reported only for coordination of care intervention (Hazard Ratio=0.49, 95% CI = 0.27-0.90). Only one study target healthcare professionals and reported significant reduction in emergency department visit in one year (Incidence Rate Ratio = 0.04, 95% CI = 0.01-0.13). There was limited evidence on the impact on primary care visits (n=2) or institutionalisation (n=3) and no significant effect were observed. The quality of evidence was moderate to high.

Discussion. This review identified a range medication management interventions tested in people with dementia with mixed impact on healthcare related outcomes. Future research should focus on developing well-designed interventions to optimise healthcare utilisation in people with dementia.

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A qualitative evidence synthesis on the unintended consequences of prescription opioid policies

Mr Patrick Lu

Biography:

Patrick Lu is an Honours student in the Bachelor of Pharmacy and Management at the University of Sydney. His research focuses on the unintended consequences of prescription opioid policies, examining how regulatory frameworks affect access, patient care, and safe and rational use of prescription opioids.

A qualitative evidence synthesis on the unintended consequences of prescription opioid policies

Patrick Lu[1], Aili V Langford[1,2], Kellia Chiu[1,3]. Sydney School of Pharmacy, Faculty of Medicine and Health, The University of Sydney[1], Sydney, NSW, Australia; Centre for Medicine Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University[2], Parkville, VIC, Australia; Temerty Faculty of Medicine, University of Toronto[3], Toronto, Canada.

Introduction. Opioids are essential medicines, vital in acute and chronic pain management, perioperative and palliative care, and opioid use disorder treatment. However, opioids also carry significant risks, and their potential for harm (e.g. dependence, overdose) contributes to public health burdens, higher healthcare costs, and structural stigma. In response, governments and institutions have introduced policies designed to ensure uniform standards for safer prescribing, equitable access to opioids, and thus reduce harm. However, such measures can also lead to unintended consequences for health systems, clinicians and patients.

Aims. This qualitative evidence synthesis explored the unintended consequences arising from implementing opioid policies at national and subnational levels, and how these were experienced across different health system levels.

Methods. We searched 4 databases to identify primary qualitative studies reporting on unintended consequences of opioid policies. These consequences were inductively coded into themes within the following levels: society and health systems (macro), organisations (meso), and individuals (micro).

Results. The synthesis included 54 studies, consisting of four macro-level themes, such as opiophobia and overly narrow societal definitions of pain management and its treatment; two meso-level themes including breakdowns in therapeutic and professional relationships; and three micro-level themes, such as the loss of autonomy by both patients and prescribers.

Discussion. While policies have been implemented to encourage safe and rational use of prescription opioids, unintended consequences have been identified at multiple levels; consequences affecting individuals may stem from unintended consequences further upstream. For example, societal perceptions of pain and its management has been delegitimised through media and reinforced by stricter policies, leading to harmful practices and outcomes across all levels. Therefore, when designing and implementing policies and interventions to improve the quality use of opioids, both negative and positive outcomes occurring at all levels of the health system need to be considered.

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Systematic review evaluating efficacy and safety of colchicine in coronary artery disease

Dr Deisi Christopher

Biography:

Dr. Deisi Christopher, Clinical Pharmacology Advanced Trainee, Flinders Medical Centre, South Australia. My previous presentation was at ASCEPT weekend in Sydney , May 2025. Title: "Colchicine in patients with acute coronary syndrome: What is the evidence?". Will be presenting my AT project on " systematic review evaluating efficacy and safety of Colchicine in coronary artery disease" at the conference.

Systematic review evaluating efficacy and safety of colchicine in coronary artery disease

Dr. Deisi Christopher, Prof. Arduino A. Mangoni, Dr. Tilenka Thynne, Department of Clinical Pharmacology, Flinders Medical Centre and Flinders University, Bedford Park, SA

INTRODUCTION: Inflammation plays a pivotal role in the development and progression of atherosclerosis. Colchicine, an anti-inflammatory agent, has shown potential in reducing residual inflammatory risk in atherosclerosis. Initial randomized controlled trials (RCTs) have highlighted the efficacy of colchicine in coronary artery disease, however more recent trial - data (Jolly et al, 2025) is conflicting, causing uncertainty for clinicians regarding the efficacy and safety of colchicine.
AIMS: A systematic review is being performed to assess the efficacy and safety of colchicine in reducing major adverse cardiovascular events (MACE) in patients with coronary artery disease (CAD) on Guideline Directed Therapy.
METHODS: Studies including adults 18 years and older with CAD (all stages) on guideline directed therapy treated with colchicine (any dose/ duration) compared with placebo or an active comparator will be considered. The primary outcome is MACE. The secondary outcome are all-cause mortality, stroke, urgent re-admissions, recurrent myocardial infarction, cardiac arrest, adverse gastrointestinal events and response of inflammatory markers e.g. high-sensitivity C-reactive protein (hs-CRP) and interleukin-2. Databases including Medline, Embase and Cochrane Central will be searched from inception to July 2025 for RCTs. Data extraction and meta-analysis will be performed using JBI SUMARI and Covidence. Relative risk and mean differences will be pooled under the random effects model. Heterogeneity will be assessed by Cochrane Q test and I^2. The risk of bias will be assessed using the Cochrane evaluation tool and certainty of evidence will be assessed using the GRADE approach. This metanalysis is registered with the PROSPERO international database for registered systematic reviews.
RESULTS: Abstracts identified in the initial screening will be imported to Covidence and duplicates will be removed. Following a pilot test, titles and abstracts will then be screened by two independent reviewers for assessment against the inclusion criteria and relevant studies will be retrieved in full.
DISCUSSION: The complete results and discussion will be presented at the conference

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Reversible inhibition of bladder mucosa contractile activity by dimethylsulfoxide (DMSO)

Prof Russ Chess-Williams

Biography:

Russ Chess-Williams is Director of the Centre for Urology Research at the Faculty of Health Sciences & Medicine, Bond University, Australia. He has previously directed research and taught at the Universities of Sheffield, Liverpool and Cardiff in the UK. At Bond University he has previously held positions as Faculty Associate Dean of Research and Head of the Biomedical Science department. His research interests focus on the development of new drug treatments for diseases of the lower urinary tract. His recent studies have focused on the role of the urothelium in regulating lower urinary tract function and bladder sensory mechanisms in health and disease. He was involved in the early pre-clinical studies with tamsulosin, solifenacin and mirabegron.. He has published >400 articles that have received >6000 citations. He has received funding from both British and Australian research councils and his published works include original papers in European Urology and Nature.

Reversible inhibition of bladder mucosa contractile activity by dimethylsulfoxide (DMSO)
Emma Falk, Russ Chess-Williams, Christian Moro, Donna Sellers· Centre for Urol Res, Bond Univ, Gold Coast, QLD

Introduction. Dimethylsulfoxide (DMSO) is a common treatment for interstitial cystitis/Bladder pain syndrome (IC/BPS), where it is instilled into the lumen of the bladder. It's mechanism of action is unknown, but it is administered intravesically (instilled into the bladder) and thus has close contract with the bladder mucosa.
Aim. The aim of this study was to investigate the effects of DMSO on contractile activity of porcine bladder mucosa.
Methods. Isolated strips of porcine bladder mucosa were set up under 1-2g tension in gassed Krebs-bicarbonate solution at 37°C and isometric developed tension recorded. Contractile activity of tissues was recorded during a 30 min incubation with DMSO (25%) and during recovery after washout. Data are presented as mean±sem values.
Results. Isolated strips of pig mucosa developed spontaneous, phasic contractile activity with a frequency of 3.16±0.23 cycles/min and an amplitude of 0.58±0.10g (n=13). DMSO (25%) abolished spontaneous contractile activity within 9 minutes of application and it also reduced the basal tension developed by the tissues by 49.1±9.4% (n=5). After 30 mins incubation, tissues were washed and the contractile activity recovered to control levels by 12.6±2.9 mins. In separate experiments, responses to carbachol (10µM) were obtained in the absence and presence of DMSO. In control tissues, carbachol (10µM) increased the frequency of contractions by 59.3±10.1% and increased the basal tension by 4.36±0.91g (n=4). However, In the presence of DMSO, responses to carbachol (10µM) were abolished.
Discussion. The results indicate that DMSO has a large depressant effect on the bladder mucosa, inhibiting phasic contractions and causing a relaxation of the tissues. It also depresses responses to muscarinic stimulation. However these effects were readily reversed once the DMSO was removed and tissues recovered completely. It therefore seems unlikely that the prolonged beneficial effects of DMSO observed in IC/BPS patients are due to effects on the bladder mucosa contractility.

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Female mice exhibit reduced hallmarks of MASH in the GAN DIO model

Miss Isabella Simon

Biography:

Isabella Simon is a highly motivated 2nd year PhD Candidate who has an immense passion for liver disease research following her own lived-experience. Following her diagnosis of autoimmune hepatitis in 2015 at age 16, and subsequent liver transplant in 2019 at 20 years of age, Isabella pursued a Bachelor of Science and Bachelor of Arts, where she was awarded First-Class Honours in Pharmacology and commenced her PhD in 2023 at Monash University. Her PhD investigates novel therapeutic avenues for metabolic dysfunction-associated steatohepatitis.

Female mice exhibit reduced hallmarks of MASH in the GAN DIO model

Isabella A. Simon[1], Timothy S. Fitchett[1], Yu-Anne Yap[2], Khashayar Asadi[3], Remy Robert[2], Robert Jones[3], Avik Majumdar[3], Robert E. Widdop[1], Mark P. Del Borgo[1]. Department of Pharmacology, Monash University[1], Clayton, VIC, Australia; Department of Physiology, Monash University[2], Clayton, VIC, Australia; Liver Transplant Unit, Austin Hospital[3], Heidelberg, VIC, Australia

Introduction. Metabolic dysfunction-associated steatohepatitis (MASH) is the progressive form of steatotic liver disease. There are suggested sex differences in disease prevalence, with lower risk seen in premenopausal women compared to men (Younossi et al, 2023). However, preclinical studies are predominantly male-biased, resulting in limited understanding of sex-specific disease mechanisms.

Aims. This study aimed to investigate sex differences in MASH development using the gold standard Gubra Amylin NASH (GAN) diet-induced obesogenic (DIO) mouse model.

Methods. Five-week-old male and female C57BL/6 mice were fed standard chow or the GAN diet for up to 36 weeks prior to euthanasia. Immunohistochemistry and immunofluorescence were performed on excised liver tissue to conduct integrated MASH Activity Score (MAS, 0-8) and fibrosis (F, 0-4) scoring, as well as individual measures of steatosis and inflammation. Second harmonic generation (SHG) was also conducted on fixed liver tissue to analyse levels of fibrillar collagen deposition and architecture.

Results. Male mice developed definitive MASH (MAS≥5) by 26 weeks, with all exhibiting clinically significant fibrosis (F≥2). In contrast, female mice showed delayed and reduced MAS scores with one-third remaining below diagnostic threshold at 36 weeks. Fibrosis severity was markedly lower in females, with only 8% reaching advanced fibrosis (F3–4) at 36 weeks versus 68% of males ($P<0.01$). Based on SHG analysis, females had significantly lower collagen deposition with shorter and fewer fibers, consistent with histological findings.

Discussion. Female C57BL/6 mice show delayed onset of MASH and fibrosis compared to males in the GAN DIO model, mirroring clinical sex differences seen in premenopausal women. These findings highlight the need for sex-balanced preclinical studies to investigate mechanisms of disease susceptibility and identify opportunities for targeted therapy.

Younossi ZM et al (2023) Hepatol Baltim Md 77:1335-1347

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Unravelling the mechanisms underlying BCG induced lower urinary tract side effects

Miss Meera Elmasri

Biography:

I am a PhD candidate in the College of Medicine and Public Health at Flinders University, working within the NeuroUrology Research Group. My research focuses on understanding and improving bladder cancer treatment, using a combination of cell culture, animal models, and bioinformatics approaches. I have a background in Medical Science, and my current work aims to uncover mechanisms of treatment response and identify potential biomarkers of therapy efficacy. I am particularly interested in the interface between cancer biology and immunology, and in translating laboratory findings into strategies that improve patient outcomes.

Unravelling the mechanisms underlying BCG induced lower urinary tract side effects

Meera Elmasri[1], Georgia Bourlotos[1], Tanvi Narke[1], Alana White[1], Giles Best[1], Luke Grundy[1]. [1]Flinders University, Adelaide, SA, Australia.

Introduction. Approximately 75% of bladder cancers are diagnosed as non-muscle invasive bladder cancer (NMIBC). The current gold-standard treatment for NMIBC is intravesical Bacillus Calmette-Guerin (BCG) immunotherapy. Whilst effective in treating NMIBC, 60-80% of patients develop lower urinary tract symptoms (LUTS), including urinary frequency, pelvic pain, and dysuria that can significantly impact quality of life during treatment. Up to 20% of patients will discontinue BCG treatment due to these LUTS, significantly increasing their risk of cancer progression.

Aims. To investigate the underlying mechanisms and develop a therapeutic strategy to prevent BCG-induced LUTS.

Methods. Mice (n=3/group) were treated with BCG ($4.2x10^6$ CFU/bladder) or PBS (SHAM) once weekly for six weeks. Mouse bladders were used for flow cytometry and bulk RNA-seq to characterise immune responses or underwent ex-vivo bladder contraction experiments to assess changes in bladder muscle function. Urothelial bladder cancer cell lines (UM-UC3, T24, and MB49) were used to assess potential impacts of Mirabegron (1μM-30μM), a β3 adrenoceptor agonist clinically approved for the treatment of LUTS in other urology disorders, on BCG efficacy in-vitro via cell senescence and cytotoxicity assays.

Results. BCG treatment induced significant immune cell infiltration in the bladder ($p<0.01$), including CD45+ cells, CD4+ T cells, neutrophils and NK cells, along with upregulation of multiple inflammatory HALLMARK pathways. A significant downregulation of the gene encoding the β3 adrenoreceptor (Adbr3) was observed in BCG treated bladders (n=6, $p=0.002$, fold change=-1.26) which correlated with a significant increase in bladder spontaneous contractions ex-vivo (n=6, $p<0.01$). Mirabegron (1μM-30μM) had no effect on BCG induced cell senescence or cytotoxicity in vitro ($p>0.05$).

Discussion. This data shows that BCG induced inflammation can alter normal bladder muscle function including downregulation of the Adbr3 gene. Targeting the β3 adrenoceptor with Mirabegron in vitro had no negative impacts on the hallmarks of BCG efficacy and thus may represent a novel and safe adjunct treatment for BCG-induced LUTS in NMIBC patients.

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Targeting endosomal metabotropic glutamate receptor 5 signalling for the treatment of pain

Dr Shane Hellyer

Biography:

Dr Hellyer is an EMCR researcher at the Monash Institute of Pharmaceutical Sciences, and it Deputy lab head of the Neuropharmacology lab within Drug Discovery Biology. His works focuses on the molecular pharmacology of GPCRs involved in neurophysiology and neuropathophysiology. In particular, Dr Hellyer is interested in the impact of single nucleotide variants found in patients populations, how they contribute to disease aetiology and how they potentially affect drug action on through changing receptor function. Dr Hellyer has published 21 peer reviewed journal articles and 1 book chapter, acting as a Chief Investigator on competitive grants worth $1.4 million.

Targeting endosomal metabotropic glutamate receptor 5 signalling for the treatment of pain

Shane D Hellyer[1], Jeffri Retamal Santibanez[1], Yifei Zhu[1], Jackson Kos[1], Rina Pokhrel[1], Nicholas Veldhuis[1], Karen J Gregory[1,2].
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[2]ARC Centre for Cryo-electron Microscopy of Membrane Proteins, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, VIC, 3052, Australia

Introduction. Targeting G protein-coupled receptors (GPCRs) within endosomes is an emerging therapeutic approach for treating pain. Metabotropic glutamate receptor 5 ($mGlu_{5)}$ is expressed on both the cell surface and intracellular membranes. Its function differs based on subcellular localisation, with reports of elevated neuronal nuclear signalling after chronic pain. However, little is known about $mGlu_5$ signalling from endosomes and the potential to therapeutically target this subpopulation for pain treatment.

Aims. To determine if, and how, $mGlu_5$ signals from endosomes, and whether targeting endosomal $mGlu_5$ using a nanoparticle formulation enhances the analgesic properties of an $mGlu_5$ inhibitor

Methods. A combination of tagged $mGlu_5$, genetically encoded resonance energy transfer and fluorescent sensors were used in HEK293A cells to assess $mGlu_5$ trafficking, localisation and signalling (intracellular Ca^{2+} and ERK1/2) in response to the orthosteric agonist glutamate and the allosteric inhibitor VU0366058. Analgesic properties of free and nanoparticle formulated VU0366058 (DIPMA-058) were tested in three *in vivo* pain models; capsaicin injection (acute pain), intraplantar complete Freund's adjuvant injection (inflammatory pain), sural nerve injury (neuropathic pain).

Results. Activated $mGlu_5$ internalises into early endosomes, where a small population recruits $G\alpha_{q/11,}$ but not $G\alpha_{s,}$ G proteins. Inhibition of $mGlu_5$ internalisation and glutamate transport into the cell differentially affected cytoplasmic and nuclear calcium and kinase activity, with sustained functional responses mediated by both processes. Selectively targeting intracellular $mGlu_5$ with DIPMA-058 achieved superior analgesia compared to free VU0366058 in inflammatory (49.4±9.0 pain reversal vs 14.6±2.5%, DIPMA-058 vs free VU0366058; $p<0.01$) and neuropathic (72.0±6.8% vs 37.4±7.2%, DIPMA-058 vs free VU0366058; $p<0.001$) mouse models of pain.

Discussion. Collectively, these data reveal $mGlu_5$ internalises into endosomes, where G protein coupling and signalling makes up a minor component of the overall sustained $mGlu_5$ signalling repertoire. Selectively targeting intracellular $mGlu_5$ represents a viable method to improve analgesic efficacy of $mGlu_5$ inhibitors.

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Untangling Polypharmacy Molecular Signature Through Network Pharmacology Approaches: Study on Hippocampal Proteomics

Mr Kevin Winardi

Biography:

Kevin is a scientific officer at the Laboratory of Ageing and Pharmacology, Kolling Institute and the University of Sydney, led by Prof Sarah Hilmer. He leads the bioinformatics analyses of omics data to investigate the molecular mechanisms of drug-related harms in old age, aiming to understand the impact of polypharmacy whether medication cessation (deprescribing) offers any molecular reversibility benefits.

Untangling Polypharmacy Molecular Signature Through Network Pharmacology Approaches: A Case Study with Hippocampal Proteomics

Kevin Winardi[1], John Mach[1], Matthew J. McKay[2], Mark P. Molloy[2], Simon Tang[3], Sarah N. Hilmer[1]. Laboratory of Ageing and Pharmacology[1] & Bowel Cancer and Biomarker Laboratory[2], Kolling Institute, University of Sydney and NSLHD, Sydney, NSW, Australia; School of Life Sciences[3], École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Introduction. Analysing the molecular signature of polypharmacy (≥5 medications) is challenging due to the complexity in monotherapy effects along with synergistic and antagonistic effects. Further, the molecular impact of deprescribing (medication cessation) is also not well described. *In silico* approaches such as network analysis can provide insights on individual drug effects within polypharmacy and deprescribing.

Aims. To apply network pharmacology approaches to disentangle the molecular signature of polypharmacy and deprescribing.

Methods. Middle-aged (12 months) C57BL/6J osteoarthritic male and female mice were given either polypharmacy (chronic oral therapeutic doses of oxybutynin, oxycodone, citalopram, simvastatin and metoprolol) or control diet (CTRL). After 4 weeks (age: 13 months), polypharmacy-treated mice either continued all medications (POLY) or had oxycodone gradually deprescribed (POLYDP). At age 14.5 months, hippocampal CA1 was collected, and proteome was measured with data-independent acquisition (DIA) using a Q-Exactive (Hfx) orbitrap mass spectrometer. Protein-drug and protein-protein interaction networks were constructed and analysed. Cell type deconvolution was conducted.

Results. Compared to CTRL mice, POLY and POLYDP induced major CA1 proteome reorganisation with 219 and 283 differentially expressed proteins, respectively, with 130 shared between POLY and POLYDP. Proteins affected include neurotransmission-related, immune, metabolic, and structural proteins. An interaction network was developed using the differentially expressed proteins permiting distinction between direct drug or indirect/downstream effects. Drug effects were either single drug (e.g., citalopram with serotonergic neurotransmission) or multi-drug effect (e.g., drug metabolism). Relationship of direct and indirect effects could be elucidated (e.g., oxycodone and axon guidance protein). Deconvolution analysis revealed that the POLY and POLYDP influenced astrocytic and interneuron functions.

Discussion. Network pharmacology is a powerful tool in hypothesis generation for molecular effects of polypharmacy and deprescribing. Future research is needed to experimentally validate these results.

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Kv1.3 blockade improves cognitive performance in APP/PS1 mice

Dr Ryan Keenan

Biography:

Dr. Ryan Keenan is a Postdoctoral Research Fellow in the Drug Delivery, Disposition and Dynamics theme at Monash Institute of Pharmaceutical Sciences. Ryan has extensive experience in rodent behavioural studies, particularly using neurodegenerative mouse models of Alzheimer's disease. Ryan completed his PhD at The University of Melbourne and Florey Institute of Neuroscience and Mental Health. Ryan's PhD research focused on the proposed bidirectional relationship between neurodegenerative disorders and sleep impairments. Ryan investigated the role that mutant tau overexpression plays in mediating sleep disruptions and cognitive deficits in a neurodegenerative tau transgenic mouse model. Ryan's experiments interrogated how genetic modulation of tau expression and pharmacological manipulation of sleep impacted the phenotype of the transgenic mouse model. In his current position, Ryan's research focuses on using novel therapeutics which target neuroinflammation to improve disease outcomes in mouse models of Alzheimer's Disease and Motor Neurone Disease.

K_V1.3 blockade improves cognitive performance in APP/PS1 mice

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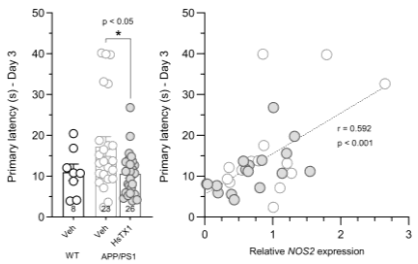

Introduction: Alzheimer's disease (AD) is a prevalent neurodegenerative disease with no known cure. Accumulating evidence highlights a prominent neuroinflammatory component in AD driven by chronically activated microglia, which release pro-inflammatory cytokines that contribute to neuronal death. Microglia express the voltage-gated potassium channel 1.3 (K_V1.3) which regulates their activation, and its expression is increased in AD. We have developed HsTX1[R14A], a potent and selective K_V1.3 blocker, which improved cognitive function in a mouse model of sporadic AD.

Aims: Investigate the anti-inflammatory and cognitive-enhancing effects of K_V1.3 blockade via chronic HsTX1[R14A] administration in a mouse model of familial AD (APP/PS1).

Methods: 8.5-month-old female APP/PS1 mice were administered HsTX1[R14A] at 1 mg/kg or saline vehicle (3 µl/g) every second day by sc injection for 8 weeks. During the last 2.5 weeks of treatment, mice underwent a battery of cognitive behavioural tests including the Barnes maze. Brain and blood samples were collected for molecular analysis of Aβ pathology and markers of neuroinflammation. Positron emission tomography (PET) imaging of 64Ga-HsTX1[R14A] assessed peptide distribution in the brain for up to 85 min post sc administration.

Results: Vehicle-treated APP/PS1 mice exhibited a longer primary latency across the 4 days of Barnes maze acquisition trials compared with WT mice. HsTX1[R14A] treatment decreased primary latency to WT levels by day 3 of acquisition. HsTX1[R14A] did not decrease soluble Aβ in the brain nor cytokine levels at either a protein or gene level, although higher pro-inflammatory (*IL-1ß, IL-6, TNF-α, NOS2*) and K_V1.3 (*Kcna3*) gene expression was correlated with poorer cognitive performance. Detectable albeit limited peptide brain uptake was observed following sc administration.

Discussion: These data further highlight the association between K_V1.3, neuroinflammation and cognitive decline using a mouse model of familial AD. The exact mechanism by which HsTX1[R14A] improves cognitive performance remains to be determined. Immunohistochemical evaluation of microglial K_V1.3 and Aβ plaques are currently in progress.

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Clinical decision-making in primary aldosteronism screening, diagnosis and management: A qualitative study

Dr Sandra Hakim

Biography:

Sandra is an early career health care researcher with a track record in biochemistry and molecular biology research, and an emerging body of work in health care, aged care and hypertension research. She is a team member of the National Aged Care Research Network (NACReN), a national aged care stakeholder engagement and knowledge translation platform. Within NACReN, she has contributed to a research priority-setting study in aged care, and is leading a preliminary evaluation of NACReN. Outside of NACReN, she has led a qualitative research study that aims to understand barriers to the diagnosis of secondary hypertension in the Australian healthcare setting.

Clinical decision-making in primary aldosteronism screening, diagnosis and management: A qualitative study

Sandra Hakim[1,2,3], Lok Him Jason Yeung[4], Grant Russell[5], Lisa Dubrofsky[6], Gregory Kline[7], Jun Yang[8,9]*, Katrina M Long[2,3,4]*

1. Sch. of Primary & Allied Health Care, Monash Univ., Australia; 2. National Centre for Healthy Ageing, Frankston Hosp., Australia; 3. Peninsula Health, Frankston Hosp., Australia. 4. Dept of OT, Sch. of Primary & Allied Health Care, Monash Univ., Australia; 5. Dept of General Practice, Monash Univ., Australia; 6. Dept of Medicine, Women's College Hosp., Canada; 7. Dept of Medicine, Cumming Sch. of Medicine, Univ. of Calgary, Canada; 8. Hudson Inst. of Medical Research, Australia; 9. Dept of Medicine, Monash Univ., Australia; *Authors contributed equally.

Introduction: Primary Aldosteronism (PA) is a potentially curable cause of hypertension, accounting for up to 14% of cases. In Australia, PA screening rates are below 1%, with underdiagnosis and/or diagnostic delay contributing to potentially preventable cardiovascular complications and end-organ damage. However, the factors underlying PA underdiagnosis and undertreatment are not well understood.

Aims: To identify clinician-reported factors influencing the screening, diagnosis and treatment of PA.

Methods: Between May and November 2024, semi-structured interviews were conducted with 8 cardiologists, 10 endocrinologists, 10 general practitioners and 10 nephrologists across Australia. Interview transcripts were analysed using deductive content analysis guided by the Consolidated Framework for Implementation Research (CFIR) and inductive reflexive thematic analysis.

Results: Four themes were developed to explain factors affecting clinician decision-making: 1) clinician experience, knowledge and perceptions; 2) complexity and burden of PA screening and diagnosis; 3) accessibility to services and information; and 4) health system, government and organisational factors. Key barriers to screening, diagnosis and treatment for all clinician groups were i) that PA screening is often considered in a narrow patient cohort, excluding older individuals and those living with multi-morbidity, and; ii) that limited access to diagnostic services compromised screening and diagnostic workup. A key facilitator was cross-disciplinary and collegial decision-making in patient management.

Discussion: These findings highlight several areas for development of clinician-targeted interventions to improve PA detection and management. Opportunities include: advocacy, education and clinical guideline updates to promote broader screening; protocol development to simplify screening test preparation and improve assay reliability; innovation in the workflow for PA diagnosis, and; development of communities of practice.

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Heart failure exacerbates renal hypoxia and acute kidney injury after cardiopulmonary bypass

Prof Clive May

Biography:

Professor Clive May founded the Preclinical Critical Care Unit at the Florey Institute of Neuroscience and Mental Health. He retired in 2022 but still provides support and mentorship to the laboratory. At the Florey, he developed clinically relevant large animal models of septic shock, cardiopulmonary bypass, heart failure, myocardial infarction/reperfusion and seizure, together with the development of techniques to continuously monitor cardiovascular, autonomic and vital organ function. These preclinical models and techniques provide a unique opportunity to investigate pathophysiology at a level of detail not possible in critically ill patients and not available in other laboratories worldwide Outcomes from these studies include the development of a new drug to treat catecholamine resistant hypertension, which has saved lives, the Stentrode, a novel brain machine interface, and the discovery that intravenous megadose sodium ascorbate can reverse the pathophysiological effects of sepsis. Professor May has over 270 publications and <15,400 citations

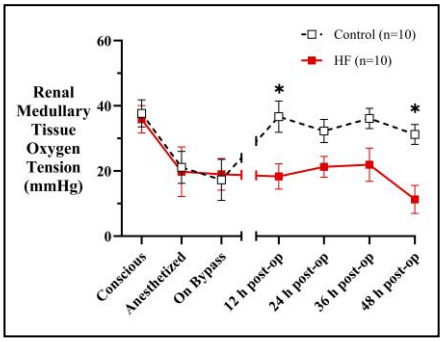
Heart failure exacerbates renal medullary hypoxia and risk of acute kidney injury after cardiopulmonary bypass

Clive N. May[1], Anton Trask-Marino[1], Taku Furukawa[1], Ian Birchall[1], Lachlan F. Miles[1,2], Sally G. Hood[1], Connie Pei Chen Ow[1], Lindsea C. Booth[1], Yugeesh R. Lankadeva[1]. [1]Preclinical Critical Care, Florey Institute of Neuroscience and Mental Health, University of Melbourne, VIC, Australia; [2]Department of Anaesthesia, Austin Health, VIC, Australia.

Introduction. Acute kidney injury (AKI) is a major complication of cardiac surgery, especially in patients with heart failure (HF). Mechanistic insight has been limited by the lack of clinically relevant models.

Aims. To determine how pre-existing HF affects renal oxygenation and function before, during and after cardiopulmonary bypass (CPB), and to identify the mechanisms underlying postoperative AKI.

Methods. Female sheep were surgically instrumented under isoflurane anaesthesia (2.0-2.5% in oxygen-air mixture), for continuous monitoring of renal blood flow (RBF), renal oxygen delivery (RDO_2), renal cortical and medullary tissue oxygenation (PO_2) and urine output during 3 phases: pre-CPB (conscious), during CPB (anesthetized), and post-CPB (conscious). HF was induced via progressive coronary ligation and defined by a ≥25% fall in ejection fraction. HF (n=10) and control (n=10) animals underwent 2-h CPB with aortic cross-clamp followed by 48-h recovery.



Results. CPB reduced RBF and renal medullary (but not cortical) tissue PO_2 in both groups (all P_{time} ≤0.001). Postoperatively, medullary PO_2 recovered in healthy controls but remained suppressed in sheep with HF (P_{group} <0.001), despite a similar recovery of RBF. Animals with HF also had persistently lower haemoglobin and RDO_2 across the perioperative phase (both P_{group} ≤0.05). In the HF group, postoperatively urine output was lower (P=0.039) and AKI occurred more frequently (50% vs. 11%; OR 9.0, P=0.14). Histopathology showed acute tubular necrosis and peritubular inflammation after CPB (50% [HF] vs. 37% [control]), with no group differences.

Discussion. Pre-existing HF amplifies renal vulnerability to CPB by preventing recovery of renal medullary oxygenation, implicating sustained tissue hypoxia as a driver of postoperative AKI and a potential target for renoprotection.

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Sex differences in response to podocyte depletion in aged mice

Dr Sarah Walton

Biography:

Dr Sarah Walton is an integrative physiologist specialising in sex differences in hypertension and kidney disease. She completed her PhD at the University of Queensland in 2016, and now conducts postdoctoral research under the mentorship of Prof Kate Denton at the Monash Biomedicine Discovery Institute. Dr Walton's work integrates advanced physiological techniques with molecular and morphological analyses to understand mechanisms driving cardiovascular disease.

Sex differences in response to podocyte depletion in aged mice

Sarah L Walton[1], Zoe M McArdle[1], Kate M Denton[1]. [1]Department of Physiology and Monash Biomedicine Discovery Institute, Monash University, Clayton, VIC, Australia.

Introduction. Up to 90% of kidney diseases originate in the glomeruli. Podocyte injury and loss in ageing can compromise the glomerular filtration barrier, contributing to kidney function decline and arterial hypertension. Significant sex differences exist in protein filtration and progression of glomerular diseases. Yet, few studies examine sex differences in podocyte biology.

Aim. To assess the effect of biological sex on podocyte depletion, a central event in glomerular disease, and proteinuria in aged mice.

Methods. We induced moderate podocyte loss in male and female Pod^{cre}iDTR mice (12-16 months of age; n=9-11/sex) by treatment with diphtheria toxin (DT, 110 ng/kg i.p.). Age- and sex-matched Pod^{cre}iDTR mice were treated with saline (i.p, n=10/sex) as controls. Six days after treatment, a 24h urine sample was collected via metabolic cage housing to measure total protein content. Mice were humanely killed seven days following treatment. Kidneys were immersion fixed for histological analysis of senescence-associated beta-galactosidase (SA-β-gal), a marker of cellular senescence and ageing.

Results. Total protein excretion over 24h was ~3.3-fold greater in vehicle-treated male mice than female mice and was not affected by age (P_{sex}=0.008; P_{age}=0.62). DT treatment induced marked proteinuria in both sexes ($P_{treatment}$<0.0001). Females displayed an enhanced proteinuric response to DT (~9-fold greater than female vehicle, p=0.002) than males (~4-fold greater than male vehicle, P=0.01). Age and DT treatment had no effect on body weight, urine flow, kidney weight, or heart weight. Expression of SA-β-gal in the renal cortex was not affected by age, sex or DT treatment.

Discussion. Our study demonstrates aged female mice exhibit an enhanced proteinuric response to a podocyte depletion event compared with males. Whether this finding reflects greater susceptibility to podocyte loss and injury in aged females will be answered by future podometric studies to assess podocyte number and injury. Given hypertension is a major contributor to glomerular injury, particularly in aged populations, its potential role in exacerbating podocyte vulnerability warrants further investigation.

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Linking Renal Medullary Hypoxia to Mitochondrial Dysfunction in Septic Acute Kidney Injury

Dr Connie Ow

Biography:

I am a mid-career post-doctoral researcher based at the Florey Institute. I currently head the sepsis research and the biochemical platform in the Translational Cardiovascular and Renal Research Group. My research focus has been on determining the role of renal tissue dysoxia in kidney diseases and to investigate therapeutic opportunities in ameliorating tissue hypoxia-induced injuries to the kidney. My earlier work on the development and validating the techniques for chronic monitoring of renal tissue oxygenation in ischemia-induced acute kidney injury further highlighted the need for direct and long-term assessment of tissue oxygenation for determining opportunistic therapeutic window in order to prevent/slow the progression of chronic kidney disease following recovery from acute kidney injury. My current research focuses on therapies aimed at ameliorating renal medullary tissue hypoxia in sepsis-induced acute kidney injury.

Linking Renal Medullary Hypoxia to Mitochondrial Dysfunction in Septic Acute Kidney Injury.

Connie Ow[1], Alemayehu Jufar[1], Darius Lane[2], Ruslan Pustovit[1], Clive May[1], Jennifer Bauquier[3], Mark Plummer[4], Yugeesh Lankadeva[1]. [1]Translational Cardiovascular and Renal Research Group and [2]Translational Neurodegeneration Laboratory, The Florey Institute of Neuroscience and Mental Health, VIC, Australia. [3]Melbourne Veterinary School, The University of Melbourne, VIC, Australia. [4]Department of Intensive Care, Royal Adelaide Hospital, Adelaide, Australia.

Introduction. Renal medullary hypoxia occurs during sepsis-induced acute kidney injury (AKI). An early onset of sepsis-induced hypoxia and inflammation can cause deficits in mitochondrial complexes I-IV thereby impairing electron transport chain function, and decrease ATP production, worsening cellular injury and organ dysfunction culminating in AKI. However, there is a paucity of evidence on renal medullary tissue mitochondrial injury in clinically relevant large animal models of septic AKI.

Aims. To quantify mitochondrial injury in the renal medulla of a clinically relevant model of ovine septic AKI.

Methods. Sepsis was induced in five Merino ewes via an intravenous bolus (2.8 x 10^9 CFU/ml) followed by a continuous infusion (1.26 x 10^9 CFU/ml/h) of live *Escherichia coli* for 31 h. At the end of 31 h sepsis, the renal medullary tissue was collected and mitochondria injury was determined by assessing for mitochondrial respiration using the gold-standard 'Seahorse' approach. Renal medullary tissue from five healthy naïve sheep served as controls for this assay. Next, we utilised quantitative real-time PCR in plasma samples collected before and after sepsis, to assess for mitochondrial DNA leakage, which is often associated with compromised mitochondrial structural integrity.

Results. Ovine septic AKI recapitulated clinical symptoms of human septic AKI, including the hypotension, hyperlactatemia and elevations in plasma creatinine and oliguria. We identified significant reductions in the activity of mitochondrial complexes I (526±34 vs 320±743 pmol/min, P=0.03) , II (137±21 vs 56 ± 13 pmol/min, P=0.01) and IV (595±47 vs 233±65 pmol/min, P=0.002) of the electron transport chain in the renal medullary tissue of septic sheep with AKI compared with healthy sheep. Mitochondrial DNA encoding components crucial to complexes I and III of the electron transport chain in plasma was significantly increased in septic sheep with AKI.

Discussion. Renal medullary hypoxia in sheep with septic AKI was associated with impaired mitochondrial respiration and structural disruption. These findings highlight mitochondria as a key therapeutic target and provide a rationale for developing interventions that preserve mitochondrial integrity to promote adaptive and functional repair in sepsis-induced AKI.

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Beyond diet and obesity: establishing a sympathetic nervous system-driven model of MAFLD

Dr Lakshini Herat

Biography:

Dr Lakshini Herat is a National Heart Foundation Postdoctoral Research Fellow in the Translational and Discovery Science Laboratory at the Dobney Hypertension Centre, UWA. Her research focuses on identifying novel mechanistic pathways of anti-diabetic and anti-obesity treatments to optimise their use and improve cardio-kidney-metabolic outcomes in patients. A passionate advocate for science and education, she actively promotes women in STEM through teaching and community outreach.

Beyond diet and obesity: establishing a sympathetic nervous system-driven model of MAFLD.

Lakshini Herat[1,2], Lois Balmer[1,3], Tharani Senavirathna[1], Ricky Lareu[4], Jiansha Wu[5], Hanane Belhoul-Fakir[5], Juliana Hamzah[5], Tim Rosenow[6], Markus Schlaich[2,7,8]. Dobney Hypertension Centre, School of Biomed Sci, UWA, Perth, WA[1]; RPH Research Foundation, Perth, WA[2]; CPH, ECU, Joondalup, WA[3]; CHIRI, Curtin University, Bentley, WA[4]; Harry Perkins Institute of Medical Research[5], Nedland, WA[5]; CMCA, UWA, Nedland, WA[6]; Dobney Hypertension Centre, Med School, UWA, Perth, WA[7]; Dept of Cardiology and Dept of Nephrology and Transplantation, RPH, Perth, WA[8].

Introduction. Metabolic dysfunction-associated fatty liver disease (MAFLD) is often linked to poor diet, obesity and insulin resistance. Additionally, chronic sympathetic nervous system (SNS) hyperactivity plays a key role in metabolic dysfunction, inflammation and liver fat accumulation. Current preclinical MAFLD models are mostly diet-induced whereas none reflect sympathetically induced MAFLD (Oligschlaeger Y et al 2020). This limits our understanding of specific neurogenic mechanisms implicated in MAFLD and the development of SNS-targeted therapies.

Aims. We sought to establish and characterise a novel mouse model of MAFLD induced by SNS hyperactivity.

Methods. BPH/J2 mice, an established model of neurogenic hypertension were fed chow or high-fat diet (HFD) for 16 weeks. We assessed changes in weekly body weight, liver fat content (using MRI), glucose tolerance and insulin resistance. Blood and liver tissues were collected at week-16 for biochemical and histological analysis.

Results. In BPH/2J HFD mice, percentage body weight and liver fat fraction were significantly higher compared to Chow-fed BPH/2J and BPN/3J (control) mice (n=4-6, $P<0.05$). Additionally, these mice demonstrated significant glucose tolerance and insulin resistance when compared to Chow-fed BPH/2J counterparts. Histological analysis in HFD-fed BPH/2J showed a significant increase in total hepatic steatosis (BPH/2J Chow 19.2%±0.5 vs HFD 51.4%±14.0; n=6-8, $P<0.001$). A significant difference was identified in total cholesterol (BPH/2J Chow 2.47±0.28 vs HFD 3.58±0.49; n=6-8 $P<0.001$) accompanied by a trend towards higher AST and ALT levels in HFD-fed mice.

Discussion. Our model enables testing of SNS-targeted therapies, such as sympatholytic drugs or hepatic denervation, with benefits beyond weight or glucose control. Future work will explore underlying mechanisms and evaluate interventions to advance neurogenic-based treatments for MAFLD.

Oligschlaeger Y et al (2020) Biomedicines, 8;8(2):28.

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Megadose sodium ascorbate attenuates splanchnic sympathetic nerve activity in Gram-negative rodent sepsis

Dr Rachel Peiris

Biography:

Rachel Peiris recently completed her PhD at the Florey Institute of Neuroscience and Mental Health, where she was supervised by Professor Yugeesh Lankadeva, Professor Clive May, Professor Robin McAllen, Doctor Lindsea Booth and Doctor Laura Cook (from the Doherty Institute).

Rachel is an Early Career Researcher whose work has redefined how the body responds to infections. She has measured sympathetic nerve activity, bacterial clearance and immune cells' function over the course of sepsis induced by live infection in small to large animal models.

Her overarching research goal is to understand immunological changes in life-threatening conditions across animal models and in patients, to facilitate the development of therapeutics. She has received several Best Student Presentation awards at premier national cardiovascular and immunology conferences.

Megadose sodium ascorbate attenuates splanchnic sympathetic nerve activity in Gram-negative rodent sepsis.

Rachel M Peiris[1], Robin M McAllen[1], Michael J McKinley[1, 2], Clive N May[1], Lindsea C Booth[1], Alemayehu H Jufar[1], Willian S Korim[2], and Yugeesh R Lankadeva[1]. Trans Cardiovasc Renal Res Grp, The Florey Inst[1], Parkville, VIC, Australia. Depart of Anat and Phys, The Univ of Melbourne[2], Parkville, VIC, Australia.

Introduction. There is evidence that the brain can suppress innate immune responses to infections via the splanchnic sympathetic nerves. Bilateral splanchnic denervation can accelerate bacterial clearance and improve clinical state in established ovine sepsis. As splanchnic denervation is an unacceptable treatment for sepsis, it is critical to assess potential pharmacological approaches.

Aims. To assess, if megadose sodium ascorbate reduces splanchnic sympathetic nerve activity (SpSNA) during rodent Gram-negative sepsis and if cerebrospinal fluid (CSF) levels of ascorbate increase with treatment.

Methods. Male and female Sprague-Dawley rats were randomised to receive iv *E. coli* (4×10^9 CFU/mL, n = 14) or lipopolysaccharide (LPS, 60 µg/kg, n = 14; control for infection). After 1-h, these groups were randomised to receive iv megadose sodium ascorbate (n = 7/group) or sodium and fluid-matched control (placebo, n = 7/group) for 3-h. The left SpSNA was continuously recorded via silver wire electrodes. Plasma and CSF samples were collected to measure ascorbate concentrations.

Results. During infection, sodium ascorbate treatment, blunted the rise in SpSNA compared with the placebo-treatment (131±68.2 vs. 227±122 % of baseline, PGroup×Time=0.041). This effect was not observed in the LPS groups. Plasma ascorbate levels increased in the *E. coli* and LPS groups treated with sodium ascorbate compared with placebo (16.2±3.48 vs. 0.21±0.06 mM and 21.9±7.68 vs. 0.11±0.07 mM, P<0.0001 P<0.0001, respectively). This was accompanied by increases in CSF ascorbate concentrations in the *E. coli* and LPS groups treated with sodium ascorbate compared with placebo (0.66±0.24 vs. 0.14±0.09 mM and 2.51±1.11 vs. 0.09±0.05 mM; P=0.001 and P<0.0001, respectively).

Discussion. Sodium ascorbate treatment attenuated the increase in splanchnic sympathetic nerve activity in rats with live *E. coli* infection but not with LPS. The reduction in splanchnic sympathetic nerve activity with sodium ascorbate during live Gram-negative infection might be due to enhanced bacterial clearance from the bloodstream.

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Meaningful engagement to develop culturally relevant health interventions with Aboriginal and Torres Strait Islander people

Dr Andrew Goodman

Biography:

Dr Andrew Goodman is an Aboriginal man from Iningai Country in Queensland. Prior to his PhD, Dr Goodman spent more than 13 years as an Indigenous Healthcare Worker in Queensland, focusing on cardiac and healthcare services for Aboriginal and Torres Strait Islander people. Currently, he is a Postdoctoral Fellow with CSIROs Australian eHealth Research Centre, exploring novel approaches and/or solutions to improve Aboriginal and Torres Strait Islander peoples' health and wellbeing using electronic Health (eHealth). Dr Goodman is a steering committee member of the National Hypertension Taskforce. Dr Goodman leads a program of research through the facilitation of e-Health research (with respect to consultation, co-design, trialling or evaluation) and the development of technologies to support health and wellbeing. With his core value system of 'Relationships before Partnerships', Dr Goodman takes a relational approach to research agenda setting anchored by a value-based accountability with prospective Aboriginal and Torres Strait Islander peoples and organisations.

Meaningful engagement to develop culturally relevant health interventions with Aboriginal and Torres Strait Islander people

Andrew G Goodman[1,2]. Australian eHealth Research Centre, Commonwealth Scientific and Industrial Research Organisation[1], Brisbane, QLD, Australia; School of Public Health, The University of Queensland[2], Brisbane, QLD, Australia.

Introduction. It is largely accepted that Aboriginal and Torres Strait Islander people are some of the most researched human beings in history. Yet this abundance of research has resulted in little to no perceived benefit by Aboriginal and Torres Strait Islander peoples. The legacy of Aboriginal and Torres Strait Islander activism has produced a raft of research protocols that mandate an ethical and responsible relationship with Aboriginal and Torres Strait Islander community. Yet, there remains a lack of understanding of how to operationalise a relational approach within health research and interventions.
Aims. To outline a set of principles, grounded within a relational approach, for entering a research partnership with Aboriginal and Torres Strait Islander communities.
Methodology. Underpinning this approach is the Indigenous knowledge framework of 'Two-Eyed Seeing', that emphasises the value of both Indigenous and non-Indigenous knowledges as equal and complimentary. Through reflective practice and innate cultural protocols, a set of principles were developed.
Results. The 'Relationships before Partnerships' principles facilitate respectful consultation that prioritises the needs and interests of Aboriginal and Torres Strait Islander peoples and organisations, as opposed to research driven priorities.
Discussion. The conversation is intended to guide the first steps of engagement, building a respectful and accountable relationship with prospective research partners. This process should be considered when attempting to develop research credibility and integrity with Aboriginal and Torres Strait Islander communities.

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Creating Opportunities for Consumer Involvement: Reflections of a Discovery Scientist and Research Centre Director

Prof Grant Drummond

Biography:

Professor Grant Drummond is a pharmacologist and vascular biologist with over 30 years of experience in research and tertiary education. He holds senior leadership appointments at La Trobe University, including Associate Dean (Partnerships) for the School of Agriculture, Biomedicine and Environment, and Co-Director of the Centre for Cardiovascular Biology and Disease Research. In the latter role, he oversees a team of approximately 60 staff and students engaged in fundamental research into the mechanisms driving cardiovascular disease. His own research focuses on how the immune system and inflammation contribute to hypertension and its complications. Professor Drummond's work has identified key roles for B cells, T cells, macrophages, and the NLRP3 inflammasome in promoting inflammation and damage to the arteries, heart, and kidneys. The long-term goal of his research is to develop novel therapies that suppress inflammation in these target organs without compromising the immune system's ability to fight infections and tumour development. Professor Drummond has published over 180 papers, with more than 19,000 citations. His research has been continuously supported by the NHMRC and the Heart Foundation of Australia for more than two decades.

Creating Opportunities for Consumer Involvement: Reflections of a Discovery Scientist and Research Centre Director

Grant Drummond. Centre for Cardiovascular Biology and Disease Research, La Trobe Institute of Molecular Sciences, La Trobe University, Melbourne, VIC, Australia.

Introduction. Engaging consumers in fundamental cardiovascular research presents unique challenges, particularly in translating complex science into accessible public understanding. La Trobe's Centre for Cardiovascular Biology and Disease Research is in the early stages of its consumer engagement journey, focused on building trust and awareness to ensure our research reflects lived experience and delivers meaningful impact.

Aims. To embed consumer voices meaningfully through a multi-layered strategy that strengthens community engagement and trust, promotes broader awareness of cardiovascular health, and enhances research relevance.

Methods. Our approach includes appointing a dedicated Engagement Officer; establishing a Steering Committee of lived experience participants, clinicians, industry professionals and researchers; hosting outreach events across metropolitan and regional Victoria; and forming strategic partnerships with La Trobe's Advancement and Alumni, Business Development and Educational Partnerships teams, and external organisations such as CAD Frontiers, the Baker Institute, and the Australian Cardiovascular Alliance. Researchers receive training in media, donor and industry engagement, and the Centre maintains an active social media presence to share research in accessible formats.

Results. Since 2022, our inclusive outreach has included events such as Heart Camp, World Heart Day, cardiovascular health webinars, and industry showcases. These have attracted over 1000 attendees from the public, including > 400 primary and secondary school students. We have run community forums at La Trobe's regional campuses, bringing together clinicians, scientists, pharmacists, and community members to explore cardiovascular health challenges. Outcomes have included development of a cardiovascular health dashboard in Midura, funding applications for a local clinical trials coordinator, feature articles/segments in local media, and discussions about establishing a cardiac care ward at Midura hospital. The Steering Committee has driven co-designed, consumer-led research initiatives which has led to philanthropic and commercial funding, MRFF applications, and the establishment of a start-up company.

Discussion. At La Trobe's Centre for Cardiovascular Biology and Disease Research, we have developed a framework for consumer engagement that connects technical science with public understanding. By embedding lived experience, industry and clinical voices into our research, we're building trust, enhancing relevance, and driving lasting impact.

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Ingredients for successful partnerships between researchers and consumers

John Stevens

Biography:

John is a stroke survivor and active consumer advisor and advocate of consumer voice in research, health policy and health programs to provide lived experience of the impact of stroke for survivors and their loved ones. John is an experienced consumer advisor with >5 years of experience as a research steering committee member, a co-author on two publications and CI on >$5.5 million of grant funding. In 2023, John was appointed both as Chair of the Lived Experience Group and member of the Steering Committee of the Menzies Cardiovascular Research Flagship, UTAS. In 2024, John delivered a national invited presentation at the Hypertension Australia Winter School to provide lived experience of consumer involvement in research and took part in a panel discussion on consumer involvement at the inaugural National Hypertension Summit in Sydney.

Ingredients for successful partnerships between researchers and consumers

Niamh Chapman[1], John Stevens[2]. Faculty of Medicine and Health, the University of Sydney[1], NSW, Australia; Independent Consumer Advisor[2], Hobart, TAS, Australia.

Introduction. Consumer involvement is increasingly recognised as essential for impactful research and prioritised by research funding bodies. However, there is a lack of practical understanding of how to establish collaborative relationships between consumers and researchers.

Aims. Our goal was to establish a meaningful, collaborative relationship to improve patient education, engagement and empowerment for hypertension management. The aim of this talk is to reflect on the principles that enabled this successful partnership.

Methods. Our approach was underpinned by participatory research methods, principles learned from consumer engagement training and regular reflection and feedback on processes.

Results. Mutual trust, empathy and respect are essential components from both researcher and consumers to establish effective collaborative relationships. Researchers need recognise that the intended research outcomes need to address the needs and priorities of consumers, as the intended beneficiaries of the research. Consumers need to appreciate the resource constraints that may impact ability to engage and have flexibility for engagement at different times in the research process. Clear, intentional communication is required to sustain engagement beyond initial interest into a collaborative partnership.

Discussion. We will each share our reflections of our consumer and researcher partnership spanning 5 years from initial 'accidental engagement' that evolved into long-term intentional collaboration that has resulted in two co-authored papers and >$5.5 million in grant funding. We will provide applicable tips for you to develop your own consumer engagement strategy.

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Translating pharmacogenomics and precision dosing in major depressive disorder: the ALIGNED study

A/Prof Kathy Wu

Biography:

A/Professor Kathy Wu is the founding Head of St Vincent's Clinical Genomics, a HGSA-certified Clinical Geneticist, physician scientist, and educator. Kathy is a senior staff specialist at St Vincent's Public & Private Hospitals and St Vincent's Clinic, with academic affiliations with the UNSW, University of Sydney, University of Notre Dame Australia, the Garvan Institute of Medical Research, and the George Institute for Global Health. Kathy is committed to translating genomics research to inform precision healthcare and improving individual and categorical patient outcomes. Kathy is one of the clinician pioneers in Australia to lead a real-world pharmacogenomics implementation body of research and has been awarded $6 million+ in MRFF Research Grants since 2020 to continue her passion in pharmacogenomics research to improve treatment outcomes for people with Major Depressive Disorder.

Translating pharmacogenomics and precision dosing in major depressive disorder: the ALIGNED study

Kathy HC Wu[1-6] and The ALIGNED Steering Committee
[1]School of Clinical Medicine, University of New South Wales, Sydney, NSW, Australia; [2]Clinical Genomics, St Vincent's Hospital, Sydney, NSW, Australia; [3]Disciplines of Medicine and Genomic Medicine, The University of Sydney, NSW, Australia; [4] School of Medicine, University of Notre Dame Australia, Sydney, NSW, Australia; [5]Garvan Institute of Medical Research, Sydney, NSW, Australia; [6]The George Institute for Global Health, Sydney, NSW, Australia

Introduction. Pharmacogenomics (PG) assesses multiple variants influencing pharmacokinetic (drug metabolism) and pharmacodynamic (drug receptor) responses of certain medications. PG-guided prescription enables tailored treatment and may be beneficial in depression treatment where current therapy is based on trial-and-error iterations.
Aims. Built on a body of work, we aimed to: (1) address current gaps in evidence, by investigating the efficacy and economic outcomes of PG-guided antidepressant therapy in people with depression; and (2) combine PG with others biomarkers of treatment response via machine learning, to develop a decision support tool.
Methods. A double-blind randomised-controlled trial of PG-guided antidepressant therapy, with within-study economic analyses, in adults with depression. Outcome measures included treatment response, symptom remission, medication changes and adherence, by validated scales, as well as health services data linkage.
Results. Differing clinician *vs* patient perspectives on PG and barriers to clinical adoption were identified by a retrospective review (n=100). A significant proportion (67%) of patients were taking incongruent medications with actionable drug-gene interactions. In a prospective pilot cohort (n=80), those taking congruent vs incongruent antidepressants had improved treatment outcomes. The ALIGNED study has recruited participants (n=550) with depression from the community via social media and general practice.
Discussion. By generating Australia-specific efficacy and economic data via a double-blind randomised-controlled trial with health services data linkage, we hope to inform future clinical guideline/policy development and public funding decisions, thereby facilitating systemic uptake and equitable access to PG. By combining existing (clinical), new (pharmacogenomics) and other emerging biomarkers of antidepressant response, via a novel machine-learning application, we hope to refine treatment outcome prediction, and develop a decision-support tool to enhance precision of psychotropic therapy in depression treatment.

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The PRESIDE (PhaRmacogEnomicS In DEpression) Trial: a double-blind RCT of pharmacogenomic-informed prescribing of antidepressants on depression outcomes in patients with major depressive disorder in primary care

Dr Sibel Saya

Biography:
Dr Saya is a senior research fellow and an academic genetic counsellor at the University of Melbourne Department of General Practice and Primary Care. Dr Saya's expertise is the implementation and translation of genetic and genomic tests into primary care and general practice and the conduct of clinical trials in this field.

The PRESIDE (PhaRmacogEnomicS In DEpression) Trial: a double-blind RCT of pharmacogenomic-informed prescribing of antidepressants on depression outcomes in patients with major depressive disorder in primary care

Sibel Saya[1], Patty Chondros[1], Cathy Mihalopolous[2], Mary-Lou Chatteron[2], Melanie Galea[5], Timothy Chen[3], Tom Polasek[4], Adrian Laughlin[1], Jane Gunn[1], Victoria Palmer[1], Elise Dettmann[1], Rachel Brooks[1], Georgia Ramsay[1], Matthew Thoenig[1], Madeline Luke[1], Anastasia Abela[1], Philip Ly[1], Jamie Liew[1], Floriy La Rocca[1], Graeme Suthers[5], Chad Bousman[6], Jon Emery[1].
The University of Melbourne, VIC[1]; Monash University, VIC[2]; The University of Sydney, NSW[3]; Certara[4]; Sonic Genetics[5]; University of Calgary, Canada[6]

Introduction: Depression affects over 280 million people worldwide and is a leading contributor to disease burden in Australia, where most patients are managed in primary care. Although antidepressants are recommended for moderate to severe depression, up to half of patients do not respond to their first medication. Pharmacogenomic (PGx) testing of CYP2C19 and CYP2D6 genotypes has been proposed to guide prescribing, but evidence from primary care settings is limited.
Methods: This double-blind, two-arm, stratified, individually randomised controlled trial was conducted in 19 general practices in Victoria, Australia from May 2021 to September 2023. Adults aged 18–65 years with moderate to severe depressive symptoms (PHQ-9 ≥10) were randomized 1:1 to have their general practitioner (GP) receive a prescribing report based on CYP2C19 and CYP2D6 genotypes (intervention) or the Australian Therapeutic Guidelines (control). The primary outcome was difference in mean change in PHQ-9 score from baseline to 12 weeks between arms. Secondary outcomes included remission, response, adherence, side effects, and quality of life.
Results: 552 participants were randomised (80.2% of eligible patients). At 12 weeks, both groups improved, but the control group showed a slightly greater reduction in PHQ-9 scores (mean change: intervention –3.45, control –4.63; difference = 0.90, 95% CI 0.06–1.75; p=0.036). Remission rates were also higher in the control group (absolute difference 7.2%, 95% CI 1.2–13.3; p=0.02). No significant differences were observed in response rates, adherence, side effects, or quality of life.
Discussion: Providing GPs with a PGx-guided prescribing report did not improve depressive symptom outcomes compared with a guideline-based report. Routine provision of PGx testing for all patients in primary care with moderate depression does not appear to be an effective implementation strategy.

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The science of delivering pharmacogenomic test results to guide prescribing in Australia

Prof Luke Hesson

Biography:

Professor Luke Hesson is a Clinical Scientist with a Ph.D in Clinical Genetics and is a Fellow of the Faculty of Science of the Royal College of Pathologists of Australasia (RCPA). He is Department Manager of Genetics at Douglass Hanly Moir Pathology, and provides scientific supervision of genetic testing including pharmacogenomics and comprehensive genomic profiling for cancer. He is affiliated with University of Technology Sydney where he lectures in genetics, epigenetics, cancer, molecular pathology and precision medicine. Luke is Chair of the Australasian Society for Diagnostic Genomics (ASDG) and co-Chair of the RCPA Pharmacogenetic Advisory Group, which recently provided guidance for prescribers, pharmacologists and pathologists regarding clinical indications for pharmacogenomics testing in Australia.

The science of delivering pharmacogenomic test results to guide prescribing in Australia
Prof Luke Hesson[1], Douglass Hanly Moir Pathology[1], Macquarie Park, NSW, Australia

Pharmacogenomic testing can enhance medication effectiveness and safety across multiple specialties. From a pathology laboratory perspective, this presentation reviews the challenges and opportunities of offering such testing in Australia, including variable clinical demand, inconsistent reimbursement, reporting standardisation, the need for clear testing indications, and the importance of selecting alleles suited to Australasian populations to maximise clinical relevance and equity.

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The value proposition: Is pharmacogenomic-guided prescribing of medicines to treat mental health conditions economically sound?

Prof Christine Lu

Biography:

Christine Lu, MSc, PhD is a Professor at the Sydney Pharmacy School and Chair of Clinical Pharmacy at Northern Sydney Local Health District. A pharmacist, health policy scientist, and pharmacoepidemiologist, she holds an MSc in Biopharmaceuticals and a PhD from the University of New South Wales. Dr. Lu completed her postdoctoral training at Harvard Medical School, where she later served as Associate Professor at both Harvard Medical School and the Harvard Pilgrim Health Care Institute before joining the University of Sydney. Internationally recognised for her impactful research, Dr. Lu's work addresses critical clinical pharmacy and health system challenges. Her research focuses on:

1. *The effects of health policies and programs on medication use and outcomes;*
2. *Access to and quality use of pharmacogenomic testing and genomic sequencing; and*
3. *The use, access, and outcomes of high-cost medicines.*

- *Academic Profile: https://www.sydney.edu.au/medicine-health/about/our-people/academic-staff/christine-lu.html*

The value proposition: Is pharmacogenomic-guided prescribing of medicines to treat mental health conditions economically sound?

Christine Y Lu[1,2]. Faculty of Medicine and Health, The University of Sydney, Sydney, NSW[1]; Kolling Institute, Royal North Shore Hospital, St Leonards, NSW[2]

Introduction. Pharmacogenomic (PGx) testing is increasingly recognized as a tool for guiding individualized prescribing in mental health care, where treatment response is variable and adverse drug reactions are common. By aligning medication selection with genetic profiles, PGx has the potential to improve outcomes and enhance efficiency.

Aims. To evaluate the economic viability of PGx-guided prescribing in mental health by examining published literature, national population-level estimates, and real-world data on potential cost savings and clinical benefits.

Methods. Published studies and real-world implementation data were reviewed to assess the economic impact of PGx in psychiatric care, with a focus on healthcare utilization, medication changes, and time to treatment response. We also drew on recent national data estimating the potential annual costs of subsidizing PGx testing for antidepressants and other PGx-relevant drugs in Australia.

Results. Evidence from existing studies suggests that PGx-guided prescribing may reduce adverse drug reactions, avoid ineffective treatment trials, and shorten time to symptom improvement—factors associated with cost savings. New Australian data show that among adults, incident prescribing of PGx-relevant antidepressants such as citalopram (1.6%), escitalopram (1.5%), sertraline (1.2%), and amitriptyline (1.2%) is common, translating into an estimated annual PGx testing cost of AUD$2.9–4.3 million depending on uptake rates. In older adults, incident use of these antidepressants also remained substantial, with predicted testing costs exceeding AUD$1.3–2.0 million annually. These findings underscore the scale of potential investment required, while also highlighting the clinical importance of integrating PGx into antidepressant prescribing.

Discussion. PGx testing may support more efficient, value-based care in mental health by improving prescribing precision and reducing unnecessary healthcare use. While implementation would entail notable upfront costs, especially for antidepressants widely used in adults and older adults, the long-term potential to reduce adverse drug reactions, accelerate treatment response, and improve outcomes strengthens the economic case for targeted PGx adoption.

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Development of a biologically-selective treatment for lung adenocarcinoma

A/Prof Nicola Smith

Biography:

Associate Professor Nicola J Smith is an expert in molecular pharmacology with a track record in exploring GPCR structure-function relationships in the context of cardiovascular disease and metabolic disorders, and more recently lung cancer. She is the Head of the Department of Pharmacology at UNSW Sydney, Australia, where her team works on a class of G protein-coupled receptors called 'orphan GPCRs'. Recently, her career focus has been interrogating receptor deorphanisation claims and calling for more stringent standards of evidence. Smith is the current President-elect of the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT).

Development of a biologically selective treatment for lung adenocarcinoma

Mariah R Stavrou[1], Olivia A. Clink[1], Sara Ballouz[2], Nan Li[1], Paige G. Pfeiffer[1], Joshua A Nillama[3], Luke Hunter[3], Kaavya Krishna Kumar[4], Madison Coward-Smith[5], Richard Y. Kim[5], David A. Jacques[1], Chantal Donovan[5], Nicola J Smith[1].
[1]School of Biomedical Science, UNSW Sydney, Kensington, NSW, Australia; [2]School of Computer Science and Engineering, UNSW Sydney; [3]School of Chemistry, UNSW Sydney; [4]Weill Cornell Medical College, NY, USA; [5]School of Life Sciences, University of Technology Sydney, Ultimo, NSW, Australia.

Introduction. Lung cancer remains the leading cause of cancer-related deaths in Australia, with a dismal 3% survival rate for patients diagnosed at stage IV—primarily due to treatment resistance. We have discovered that mRNA expression of the orphan G protein-coupled receptor bombesin 3 (BB_3) is increased in lung adenocarcinoma (LUAC), a subtype of non-small cell lung cancer, and not found in healthy tissue. This presents a compelling drug opportunity.
Aim. To comprehensively characterise the pharmacology of BB_3 to inform future LUAC drug development strategies.
Methods. BB_3 expression in LUAC was assessed using bioinformatics and qPCR. LUAC cell survival was evaluated in response to current standard-of-care treatments with or without BB_3 ligands, in cells expressing endogenous or exogenous BB_3, with or without BB_1 and BB_2. BB_3 signalling pathways were investigated using bioassays for canonical GPCR signalling in HEK293 cells overexpressing BB_3. BB_3 protein was subsequently purified from Expi293 cells in the presence of an antagonist for downstream applications.
Results. BB_3 was expressed in 83% of LUAC cases—more frequently than any other LUAC marker (<44%)—but showed no correlation with patient survival or known LUAC drivers. BB_3 agonism or antagonism did not influence LUAC cell viability or the efficacy of existing treatments. We found BB_3 to be constitutively active, capable of engaging multiple GPCR signalling pathways, and likely to possess an allosteric binding site. Negative stain electron microscopy confirmed successful purification of monodisperse BB_3 protein.
Discussion. BB_3 exhibits exceptional tissue selectivity and is present in the majority of LUAC cases. Our finding that BB_3 does not contribute to LUAC progression supports its use as a therapeutic conduit for cytotoxic delivery or antibody-mediated cell death. With our highly purified BB_3 protein and detailed pharmacological characterisation of BB_3 ligands, we are now positioned to develop targeted therapies via this receptor. Future work will focus on elucidating BB_3 internalisation mechanisms, characterising orthosteric and allosteric binding sites through molecular pharmacology and structural biology, and computationally designing ligand-cytotoxic or ligand-radiochemical conjugates.

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A novel model of air pollution-induced lung cancer

Dr Chantal Donovan

Biography:

Dr Chantal Donovan is a respiratory pharmacologist and Head of the ImmunoPharmacology Research Group (IPRG) at the University of Technology Sydney (UTS) and Woolcock Institute of Medical Research. She completed her PhD in Pharmacology at The University of Melbourne in 2015 and postdoctoral training at Monash University and the University of Newcastle (Immunology & Microbiology). She was awarded an NHMRC Early Career Fellowship (2017-2020) and NHMRC New Investigator grant (2018-2021) and was recruited to UTS as a faculty member in 2019.

Her research specialises in drug discovery and pharmacological testing of novel treatments for lung diseases, using novel pre-clinical models of lung cancer, asthma and chronic obstructive pulmonary disease, combined with cutting-edge techniques to measure lung physiology, pharmacology and immunological mechanisms (e.g. precision cut lung slices, flow cytometry).

She is currently on the Board of Directors of Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT) and convenes the ASCEPT Respiratory and Inflammation Special Interest Group.

A novel model of air pollution-induced lung cancer

Chantal Donovan[1,2], Meng Wang[1,2], Madison Coward-Smith[1,2], Maija R J Kohonen-Corish[2], Hui Chen[1], Brian G Oliver[1,2], Richard Y Kim[1,2]. School of Life Sciences, University of Technology Sydney[1], Sydney, NSW, Australia; Woolcock Institute of Medical Research[2], Sydney, NSW, Australia.

Introduction. Epidemiological evidence strongly associates airborne particulate matter (PM), the dust components of polluted air, with increased incidence and mortality of lung cancer. PM2.5 (PM less than 2.5 µm) from traffic related sources carries different toxic substances, such as sulfates, organic compounds, polycyclic aromatic hydrocarbons, and heavy metals, which are considered major carcinogens that increase lung cancer risk (Wang *et al Brit J Cancer* 2025). However, the mechanisms of this association are largely unexplored.

Aims. To develop a novel mouse model of air pollution and lung cancer.

Methods. Male and female A/J mice (6-8 weeks of age) were randomly allocated into 4 groups (saline, NNK [carcinogen], PM, NNK+PM; n=10-12 mice/group). Mice received IP injection of NNK (0.1mg/g; 200µL) or Saline (200µL) 3 times over 2 weeks. From week 3-26, mice were treated daily intranasal with low dose PM (10µg/50µL) or vehicle (50µL). Endpoint analyses included tumour characterisation (tumour burden, multiplicity, volume, histological analyses) and flow cytometric analysis of lung and upper airways.

Results. In PM-treated mice, tumour incidence was 16% in males and 9% in females and predominately lung adenocarcinomas. For NNK- and NNK/PM-treated mice, there was 100% tumour incidence, irrespective of sex. NNK and PM+NNK groups had similar lung tumour burden. Interestingly, females had a higher numbers of tumours per lung but these were smaller in volume, compared to males who had less tumours but larger in volume.

Discussion. Understanding the molecular drivers underpinning air pollution-induced lung cancer will provide knowledge for future drug development for the prevention of lung cancer.

Wang M (2025) Br J Cancer 2025 Jun;132(11):986-996

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TRACKER Biobank: empowering lung cancer breakthroughs

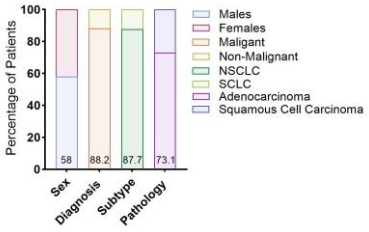
Dr Senthuran Shivakumar

Biography:

Dr. Senthuran Shivakumar is a Respiratory Physician and Clinical Pharmacologist based at Austin Health and the Olivia Newton-John Cancer Research Institute in Melbourne, Victoria. He is currently pursuing a PhD focused on identifying biomarkers for immunotherapy-related pneumonitis. Dr. Shivakumar's research investigates the intricate immunobiology underlying this form of drug-induced ILD, which is associated with significant morbidity and mortality in cancer patients. By examining the cellular, molecular, and microbial factors driving immunotherapy-related pneumonitis, his work aims to find predictive and diagnostic biomarkers as well as potential therapeutic targets that could improve management. His overall goal is to improve the survivorship of cancer patients receiving immunotherapy through improved safety and precision medicine.

TRACKER Biobank: empowering lung cancer breakthroughs

S. Shivakumar[1,2,3,4], N. Vukelic[4], F. Atashrazm[4], V. Naranbhai[5], J. Da Gama Duarte[4,5], N. Goh[1,2,3], S. Parakh[1,4] T. Leong[1,2,3,4]
1 Austin health, VIC, 2 University of Melbourne, VIC, 3 Institute for Breathing and Sleep, VIC, 4 Olivia Newton John Cancer Research Institute VIC, 5Monash University, VIC



Introduction. Lung cancer is the leading cause of cancer death in Australia, with over half of cases diagnosed advanced stage. There remains a critical lack of biospecimens to drive breakthroughs in areas of unmet need, including immunotherapy resistance and treatment-related side effects.

Aims. TRACKER is a first-of-its-kind national biobank collecting biospecimens with clinical data from lung cancer patients at diagnosis, during treatment, and at progression. Multi-omic analysis will investigate biomarkers of immunotherapy resistance and checkpoint inhibitor pneumonitis. We report findings from the first 149 participants.

Methods. Patients were recruited at Austin Health (VIC), the Royal Melbourne Hospital (VIC), Macquarie University Hospital (NSW), St Vincent's Hospital (NSW), and the Royal Adelaide Hospital (SA), with expansion planned across an additional six sites. Planned multimodal analyses include Whole Exome Sequencing, CITE-seq, FACS, metagenomics, and circulating tumour DNA.

Results. Of 149 participants (median age 65; 67.3% male), 81.6% had lung cancer, predominantly NSCLC (93.8%). Subtypes included adenocarcinoma (70.4%) and squamous cell carcinoma (25%). A total of 108 EBUS, and 256 longitudinal blood samples have been collected to date. Immunotherapy was received in 54.7% of patients; among those with response data, 70% showed early response and 30% primary resistance.

Discussion. Early findings confirm TRACKER's feasibility and its value as a unique, longitudinal national biobank supporting innovative research with the potential to significantly improve lung cancer care and outcomes.

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Sequencing approaches for improving diagnosis – insights from industry

Dr Baoming Wang

Biography:

Dr. Baoming Wang is a research fellow at the University of Technology Sydney and the Woolcock Institute of Medical Research, specialising in translational oncology and molecular diagnostics. After earning his PhD in Life Sciences from UTS in early 2021, he returned to China and spent three years in the biotechnology industry. He worked at Genetron Health Co., Ltd., a NASDAQ-listed precision oncology company, where he led the development of CE-certified RNA NGS panels (FusionCapture™ and FusionScan™) for detecting clinically actionable gene fusions. These panels have been applied in over 25,000 cancer patients and adopted by biopharma partners for clinical trial stratification and companion diagnostics. During his time in industry, he collaborated closely with clinicians from multiple hospitals and co-authored seven peer-reviewed clinical publications—six of which as co–first author. In late 2024, he returned to academia, integrating his industry experience into research on extracellular vesicles, environmental exposures, and lung cancer.

Sequencing approaches for improving diagnosis – insights from industry

Baoming Wang [1,2]

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Introduction. Conventional cancer therapies such as chemotherapy and radiotherapy remain common but are often associated with significant toxicity. In contrast, targeted therapies offer more precise and less toxic options. Their success, however, relies on accurate identification of actionable mutations, particularly gene fusions, which are key therapeutic targets across various cancers. Detecting these fusions is thus essential for enabling personalised treatment.

Aims. To develop a high-throughput, cost-effective sequencing strategy capable of efficiently detecting gene fusions across diverse cancer types, and to evaluate its translational value in clinical diagnostics.

Methods. Using hybrid-capture technology, we developed and optimised DNA- and RNA-based NGS panels (OncoPanScan™ and FusionCapture™) for fusion detection. Drawing from my experience in panel design and biomarker selection, we assessed the diagnostic performance and clinical relevance of DNA-NGS versus RNA-NGS, with a focus on their complementary value in routine oncology workflows.

Results. DNA-NGS panels are limited by intronic complexity, which restricts fusion coverage and increases panel size. In contrast, RNA-NGS panels target exonic regions, enabling more compact designs, higher fusion detection rates, and lower cost. Importantly, several DNA-detected fusions were not transcriptionally active, underscoring the clinical importance of RNA-level validation. The combined approach provided broader and more functionally relevant fusion profiling

Discussion. This work supports a sequential or combined use of DNA- and RNA-NGS in clinical practice to improve the detection of druggable fusions. The panels developed have been implemented in clinical settings and adopted by biopharma partners for patient stratification and companion diagnostics, bridging cutting-edge genomics with translational oncology.

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Nitrogen metabolism in salt-sensitive hypertension

A/Prof Jens Titze

Biography:

I began working on salt and water homeostasis as a medical student in 1991. At that time, the generally accepted belief was that body Na+ content is constant, and that any increase would elevate blood pressure. Measuring Na+ balance in humans preparing for long-term space missions, however, we found that rhythmically Na+ dis- and re-appeared from an at that time invisible storage site. Developing novel tools, we saw that rodents and humans store large amounts of Na+ under their skin and in skeletal muscle, and that the storage process is physiologically regulated. This new way of thinking about the body fluids quickly delivered new research avenues in immunology (immunological host defence and auto-immunity), endocrinology (insulin resistance, diabetes mellitus, and metabolic muscle function), and cardiovascular disease (hypertension research, heart failure).
Today, our clinical research revolves around the fact that Na+ storage is secondary to intracellular K+ depletion, and that increasing K+ intake effectively reverses this process; with beneficial effects on blood pressure. In the basic research arena, we dream of solving a general methodological-physiological root problem in the field: our inability to visualize and quantify Na+ and K+ distribution disorders inside diseased cells at the µm scale in intact, hydrated organs.

Nitrogen metabolism in salt-sensitive hypertension

Jens Titze, Signature Program on Cardiovascular Metabolic Disorders, Duke NUS, Singapore

Introduction. Nitrogen-driven water conservation is part of an evolutionary conserved body hydration principle known as aestivation. A key biological feature of this water conservation process during states of high salt intake is natriuretic-ureotelic water conservation, where nitrogen from muscle protein is biochemically transformed into water-conserving organic solute. The role of nitrogen metabolism is salt-sensitive hypertension is largely unexplored.
Aims. To test the hypothesis that experimental salt-sensitive hypertension initiates with potassium-driven water loss (Aim 1) and a negative nitrogen balance with catabolic muscle wasting (Aim 2).
Methods. We tested the effect of deoxycorticosterone acetate (DOCA; 25 mg pellet) in mice on low Na^+ diet (0.02-0.03%) with tap water, or with Na^+ in their drinking water (1% NaCl), on body Na^+, K^+, and water content 2, 6, and 12 days after treatment initiation. In addition, we monitored blood pressure (BP) with radiotelemetry, body fluid homeostasis, and renal and cutaneous blood flow. We studied the accompanying changes in body weight, stationary amino acid metabolome, and transamination and deamination enzyme activities in muscle, liver, and kidney.
Results. Aim 1: Two days after treatment initiation, DOCA NaCl treatment reduced intracellular K^+ and water content, and elevated BP; resulting in cellular dehydration. The adaptive multi-organ water conservation response included compensatory intracellular Na^+ retention, reduced dermal blood flow to reduce transcutaneous water loss, and increased fluid intake with reduced renal free-water clearance. Aim 2: This water conservation pattern was accompanied by excess mobilization of amino acids from skeletal muscle with catabolic muscle mass loss, reduced utilization of amino acid for ureagenesis in the liver, but increased renal ammonium production and excretion. As a result, the animals showed lower glucose and urea levels, but metabolic alkalosis with reduced plasma HCO_3^- levels.
Discussion: DOCA salt-sensitive hypertension initiates with K^+-driven potassium loss. The BP increase is explainable by secondary-adaptive multi-organ water conservation physiology. This water conservation response is accompanied by catabolic nitrogen mobilization from skeletal muscle, however, without an accompanying increase in hepatic ureagenesis. The nitrogen is instead excreted as ammonium, indicating a switch from hepatic gluconeogenesis/ureagenesis to preferential renal gluconeogenesis/ammoniagenesis.

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Implementing potassium-enriched salt substitutes in Australia and globally to reduce blood pressure on a population level

Prof Alta Schutte

Biography:

Alta (Aletta E.) Schutte PhD FESC FRRSAf ISHF is SHARP Professor and Principal Theme Lead of Cardiac, Vascular and Metabolic Medicine in the Faculty of Medicine and Health at UNSW Sydney, Australia. She is also the Global Co-Director of the Cardiovascular Program and Head of the Blood Pressure Program at The George Institute for Global Health. She is a NHMRC Investigator Grant Leadership Fellow. She has extensive experience in working in clinical and population-based studies with a focus on raised blood pressure, hypertension and cardiovascular disease. She has been the Chief Investigator of several multidisciplinary studies, published >500 papers in the field of blood pressure and cardiovascular disease, and supervised over 85 postgraduate students.

She is the senior author of the 2020 International Society of Hypertension Global Hypertension Guidelines. She has been acknowledged for her work as winner of several awards, most recently the 2022 Harriet Dustan Award of the American Heart Association's Hypertension Council and 2023 Peter Sleight Excellence Award in Hypertension Clinical Research from the World Hypertension League. In 2023 and again in 2024, she was recognised as the Leading Researcher in Vascular Medicine by The Australian, and in 2024 received the Fiona Stanley Award from the NHMRC as the highest ranked applicant awarded with a $5 million SYNERGY grant. She serves as Associate Editor of Hypertension and is on the Editorial Board of several major hypertension and cardiovascular journals. She is Company Secretary of the Australian Cardiovascular Alliance, Board Member of Hypertension Australia, Fellow of the European Society of Cardiology, the International Society of Hypertension and the Royal Society of South Africa, and Past President of the International Society of Hypertension (ISH). She is Co-Chair of the National Hypertension Taskforce of Australia.

Implementing potassium-enriched salt substitutes in Australia and globally to reduce blood pressure on a population level

Aletta E Schutte[1,2]. School of Population Health, University of New South Wales[1], Sydney, NSW, Australia; The George Institute for Global Health[2], Sydney, NSW, Australia.

High blood pressure remains the leading modifiable risk factor for cardiovascular disease and premature mortality worldwide. Excess sodium intake and insufficient potassium intake are major contributors, yet decades of public health efforts have achieved limited success. Potassium-enriched salt substitutes – typically comprising 75% sodium chloride and 25% potassium chloride – offer a practical, scalable solution by simultaneously reducing sodium and increasing potassium intake. Evidence from large, randomized trials and meta-analyses demonstrates that replacing regular salt with potassium-enriched salt lowers systolic blood pressure by approximately 4–5 mmHg and reduces major cardiovascular events and mortality by 11–13%. Acceptability is high, with long-term adherence exceeding 90% in pragmatic trials.

Despite strong evidence and World Health Organisation endorsement, global guideline recommendations remain inconsistent. A recent review of 32 hypertension guidelines found universal advice for sodium reduction, but only four mentioned potassium-enriched salt and two recommended its use. Recent updates from the European Society of

Hypertension (2023), European Society of Cardiology (2024), and American Hypertension Guidelines (AHA/ACC)(2025) now include specific recommendations.

In a recent position statement, the National Hypertension Taskforce of Australia advocates for incorporating potassium-enriched salt into Australian hypertension guidelines and promoting its use across clinical and food industry settings. This simple intervention could deliver substantial population-wide blood pressure reductions and cardiovascular benefits, provided contraindications such as advanced kidney disease are managed through routine screening.

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Salty guts: A high salt diet promotes atherosclerosis through a gut-bone marrow axis

Prof Andrew Murphy

Biography:

Professor Andrew Murphy obtained a BSc(Hons) in Biotechnology from the Queensland University of Technology (QUT) in Brisbane and a PhD (Monash University) at the Baker Heart and Diabetes Institute, funded by an industry scholarship from the Swiss biotech company Actelion. During this time, he discovered an anti-inflammatory role for HDL on circulating monocytes and neutrophils both published in ATVB. Upon completing his PhD, Andrew moved to Columbia University in New York under Professor Alan Tall, where he was funded by a prestigious American Heart Association Fellowship. His work shifted to examining the role of cholesterol efflux pathways on the proliferation and mobilisation of haematopoietic stem cells (HSCs) in the bone marrow. Specifically, he defined a cell-intrinsic role for ApoE in regulating HSC proliferation and showed that increased numbers of circulating monocytes resulted in larger lesions, which was published in the Journal of Clinical Investigation. He also discovered the haematopoietic role of the cholesterol transporter ABCG4 in platelet production and atherosclerosis, along with defining an important feedback loop for the thrombopoietin receptor c-MPL, published in Nature Medicine.

Professor Murphy also initiated several collaborations in New York, in particular with Professor Ira Goldberg and Professor Edward Fisher (NYU) along with A/Professor Prabhakara Nagareddy (University of Oklahoma Health and Sciences Center) to explore the mechanisms of diabetes (hyperglycaemia) on monocyte production. They were the first to show that the novel glucose-lowering agent (SGLT2 inhibitors) could reduce circulating monocyte levels and facilitate atherosclerotic lesion regression. They discovered the damage associated molecular pattern molecules as important mediators of this event. These studies published in Cell Metabolism have triggered an extensive and collaborative research program run by these investigators with publications in Cell Metabolism, Circulation and Circulation Research, Journal of Clinical Investigation, etc.

Salty guts: A high salt diet promotes atherosclerosis through a gut-bone marrow axis

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Introduction. Salt intake is often associated with increased risk of cardiovascular disease through its relationship with hypertension. However, a high salt diet (HSD) can directly modulate immune cells.

Aims. We aimed to determine if a HSD promoted atherosclerosis independent of blood pressure and the associated mechanisms.

Methods. Using various mouse model fed a normal or HSD we explore guy health, immune cell abundance (floe cytometry) and atherosclerosis.

Results. We found that a HSD increases IL-17A-producing T helper (T_H17) cells in the bone marrow (BM), which promotes hematopoietic stem and progenitor cells (HSPCs) mobilization into the spleen, expanding the population of monocytes to impact atherosclerosis. We discovered that a HSD causes gut permeability, increases gut T_H17 cells which is associated with microbial dysbiosis. To explore how the HSD-induced effects in the gut influences HSPC mobilization, we took a stepwise approach, first blocking T_H17 cell migration from the gut with anti-CCL20. This resulted in a reduction in T_H17 cells in the BM and HSPC mobilization. We then blocked intestinal permeability using AT-1001 (Larazotide), demonstrating that dampening permeability prevented HSD-induced HSPC mobilization. Moreover, restoring the microbiome with prebiotics increased microbial diversity, decreased gut permeability and T_H17 cell abundance, which was associated with a reduction in BM T_H17 cells, an improvement in the BM microenvironment and retention of HSPCs within the BM. Finally, to determine how dampening gut inflammation influences HSD-induced atherosclerosis, we placed *Apoe*$^{-/-}$ mice on a NSD or HSD with or without prebiotics for 12 weeks. We found that supplementing HSD-fed mice with prebiotics not only decreased T_H17 cells in the gut, blood, and BM, but also prevented HSPC mobilization from the BM to the blood and spleen, thereby reducing myelopoiesis and atherosclerosis.

Discussion. This suggests that targeting the gut using prebiotics can reduce T_H17-driven myelopoiesis and atherosclerosis.

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Sodium & Sensibility: The Gendered Tale of Salt Regulation

Dr Zoe Mcardle

Biography:

Dr Zoe McArdle is a research fellow in Cardiovascular Disease Program, Monash Biomedicine Discovery Institute and the Department of Physiology, Monash University. Zoe's research focusses on maintaining kidney health and blood pressure throughout life. Hypertension is both a cause and consequence of chronic kidney disease. It damages the kidneys over time, and impaired kidney function can further elevate blood pressure, creating a vicious cycle. To-date my research has unveiled key mechanisms underlying the progression of kidney disease and hypertension. These include whether adverse events in-utero, that can lead to elevated cardiovascular disease risk in the future, can be re-programmed in the early post-natal period (JASN), the role of the renal nerves in hypertension and kidney disease (J Am Coll Cardiol). Current work focuses on understanding sex differences in blood pressure salt sensitivity and the role of the kidney transport profile in the response to high sodium intake.

Sodium & Sensibility: The Gendered Tale of Salt Regulation.

Zoe McArdle. Cardiovascular Disease Program, Monash Biomedicine Discovery Institute and the Department of Physiology, Monash University, Melbourne, Vic, Australia

Sex differences in sodium regulation are a compelling example of how biological sex influences core physiological processes. Emerging evidence reveals distinct profiles of sodium transporters in the kidney: males predominantly express NHE3 in the early proximal tubule, promoting sodium reabsorption, whereas females exhibit greater ENaC activity in the distal nephron, thereby enhancing fine-tuned sodium excretion. These differences contribute to sex-specific responses to dietary salt intake and sodium loading.

Women, particularly postmenopausal women, are more sensitive to salt than men, exhibiting greater increases in blood pressure in response to high sodium intake. This heightened sensitivity is linked to hormonal changes, endothelial dysfunction, and altered activation of the renin-angiotensin-aldosterone system. Additionally, females tend to excrete sodium loads more efficiently, a process influenced by estrogen and progesterone, which regulate the renal and gastrointestinal handling of sodium and water.

Understanding these sex-based differences in sodium regulation is critical for developing personalised strategies in managing hypertension and fluid balance disorders. This talk examines the nuanced mechanisms by which males and females regulate sodium balance, with implications for blood pressure control and fluid homeostasis.

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Therapeutic Potential of Human Amnion Epithelial Cells for Improving Post-Stroke Cognitive Outcomes

Mr David Wong Zhang

Biography:

David Wong Zhang is a final year PhD Candidate from the Centre of Cardiovascular Biology and Disease Research (led by Prof. Grant Drummond and Prof. Chris Sobey). He completed his Master of Science in 2021 in the department of Microbiology, Anatomy, Physiology and Pharmacology at La Trobe University. David has received recognition of his work through awards from the Australian & New Zealand Microcirculation Society (ANZMS), and Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT).

Alongside his PhD, David is an anatomy and physiology demonstrator and is passionate about research and education. His current research focuses on the use of human amniotic epithelial cells as therapy for stroke, using techniques such as neurobehavioral testing, immunohistochemistry, RT-qPCR, and single-cell transcriptomics to uncover the mechanisms of cognitive repair.

Therapeutic Potential of Human Amnion Epithelial Cells for Improving Post-Stroke Cognitive Outcomes

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Introduction. Stroke is a leading cause of death and long-term disability worldwide. Up to 70% of stroke patient will experience cognitive impairment after stroke. However, there are limited treatment options to improve cognition following stroke. Due to their multiple protective effects, human amnion epithelial cells (hAECs) are an attractive candidate for stroke therapy. Whether hAECs improve post-stroke cognitive impairment remains unknown.

Aims. This study aims to investigate the long-term cognitive outcomes of hAEC treatment post-ischaemic stroke. Furthermore, to determine the mechanisms by which hAECs contribute to their pro-cognitive effects.

Methods. Male C57Bl/6 mice randomly assigned to undergo either sham or stroke surgery targeting the prefrontal cortex. Saline or hAECs (1 x 10^6 cells IV) was administered 24 h later. Cognition was assessed using the Barnes maze 36 d days later. Brain injury was evaluated using histology and transcriptomic changes relating to synaptic plasticity and cognitive processes was analysed using single-cell RNA sequencing and validated by qPCR.

Results. In the Barnes maze, delayed escape latency (EL) was observed in stroke+saline (day 5 EL=106±20s, $P>0.05$) but not stroke+hAEC (day 5 EL=66±12s, $P>0.05$) compared with sham mice. Infarct volume was significantly reduced following hAEC treatment (1.3±0.2 vs 0.4±0.2mm3, $P<0.05$).

Conclusion. Early hAEC administration following stroke attenuates cognitive impairment and reduces brain injury. The combination of behavioural improvements, reduced infarct pathology, and distinct transcriptomic changes supports hAEC as a promising therapeutic approach for preventing stroke-induced cognitive decline.

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FPR2 agonist attenuates pulmonary arterial hypertension and right ventricular dysfunction in mice

Miss Ting Fu

Biography:

Ting is a third-year PhD student at the Monash Institute of Pharmaceutical Sciences, where she has the privilege of working under the esteemed guidance of a dynamic team of researchers, including Dr. Chengxue Helena Qin, Professor Rebecca Ritchie, Associate Professor Barbara Kemp-Harper, and Dr. Peishen Elva Zhao. Her research focus is centred on unravelling the intricate regulation of formylpeptide receptors, with a particular emphasis on their role in Cardiopulmonary diseases

FPR2 agonist attenuates pulmonary arterial hypertension and right ventricular dysfunction in mice

Ting Fu[1], Chloe Landy[1], Yuchi Sun[1], Miles J De Blasio[1], Jaideep Singh[1], Anida Velagic[1], Owen L Woodman[1], Barbara Kemp-Harper[2], Peishen Zhao[1], Rebecca H Ritchie[1,2], Chengxue Qin[1*]. [1]Drug Discovery Biology and [2]Department of Pharmacology, Monash Univ, VIC; Australia.

Introduction. Pulmonary arterial hypertension (PAH) is characterised by vascular remodelling, including intimal hyperplasia, fibrosis, and inflammation, which progressively increase pulmonary vascular resistance and vasoconstriction. The selective FPR2 agonist BMS-986235 enhances pro-resolving macrophage activity and improves cardiac remodelling post-myocardial infarction[1], but its therapeutic potential in PAH remains unknown.

Aim. To investigate the therapeutic effects of FPR2 agonist in preventing PAH progression.

Methods. Male C57BL/6J mice (9 weeks old) were allocated to normoxia (21% O_2) or sugen/hypoxia (SuHx, 10% O_2 plus weekly sugen 5416, 20 mg/kg) for 4 weeks. The SuHx cohort was randomly divided into three groups: (i) treatment-vehicle, (ii) BMS-986235 (3mg/kg/day), or standard clinical treatment (iii) sildenafil (0.3mg/kg/day). The normoxia cohort received the treatment-vehicle (10% DMSO in 0.8% Tween 80 in saline). At experimental endpoint, haemodynamics were assessed, and lungs and hearts were collected for histological and molecular analyses.

Results. SuHx mice displayed elevated right ventricular systolic pressure (RVSP), decreased tricuspid annular plane systolic excursion (TAPSE), complete muscularisation of small pulmonary arteries, and upregulated pro-inflammatory gene expression (*mIl-6*) in the lungs. BMS-986235 treatment reduced RVSP, increased TAPSE, limited pulmonary arterial muscularisation, and downregulated *mIl-6* and *mTnf-α* expression, comparable to or exceeding the effects of sildenafil.

Discussion. Our study demonstrates that BMS-986235 lowers RVSP and limits vascular remodelling, similar to current clinical therapies, while additionally reducing inflammation and preserving RV function, highlighting its potential advantages beyond haemodynamic improvement.

	Normoxia + Vehicle	SuHx + Vehicle	SuHx + BMS-986235	SuHx + Sildenafil
RVSP (mmHg)	25±1 (n=12)	40±2**** (n=12)	34±2$$$ (n=16)	30±1$ (n=13)
TPASE (mm)	1.03±0.06 (n=16)	0.56±0.06*** (n=19)	0.78±0.04 (n=15)	0.69±0.05 (n=13)
PA muscularisation (%)	15.0±4.2 (n=5)	57.0±7.5*** (n=5)	26.0±7.0$$ (n=5)	33.1±5.2$ (n=6)
M*il-6* (fold increase)	1.0±0.2 (n=11)	1.9±0.3* (n=13)	0.9±0.3$ (n=11)	1.0±0.3 (n=10)
m*Tnf-α* (fold increase)	1.0±0.2 (n=11)	1.8±0.5 (n=13)	0.8±0.2$ (n=11)	1.0±0.1 (n=10)

*P<0.05, ***P<0.001, ****P<0.0001 vs Normoxia + vehicle;$P<0.05, $$P<0.01,$$$P<0.001 vs SuHx + vehicle, (One-way ANOVA with Šídák's multiple comparisons test). RVSP: Right ventricular systolic pressure, TAPSE: Tricuspid annular plane systolic excursion, PA: Pulmonary arteries, m*il-6*: Interleukin6, m*Tnf-α*: Tumour necrosis factor-α.

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IRAP – A novel target in the treatment of Pulmonary Arterial Hypertension

Miss Supitchaya Watakul

Biography:

Supitchaya (Leena) is a second-year PhD student in the Department of Pharmacology at Monash University as part of the IRAP Pharmacology Group and Cardiovascular and Pulmonary Pharmacology Group. Her area of research focuses on identifying novel therapeutic targets to treat Pulmonary Hypertension (PH). After completing her Honours at Monash, she worked as a research assistant at the Garvan Institute of Medical Research, testing compounds in preclinical mouse models of pancreatic cancer. Now, she continues her work in PH, investigating IRAP as a novel therapeutic target. This involves testing IRAP inhibitors and performing right heart catheterisation in mouse models of PH, and utilising immunohistochemistry to explore pathological changes within the lungs. She hopes to contribute to cardiovascular therapeutic testing and discover novel treatments to improve patient outcomes.

IRAP – A novel target in the treatment of Pulmonary Arterial Hypertension

Supitchaya Watakul[1], Peng-Cheng Wang[1], Jana Goldenberg[1], Robert E Widdop[1], Barbara K Kemp-Harper[1] and Tracey A Gaspari[1]. Dept of Pharmacol, Monash University[1], Clayton, VIC, Australia.

Introduction. Pulmonary Arterial Hypertension (PAH) is a progressive and incurable disease with a high mortality rate. Current vasodilator therapies modestly lower pulmonary arterial pressure yet have limited ability to halt or reverse the cardiopulmonary remodelling associated with the disease. Insulin-regulated aminopeptidase (IRAP) inhibitors have demonstrated vasoprotective, anti-inflammatory and anti-fibrotic actions in multiple preclinical cardiovascular disease models and thus present as a potential novel treatment for PAH, a disease characterised by inflammation, vascular remodelling and right ventricular hypertrophy (RVH).

Aims. To investigate IRAP inhibitors as a novel treatment for PAH in a murine pre-clinical model.

Methods. PAH was induced in male and female C57BL/6J mice using the gold standard sugen-hypoxia (SuHx; 42 days, 10% O_2) model. Lung IRAP expression was assessed during the development of PAH (14, 21, 35 and 42 days, n=6-9/timepoint) using immunofluorescent staining. Subsequently, SuHx mice were treated with the IRAP inhibitor, HFI-419 (0.72mg/kg/day; minipump) or the current standard-of-care, the phosphodiesterase 5 (PDE5) inhibitor, sildenafil (30mg/kg/day; oral) from day 21 to 42 (n=5-6/group). Endpoint measures included: right ventricular systolic pressure (RVSP), RVH and histological analysis of pulmonary vascular remodelling.

Results. Lung IRAP expression was ~6-fold higher in normoxic females compared to males. However, IRAP expression increased up to 10-fold throughout the time course of PAH development in male but not female mice, such that IRAP expression in males at day 42 was similar to that of females at day 42. The SuHx model was associated with increased RVSP, RVH, pulmonary vessel wall thickness and lung weight in both sexes. Treatments did not decrease RVH or lung weight/tibial length ratio in male and female SuHx mice. In male SuHx mice, both sildenafil and HFI-419 reduced RVSP (38.6±1.4 and 38.8±1.1 vs 45.2±1.7 mmHg respectively; $P<0.05$). By contrast, none of the treatments reduced RVSP in female SuHx mice. Interestingly, targeting IRAP inhibitors significantly reduced pulmonary vessel wall thickness ($P<0.01$) in SuHx male and female mice, an effect not observed with the PDE5 inhibitor sildenafil.

Discussion. IRAP inhibition shows promise as a novel target for vascular remodelling in PAH in both males and females. Future studies will explore the efficacy of IRAP inhibitors in combination with the current standard-of-care (sildenafil).

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Characterising BB3: a novel therapeutic target in lung adenocarcinoma

Miss Mariah Stavrou

Biography:

Mariah is a final year PhD candidate at UNSW Sydney, supervised by A/Prof Nicola Smith. Her research focuses on the molecular pharmacology of BB3, an understudied G protein-coupled receptor with untapped therapeutic potential in lung cancer. Since 2023, she has served as Treasurer of the ASCEPT Student Committee, where she has organised career workshops and networking dinners for students at the annual ASCEPT conferences.

Characterising BB_3: a novel therapeutic target in lung adenocarcinoma

Mariah R Stavrou[1], Olivia A. Clink[1], Sara Ballouz[2], Joshua A Nillama[3], Luke Hunter[3], Madison Coward-Smith[4], Richard Y. Kim[4], Chantal Donovan[4], Nicola J Smith[1]. School of Biomedical Sciences, UNSW Sydney[1], Kensington, NSW, Australia; School of Computer Science and Engineering, UNSW Sydney[2]; School of Chemistry, UNSW Sydney[3]; School of Life Sciences, UTS[4], Sydney, NSW, Australia.

Introduction. Highly innovative strategies are urgently needed to target lung cancer, one of the biggest killers of Australians. Early evidence suggests that the orphan G protein-coupled receptor, bombesin 3 (BB_3), may be overexpressed in lung cancer and absent in healthy tissue. We seek to improve outcomes for lung adenocarcinoma (LUAC), a subtype of non-small cell lung cancer, by exploiting the biological selectivity of BB_3.

Aims. To deconvolute the expression, activation and signal transduction of the poorly defined receptor, and then determine any possible interactions between BB_3 ligands and standard therapeutics.

Methods. To determine the extent of BB_3's biological selectivity, gene expression data was mined from RNA-sequencing databases. To validate the pharmacological properties of BB_3, the following assays were used: reporter gene assays to investigate $G\alpha_{q/11}$, $G\alpha_{12/13}$, and $G\alpha_s$ signalling; NanoBiT assay for β-arrestin recruitment; and BRET1-based biosensors for ERK1/2 phosphorylation and cAMP accumulation. To assess the impact of BB_3 activity in cancer, a panel of lung cancer cell lines was assessed for BB_3 expression via qPCR, and the effect of agonist stimulation was measured using the CellTiter-Glo cell viability assay.

Results. BB_3 mRNA was found exclusively in LUAC, and not in healthy human tissue. BB_3 expression in LUAC was more prevalent (83%) than any other LUAC marker (<44%). BB_3 signals in the absence of ligand via the $G\alpha_{q/11}$, $G\alpha_{12/13}$, and $G\alpha_s$ pathways (Emax = 439.8, 174.2, 118.7 RLU respectively), and agonism increases Ca^{2+} (MK-5046 pEC_{50} = 8.75, BAG-1 pEC_{50} = 9.63). Cell lines expressing BB_3 were susceptible to traditional cancer therapies, but targeted BB_3 ligands had no effect on cell viability.

Discussion. BB_3 appears to be a cell-surface biomarker of LUAC, making it an ideal candidate for selective targeting in a disease with high treatment resistance. By characterising BB_3's pharmacology and demonstrating its selective expression in LUAC, we provide a strong foundation for the future development of BB_3-targeted therapies.

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Protection in IRAP deficient mice differs between photothrombotic and MCAO induced stroke

Ms Rianna Tadd-Lennox

Biography:

Rianna Tadd-Lennox is a second-year PhD student in the Department of Pharmacology, Monash University. She is passionate about neuropharmacology and cardiovascular research, and her work aims to reduce the devastating neurological deficits that follow ischemic stroke. Her research utilizes the photothrombotic model of stroke to assess the impacts of targeting insulin-regulated aminopeptidase (IRAP) as a novel ischemic stroke therapeutic. Ultimately, her work aims to bridge the gap between preclinical discoveries and clinical treatments to improve outcomes for stroke patients.

Protection in IRAP deficient mice differs between photothrombotic and MCAO induced stroke.

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Introduction. Ischemic stroke is a major cause of death and disability. The only pharmacological treatment is the clot buster, recombinant tissue plasminogen activator, which <10% of Australian patients are eligible to receive[1]. Insulin-regulated aminopeptidase (IRAP) is a potential target for treatment, with IRAP deletion and IRAP inhibition protecting against damage induced by middle cerebral artery occlusion (MCAo) in mice[2] and spontaneously hypertensive rats[3] respectively. These benefits are yet to be tested in females or in models of cerebral microvascular occlusion.

Aims. To investigate the effect of IRAP gene deletion on photothrombotic stroke outcomes in male and female mice.

Methods. Photothrombotic stroke was induced in IRAP wild type (WT) and knock out (KO) male and female mice (n= 10/group, aged 6-8 months). Motor and sensory function were assessed at baseline and days 1 and 3 following surgery using the hanging wire and adhesive removal tests. At 3 days post-surgery, mice were culled, and brains were taken for analysis of infarct volume and expression of IRAP, activated astrocytes, and apoptosis.

Results. Photothrombotic stroke induced significant infarct in the cortex, impaired function, and increased levels of neuroinflammation and apoptosis. Male mice had significantly larger infarcts (WT:22.90 ±2.19 mm^3, KO: 23.97 ± 2.90 mm^3) than female mice (WT: 16.7 ±1.82 mm^3, KO: 18.53 ± 2.48 mm^3). IRAP deletion protected against weight loss in male mice; however, for all other outcomes, there was no genotype. Interestingly in the peri-infarct region of WT female mice had higher IRAP expression than male mice (9.11±1.07% vs 4.28 ± 0.58%)

Discussion. IRAP gene deletion did not protect against photothrombotic stroke. This contrasts with previous protection against MCAO-induced ischemic damage with IRAP gene deletion and IRAP inhibition, potentially due to lack a lack of penumbral region and contralateral blood flow in photothrombotic stroke. This suggests that part of the protection of IRAP gene deletion/inhibition may result from partial restoration of cerebral blood supply to the ischemic region.

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Modeling acute silica-induced inflammation using precision-cut lung slices

Miss Varuni Premaratne

Biography:

Varuni Premaratne holds a Bachelor of Medicine and Bachelor of Surgery and has over three years of clinical experience across anaesthesia, intensive care, surgery, and internal medicine. Building on this foundation, she is currently completing a Master of Biomedical and Health Science at Monash University, where her research focuses on developing a novel precision-cut lung slice model of silicosis to explore pharmacological responses in ex vivo tissue.

Her dual background in medicine and biomedical science fuels her passion for translational research, particularly in bridging laboratory findings with clinical application to improve patient care. She aspires to develop her career as a clinician-researcher, combining her clinical insight and scientific training to drive innovative research that enhances health outcomes and directly benefits patients.

Modeling acute silica-induced inflammation using precision-cut lung slices

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Introduction. Silicosis is an occupational lung disease caused by the inhalation of respirable crystalline silica, characterized by chronic inflammation and progressive massive fibrosis. Current *in vivo* and *in vitro* models present limitations in replicating the pathophysiological features of silicosis, hindering the development of effective therapies.

Aims. To establish a novel *ex vivo* model to investigate acute inflammatory responses in both mouse (mPCLS) and human (hPCLS) precision-cut lung slices exposed to different types of commercial silica.

Methods. PCLS from male C57BL/6 mice (n=5) and human lung tissue resections (n=5) were untreated (control) or treated with silica (Min-U-Sil 5, NIST 1878b or quarry-derived DQ12) at 200 or 400 µg/mL, in the absence or presence of lipopolysaccharide (LPS; 10ng/mL) for 5 days. PCLS viability (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay; MTT) and silica-induced cytotoxicity (lactate dehydrogenase assay; LDH) were assessed. Silica uptake was determined via polarized light microscopy, and secretion of cytokines (TNFα, IL-6, IL-1β, IL-10, TGF-β) and procollagen were quantified by ELISA of PCLS conditioned media. Collagen deposition (Masson's trichrome), macrophage number (F4/80), and α-SMA expression were assessed in fixed histological sections of PCLS.

Results. Viability of mPCLS and hPCLS was preserved with all silica treatments, but high cytotoxicity was observed with DQ12 and NIST 1878b silica (mPCLS). Macrophage uptake of Min-U-Sil 5, NIST 1878b, and DQ12 was confirmed in both mPCLS and hPCLS, with cell aggregation around silica particles and evidence of activated and foamy macrophages, apoptotic bodies, and macrophage disintegration visualised by histology in mPCLS. Silica-induced cytokine secretion of IL-1β, TNF-α, and IL-10 was highest in DQ12-treated hPCLS co-stimulated with LPS. Despite modest increases in procollagen secretion, there was no collagen deposition or increased α-SMA expression in silica-treated mPCLS regardless of LPS, at the 5-day endpoint.

Discussion. Silica treatment of PCLS effectively induced acute inflammation, recapitulating aspects of the initiation of silicosis, but without establishing fibrosis. This model could be utilised to compare the damaging effects of exposure to different types of silica, study mechanisms driving early silicosis, and screen novel therapeutics.

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Effects of prebiotic HAMSAB supplementation on 24-hour ambulatory blood pressure indices

Dr Rikeish R Muralitharan

Biography:

Dr. Rikeish R. Muralitharan (rikeish.bsky.social & @rikeishm) is a research fellow who completed his PhD in 2023 at the Hypertension Research Lab at Monash University under the supervision of Prof. Francine Marques, Prof Charles Mackay, and Dr Joanne O'Donnell. Driven by a passion for discovery science, Rikeish embarked on his PhD journey after completing a medical degree and clinical training in Malaysia. Dr. Muralitharan's research focuses on leveraging the gut microbiota and host signalling of gut microbiota-derived metabolites to develop innovative treatments for hypertension and other cardiovascular diseases.

Currently he is leading the GRAINS-BP trial investigating the role of the gut-brain axis in mediating the beneficial effects of dietary fibre supplement in blood pressure regulation. Beyond the lab, he enjoys walking and traveling, finding inspiration in exploring new places and experiences.

Effects of prebiotic HAMSAB supplementation on 24-hour ambulatory blood pressure indices

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Introduction. The gut microbiome has emerged as a non-traditional risk factor for hypertension. We recently demonstrated that supplementation with microbial metabolites acetate and butyrate using high-amylose maize starch – acetylated and butyrylated (HAMSAB) significantly reduced 24-hour systolic blood pressure (SBP) in untreated hypertensive participants, independent of age, sex, and BMI. The primary endpoint, 24-hour SBP, was reduced by –6.1 mmHg, equivalent to a single anti-hypertensive medication. Other ambulatory blood pressure monitoring (ABPM) indices acquired in this study, such as nocturnal dipping, pulse wave velocity (PWV), and reflection magnitude (RM), are predictors of cardiovascular risk but have not been evaluated with microbial interventions.

Aims. To investigate whether HAMSAB supplementation influenced additional BP and vascular indices measured via ABPM, and to explore associations between these indices and gut microbial composition.

Methods. In a double-blind, randomised, placebo-controlled, crossover trial, 20 participants (mean age 55.8±11.2 years, 30% female) underwent ABPM at baseline and after each 3-week intervention (placebo and HAMSAB). We evaluated systolic/diastolic dipping, percentage of time above normal BP limits, PWV, and RM.

Results. Compared to placebo, HAMSAB did not alter 24-hour PWV (placebo-subtracted effect: 8±1.4 m/s, P=0.063), RM (66.5±4.4%, P=0.066), or percentage of time with SBP (42.6±26.7%, P=0.154) and DBP (47.5±28.1%, P=0.281) above normal limits. No differences were seen in systolic (13.6±6.4%, P=0.874) or diastolic (17.8±7%, P=0.359) dipping. Similar associations were observed in both day and night indices. However, exploratory analyses revealed that PWV inversely correlated with the relative abundance of the genus *Coprobacter*, a known short-chain fatty acid producer (q=0.00328, adjusted for age, sex, BMI, and diet).

Discussion. HAMSAB lowered 24-hour SBP but did not significantly affect other ABPM-derived indices over 3 weeks. This may reflect limited power, short intervention, or a brachial SBP–specific effect. Importantly, the association between PWV and *Coprobacter* suggests that vascular stiffness may be linked to specific gut microbial taxa, highlighting a potential pathway for future microbiome-targeted interventions. Larger and longer studies are needed to assess whether supplementation with microbial metabolites modulates additional cardiovascular risk markers.

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IRAP Inhibition as a Novel Anti-Fibrotic Strategy for Post-MI Heart Failure

Dr Yan Wang

Biography:

Dr Yan Wang is an Early Career Researcher who has a strong passion for translational drug discovery. Yan has extensive experience in cardiovascular/renal pharmacology (both in vivo and in vitro). Her research focuses on novel treatments for cardiovascular and renal diseases, especially for end-organ damage (fibrosis) affecting the heart and kidney. Yan's PhD work successfully led to a patent filing in 2018, on which she is one of the co-inventors. Yan has published 10 peer reviewed articles.
Yan has presented her research in > 15 national and international conferences and has received >13 competitive awards. Yan has a strong passion about inspiring the next generation of scientists. She has (co)supervised 9 undergraduate research students, 5 Honours students and 2 Masters students.

IRAP Inhibition as a Novel Anti-Fibrotic Strategy for Post-MI Induced Heart Failure

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Introduction. Cardiac fibrosis is directly linked to reduced cardiac function that results in chronic heart failure (HF), which is responsible for ~15% of all deaths in Australia in 2022 (AIHW). This underpins the need for effective anti-fibrotic therapies, as current treatments slow down progression to HF but do not stop or reverse the damage.
Aims. This study aims to identify novel anti-fibrotic drugs and test their protective effects on MI-induced HF in mice.
Methods. A high-content 96-well plate imaging assay was developed using transforming growth factor (TGF)-β1-stimulated human cardiac fibroblasts (HCFs). Cells were stained with fibrotic markers (collagen, α-SMA), DAPI, and CellMask, then imaged via the Opera Phenix automated microscopy. Harmony software was trained to distinguish fibrotic from non-fibrotic cells based on cell/nuclei area, texture, intensity, and marker staining. The most effective anti-fibrotic compound was then evaluated in a 7-day myocardial infarction (MI) mouse model, assessing cardiac fibrosis (picrosirius red), function (echocardiography), injury (troponin, caspase-3), inflammation (CD68), myofibroblast presence (α-SMA), and cellular senescence (p21) via immunohistochemistry.
Results. TGF-β1 (1 ng/ml) induced a pro-fibrotic phenotype in HCFs after 72 hours, increasing fibrotic cells from 25% to 70%. Among 30 compounds tested, three IRAP inhibitors showed stronger anti-fibrotic effects than standard HF therapies. The IRAP inhibitor, AL-11, reduced TGF-β1-induced fibrosis by ~30%, compared to <10% reduction by AT1R antagonists, ACE inhibitors, SGLT2 inhibitors, and ARNI. IRAP expression was upregulated 5-fold in infarcted mouse hearts and correlated with elevated IRAP gene expression in human aortic stenosis tissue. AL-11 (0.72 mg/kg/day) significantly suppressed IRAP expression, reduced MI-induced fibrosis (15.5% to 9.7%), myofibroblast differentiation, and cellular senescence (*$p < 0.05$ vs MI, n=4). AL-11 also prevented MI-induced cardiac injury, apoptosis, and inflammation, leading to reduced infarct size and improved ejection fraction (from 39% to 49% post-MI).
Discussion. High-content imaging identified IRAP inhibitors as superior to standard HF therapies in reducing fibrosis. This study demonstrates a potential correlation between increased IRAP expression and fibrotic cardiac disease whilst highlighting inhibition of IRAP as a potential effective treatment for cardiac fibrosis and HF.

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Low dietary fibre: a sex-dependent regulator of inflammation and blood pressure

Dr Joanne O'Donnell

Biography:

Dr O'Donnell is an NHMRC Early Career Research Fellow and co-deputy lab head in the Hypertension Laboratory, Monash University, with A/Prof Francine Marques. She completed her PhD at WEHI, Melbourne, and postdoctoral studies at the University of Massachusetts Medical School, Boston, where she studied the interplay between cell death, immune cell activation and autoimmune disease. Her research focuses on understanding the interplay between the gut microbiome and the immune system during hypertension.

Low dietary fibre: a sex-dependent regulator of inflammation and blood pressure

Joanne A. O'Donnell[1,2], Wendy Qin[1,2], Rikeish R Muralitharan[1,2], Chudan Xu[1,2], Evany Dinakis[1,2], Simona Antonacci[1,2], Dovile Anderson[3], Matthew Snelson[1,2], Francine Z. Marques[1,2]. 1. Hypertension Research Laboratory, Department of Pharmacology, Biomedical Discovery Institute, Monash University, Clayton, VIC, Australia; 2. Victorian Heart Institute, Monash University, Clayton, VIC, Australia; 3. Monash Proteomics and Metabolomics Facility, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, VIC, Australia.

Introduction. Dietary fibre lowers blood pressure (BP) via the gut microbiome, through the production of the metabolites short-chain fatty acids (SCFAs), which are potent immunomodulators. Suboptimal fibre intake, which is observed in 9 out of 10 Australians, contributes to hypertension development. However, how fibre deficiency promotes hypertensive development remains unknown.

Aims. To investigate how long-term low fibre intake impacts BP and the immune system in mice.

Methods. Male and female C57BL/6 mice were fed a control or low fibre diet from weaning to 6 or 12 months of age (N=8-10/sex/diet/timepoint). BP was assessed by non-invasive CODA tail-cuff every 2-3 weeks. Body composition was determined by EchoMRI. Gut permeability was assessed using FITC-dextran. Deep immunoprofiling was performed in the spleen and aorta using flow cytometry by Cytek Aurora. Caecal SCFAs were quantified by mass spectrometry.

Results. 12 months of low fibre intake did not alter BP, body composition or gut permeability. Male mice on a low fibre diet for 6 months had elevated splenic NK cells (P=0.049) and CD4+ T cell subsets (P=0.045). Aortic macrophages (P=0.033), neutrophils (P=0.013) and monocytes (P=0.015) were also increased. While splenic or aortic inflammation was not evident at 12 months, splenic CD8+ T cells with an exhausted phenotype were elevated (P=0.045). Conversely, no changes to immune profiles were evident in female mice at 6 or 12 months. The SCFA butyrate was decreased in the caecum of low fibre-fed males (P=0.001), whereas propionate was lower in females (P=0.02) at 12 months, compared to those fed a control diet.

Discussion. Long-term intake of low dietary fibre promotes inflammation in male, but not female, mice. This inflammation progressed into an exhausted T cell profile, where T cells progressively lose their effectiveness. The sex differences in inflammation correlated with sex-specific changes in SCFA production. This suggests the inflammation is driven by lack of specific SCFAs, which underlies the susceptibility to hypertension caused by low dietary fibre intake.

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Ad hoc use of home blood pressure monitoring undermines clinical utility

Dr Annika Wilson

Biography:

Dr Annika Wilson is a clinical dentist and postdoctoral research fellow at the University of Tasmania. Her work focuses on public health and cardiovascular disease, using mixed-methods and implementation science approaches. She also lectures in the Tasmanian School of Medicine and Public Health Programs and has published across health and exploratory research.

Ad hoc use of home blood pressure monitoring undermines clinical utility

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Introduction. Hypertension guidelines recommend home blood pressure monitoring (HBPM) using a standardised protocol to ensure accuracy and guide effective management. However, the extent to which HBPM is performed according to standardised protocol is unclear.

Aims. This study aimed to explore how HBPM is used and understood by both health professionals and community members who regularly engage in BP monitoring.

Methods. A targeted, inductive content analysis to identify themes related to HBPM was undertaken from data collected at 19 co-design workshops with primary health professionals (general practitioners, general practice staff, nurses, health workers, pharmacists, n=85) and community members (adults with known or suspected hypertension, n=61). Workshops explored experiences with HBPM, perceptions of accuracy, and practices in BP measurement and were conducted across three Tasmanian regions.

Results. Both community members and health professionals reported HBPM to be valuable and practical for hypertension management. However, there was variability in HBPM technique and limited awareness of evidence-based protocols. Instead, participants described ad hoc, individualised, and often incorrect methods for measuring and recording BP at home.

Discussion. HBPM is an acceptable and widely used strategy for managing hypertension, but ad hoc use in practice undermines its accuracy and clinical utility. Addressing barriers to standardisation through validated devices, protocol-based education, and integration into primary care, are essential for optimising the role of HBPM in hypertension management.

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Deep immunophenotyping reveals associations with human blood pressure

Miss Evany Dinakis

Biography:

Evany Dinakis is a final year PhD student in the Hypertension Research Laboratory led by Professor Francine Marques, and her research primarily focuses on the interplay between hypertension, the immune system and pH-sensing mechanisms. In particular, Evany has explored whether acidic by-products from dietary fibre fermentation act via pH-sensing G-protein receptors such as GPR68 under hypertensive conditions, with findings recently published. Currently, Evany is working on further characterising the peripheral immune system to better understand its role in human blood pressure regulation.

Deep immunophenotyping reveals associations with human blood pressure

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Introduction. Substantial evidence in preclinical models has demonstrated the pivotal role of the innate and adaptive immune systems in hypertension. However, clinical evidence remains limited.
Aims. We aimed to comprehensively characterise the peripheral immune system in human blood pressure (BP) regulation and delineate immune cell composition differences between participants with normal and high BP.
Methods. Normotensive (n=15; 67% female) and untreated hypertensive (n=23; 26% female) participants underwent 24-hour ambulatory BP measurements. Deep immunoprofiling was performed on peripheral blood mononuclear cells isolated from whole blood using the Cytek Aurora (n=38). The relationship between continuous 24-hour BP measurements and 121 circulating immune cell populations/subtypes (including expression of activation markers and cytokine production) was analysed using Spearman's correlation. Differences in circulating immune cell counts between participants with normal and high BP were determined using the Mann–Whitney U test.
Results. Fifty-nine significant positive associations were reported between 24-hour BP and immune cells (P=0.00035-0.049); 23 were $CD4^+$ subtypes and 31 were $CD8^+$ T cell subtypes. Activated ($CD69^+$/HLA-DR^+), effector memory, IFNγ-, IL-17A-, IL-2- and TNFα-producing, as well as CTLA-4^+ and PD-1^+ activated $CD4^+$ and $CD8^+$ T cells were all associated with increasing BP. Strikingly, 54 and 49 significant correlations were associated with 24h night-time systolic and diastolic BP, respectively. Categorical analysis further revealed that untreated hypertensives had higher terminally differentiated effector memory $CD8^+$ T cells (P=0.0159), IL-17A-producing activated $CD8^+$ (P=0.0327), $CD161^+$ $CD8^+$ T cells (P=0.0427) but no differences in T regulatory cell numbers (P=0.79) compared to normotensive participants.
Discussion. Elevated 24-hour BP, particularly night-time BP, was strongly associated with elevated circulating $CD4^+$ and $CD8^+$ T cell subtypes, with $CD8^+$ populations emerging as the predominant immune signature distinguishing hypertensives from normotensives. These pro-inflammatory immune cells are likely key drivers of inflammation during BP increase.

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Distinct endothelial cell subtype promotes vascular inflammation and remodelling during aortic stiffening

Ms Tayla Gibson Hughes

Biography:

Tayla is a final year PhD student in the Hypertension and Immunobiology lab within the Centre for Cardiovascular Biology and Disease Research at La Trobe University. Her primary research goal is to understand the cellular drivers of vascular fibrosis, with a focus on the aortic endothelium and fibroblasts. To decipher this, Tayla uses single-cell RNA sequencing, spatial transcriptomics, in-vitro and in-vivo techniques to decipher the cellular changes attributed to vascular fibrosis.

Distinct aortic endothelial cell subtype promotes vascular inflammation and remodelling during angiotensin II-induced aortic stiffening

T A Gibson Hughes[1,2], M I Dona[1,2], B Wickramasinghe[1], V Tran[1], G Farrugia[1,2], T Gaynor[2], A Pinto[1,2], G Drummond[1], M Jelinic[1], A Vinh[1]. [1]Centre for Cardiovascular Biology and Disease Research, La Trobe University, Bundoora, VIC, Australia. [2]Baker Heart and Diabetes Institute, VIC, Australia.

Introduction. Hypertension is the leading cause of death, affecting one third of adults worldwide. Aortic stiffening, inflammation and endothelial dysfunction are hallmarks of hypertension, however the interactions between these conditions remain largely unknown.

Aims. We aimed to characterise endothelial cell (EC) heterogeneity and compare aortic EC phenotypes in healthy and hypertensive settings.

Methods. Hypertension was induced by angiotensin (Ang) II (0.7 mg/kg/day) infusion into 12-week-old male C57BL/6 mice via osmotic minipump (*s.c.*). Normotensive control mice received saline. After 28 days, aortae were harvested and enzymatically dissociated into single-cell suspensions. Metabolically active live cells were collected using FACS and prepared for single cell RNA-sequencing using Chromium 10x and NovaSeq genomics platforms.

Results. Single-cell analysis of 22,207 cells identified 17 cell types including 3 distinct Pecam1-expressing EC subclusters, one being a lymphatic EC. Interestingly, von Willebrand factor (vWF), a widely accepted EC marker, was solely expressed in one EC cluster (EC2). Immunofluorescence and flow cytometry confirmed the presence of three distinct EC populations. To determine regional heterogeneity, flow cytometry was performed on thoracic and abdominal aortas from male and female mice and showed male mice harboured a higher percentage of vWF+ ECs. Irrespective of sex, the abdominal aorta had a higher proportion of vWF+ ECs compared to thoracic aorta. Gene ontology analysis revealed hypertension enriched for biological processes associated with *ECM organisation*, *cell adhesion* and *migration* in EC2, suggesting a pro-fibrotic phenotype. Cell-cell communication analysis showed profibrotic signalling pathways enriched in EC2 from hypertensive mice including *Thbs1*, *Fn1*, *Bmp* and Icam1, which was uniquely associated with EC2-macrophage cross talk.

Discussion. Characterising the distinct roles of aortic EC subtypes may provide crucial insights into EC- driven molecular mechanisms of aortic stiffening and inflammation in the context of hypertension.

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Microbial metabolite supplementation reduces blood pressure by improving vascular function

Ms Phoebe Cheong

Biography:

Phoebe Tsin Tse Cheong is a second-year PhD student at the Biomedicine Discovery Institute of Monash University, and the Victorian Heart Institute (VHI) of the Victorian Heart Hospital in Clayton, VIC. She holds a Masters degree in Microbiome in Health and Disease from King's College London, UK, and Bachelor's degree in Food Science and Nutrition, Universiti Malaysia Sabah.

Phoebe's academic journey has compelled her to integrate methodologies from interdisciplinary aspects to uncover the potential of the gut microbiome for biotherapies. Her keen interest is in the modulation of the gut microbiome in health and diseases, particularly in blood pressure regulation. Phoebe's dedication to research has been recognized with the VHI travel grant, which has enabled her to present her findings at the Human Microbiome Symposium, in EMBL Heidelberg, Germany. Phoebe aspires to contribute to the growing field of microbiome research and its translational potential in precision and personalised nutrition.

Microbial metabolite supplementation reduces blood pressure by improving vascular function

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Introduction: Short-chain fatty acids (SCFAs), gut microbial metabolites derived from dietary fibre fermentation, reduce BP in mice and humans. In a clinical trial, total vascular resistance was reduced in the SCFA arm of participants untreated for hypertension. Whether this is a primary BP-lowering mechanism remains unclear.
Aim: To determine whether dietary SCFAs lower BP via vascular function in experimental hypertension.
Methods: Male C57BL/6 mice (n=16/group) received minipumps with angiotensin II (Ang II, 0.75mg/kg/day) or saline (sham) and drinking water with 0.9% sodium chloride for 4 weeks. Mice were fed on high-SCFA or control diet after surgery. Aortic elastin content was determined using Verhoeff van Giesen (VVG) staining, aorta contractile forces by wire myography and function by ultrasound. BP was measured by tail-cuff, immune system by flow cytometry, gut microbiome via 16S rRNA sequencing, and caecal SCFAs via NMR.
Results: SCFAs significantly increased elastin content in sham mice aortas (p=0.0041). Improved relaxation (*p*=0.0041) and resistive index (*p*=0.027) were observed with SCFAs, irrespective of hypertension status. SCFAs decreased BP (p=0.02) and increased caecal SCFAs (p=0.015) in Ang II-treated mice compared to control diet. The gut microbiome was significantly modulated by SCFAs, regardless of hypertension status (Shannon index, p<0.001; Weighted UniFrac distance, adjusted p-value<0.05). No significant changes to aortic immune cells were observed.
Discussion: SCFAs directly improves vascular function *in vivo*, via BP-reducing gut microbial metabolites.

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Arterial stiffness shows stronger association with cognitive function in females than males

Miss Genevieve Shek

Biography:

Genevieve Shek is a fourth-year Honours medical student at the University of New South Wales with a strong interest in cardiology, particularly hypertension and vascular ageing. Her current research project investigates the relationship between arterial stiffness and cognitive function in older adults, aiming to better understand the interplay between cardiovascular and neurological health. Through this work, she hopes to contribute to strategies for early detection and prevention of cognitive decline, with a focus on sex-specific differences in vascular risk.

Arterial stiffness shows stronger association with cognitive function in females than males

Genevieve Shek[1], Elza Plotz[2], Charlene Melencion[2], Andy Lee[2], Arthiga Vickneswaran[2], Katherine Samaras[1,2], Audrey Adji[1,3,4]. St Vincent's School of Clin Med, UNSW[1], Sydney, NSW; Garvan Institute of Med Research, Sydney, NSW; Cardiology, St Vincent's Hosp[3], Sydney, NSW; MCSR Lab, Victor Chang Cardiac Research Institute[4], Sydney, NSW.

Introduction. Arterial stiffness increases with age, transmitting higher pulse pressures to cerebral microvasculature and potentially accelerating cognitive decline. Postmenopausal arterial stiffening may contribute to faster cognitive deterioration and higher dementia rates in females.

Timepoint	β (male − female slope)	95% CI	p-value
0 months	-0.11	-0.39 to 0.17	0.448
6 months	-0.66	-1.19 to -0.13	0.015
12 months	-0.57	-1.21 to 0.06	0.077

Aims. To examine the association between carotid-femoral pulse wave velocity (cfPWV, a marker of arterial stiffness) and cognition, measured using Montreal Cognitive Assessment (MoCA), in older adults with mild cognitive impairment.

Methods. Data were obtained from 255 participants (130 males, 125 females; MoCA <26) in the MetMemory Study, a 3-year randomised, double-blind, placebo-controlled trial of metformin. Mean ± SD age was 71.7±6.6 years and BMI 29.7±4.9 kg/m^2. BP, cfPWV (SphygmoCor XCEL) assessments and MoCA were conducted at 0, 6, and 12 months. Sex differences were evaluated at baseline using two-sample t-tests. Linear regression models assessed the relationship between cfPWV and MoCA, including sex-stratified and interaction analyses.

Results. Females had lower BMI (28.7±4.8kg/m^2) and diastolic ((77 ± 9mmHg) brachial, (78 ± 9mmHg) central) pressure than males (all p<0.001). Across the whole cohort, higher cfPWV was associated with lower MoCA scores at 0 (p < 0.001) and 12 months (p=0.005). Sex-stratified analyses revealed this association was significant only in females at 0 (n=115, p=0.003), 6 months (n=104, p=0.013), and 12 months (n=109, p=0.004). A cfPWV×Sex interaction revealed a stronger association between cfPWV and MoCA in females than males, reaching significance at 6 months (Table).

Discussion. Increased arterial stiffness is more strongly associated with lower cognitive function in females than males. This could reflect greater cerebral vulnerability from higher central haemodynamic load and lower diastolic perfusion. These findings reinforce the importance of sex-specific approaches to vascular ageing and dementia prevention.

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Human amnion epithelial cell therapy modulates brain cell heterogeneity in experimental stroke

Mr Yeshwanth Reddy Yeraddu

Biography:

I am a final-year PhD candidate at the Centre for Cardiovascular Biology and Disease Research, led by Prof. Chris Sobey and Prof. Grant Drummond. I completed my Master's in Biomedical and Health Sciences at Monash University in 2020. My research uses single-cell and spatial transcriptomics to investigate the role of human amnionic epithelial cells (hAECs) in stroke, focusing on their neuroprotective effects and impact on cognition. I aim to investigate the effects of stroke on transcriptional changes in brain cell populations and characterize how hAECs influence recovery processes. My work incorporates advanced techniques such as the photothrombotic stroke model, neurobehavioral testing, transcriptomics, and bioinformatics tools to better understand the mechanisms underlying stroke recovery.

Human amnion epithelial cell therapy modulates brain cell heterogeneity in experimental stroke.

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Introduction. Stroke is a leading cause of death and disability worldwide. Current treatment options have a narrow therapeutic window and do not address secondary injury. Human amnion epithelial cells (hAECs) have several properties that make them a promising cell-based therapy. Ischaemic injury leads to loss of brain cells within minutes, but the transcriptional changes that occur during the delayed phase after stroke in response to hAEC therapy are unknown.
Aim. To investigate the effects of stroke and hAEC therapy on transcriptional changes in brain cell populations using single-cell transcriptomics.
Methods. Male and female C57Bl6 mice (14-18 weeks, *n*=3 per group) underwent sham or photothrombotic stroke surgery targeting the prefrontal cortex and received saline or 1×10^6 hAECs intravenously 24 hours post-stroke. Five weeks after stroke, brains were collected. A 3 mm section from the infarct region was prepared for single-cell RNA sequencing. Data were quality filtered, clustered, and analysed for differential gene expression and gene ontology to identify treatment-associated molecular changes.
Results. Single-cell analysis identified 12 brain cell populations. Additionally, we identified multiple clusters in saline- or hAEC-treated mice. hAEC therapy modulated cell transcriptional profiles, with upregulation of genes related to survival, and neuroprotection, and downregulation of pro-apoptotic and inflammatory pathways. Unique cell subpopulations in the hAEC group displayed enhanced repair signatures and reduced injury markers. Gene ontology analysis supported these findings, suggesting a shift towards a reparative phenotype with hAEC treatment.
Discussion. The modulation of gene expression by hAEC treatment suggests a potential role in promoting brain repair mechanisms after stroke. Further investigation of additional brain cell populations and their interactions will be important to fully elucidate the therapeutic effects of hAECs.

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Gut microbial metabolite acetate and prevention of cardiovascular disease in high-risk women

Mr. Chaoran Yang

Biography:

Chaoran Yang is a second-year PhD student of the Hypertension Research Lab under supervision of Prof Marques, Prof. Professor El-Osta. He holds a research-based Master's degree from Tohoku University and a Master's degree in Statistics from Ghent University. Currently, he is immersed in exploring the personalised response to dietary fibre using bioinformatic and biostatistic method.

Gut microbial metabolite acetate and prevention of cardiovascular disease in high-risk women

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Introduction: Sex hormone alterations, such as estrogen deficiency or testosterone excess, significantly disrupt cardiometabolic health in women, increasing their risk of cardiovascular disease (CVD). While dietary fibre and its microbial by-products, short-chain fatty acids (SCFAs), are known to support cardiovascular health, it remains unclear whether these benefits extend to women with an altered sex hormone profile.

Aims: To investigate whether dietary fibre intake, measured via plasma acetate—the most abundant SCFA—is associated with improved cardiovascular health in women with an altered sex hormone profile.

Methods: This cohort study analysed data from 89,188 and 123,576 female participants in the UK Biobank, recruited between 2006 and 2010. Analyses focused on plasma-free testosterone levels and early menopause (menopause<45 years: surrogate for estrogen deficiency), with up to 10 years of follow-up.

Results: Overall, acetate were associated with lower systolic blood pressure (SBP), diastolic BP (DBP) and 10-year major cardiovascular events (MACE) incidence in females. A significant interaction was observed between plasma acetate and free testosterone on SBP ($\beta=6.94\times10^{-4}$; 95% CI, 8.04×10^{-5} to 8.60×10^{-4}; P=0.018). Around 16 pmol/L of free testosterone halved the effect of acetate on SBP. Mediation analysis revealed that central obesity (waist-hip ratio) and inflammation (C-reactive protein) partially mediated this interaction. Moreover, in women with free testosterone levels below the median, elevated acetate levels (15.14µmol/L) were associated with a significantly lower 10-year MACE risk (HR=0.83; P=0.026). Elevated acetate levels also attenuate the increased MACE risk associated with early menopause (early-menopause vs non-early menopause: HR=0.72; P=0.199) relative to those with below-median acetate (early-menopause vs non-early menopause: HR=4.58; P=0.006).

Discussion. Higher plasma acetate levels were associated with lower BP and reduced cardiovascular risk in women, particularly those with lower free testosterone or early menopause. These findings highlight the importance of individual hormonal profiles when considering CVD prevention strategies such as dietary fibre supplementation.

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Neuroinflammation without Hypoxia, and Brain Injury Biomarkers after Cardiopulmonary Bypass in Sheep

Dr. Taku Furukawa

Biography:

Dr. Taku Furukawa is a PhD candidate at the Florey Institute of Neuroscience and Mental Health, University of Melbourne and a dual-trained intensivist and anaesthetist. He is completing his PhD under the supervision of Prof. Yugeesh Lankadeva, Prof. Clive May, Dr. Connie Ow, and the late Prof. Rinaldo Bellomo. His research focuses on the mechanisms of acute kidney and brain injury arising from cardiac surgery and sepsis, aiming to develop novel diagnostics and therapeutics. He received the Best Oral Presentation Award at the Hypertension Australia ASM 2023 and represented the society at the British and Irish Hypertension Society meeting in 2024.

Neuroinflammation without Hypoxia and Brain Injury Biomarkers after Cardiopulmonary Bypass

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Introduction. Delirium occurs in ~50% of patients undergoing cardiopulmonary bypass (CPB) in the first 48-h postoperative period. Cerebral hypoxia and neuroinflammation have been proposed as important contributing factors, but their duration and severity after CPB remain unclear. Furthermore, blood biomarkers for early detection or prognostication are not yet established, and their direct relationship with histological injury remains unknown.

Aims. To investigate the effects of CPB on cerebral microcirculation, neuroinflammation, and blood biomarkers of neurological injury over a postoperative period of up to 4 weeks in a clinically relevant sheep model

Methods. Healthy adult merino ewes underwent CPB for 2 h and were recovered for either 48 h (n=8) or 4 weeks (n=8). Frontal cortical tissue oxygen tension (PO_2) was monitored before, during, and after CPB. Neuroinflammation was quantified by morphometric analyses of microglia and astrocytes in the frontal cortex in both CPB groups and healthy naïve controls (n = 5). Plasma neurofilament light chain (NfL; neuronal injury marker) and glial fibrillary acidic protein (GFAP; astrocyte injury marker) were measured at baseline, 2-h of CPB, and 24 h and 48 h post-CPB.

Results. Compared with baseline, cerebral PO_2 did not change at 48-h or over 4-weeks post-CPB. Compared with controls, at 48 h post-CPB, there was microglial activation characterised by increased number of microglia (mean ± SD, 54 ± 3 vs 71 ± 3 cells, $P < 0.001$) and reduced sphericity (0.83 ± 0.01 vs 0.79 ± 0.02, $P < 0.05$). Astrocyte reactivity was characterised by increased GFAP-stained area (17 ± 2 % vs 10 ± 2 %, $P = 0.026$). At 4-weeks post-CPB, these measures did not differ from controls. Peak elevations in NfL levels (median [IQR]) occurred from 138 [96, 185] pg/mL at baseline to 198 [149, 265] pg/mL at 48 h CPB ($P = 0.0007$), while GFAP rose from 3.0 [1.3, 4.5] pg/mL at baseline to a peak at 2-h of CPB (14.4 [4.7, 32.4] pg/mL, $P < 0.0001$).

Discussion. Even in absence of tissue hypoxia, neuroinflammation in the frontal cortex was evident 48 h after CPB, which coincides with the clinical window in which cardiac surgery-associated delirium occurs. This neuroinflammatory response was accompanied by elevated blood biomarkers of neurodegeneration. Therapeutic strategies targeting neuroinflammation may help prevent CPB-related brain injury, and blood-based biomarkers such as NfL and GFAP show promise as surrogate markers for monitoring treatment efficacy in future clinical trials.

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Team-based hypertension care in Australia: A qualitative study among primary care providers

Dr Gautam Satheesh

Biography:

Gautam Satheesh is a PhD candidate at the Faculty of Medicine and Health, University of Sydney, and a researcher at The George Institute for Global Health in Sydney. His doctoral research focuses on strengthening team-based care for hypertension in Australia, with particular emphasis on enhancing the roles of nurses and pharmacists in supporting evidence-based blood pressure management. His work applies mixed methods and implementation science approaches to explore provider perspectives, workforce modelling, and system-level reforms that can expand access and equity in hypertension care. Gautam has also contributed to global policy efforts, including the World Heart Federation's efforts on Single Pill Combinations and the WHO HEARTS technical package on hypertension control. His broader research interests span cardiovascular disease prevention, access to essential medicines, and innovative service delivery models in low- and middle-income countries. He is passionate about building evidence that bridges clinical practice, health systems, and policy for population-level impact.

Team-based hypertension care in Australia: A qualitative study among primary care providers

Gautam Satheesh[1,2], Kaylee Slater[1], Ritu Trivedi[1], Eleanor Clapham[3], Florence Lopez[1], Aletta E Schutte [2,4], J. Jaime Miranda[1], Brendan McCormack[1], Niamh Chapman[1,3]. [1]Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia; [2]The George Institute of Global Health, Sydney, NSW, Australia; [3]Menzies Institute for Medical Research, University of Tasmania, Australia; [4]School of Population Health, UNSW, Sydney, NSW, Australia

Introduction. Hypertension care in Australia is burdened by poor BP control (32%) and a projected shortage of 5,000 general practitioners (GPs) by 2030, underscoring the need to expand team-based care with pharmacists and nurses.
Aims. To explore barriers and attitudes among primary care providers towards team-based hypertension care.
Methods. We conducted 43 semi-structured interviews with GPs (N=21), nurses (N=11), and pharmacists (N=11), purposively recruited from diverse primary care settings. We employed framework analysis, combining deductive analysis, based on Theoretical Domains Framework embedded within COM-B (Capability, Opportunity, Motivation–Behaviour), with inductive analysis to identify emergent themes across individual and system levels.
Results. Hypertension management remained GP-centred, with nurses and pharmacists confined to supporting roles for BP measurement, follow-up, and counselling. Contributions of nurses and pharmacists were constrained by barriers at both individual/practice (e.g., mistrust among GPs) and system levels. Nurses described being "hamstrung" by workload and absence of direct funding for hypertension services, despite being critical in care planning. Pharmacists reported that unreimbursed BP checks and capped MedsChecks hindered sustainability. Communication across providers was largely fragmented, with pharmacists noting almost no referral pathways to GPs. Role ambiguity and absence of protocols on shared workflow further limited collaboration, with concerns about overstepping professional boundaries. Attitudes towards team-based care ranged from active disregard (outright rejection), through more passive/conditional acceptance, to active uptake (strong endorsement).
Discussion. Hypertension care in Australia remains largely GP-centred, despite demonstrated willingness and potential among nurses and pharmacists to alleviate burden on GPs and provide quality care. Addressing provider-level barriers of workload and trust, alongside system-level barriers of funding and authority, is critical for sustainable workforce planning, task sharing and team-based care.

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Hypertension awareness, treatment and control in Australian young adults

Dr Ritu Trivedi

Biography:

Ritu is a Postdoctoral Research Fellow at the University of Sydney. Her PhD explored digital health technologies for supporting patients with atrial fibrillation and her postdoctoral research work is focused on the accuracy of devices used by Australians to measure their blood pressure at home. Ritu's research interests are in optimising self-management for those with cardiovascular diseases.

Hypertension awareness, treatment and control in Australian young adults

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Introduction. High blood pressure (BP) in young adults is associated with greater risk of cardiovascular disease (CVD) in later life. Hypertension may remain undiagnosed in young adults and could remain uncontrolled for several reasons including lower engagement with healthcare and lack of awareness of high BP. Moreover, the most recent absolute CVD risk algorithms for Australia is only recommended for people from the general community who are aged 45-79 years. This potentially means opportunities for risk factor modification to reduce BP among younger adults may be missed.
Aims. To understand hypertension awareness, treatment and control rates in young Australian adults.
Methods. A cross-sectional analysis of Australian National Health Survey 2017-18 among adults aged 18 to 39 years. Descriptive analyses to determine hypertension awareness, treatment and control was performed and stratified by sex and history of cardiometabolic risk factors (high cholesterol (self-reported), obesity (body mass index ≥30 kgm^{-2})). BP was categorised according to the 2016 Australian hypertension guidelines. Hypertension was defined as people who had measured high BP (≥140/90 mmHg), or normal measured BP and were taking antihypertensive medications.
Results. The analysis included 7.5 million adults aged 18 to 39 years (48.9% women). Among those with hypertension (802,493, 10.7%), only 9.4% (75,690) were aware of their high BP, 6.8% (54,930) were treated and only 4.5% (35,888) were controlled. Among 358,632 young adults with obesity and hypertension, awareness (28,788, 8.0%), treatment (17,991, 5.0%) and control (4,968, 1.4%) were lower than in the general population. However, in the 27,963 young adults with high cholesterol and hypertension (awareness: 23,813, 85.2%; treatment: 20,124, 72.0%; control: 10,730, 38.4%) was higher than in the general population.
Discussion. Young Australian adults with hypertension were found to have low awareness, control and treatment rates. Tailored approaches to raise awareness of high BP, including pathways to confirm high BP in young adults and methods to lower BP are required to support young adults with hypertension to improve their overall CVD risk factor profile.

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The impacts of an intracerebrally-administered hydrogel therapeutic-delivery system on the brain post-stroke

Dr Adriana Knezic

Biography:

Dr Adriana Knezic completed her PhD in the Department of Pharmacology at Monash University in 2023, where she investigated the pathophysiology and therapeutic targeting of stroke in several preclinical models. She is now a Postdoc in the Department under the mentorship of A/Prof. Brad Broughton. Her current research focuses on developing novel therapeutics for stroke, including various stem cell-based approaches, using compounds to target the organ-protective effects of alternative arms of the renin-angiotensin system (such as the AT2R) and Relaxin Family Peptide Receptors, as well as hydrogel-based delivery systems for the brain. Beyond her research, she chairs the ECR Career Development Subcommittee of the Monash Biomedicine Discovery Institute, serves on the Hypertension Australia ECR committee and is the secretary of the ASCEPT Cardiovascular SIG.

The impacts of an intracerebrally-administered hydrogel therapeutic-delivery system on the brain post-stroke
Adriana Knezic[1], Ketav Kulkarni[2], Charlie Lines-Perrier[1], Niyoti Dhond[1], John Forsythe[3], Mibel Aguilar[2], Brad RS Broughton[1]. Dept of Pharmacology[1], Dept of Biochemistry[2], Dept of Materials Science and Engineering[3], Monash University, Clayton, VIC, Australia.

Introduction. Stroke is the second leading cause of death world-wide, yet no treatments exist which can target cell death directly or promote neuroregeneration. Many promising drug- and cell-based therapies have failed due to poor brain penetration or short half-lives. To overcome these challenges, we have developed and patented an injectable, brain-compatible β-peptide hydrogel that can encapsulate therapeutics, enabling direct delivery to the infarct core with sustained release.

Aims. To assess the impact of the hydrogel on the brain of mice subjected to middle cerebral artery occlusion (MCAO)

Methods. 8-week-old male C57Bl/6 mice were subjected to a 30-min MCAO or sham-surgery (ketamine-xylazine anaesthesia, 80mg/kg + 16mg/kg ip; n=6-8/group). 6-h post-stroke mice were re-anaesthetised (2% inhaled isoflurane) and injected with or without 5µl of hydrogel into the infarct core. Pre-stroke and 24- and 72-h post-stroke, motor function was assessed via the neurological score, ANY-maze and hanging wire tests. 72-h post stroke, infarct volume was determined via thionin staining and neuronal loss and brain inflammation assessed via immunofluorescence.

Results. In sham-mice, injected β-peptide hydrogel within the brain did not significantly impact motor function, neuronal loss, or trigger an immune response. As expected, mice subjected to stroke had an infarct region that included significant neuronal loss, worse motor function and brain inflammation compared to sham mice. While the β-peptide hydrogel did not affect infarct volume, neuronal loss or motor function, it did cause a trend for increased neutrophil and macrophage infiltration into the ischaemic hemisphere.

Discussion. Intracranial administration of β-peptide hydrogel did not impair motor function or neuronal survival in mice subjected to sham-surgery or MCAO. However, there were trends for increased immune cell infiltration in response to the hydrogel. Future studies will assess the long-term impacts of this hydrogel to assess gel degradation and chronic cellular responses. However, the impact of the hydrogel in its intended use, as a therapeutic delivery system, is yet to be assessed. Future studies will assess the implantation of our β-peptide hydrogel encapsulating therapeutics known to have anti-inflammatory and/or neuroregenerative effects.

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Impact of dialysis on cardiovascular, cerebrovascular and renovascular hemodynamics in sepsis

Dr Munenori Kusunoki

Biography:

Dr. Munenori Kusunoki is a dual-trained anaesthesiologist and intensive care physician. He earned his medical degree in 2010 and completed a PhD at Kansai Medical University in 2020, studying the effects of hypoxia on organ injury and metabolism, and the impact of anaesthetics on insulin secretion. He currently serves as an Assistant Professor at Kansai Medical University Hospital, teaching medical students and fellows, and providing anaesthesia and intensive care for approximately 2,500 patients annually. He has published 16 peer-reviewed articles and received multiple awards and research grants. In May 2024, he joined the Translational Cardiovascular and Renal Research Group at the Florey Institute of Neuroscience and Mental Health in Australia as a Clinician Research Fellow. His research focuses on haemodynamics and organ injury in sepsis-associated acute kidney injury requiring continuous renal replacement therapy. His overarching goal is to improve cardiovascular, brain, and kidney outcomes in critically ill patients.

Impact of dialysis on cardiovascular, cerebrovascular and renovascular hemodynamics in sepsis

Munenori Kusunoki[1], Taku Furukawa[1], Jonathan Nübel[1,2], Connie P C Ow[1], Clive N May[1], Yugeesh R Lankadeva[1]. 1. Translational Cardiovascular and Renal Research Group, Florey Institute of Neuroscience and Mental Health, Univ of Melbourne, Parkville, VIC, Australia. 2. Dept of Intensive Care, Austin Hosp, Heidelberg, VIC, Australia.

Introduction. Sepsis is a life-threatening condition that often leads to cardiovascular failure and sepsis-associated acute kidney injury (SA-AKI), which is associated with high mortality and prolonged hospitalisation. Continuous renal replacement therapy (CRRT), a form of dialysis, is widely used to support renal function for SA-AKI in intensive care units. However, the effects of CRRT on cardiovascular, cerebrovascular and renovascular hemodynamics are unclear.

Aims. To assess the effects of CRRT on cardiovascular function and on microcirculation in the brain and kidneys in a sheep model of SA-AKI.

Methods. Adult female sheep (n = 16) were induced with sepsis with intravenous (iv) infusion of live *Escherichia coli* for 31-h. At 23-h of established SA-AKI, sheep were randomised into two groups: sedation only or sedation with CRRT (n = 8 each). All sheep were sedated with fentanyl (5 µg/kg/h, iv), propofol (20 mg/kg/h, iv), and midazolam (0.5 mg/kg/h, iv), followed by intubation and mechanical ventilation. CRRT was applied for 4-h in the CRRT group. Systemic haemodynamics and microcirculatory perfusion and oxygenation in the frontal cortex, renal cortex and renal medulla were recorded. Noradrenaline was titrated to maintain a mean arterial pressure (MAP) of 70 mmHg after sedation.

Results. At 23 h following *Escherichia coli* infusion, SA-AKI was characterised by reduced MAP (91.47 ± 2.34 to 77.98 ± 2.96 mmHg; $P < 0.001$), increased arterial blood lactate (0.54 ± 0.05 to 1.56 ± 0.34 mmol/L; P=0.0389) and increased serum creatinine levels (70.50 ± 5.63 to 129.5 ± 19.67 µmol/L; P=0.0994). CRRT did not alter perfusion or oxygenation in the frontal cortex, renal cortex and renal medulla. Following sedation, septic sheep undergoing CRRT required higher doses of noradrenaline to maintain target MAP of 70 mmHg compared with those who underwent sedation alone (0.28 ± 0.02 vs. 0.54 ± 0.04 µg/kg/min, p=0.0309).

Discussion. In a clinically relevant sheep model of SA-AKI, CRRT did not enhance cerebral or renal perfusion or oxygenation but was associated with increased vasopressor requirements. These findings suggest that, in the acute phase of septic AKI, the cardiovascular hemodynamic instability of CRRT may offset potential benefits, emphasizing the importance of optimizing timing and patient selection when initiating CRRT in critically ill patients.

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Inadequate fibre intake increases gut-derived uremic toxins that contribute to hypertension

Dr Chudan Xu

Biography:

Dr Chudan Xu is a postdoctoral research fellow at the Hypertension Research Laboratory, Monash University. Their research investigates the impact of dietary fibre deficiency on the development of hypertension, integrating insights from animal models and human studies. By combining analyses of the gut microbiome, host metabolome, and translational approaches, Dr Xu aims to uncover the mechanisms through which fibre insufficiency contributes to cardiovascular risk. Beyond research, Dr Xu is involved in teaching and committee work, with a strong commitment to mentoring and supporting early-career scientists. Their long-term goal is to translate fundamental discoveries into preventive and therapeutic strategies that improve cardiovascular health.

Inadequate fibre intake increases gut-derived uremic toxins that contribute to hypertension

Chudan Xu[1,2], Liang Xie[1,3]*, Christopher Barlow[4,5]*, Leticia Camargo Tavares[1,2]*, Evany Dinakis[1,2], Panayiotis Louca[6], Julia El-Sayed Moustafa[6], Chaoran Yang[1,2], Michael Nakai[1], Xiaosuo Wang[7], Giovanni Guglielmi[7], Dakota Rhys-Jones[8], Joanne O'Donnell[1,2], Stephanie Yiallourou[9], Melinda J. Carrington[9], Gavin W. Lambert[10], Jane Muir[8], Charles Mackay[11], Darren Creek[12], David Kaye[9,13,14], Kerrin Small[6], John O'Sullivan[7,15#], Cristina Menni[6,16,17#], Francine Z. Marques[1,2,9*]

Introduction: Over 70% of Australians do not consume enough dietary fibre. This has now emerged as a risk factor for hypertension. However, how it increases BP remains unknown. **Aim**: To elucidate how a lack of dietary fibre contributes to hypertension. **Methods:** The gut microbiome and the plasma metabolome of 16 mice fed either a low- or high-fibre diet were profiled. Caecal and distal colon tyrosine levels were measured. Mice were treated with antibiotics to confirm that metabolites were dependent on the gut microbiota. The TwinsUK cohort (n=1,536) was used to confirm these associations. Mendelian Randomisation (MR) was performed to test the causal associations between metabolites and BP. Finally, we investigated whether a high-fibre diet reduced metabolites in a crossover randomised clinical trial. **Results:** Low-fibre-fed mice had a distinct gut microbiota composition, which shifted microbial resource preference, consuming tyrosine throughout the colon. This increased *p*-cresol-derived metabolites in the host circulation compared to high-fibre-fed mice. The gut microbiota ferments tyrosine and releases *p*-Cresol, which is metabolised into *p*-Cresol glucuronide (PCG) by the host enzymes. Indeed, low-fibre-fed mice had higher levels of plasma PCG relative to high-fibre-fed mice. Using antibiotics, we confirmed that this was dependent on the gut microbiota. In the TwinsUK cohort, plasma PCG was associated with dietary fibre intake (p=0.011) and hypertension (p=0.002), and was co-expressed with 243 genes, with a negative correlation with the regulation of inflammatory pathways and endothelial cell development. The MR analysis confirmed PCG is causally associated with higher systolic (b_{xy}=0.169, p=0.029) and diastolic BP (b_{xy}=0.140, p=0.004). An MR sensitivity analysis conditioning PCG results on eGFR genetic effects indicated that the causal effect of PCG on BP depends on renal function. Finally, 3 weeks of dietary fibre intervention in 20 participants untreated for hypertension decreased plasma PCG (q<0.001) and *p*-Cresol (q=0.023) compared to the placebo arm. **Discussion**: In a low-fibre diet setting, gut microbiota increases the production of the uremic toxin PCG, which is causally associated with BP traits.

Affiliations

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VEGF inhibitor-induced hypertension is ameliorated by DMSC-EVs in male rats

Dr Katrina Mirabito Colafella

Biography:

Dr Katrina Mirabito Colafella leads the Molecular and Integrative Mechanisms of Vascular Biology Laboratory at Monash University's Biomedicine Discovery Institute (BDI), where she also serves as the inaugural Monash BDI Anita Castan Fellow. Her research vision is to transform the treatment of hypertension and cardiovascular disease through precision medicine, with a focus on sex-specific mechanisms in blood pressure regulation. She is also at the forefront of research into the cardiovascular side effects of cancer therapies, aiming to develop innovative strategies that prevent or reverse these complications. Through her work, Dr Mirabito Colafella is redefining how we understand and treat cardiovascular disease in vulnerable populations, with the ultimate goal of improving long-term health outcomes.

VEGF inhibitor-induced hypertension is ameliorated by DMSC-EVs in male rats

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Introduction: Vascular endothelial growth factor (VEGF) inhibitors are effective cancer therapies, but are associated with significant cardiotoxicity, particularly hypertension, and kidney injury. These adverse effects are driven by activation of the endothelin (ET) system, endothelial dysfunction and oxidative stress. Decidual mesenchymal stromal cells (DMSCs) and their extracellular vesicles (EVs) are highly resistant to oxidative stress and can restore endothelial function. We hypothesised that DMSC-EVs can mitigate VEGF inhibitor-induced hypertension and kidney injury.

Aims: To assess the effects of DMSC-EVs on VEGF inhibitor-induced hypertension and kidney injury, and to determine whether these effects are sex-dependent.

Methods: Twelve-week-old male and female Sprague Dawley rats were treated with the VEGF inhibitor, sunitinib (14 mg/kg/day o.p.) or vehicle (Nutella) for 7 days. On days 4 and 6, rats received either DMSC-EVs (50 μg in 200 μl saline, i.v.) or vehicle. Mean arterial pressure (MAP) was measured via radiotelemetry on days 1-6. On day 7, 24h urine was collected to determine proteinuria. Plasma ET-1, PGI_2 and PGF2α levels were measured via ELISA. Endothelial function was assessed in mesenteric and kidney vessels.

Results: Sunitinib induced a rapid and sustained increase in MAP in both males (24±2 versus 1±1 mmHg in vehicle on day 6; $P<0.001$) and females (22±2 versus 1±1 mmHg in vehicle on day 6; $P<0.001$). Co-treatment with DMSC-EVs reduced the pressor response to SU by 50% in males (11±3 mmHg on day 6; $P<0.05$ versus SU), but not in females. Sunitinib significantly impaired endothelial nitric-oxide (NO)-dependent vasodilator function in mesenteric and kidney arteries in males but not in females. Sunitinib also increased the sensitivity to ET in these arteries in males. DMSC-EVs restored NO function and ET sensitivity in both arterial beds in males. In addition, DSMC-EVs alone had no effect on MAP or vascular function.

Discussion: These findings suggest sex-specific mechanisms in VEGF inhibitor-induced hypertension and that DMSC-EVs may be a novel intervention to allow male cancer patients to gain the full benefit of VEGF inhibitor therapy without adverse cardiovascular and kidney effects.

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Breathing Life into Physiologically Based Pharmacokinetics (PBPK): Modeling Inhaled Oxytocin for Postpartum Care

Prof Carl Kirkpatrick

Biography:

Carl is Professor of Pharmacy Practice, Medicine Use and Safety. He has a significant portfolio of research in optimising pharmacotherapy via pharmacokinetic/pharmacodynamic modelling techniques to improve patient outcomes. His research interests include population pharmacokinetic and pharmacodynamic modelling, monitoring and bayesian optimisation of dosing of antibacterial agents (especially aminoglycosides), optimisation of dosing in renal dysfunction, pharmacokinetics and dosing in obesity, drugs in breast milk and quality use of medicines.

Breathing Life into Physiologically Based Pharmacokinetics (PBPK): Modeling Inhaled Oxytocin for Postpartum Care

Carl M Kirkpatrick[1], Pete Lambert[1]. Rory Marriott[1], Siladitya R Chaudhuri[2], David Polidori[2], Bart Remmerie[2], Michelle P McIntosh[1], Monash Institute of Pharmaceutical Sciences[1], Monash University, Melbourne, VIC, Australia, [2]Johnson & Johnson Innovative Medicine

Introduction Postpartum haemorrhage (PPH) remains the leading direct cause of maternal mortality worldwide. In lower-middle-income countries (LMICs), approximately 40% of oxytocin injection products used to manage PPH fail to meet internationally recognised quality standards, with many degrading during distribution due to unreliable cold-chain infrastructure. To address this challenge, Monash researchers have developed a single-use dry powder inhaler for oxytocin (inhaled oxytocin – IHO). This formulation and device are designed to simplify administration, eliminate the need for consumables, and remain stable outside the cold chain—even in hot and humid climates. This innovation has the potential to overcome key limitations associated with injectable oxytocin in LMICs.

Aims i) To develop and validate a physiologically-based pharmacokinetic (PBPK) model to support dose selection of inhaled oxytocin for clinical evaluation.ii) To conduct a Phase 1 study assessing the pharmacokinetics and safety of selected doses of an optimised inhaled oxytocin product in healthy, non-pregnant female participants.

Methods A specific PBPK model for inhaled oxytocin was developed and validated using GastroPlus®, configured to represent a standard 28-year-old female lung. The model incorporated in vitro deposition data generated using the Next Generation Impactor (NGI) and was used to predict clinical exposure across various device and deposition profiles. Doses of 50, 200, 400, and 600 µg were evaluated. Model outputs informed dose selection for a randomised, placebo-controlled, fixed-sequence Phase 1 study, which included a partial cross-over design comparing inhaled oxytocin to standard intravenous and intramuscular dosing.

Results The PBPK model, developed for a new device and formulation, predicted key pharmacokinetic parameters within two-fold of observed values. Inhaled oxytocin demonstrated pharmacokinetics comparable to intramuscular administration, with the 150 µg and 600 µg inhaled doses bracketing the exposure of a 10 IU intramuscular dose. Repeat dosing was well tolerated, with no significant treatment-related adverse events or clinical findings reported.

Discussion/Conclusion. A validated PBPK model successfully predicted systemic oxytocin exposure following inhaled administration and was effectively used to select and optimise clinical doses for further evaluation.

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Enhancing Physiologically Based Pharmacokinetic Models with Lymphatic Flow to Predict mRNA-LNP Biodistribution in Rats

Dr Jess Tait

Biography:

Dr Jessica R. Tait is a Postdoctoral Research Fellow at the Monash-Moderna Quantitative Pharmacology Accelerator, based at Monash University in Parkville, Australia. Her research supports the development of mRNA-based vaccines and therapeutics through quantitative pharmacology, including pharmacokinetics, pharmacodynamics and physiologically-based pharmacokinetics modelling approaches. She completed her PhD in 2023 under the supervision of Associate Professor Cornelia Landersdorfer, with her thesis titled 'Dynamic infection models, metabolomics and mechanism-based modelling to investigate pharmacodynamic challenges of Pseudomonas aeruginosa'. Dr Tait has co-authored over 15 peer-reviewed publications in leading journals and has presented numerous posters and oral presentations at premier pharmacology and anti-infective conferences.

Enhancing Physiologically Based Pharmacokinetic Models with Lymphatic Flow to Predict mRNA-LNP Biodistribution in Rats

Jessica R Tait[1], Kenji Miyazawa[2], Natalie L Trevaskis[1], Hojjat Bazzazi[2], Linh Van[2], Rory S Marriott[1], Noelia Nebot[1], Carl MJ Kirkpatrick[1], Cornelia B Landersdorfer[1]. Monash University, Parkville, VIC, Australia[1]. Moderna, Cambridge, MA, USA[2].

Introduction. Minimal physiologically based pharmacokinetic and quantitative systems pharmacology (mPBPK-QSP) models are well-suited to characterize the biodistribution of therapeutic messenger RNA encapsulated in lipid nanoparticles (LNP-mRNA) and inform drug development. Despite playing an important role in the redistribution of macromolecules, the lymphatic system is rarely considered in mPBPK models for nanoparticles. Indeed, few mPBPK models in rodents incorporate lymph flow, often assumed to be 0.2% of blood flow.

Aims. To incorporate physiologically determined lymph flow values to an mPBPK-QSP model and describe the biodistribution of LNP-mRNA (containing Lipid 5) in rats.

Methods. A published mPBPK-QSP platform model was used as the base model (Miyazawa et al, Front. Nanotechnol. 2024; 6:1330406). Public domain data was sourced from Ci et al (PMID: 37208184) which reported a single dose of LNP-mRNA (containing ionizable lipid, Lipid 5, and 2 mg/kg mRNA), and plasma and liver mRNA concentrations over time. The mPBPK-QSP platform model was enhanced to include lymph flow based on physiologically measured values in rats (Yadav et al. PMID: 29305921; Trevaskis et al. PMID: 32670074; Humphreys et al. PMID: 16992278). This enhanced model was then utilized to explore non-linear transport mechanisms to describe the pharmacokinetic profiles. All model building and calibration was undertaken with MATLAB SimBiology (R2023b).

Results. The addition of physiologically determined lymph flow to the mPBPK-QSP platform model improved the ability to describe mRNA pharmacokinetics following dosing of the LNP-mRNA in rats. Including non-linear transport of mRNA from plasma to the interstitial space improved the maximal concentration (Cmax) fit in plasma and liver tissue. Adapting cellular uptake to include capacity-limited phagocytosis for macrophages and Kupffer cells improved the shape of the terminal slopes of mRNA concentrations in plasma and liver tissue.

Discussion. The physiologically correct parameterization in our mPBPK-QSP model provides greater understanding of plasma and liver pharmacokinetics of LNP-mRNA. This enhanced model could quantify the impact of food or disease on lymphatic flow to inform and optimize the drug development of LNP-mRNA therapeutics.

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What lies beneath - PBPK modelling to support subcutaneous administration of Anakinra in preterm neonates

Miss Jia Li

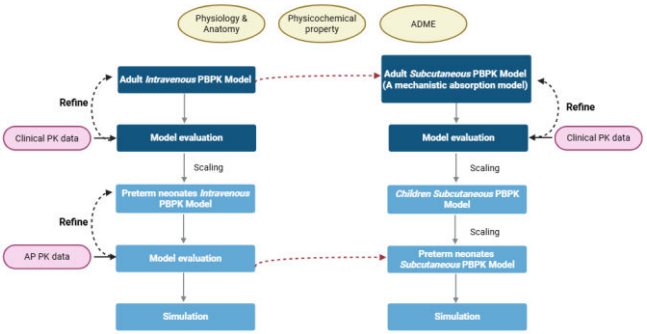
Biography:

Jia Li is a PhD candidate at the Centre for Medicine Use and Safety, Monash University. Her research focuses on model-informed drug development of anakinra in preterm neonates, including population pharmacokinetic (PPK), physiologically based pharmacokinetic (PBPK), and pharmacokinetic/ pharmacodynamic (PPK/PD) modelling approaches. Her work integrates the unique physiological characteristics of premature neonates to optimize dosing strategies and support clinical development. Jia holds a Bachelor's degree in Pharmacy and a Master's degree in Medicinal Chemistry. She has diverse experience across academia and the pharmaceutical industry, including roles as a manager coordinating preclinical and clinical studies in autoimmunology and oncology, and a researcher investigating the pathogenesis of neurodegenerative diseases.

What lies beneath - PBPK modelling to support subcutaneous administration of Anakinra in preterm neonates

Jia Li[1], Carl Kirkpatrick[1]. Monash Institute of Pharmaceutical Sciences, Monash University[1], Melbourne, VIC, Australia

Introduction. Anakinra (IL1Ra) is approved for subcutaneous (SC) administration for chronic inflammatory diseases in adults & paediatric populations. There is growing evidence that IL1Ra may ameliorate complications associated with inflammation of prematurity i.e., 24-28 weeks post menstrual age. However, the distinct physiological features of premature neonates in skin composition, perfusion & organ function, can significantly alter absorption, distribution, metabolism & excretion (ADME) processes, particularly influencing drug absorption via SC route. Indeed, due to skin fragliity current clinical practice does not recommend SC in preterm neonates.



Aim. To develop a physiologically based pharmacokinetic (PBPK) model of IL1Ra in preterm neonates (preterm) to support the dose posology for an intravenous (IV) to SC switch at >2 weeks PNA.

Methods. Using PK-Sim and MoBi, a preterm IV PBPK model of IL1Ra to characterise the elimination was developed by scaling an optimised whole-body PBPK model. A preterm SC PBPK model was then developed incorporating a mechanistic absorption model, including adjusted lymphatic flow, capillary density, and SC site volume.

Results. The scaled PBPK models with mechanistic absorption described the pharmacokinetics (PK) of IL1Ra following IV and SC dosing. At birth, the kidney plasma clearance of IL1Ra in preterm neonates was 23.3% relative to adults, i.e., 0.03 L/h/kg and 0.15 L/h/kg, respectively. The SC model predicted an earlier time to maximum concentration (T_{max}) in neonates compared to adults (i.e., 3 h vs. 4 h).

Discussion. This PBPK model for IL1Ra describes IV and SC dosing, providing valuable insights for PK and dose posology in preterm neonates. The model provides a quantitative foundation to guide future clinical development and optimised dosing strategies in this vulnerable population.

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In Vitro Models Integrating Metabolism and Transport to Support Mechanistic PK Modeling in Early Drug Discovery

Dr Kenneth Brouwer, PhD, RPh

Biography:

Kenneth Brouwer is Vice President, ADME Tox Research at BioIVT. A pharmacologist by training, Dr. Brouwer has led in vitro ADME programs at GSK and at PPD. He later led development of B-CLEAR technology, a method to quantitate hepato-biliary excretion. He was a founder of Qualyst Transporter Solutions, where he expanded applications of B-CLEAR technology and developed assays that integrate uptake, efflux, and regulatory function of cells. In 2017, BioIVT acquired Qualyst, and Dr. Brouwer now helps biopharmaceutical clients design and implement in vitro ADME research programs to achieve their drug R&D and regulatory submission objectives.

In Vitro Models Integrating Metabolism and Transport to Support Mechanistic PK Modeling in Early Drug Discovery

Kenneth Brouwer, PhD, RPh[1], BioIVT

In vitro systems are used extensively in the drug discovery and drug development process. They facilitate rapid screening for specific compound properties (efficacy, toxicity, distribution, metabolism, elimination) and also help determine the mechanism of drug action. The liver is the primary organ of metabolism and disposition for most drugs. Blood from the gastrointestinal tract flows via the portal vein through the liver and into the systemic circulation. Drugs are taken up into the hepatocytes through passive diffusion and/or active uptake by transport proteins present on the basolateral membrane of the hepatocytes. Once inside the hepatocyte, drugs may undergo metabolism, and the drug and/or generated metabolites may be effluxed across the canalicular membrane into the bile or across the basolateral membrane into the systemic circulation. The farnesoid X receptor (FXR) is a nuclear receptor that regulates genes involved in the homeostasis of bile acids. Accumulation of bile acids can lead to activation of FXR which protects against the toxic accumulation of bile acids by decreasing bile acid synthesis and regulating bile acid transport through induction of canalicular and basolateral efflux transporters. Sandwich-cultured human hepatocytes (SCHH) are a physiologically relevant model that maintains metabolic and transporter function, morphology, and regulatory machinery and therefore, is an ideal system to study bile acid metabolism and the regulation of bile acid transporters after treatment of hepatocytes with FXR agonists.

In this study, mechanistic pharmacokinetic (PK) modeling of data obtained from SCHH using B-CLEAR® technology was used to characterize the functional changes in bile acid transporters that occur with FXR activation. Changes in the basolateral uptake clearance, intrinsic basolateral efflux clearance, and intrinsic biliary clearance of an exogenously administered model bile acid, d8-TCA, were evaluated in SCHH after 72-hour treatment with obeticholic acid (OCA) and chenodeoxycholic acid (CDCA) to reflect the transporter function. In addition, the protein expression of TCA uptake and efflux transporters was assessed by immunoblot analysis. The combination of mechanistic PK modeling and molecular analysis provided a comprehensive data set for understanding the mechanisms of OCA- and CDCA-mediated alterations in hepatic bile acid transporters. Increases in the basolateral efflux clearance and biliary clearance were consistent with a pronounced upregulation of OSTβ protein expression and a smaller increase in BSEP protein expression. This study demonstrated the advantages of PK modeling in assessing changes in concurrent clearance pathways in a whole cell system.

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Unique translational clinical pharmacology challenges with novel, non-traditional drug molecules: the example of siRNA therapeutics

Dr Tom Polasek

Biography:

Dr. Tom Polasek is a Clinical Pharmacologist who works in the healthcare, life sciences and tertiary education sectors. Tom's main interest is the application of clinical pharmacology principles to improve patient care. He is the author of 150 peer-reviewed articles and conference presentations. Tom has been an Investigator on over 150 clinical studies and has supported countless drug development programs. Tom is Associate Medical Director of CMAX Clinical Research in Adelaide and is an Adjunct Senior Research Fellow at Monash University in Melbourne. Tom is also a Fellow of the American College of Clinical Pharmacology

Unique translational clinical pharmacology challenges with novel, non-traditional drug molecules: the example of siRNA therapeutics

Thomas M Polasek[1,2]. Centre for Medicine Use and Safety, Monash University[1], Melbourne, VIC, Australia; CMAX Clinical Research[2], Adelaide, SA, Australia.

Drugs are traditionally low molecular weight chemicals ("small molecules") or high molecular weight proteins ("large molecules"). But many other types of drug molecules are being developed and increasingly entering clinical use. Examples include RNA therapeutics (e.g., mRNA vaccines), cell-based therapies (e.g., CAR-T), various genomic editing technologies (e.g., CRISPR), and complex multi-specific drug conjugates (e.g., T-cell engagers). Most clinical development programs start with first-in-human (FIH) studies in healthy volunteers using single- and multiple ascending dose (SAD and MAD) designs, with pharmacokinetics, safety and tolerability the primary objectives. This translational step from nonclinical to clinical work is a major milestone in drug development, but poses unique clinical pharmacology challenges when developing novel, non-traditional drug molecules. This presentation covers some of these challenges using small interfering RNA (siRNA) therapeutics as examples. Key points include the following:

1. Relevance of nonclinical data for predicting target organs of toxicity and human safety
2. Selection of FIH clinical trial populations and starting doses
3. Accurate measurement of drugs in biological fluids for pharmacokinetic analyses
4. Data requirements for dose escalation decisions
5. Importance of pharmacokinetic-pharmacodynamic modelling to guide go/no-go decisions
6. Selection of recommended phase 2 dose(s)
7. Requirements for "special population" studies, including drug-drug interactions, QT-interval etc.
8. Evolving regulatory environments

Guidance with these challenges can be sort from similar past programs, where information is available, and by working with expert reviewers on HRECs, FIH trial clinicians with experience, sponsors with previous successes with a given type, and international regulators. Translational clinical pharmacology is an exciting field with unique challenges for novel, non-traditional drug molecules. Scientists and clinicians who enjoy turning principles into practice are urgently needed at the nonclinical-clinical interface to ensure new drug types enter human trials safely and efficiently.

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The challenges of conducting psychedelic clinical trials

Dr Jonathan Brett

Biography:

Dr Jonathan Brett is a senior staff specialist in clinical toxicology and addiction medicine at St. Vincent's Hospital, Sydney, clinical director of the Psychiatry and Non-Prescription Drug and Alcohol Unit and a clinical toxicologist with the NSW Poison's Information Centre. He has fellowships with the Royal Australian College of Physicians in clinical pharmacology, toxicology and addiction medicine. He is a conjoint Professor with St. Vincent's Clinical School, UNSW and a Senior NHMRC Research Fellow with the Medicines Policy Unit of Centre for Big Data Research in Health, UNSW. He is president elect of the Royal Australian College of Physicians Chapter of Addiction Medicine. He completed his PhD in biostatistics in 2018 with a focus on the use of big data measure the quality use of psychotropics in mental health and has a research interest in psychopharmacology.

The challenges and experiences with conducting psychedelic clinical trials

Jonathan Brett
St. Vincent's Clinical School, St. Vincent's Hospital, UNSW, Sydney.

The rapid expansion of psychedelic assisted psychotherapy interest and research has led to some unique challenges around clinical trial design and regulatory pipelines. Here I discuss some of our local experiences in conducting clinical trials and then some of the broader considerations including issues with masking, selection bias, safety, intervention complexity and regulatory challenges that face this area.

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Challenges of conducting trials with Complement inhibitors

Dr Millie Wang

Biography:

Millie Wang is a research physician at New Zealand Clinical Research, where she has worked as a collaborative investigator in more than 100 clinical trials. Her key research interests are in first-in-human / early phase clinical research, with a particular focus on immunology and metabolic studies. She graduated from the University of Auckland in 2011 with a Bachelor of Medicine and Bachelor of Surgery and obtained her Fellowship of the Royal Australasian College of Physicians in 2022, specialising in general and acute care medicine. She has since embarked on her clinical pharmacology training and is due to complete this in 2026.

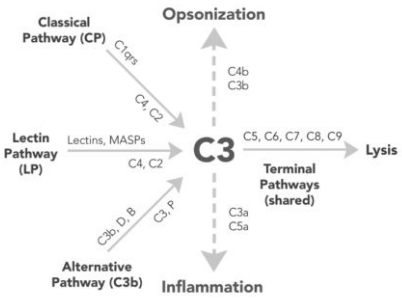
Challenges of conducting trials with Complement inhibitors

Millie Y Wang[1], New Zealand Clinical Research[1], Auckland, New Zealand

Introduction. Clinical trials involving complement inhibitors may predispose participants to infections caused by encapsulated organisms. This risk is determined by the drug target (proximal / unselective versus distal / selective pathway inhibition) and the varying extent of inhibition with ascending doses. Safety often requires vaccinations and / or prophylactic antibiotics, increasing complexity of the study design.

Aims. To provide an overview of some of the challenges faced when performing complement inhibitor studies at an early phase clinical trials unit.

Methods. A brief summary of the complement pathway and types of complement inhibitor studies will be presented, along with examples of different vaccination and antibiotic regimens. This will be followed by a discussion of the common challenges faced.



Results. Challenges of vaccinations included timing of vaccine administration, as well as vaccine related adverse events. Selection of the best antibiotic regimen for the type of complement inhibition was complicated by limited available evidence. Ease of administration and tolerability had to be considered as well. In addition, there were challenges associated with conditional follow up of participants whose complement levels had not returned to baseline at the end of study.

Discussion. Vaccination was considered the most important step in terms of reducing the risk of infection caused by encapsulated organisms. Haematology patients receiving approved complement inhibitors generally did not require prophylactic antibiotics if they were adequately vaccinated. However, do we have a greater duty of care towards healthy volunteers? With the lack of robust evidence, are we doing more harm than good when administering prolonged courses of prophylactic antibiotics to participants, both individually and from the perspective of antibiotic stewardship? To avoid unblinding, participants often received longer courses of antibiotics than was necessary.

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Technical aspects of modern early phase study design – what does the future of early phase clinical studies look like?

Prof Sepehr Shakib

Biography:

Professor Shakib is Professor of Clinical Pharmacology at the University of Adelaide, and has been involved in over 300 phase I clinical trials since 1997

Technical aspects of modern early phase study design – what does the future of early phase clinical studies look like?

Sepehr Shakib, Consulting Medical Director, CMAX Clinical Research, Adelaide, SA, Australia. Professor, Clinical Pharmacology, University of Adelaide, Adelaide, SA, Australia .

Introduction. Over the last 20 years there has been a steady increase in the number and complexity of phase I studies being performed**.** What can we learn that will help determine the challenges of future early phase clinical trials?

Aims. To summarise the changes in the designs of early phase trials as well as clinical trial ecosystem in which they are conducted, to highlight the likely future challenges

Discussion: The presentation will review the impact of trends in early phase drug development such as the emergence of novel therapeutic approaches (monoclonal antibody, and SiRNA development), growth in number of Contract Research Organizations, drug repurposing, and the desire for accelerated development and earlier biomarker data on current and future aspects of early phase clinical trials.

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Vascular smooth muscle cell heterogeneity: New insights into coronary artery atherosclerosis

Dr Maria Jelinic

Biography:

Hypertension, obesity and diabetes are leading causes of cardiovascular disease. Dr Maria Jelinic hopes to make this a problem of the past. Since completing her PhD in vascular physiology, Maria's research has focused on elucidating mechanisms that drive cardiac, vascular and renal complications in cardiometabolic disease. Her research investigates novel inflammatory mechanisms that drive renal and vascular complications in these disease states. Maria specializes in using pharmacological interventions and genetic modifications in rodent models of cardiovascular disease to test new therapeutic strategies that target immune cells to reduce end organ-damage in these disease settings. In her short career to date, she has produced 34 publications (with over 1000 citations), and secured over $3.7M in competitive funding. She is also passionate about training the next generation of scientists to build on Australia's capacity in biomedical research and has over 12 years' experience training both undergraduate and HDR students in physiology and pharmacology.

Vascular smooth muscle cell heterogeneity: New insights into coronary artery atherosclerosis.

Jake Robertson[1], Helen McGuire[2,3], Sean Lal[3], Alex Bobik[1,4], Chris G Sobey[1], Gemma Figtree[2,3], Antony Vinh[1], Grant R Drummond[1], Maria Jelinic[1,4]

[1]Centre for Cardiovascular Biology and Disease Research, La Trobe University, Melbourne, VIC, 3086, Australia. [2]School of Medical Sciences, Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia. [3]Charles Perkins Centre, The University of Sydney, Sydney, NSW, Australia. [4]Baker Heart and Diabetes Research Institute, Prahran, VIC, Australia.

Introduction. Myocardial infarction remains the leading global cause of death, primarily driven by coronary artery atherosclerosis (CAA). CAA involves plaque formation through lipid accumulation, immune cell infiltration, and vascular smooth muscle cell (VSMC) phenotype changes. Up to 70% of infarctions result from plaque rupture due to fibrous cap instability, yet the mechanisms driving this instability are poorly understood.

Aims. To identify key cell types involved in fibrous cap formation and degradation in human coronary arteries. We hypothesised that synthetic VSMCs contribute to cap formation, and that their transition to a lipid-scavenging, macrophage-like phenotype underlies plaque instability in advanced disease.

Methods. Eight cryopreserved human left anterior descending (LAD) coronary artery samples with varying CAA severity were analysed using single-cell RNA sequencing (scRNAseq), spatial transcriptomics, and imaging mass cytometry. Transcriptomic data were processed using the Seurat package in R to assess cellular heterogeneity, localization, and interactions.

Results. Analysis of 32,481 cells revealed nine major cell clusters, including four VSMC subtypes: contractile, synthetic, proinflammatory, and macrophage-like. Gene ontology analysis showed distinct biological roles for each subtype. Synthetic VSMC signatures were enriched in early-stage plaques, particularly within the fibrous cap, but diminished in advanced disease. In contrast, macrophage-like VSMCs were absent in healthy arteries, appeared in early plaques, and were highly enriched in the fibrous cap of advanced lesions.

Discussion. Our findings reveal dynamic VSMC heterogeneity in human CAA and suggest that synthetic VSMCs may drive plaque instability by transitioning to a macrophage-like phenotype. Targeting these cellular transitions could offer new therapeutic strategies to prevent plaque rupture and myocardial infarction.

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Machine learning and spatial multiomics to study drug targets and responses

A/Prof Quan Nguyen

Biography:

Associate Professor Nguyen is a head of the Genomics and Machine Learning lab and a scientific director of the National Centre for Spatial Tissue and AI Research. With supports from multiple prestigious fellowships, he established his leadership in addressing cancer complexity at single cell and tissue levels. He has led multiple large-scale projects/programs, funded nationally (e.g., ARC, NHMRC, MRFF) and internationally (e.g., DoD, NCI, Wellcome Trust).

Machine learning and spatial multiomics to study drug targets and responses

A/Prof Quan Nguyen, QIMR Berghofer

Spatial multiomics technologies allow for the profiling of RNA, proteins, and metabolites within tissue sections, while preserving their spatial context. In this talk, I will present our approach to identifying potential drug targets using spatial transcriptomics, focusing on ligand-receptor interaction analysis and integration with knowledge graphs.

I will showcase examples where combined spatial transcriptomics and proteomics analyses provide insights into treatment outcomes following chemotherapy and immunotherapy. Finally, I will introduce our integrated spatial metabolomics and transcriptomics methodology, which enables mapping of drug distribution alongside the corresponding transcriptional responses.

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Using spatial proteomics on human cardiac organoids to map cardiac cell-cell and cell-matrix interactions in fibrosis

Dr Lynn Devilee

Biography:

I am a postdoctoral researcher in the Cardiac Drug Discovery Laboratory at QIMR Berghofer. After finishing my BSc in Biomedical Sciences and MSc in Molecular Mechanisms of Disease at the Radboud University, Nijmegen, The Netherlands, I completed my PhD in the Cardiac Bioengineering Laboratory at QIMR Berghofer working with Prof James Hudson. The primary focus of my work was to better understand why the endotherm heart fails to regenerate after injury. Using human cardiac organoids, microscopy and a multi-omics approach, I studied the regulation of the cardiac cell cycle. Since finishing my PhD in November 2024, I have been working with Dr. Simon Foster in the Cardiac Drug Discovery Laboratory. Here, I am following my passion for fundamental science and understanding why cells/organs/tissues work the way they do. I am applying my skills in organoid culture, functional analysis and microscopy to improve our understanding of the dynamics of extracellular matrix remodeling, how this impacts cardiac function and vice versa under physiological and pathological conditions, including fibrosis. I am also working on setting up a cardiac panel for spatial proteomics to map the spatial cellular and ECM interactions in response to pathological stimuli.

Using spatial proteomics on human cardiac organoids to map cell-cell and cell-matrix interactions in fibrosis

Lynn Devilée[1], Harley Robinson[1], Ashwini Potadar[2], Clay Winterford[2], Tam Hong Nguyen[2], Simon Foster[1]. Cardiac Drug Discovery Laboratory, QIMR Berghofer[1], Brisbane, QLD, Australia; Scientific Services, QIMR Berghofer[2], Brisbane, QLD, Australia

Introduction. Cell-cell and cell-matrix interactions regulate cardiac tissue homeostasis and disease development. Spatial mapping of these interactions and changes to tissue architecture can be done through immunohistochemistry (IHC), though this is limited to a few markers per sample. Recent years, major strides have been made towards multiplexing IHC, now making it possible to image ~100 different markers on one sample. This allow us to study the dynamics of extracellular matrix (ECM) remodelling in cardiac fibrosis into greater detail and with higher throughput.

Aims. To develop a spatial-proteomics workflow using the Akoya PhenoCycler to study cell-cell and cell-matrix interactions in a 3D human cardiac organoid (hCO) model.

Methods. A high throughput stem-cell derived hCO model, consisting of cell types found in the human heart, including cardiomyocytes, fibroblasts, epicardial cells and endothelial cells, was used to model fibrosis in response to fibrotic stimuli (TGFβ and endothelin-1). Functional parameters (force, rate, activation and relaxation time) were analysed along with IHC for classic fibrosis markers (tenascin C, fibronectin). In addition, hCOs were pooled, organised in an arrayed format (6 x 4-5), and fresh-frozen in OCT-compound, while maintaining treatment group identity. OCT blocks were sectioned (7 µm), with sections placed onto coverslips to image using the Akoya PhenoCycler format. A custom cardiac antibody panel with over 20 markers was generated through antibody-barcode conjugation, including cardiac (TNNI3, NKX2-5), fibroblast (DCN, αSMA), endothelial (CD31), epicardial (WT-1) and ECM (TNC, FN, COL1A1) markers to enable multiplexed cell type identification and ECM localisation.

Results. Fibrotic mediators resulted in distinct functional alterations and IHC demonstrated robust changes in fibrosis markers. Initial PhenoCycler runs have been performed, providing evidence of feasibility, successful antibody conjugation and marker specificity.

Discussion. We have applied spatial proteomics using a custom-made antibody panel for the first time on hCOs to enable high throughput visualisation of ECM remodelling and cell-cell interactions. Current work is focussed on further optimising sample processing, expanding the antibody panel and establishing quantitative analysis pipelines.

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End-to-end spatial transcriptomics analysis with VR-Omics

Prof Mirana Ramialison

Biography:

Professor Mirana Ramialison is Group Leader of the Transcriptomics and Bioinformatics Laboratory at the Murdoch Children's Research Institute in Melbourne, and co-Director of the reNEW Bioinformatics Hub of the Novo Nordisk Foundation for Stem Cell Medicine. Prof Ramialison received her Engineering degree from the University of Luminy in France, after which she worked as a programmer at the ERATO differentiation project in Kyoto. She obtained her PhD from the European Molecular Biology Laboratory in Heidelberg in 2007, and joined the Victor Chang Cardiac Research Institute in Sydney as an EMBO and HFSP Post-Doctoral Fellow in 2010. As an NHMRC/Heart Foundation Career Development Fellow, she established her first laboratory at the Australian Regenerative Medicine Institute (Monash University) in 2014. She is currently a Heart Foundation Future Leader Fellow. Prof Ramialison has delivered a number of algorithms that enable the generation of new knowledge in our understanding of embryonic development and she is pioneering the field of spatial transcriptomics, having published the first 3D transcriptome map of the mammalian heart and, the first visualisation of spatially-resolved transcriptome data in immersive environments. https://ramialison-lab.github.io/

End-to-end spatial transcriptomics analysis with VR-Omics

Mirana Ramialison, Novo Nordisk Foundation Center for Stem Cell Medicine (reNEW), Murdoch Children's Research Institute, Parkville, Victoria, 3052, Australia

The field of spatial transcriptomics (ST) is progressing rapidly, driven by technological advances that offer higher resolution, increased throughput, processing of larger sample sizes, and multimodal capabilities. Despite these developments, there is a lack of comprehensive and intuitive tools for the automated integration and analysis of complex multi-slice datasets—particularly those arranged in co-planar (2D) or stacked (3D) formats.

To address this gap, we developed VR-Omics, a free, platform-agnostic software that enables end-to-end automated processing of spatial transcriptomics data via a user-friendly interface. Starting from raw vendor data, VR-Omics supports data preprocessing, analysis and visualisation in both standard desktop environments and immersive virtual reality, enhancing user engagement and interpretability.

VR-Omics is built on the Unity game engine and integrates Python-based analytical workflows. This modular architecture allows seamless incorporation of state-of-the-art ST analysis packages, ensuring flexibility and scalability as the field evolves.

By integrating sequential 2D spatial transcriptomics slices, VR-Omics can reconstruct comprehensive 3D datasets that capture gene expression dynamics across spatial and temporal dimensions. This enables researchers to investigate the spatial organisation of gene regulatory networks and their disruption in disease, providing deeper insights into complex biological systems.

Benchmarking against existing tools highlights VR-Omics' unique capabilities in handling multi-slice datasets in both co-planar (2D) and stacked (3D) configurations. In a case study of rare paediatric cardiac rhabdomyomas, VR-Omics uncovered previously undetected dysregulated metabolic networks through co-planar slice analysis, demonstrating its potential to reveal novel biological insights.

https://ramialison-lab.github.io/pages/vromics.html

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Improving Cardiometabolic disease outcomes for people with intellectual disability

Prof Julian Trollor

Biography:

Julian is a Scientia Professor, NHMRC Leadership Fellow, Director of the National Centre of Excellence in Intellectual Disability Health at UNSW Sydney. He was appointed a Member of the Order of Australia (AM) in 2025 for significant service to people with disability, particularly as a clinician and academic. He previously held UNSW's inaugural Chair of Intellectual Disability Mental Health (UNSW Sydney) and was head Department of Developmental Disability Neuropsychiatry (3DN).

Julian and the Centre work to improve health policy, practice and supports for people with an intellectual or developmental disability. They lead educational resource development, health promotion, consultancy, advocacy and contributions to policy and legislation. The team also conducts translational research of benefit to people with disability and the health sector.

Improving Cardiometabolic disease outcomes for people with intellectual disability

Julian N. Trollor[1], Preeyaporn Srasuebkul[1], Janelle Weise[1,2], Rebecca Koncz[1], Jessica Bellamy[1,3], Emma Suzuki[1], Katherine Samaras[4,5], Anurag Sharma[6], Benn Harris-Roxas[6], Janet C. Long[7], Anne Kavanagh[8]

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[2]Discipline of Occupational Therapy, Sydney School of Health Sciences, Faculty of Medicine and Health, University of Sydney
[3]School of Medical, Indigenous & Health Sciences, Faculty of Science, Medicine & Health, University of Wollongong, NSW, Australia
[4]Department of Endocrinology, St Vincent's Hospital Sydney, Darlinghurst, NSW, Australia
[5]St Vincent's Clinical School, UNSW Medicine and Health, UNSW Sydney, NSW, Australia
[6]School of Population Health, UNSW Medicine and Health, UNSW Sydney, NSW, Australia
[7]Australian Institute of Health Innovation, Macquarie University, Sydney
[8]Melbourne School of Population and Global Health, University of Melbourne, Melbourne, Australia

Introduction. People with intellectual disability experience significantly higher mortality rates[1], including a disproportionate number of potentially avoidable deaths compared to the general population[2]. Deaths related to cardiovascular conditions, overweight/obesity and diabetes are the most prevalent[2] and are exacerbated by undertreated or untreated preventable risk factors.

Aims. This work aims to explore the population health needs and emerging evidence concerning the prevalence and prevention of cardiometabolic diseases in individuals with intellectual disability.

Methods. We present findings from a mixed-methods research program conducted by the National Centre of Excellence in Intellectual Disability Health, focusing on cardiometabolic health.

Results. Our analysis reveals substantial gaps in preventive healthcare policy and practice for people with intellectual disability. Using linked administrative data from Australia, we report the prevalence of specific cardiometabolic conditions in this population. Additionally, we outline a targeted strategy for reducing cardiometabolic disease burden.

Discussion. We propose a comprehensive, multipronged approach to improving cardiometabolic health outcomes for people with intellectual disability, inviting further discussion, engagement and collaboration.

[1]Florio T, Trollor J. Mortality among a Cohort of Persons with an Intellectual Disability in New South Wales, Australia. J Appl Res Intellect Disabil. 2015 Sep;28(5):383-93. doi: 10.1111/jar.12190. Epub 2015 May 21. PMID: 25994286.

[2]Trollor J, Srasuebkul P, Xu H, et al Cause of death and potentially avoidable deaths in Australian adults with intellectual disability using retrospective linked data BMJ Open 2017;**7:**e013489. doi: 10.1136/bmjopen-2016-013489

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Understanding the mechanisms of cardiac and metabolic risk in individuals with intellectual disability

A/Prof Elisabeth Lambert

Biography:

A/Prof Elisabeth Lambert joined the School of Health Science and Iverson Health Innovation Research Institute in February 2017. She previously worked at the Baker Heart and Diabetes Institute for 18 years. Elisabeth's research program focusses on mechanisms, treatments and prevention of cardiovascular and metabolic diseases, with a particular interest on the role played by the sympathetic nervous system in the development of metabolic abnormalities and organ damage. She has led multiple clinical cross-sectional, and interventional investigations in various conditions such as hypertension, obesity, type-2 diabetes, chronic kidney disease, orthostatic intolerance, anorexia nervosa as well as studies in people living with intellectual disability. She has published around 220 papers and has been a chief investigator on 12 NHMRC grants.

Recent major achievements of her group include:

• Refinement and application of techniques for identifying brain areas involved in muscle sympathetic nerve activity in the context of hypertension and obesity (NHMRC Idea grant 2022-2024). Techniques include direct nerve recording using microneurography, magnetoencephalography (MEG) and magnetic resonance imaging (MRI).

• Demonstration that young women with anorexia and those who have recovered from the condition have enhanced arterial stiffness, a marker of vascular aging.

• Demonstration that young normotensive individuals with excess adiposity have subclinical organ damage (cardiac, renal and endothelial) and that the degree of organ dysfunction is directly related to the degree of sympathetic activation.

• Demonstration of the link between sympathetic activity and endothelial dysfunction in women with dyslipidemia.

Understanding the mechanisms of cardiac and metabolic risk in individuals with intellectual disability

Elisabeth Lambert, Clara Zwack, Rachael McDonald
Swinburne University of Technology, Hawthorn, Victoria

Young adults with intellectual disability (ID) are at higher risk of premature death and experience increased prevalence of chronic diseases compared to the general population. Cardiovascular and metabolic risk factors in this population remain to be determined. It is unclear whether it is underlying biological factors – perhaps related to the aetiology of ID – that confer elevated physiological risk, or whether modifiable health behaviours and the environment lead to substantial health challenges and risks. Hence, we investigated the cardiometabolic health profile of people with ID aged 18–45 years to understand whether this population is more pre-disposed to display early signs of cardiometabolic disease compared to the general population, and to identify whether their environment and lifestyle may contribute to increased cardiometabolic risk. Investigators collected clinical data through a non-invasive cardiovascular and metabolic assessment, blood sample analysis and delivery of questionnaires relating to behavioural and environmental factors. The findings indicate that young adults with ID demonstrate increased prevalence of cardiometabolic risk factors compared to those without ID including increased frequency of hypertension, high body mass index, high levels of plasma Hba1c and impaired

autonomic nervous system function. Young adults with ID have increased stress levels and experience social and community isolation, reduced physical activity and poor diets. Our results indicate that many modifiable risk factors were linked to cardiometabolic risk factors. Screening for traditional, subclinical, modifiable health-related behaviours and environmental risk factors in young adults with ID could prove a useful tool in early detection of cardiometabolic disease in this cohort.

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Using co-design to improve health outcomes in disadvantaged communities

Professor Rachael Mcdonald

Biography:

Professor Rachael McDonald is the Director of the MedTechVic Hub. The MedTechVic hub creates innovative enabling technology, products and services to enhance lives for people with disability, their families and the people who support them. The hub does this through Development of enabling technology products, Consulting on co-design and manufacture, Best-practice research and development and Educational services, including fellowships and training.

Professor McDonald is a clinical, research and teaching Health Professional with an interest in enabling people with lifelong disabilities to participate in life situations. She has worked extensively in this field, with in both children's services and adult settings. She has or is supervising 31 research (honour's, MSc and PhD) students specialising in the care of people with complex disability as well as development and evaluation into the effectiveness of assistive technologies, and has published widely (over 150 outputs). She has qualifications in occupational therapy, biomechanics and higher education in addition to her Doctorate and has attracted over $11m in competitive grant funding.

Using co-design to improve health outcomes in disadvantaged communities

Rachael McDonald, MedTechVic Hub, Swinburne University of Technology, Melbourne, VICTORIA, Australia

Introduction. Approximately 2% of Australians live with intellectual disability (ID), experiencing higher rates of preventable death, reduced life expectancy and significant cardiometabolic risk, including hypertension, obesity and diabetes. Despite this, health promotion programs rarely incorporate the perspectives of people with ID, limiting relevance, uptake and sustainability. MedTechVic provides an innovation ecosystem that brings together people with lived experience, clinicians, researchers and industry to co-design health technologies and interventions.

Aims. This seminar will demonstrate how MedTechVic's co-design framework can be applied to the development of health promotion strategies to reduce cardiovascular risk in people with ID, highlighting practical processes for engaging disadvantaged populations in research about their own health.

Methods. Drawing on MedTechVic's structured approach, individuals with ID, carers and service providers are engaged from the outset of research to define priorities, shape intervention design and evaluate feasibility. Participatory workshops, accessible communication methods, and iterative prototyping ensure equity of input and shared decision-making.

Results. Co-design processes have enabled the creation of tailored digital and hybrid health programs, accessible nutrition and exercise resources, and inclusive evaluation methods. Involving end users has identified barriers not evident to clinicians alone (e.g., fatigue, sensory sensitivity, accessibility of technology), allowing for adaptation to ensure feasibility and effectiveness.

Discussion. MedTechVic's approach demonstrates that embedding end users in research and design enhances the equity, inclusivity and translational potential of health promotion strategies. By centring the voices of people with ID, co-design provides a scalable framework that can also be applied to other disadvantaged groups at high risk of cardiometabolic disease.

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Designing and implementing the Food and Lifestyle Information Program (FLIP) culinary nutrition intervention for adults with intellectual disability

Dr Roberta Asher

Biography:

Dr Roberta Asher is an Accredited Practising Dietitian (APD) and Postdoctoral Researcher at The University of Newcastle.

Roberta completed a Bachelor of Nutrition and Dietetics in 2010 after a 10-year career as a trade qualified chef working in restaurant and international hotel kitchens in Australia and overseas. She has worked as a clinical dietitian, a community culinary nutrition educator and research assistant. In 2024 Roberta completed her PhD at the University of Newcastle researching cooking skill development and nutrition education for people with disability using co-design methods.

Roberta's research work focusses on programs that aim to improve diet quality, health and wellbeing through cooking and food skill development. Working in a multidisciplinary collaboration, she has also developed resources that can be used by other culinary education program developers, across a range of settings and target groups, to guide program planning, curriculum development and evaluation.

Designing and implementing the Food and Lifestyle Information Program (FLIP) culinary nutrition intervention for adults with mild to moderate intellectual disability

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Introduction. Healthy food provision and preparation can present unique and complex challenges for people with intellectual disability. Programs to address these challenges are a promising strategy to improve nutrition-related health. However, people with intellectual disability are infrequently included in program development.

Aims. To describe the development and pilot study of the Food and Lifestyle Information Program (FLIP), a culinary nutrition program for adults with mild-to-moderate intellectual disability.

Methods. FLIP was initiated by a disability service provider. Guided by inclusive research principles, the FLIP program and pilot study was developed in partnership with an academic research team and co-researchers with lived experience of intellectual disability. The eight-session pilot evaluated feasibility (recruitment, retention, engagement, adverse outcomes), acceptability (interactive process evaluation), and preliminary effectiveness (cooking frequency, food skill confidence, diet quality) using measures adapted for people with intellectual disability.

Results. Six of eight participants completed the pilot with high attendance and engagement. The FLIP eight-week small-group program featured cooking and nutrition education activities, Easy Read paper-based resources, and opportunities for participant choice. Co-researchers with intellectual disability contributed to the design of recipes, program materials and evaluation tools, enhancing accessibility of the program Overall, FLIP was well received by participants and was feasible to run. Diet quality was feasible to measure.

Discussion. Inclusive design and implementation enhanced program relevance and engagement. Future studies will enable further iterative development and can evaluate whether FLIP can improve participants' cooking and meal planning skills, diet quality, health and wellbeing.

Asher RC et al. (2024) J Appl Res Intellect Disabil 2024 Vol. 37 Issue 5 Pages e13281

P500

IRAP inhibitors offer reduced protection following endothelin-1 induced stroke in normotensive rats.

Mr Barisa Degal

Biography:

Student at Monash University, currently completing a PhD in Pharmacology in the Integrative Cardiovascular Pharmacology Group in ischemic stroke. A Graduate of a Bachelor of Science with majors in Physiology and Pharmacology, as well as an Honours degree in Pharmacology. Barisa's project is to investigate the effects of IRAP inhibition following endothelin-1-induced ischemic stroke in normotensive rats. Ultimately, the project aims to bridge the gap between preclinical discoveries and clinical treatments, thereby improving neurological outcomes for stroke patients.

IRAP inhibitors offer reduced protection following endothelin-1 induced stroke in normotensive rats.

Barisa Degal[1], Robert Widdop[1], Adriana Knezic[1]. Siew Yeen Chai[2], Tracey Gaspari[1], [1]Pharmacology Department, [2]Physiology Department, Monash University, Melbourne, VIC, Australia

Introduction. Stroke is the third leading cause of death and the top cause of disability in Australia. The only approved drug, tissue plasminogen activator (t-PA), must be administered within ~4.5 hours, excluding nearly 90% of patients. Insulin-regulated aminopeptidase (IRAP) is a promising target: its deletion improves outcomes and blood flow in normotensive mice with middle cerebral artery occlusion[1], and inhibition reduces infarct size in the endothelin-1 model of ischemic stroke in hypertensive rats[2]. However, its efficacy remains untested in normotensive animals.

Aim. To determine if inhibition of IRAP is protective against focal ischemic damage in a conscious model of stroke using normotensive Sprague-dawley (SD) rats.

Methods. Cannulas were implanted in 10-week-old SD rats with endothelin-1 (ET-1) administered to conscious rats until severe stroke behaviours were achieved; sham (vehicle) group received saline. Treatment of either vehicle (n=10) or the IRAP inhibitor, HFI-419 (1nmol; n=10) was given blinded by icv infusion at 6,24,48 and 70h post stroke. Motor and sensory function was assessed using ledge beam and adhesive sticker test. At 72h post-stroke, rats were culled and brains taken for ex vivo analysis.

Results. ET-1 induced significant infarcts in both vehicle and HFI-419 groups; however, only vehicle-treated rats showed significant motor impairment on the ledge beam at 24 and 72h post-stroke. Treatment had no effect on adhesive sticker removal time, with both groups taking significantly longer than the sham group. For all other markers, despite positive trends, there was no significant drug effect with HFI-419.

Discussion. These results suggest IRAP inhibition has reduced protection in a normotensive model of stroke compared to effects reported in the spontaneously hypertensive rat strain using the ET-1 model. Therefore, moving forward either: 1. A higher dose of drug is required to overcome the effects in a normotensive setting; or 2. Protection is being mediated by treating the high blood pressure in the co-morbid model, improving cerebral blood supply through other vasodilatory factors.

1. Pham, V. et al (2011). Journal of Neurotrauma 29: 1243-1248. doi:10.1089/neu.2011.1824.
2. Telianidis, J et al (2023). Scientific Reports 13: 19722. doi:10.1038/s41598-023-46072-5.

P501

Vasorelaxation by NO in thoracic aorta is unaffected by additional endothelial autacoids

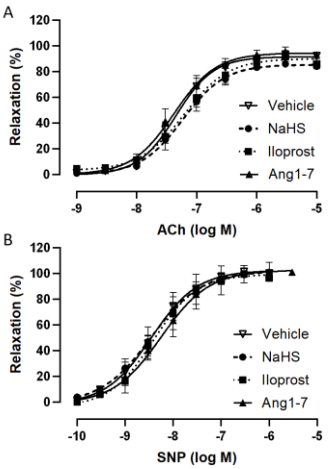
Ms Beidong Huang

Biography:

Beidong Huang is an overseas-trained and qualified medical doctor undertaking a PhD at the University of Adelaide. Her work focuses on translational cardiovascular physiology/pathophysiology, examining how the main compartments of endothelial function interact in health and disease. It is the goal of her research to bridge bench and bedside to optimise outcomes in diabetes, heart failure, and related conditions.

Vasorelaxation by NO in thoracic aorta is unaffected by additional endothelial autacoids

Beidong Huang[1,2], Irene Stafford[2], Michael P Frenneaux[1,2], Cher-Rin Chong[1,2], John D Horowitz[1,2]. Fac of Hlth and Med Sci, Univ of Adelaide[1], Adelaide, SA; Cardiovasc Pathophysiol & Therapeutics Grp, Basil Hetzel Inst for Transl Hlth Res, the Queen Elizabeth Hosp[2], Woodville South, SA.



Introduction. Endothelial-dependent vasodilatation, studied mainly in isolated large arteries, has been largely attributed to release of nitric oxide (NO), but some studies have raised the possibility of additive/synergistic interactions with other endothelial autacoids, with which NO shares components of signalling pathways.

Aims. We sought to delineate the extent of interactions between NO and other endothelial autacoids in normoxic large arteries.

Methods. Male Sprague-Dawley rats were anaesthetised with 4% inhaled isoflurane. Thoracic aortic rings were mounted in normoxic organ baths, and precontracted with phenylephrine. Concentration-response curves for ACh (NO synthase activator) and SNP (direct NO donor) alone, or with subthreshold concentrations of sodium hydrogen sulphide (NaHS, hydrogen sulphide donor), Iloprost (prostacyclin analogue) and Angiotensin-(1-7) [Ang-(1-7), ACE2 product]. EC_{50} values were derived from concentration-response curves (see Figure) using logit transformation.

Results. EC_{50} values (log M) for ACh and SNP were -7.04±0.17, and -8.434±0.11 respectively. Ang-(1-7) induced no intrinsic vasodilator effects, and 100 nmol/L was utilized for co-incubation; subthreshold concentrations of NaHS and Iloprost were 100 µmol/L and 30 nmol/L respectively. None of these co-incubations significantly altered responses to either ACh or SNP (n=4-6, see Figure).

Discussion. These data exclude significant vasodilator interactions between either NOS activation or NO signalling and subthreshold concentrations of other vasodilatory autacoids in a normoxic isolated vessel preparation. Further experiments will address variability in intrinsic autacoid interactions, such as, the influence of hypoxia/redox stress, and heterogeneity between macro- and microvasculature. Clinically, these data will elucidate mechanisms for some of the variability in NO effect seen in pathological states such as heart failure, sepsis and tissue anoxia.

P502

Protection in IRAP deficient mice differs between photothrombotic and MCAO induced stroke

Ms Rianna Tadd-Lennox

Biography:

Rianna Tadd-Lennox is a second-year PhD student in the Department of Pharmacology, Monash University. She is passionate about neuropharmacology and cardiovascular research, and her work aims to reduce the devastating neurological deficits that follow ischemic stroke. Her research utilizes the photothrombotic model of stroke to assess the impacts of targeting insulin-regulated aminopeptidase (IRAP) as a novel ischemic stroke therapeutic. Ultimately, her work aims to bridge the gap between preclinical discoveries and clinical treatments to improve outcomes for stroke patients.

Protection in IRAP deficient mice differs between photothrombotic and MCAO induced stroke.

Rianna Tadd-Lennox [1], Brad Broughton[1], Siew Chai[2], Adriana Knezic[1], Robert Widdop[1], Tracey Gaspari[1]. [1]Pharmacology Department, [2]Physiology Department, Monash University, Melbourne, VIC, Australia

Introduction. Ischemic stroke is a major cause of death and disability. The only pharmacological treatment is the clot buster, recombinant tissue plasminogen activator, which <10% of Australian patients are eligible to receive[1]. Insulin-regulated aminopeptidase (IRAP) is a potential target for treatment, with IRAP deletion and IRAP inhibition protecting against damage induced by middle cerebral artery occlusion (MCAo) in mice[2] and spontaneously hypertensive rats[3] respectively. These benefits are yet to be tested in females or in models of cerebral microvascular occlusion.

Aims. To investigate the effect of IRAP gene deletion on photothrombotic stroke outcomes in male and female mice.

Methods. Photothrombotic stroke was induced in IRAP wild type (WT) and knock out (KO) male and female mice (n= 10/group, aged 6-8 months). Motor and sensory function were assessed at baseline and days 1 and 3 following surgery using the hanging wire and adhesive removal tests. At 3 days post-surgery, mice were culled, and brains were taken for analysis of infarct volume and expression of IRAP, activated astrocytes, and apoptosis.

Results. Photothrombotic stroke induced significant infarct in the cortex, impaired function, and increased levels of neuroinflammation and apoptosis. Male mice had significantly larger infarcts (WT:22.90 ±2.19 mm^3, KO: 23.97 ± 2.90 mm^3) than female mice (WT: 16.7 ±1.82 mm^3, KO: 18.53 ± 2.48 mm^3). IRAP deletion protected against weight loss in male mice; however, for all other outcomes, there was no genotype. Interestingly in the peri-infarct region of WT female mice had higher IRAP expression than male mice (9.11±1.07% vs 4.28 ± 0.58%)

Discussion. IRAP gene deletion did not protect against photothrombotic stroke. This contrasts with previous protection against MCAO-induced ischemic damage with IRAP gene deletion and IRAP inhibition, potentially due to lack a lack of penumbral region and contralateral blood flow in photothrombotic stroke. This suggests that part of the protection of IRAP gene deletion/inhibition may result from partial restoration of cerebral blood supply to the ischemic region.

1. Stroke Foundation. (2023). National Stroke Audit – Acute Services Report 2023. Melbourne, Australia.
2. Pham, V. (2011). Journal of Neurotrauma 29: 1243-1248. doi:10.1089/neu.2011.1824.
3. Telianidis, J (2023). Scientific Reports 13: 19722. doi:10.1038/s41598-023-46072-5.

P503

Left ventricular effects from polypharmacy across age and sex in mice

Mr Kevin Winardi

Biography:

Kevin is a scientific officer at the Laboratory of Ageing and Pharmacology, Kolling Institute and the University of Sydney, led by Prof Sarah Hilmer. His work primarily focuses on exploring the complex molecular basis of drug-related harms in old age and whether medication withdrawal offers any molecular reversibility benefits. Using the established preclinical murine model, Kevin employed big molecular data analysis to study complex age-related drug-drug interactions across various different organs, including the heart.

Consequences of polypharmacy on left ventricular function, structure, and proteome across age and sex in mice

Kevin Winardi[1], Trang Tran[1], Scott P. Levick[2], Alexander Widiapradja[2], Gizem Gemikonakli[1], Susan E. Howlett[3], Matthew J. McKay[4], Mark P. Molloy[4], John Mach[1], Sarah N. Hilmer[1]. Laboratory of Ageing and Pharmacology[1], Kolling Institute, University of Sydney and NSLHD, Sydney, NSW, Australia; Department of Physiology, Pharmacology, and Toxicology[2], West Virginia University, Morgantown, West Virginia, USA; Departments of Pharmacology and Medicine (Geriatric Medicine)[3], Dalhousie University, Halifax, Nova Scotia, Canada; Bowel Cancer and Biomarker Laboratory[4], Kolling Institute, University of Sydney and NSLHD, Sydney, NSW, Australia

Introduction. Polypharmacy (≥5 medications) is prevalent in older individuals with cardiovascular conditions and is associated with adverse drug reactions. However, the specific adverse effects on the cardiovascular system in different age and sex groups are not well characterized.

Aims. To assess the impact of polypharmacy in the cardiac left ventricular (LV) function, structure, and proteome across age and sex in mice.

Methods. Young (4 months) and old (22 months) C57BL/6JArc mice of both sexes were treated with a polypharmacy regimen that included two cardiovascular drugs (chronic oral therapeutic doses of simvastatin and metoprolol plus oxybutynin, oxycodone, and citalopram). After 9 weeks of treatment, the LV structure and function were assessed via echocardiography. At week 10, LV tissue was collected for proteomic analysis using data-independent acquisition (DIA) with Q-Exactive HF-X Orbitrap mass spectrometry.

Results. Polypharmacy induced both non-specific and age-/sex-specific effects. Heart rate was reduced across all age and sex groups, whereas LV structure was primarily affected in old males. Specifically, polypharmacy increased relative wall thickness due to decreased LV diameter and volume. When comparing age- and sex-matched polypharmacy against control, a total of 195 unique differentially expressed proteins were identified, with old males experiencing most at 141 proteins. These include structural proteins, calcium handling proteins, metabolic enzymes, and antioxidants. Network analysis identified specific proteins associated with specific changes in cardiac function and structure observed with polypharmacy.

Discussion. The finding highlights the varying impact of polypharmacy in the cardiac pathophysiological and molecular domains across age and sex.

P504

Therapeutic Potential of Human Amnion Epithelial Cells for Improving Post-Stroke Cognitive Outcomes

Mr David Wong Zhang

Biography:

David Wong Zhang is a final year PhD Candidate from the Centre of Cardiovascular Biology and Disease Research (led by Prof. Grant Drummond and Prof. Chris Sobey). He completed his Master of Science in 2021 in the department of Microbiology, Anatomy, Physiology and Pharmacology at La Trobe University. David has received recognition of his work through awards from the Australian & New Zealand Microcirculation Society (ANZMS), and Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT).

Alongside his PhD, David is an anatomy and physiology demonstrator and is passionate about research and education. His current research focuses on the use of human amniotic epithelial cells as therapy for stroke, using techniques such as neurobehavioral testing, immunohistochemistry, RT-qPCR, and single-cell transcriptomics to uncover the mechanisms of cognitive repair.

Therapeutic Potential of Human Amnion Epithelial Cells for Improving Post-Stroke Cognitive Outcomes

David E. Wong Zhang[1], Yeshwanth Yerradu[1], Shenpeng R. Zhang[1], Hyun Ah Kim[1], Grant R. Drummond[1], Siow Teng Chan[2], Christopher G. Sobey[1], & T. Michael De Silva[1].

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Introduction. Stroke is a leading cause of death and long-term disability worldwide. Up to 70% of stroke patient will experience cognitive impairment after stroke. However, there are limited treatment options to improve cognition following stroke. Due to their multiple protective effects, human amnion epithelial cells (hAECs) are an attractive candidate for stroke therapy. Whether hAECs improve post-stroke cognitive impairment remains unknown.

Aims. This study aims to investigate the long-term cognitive outcomes of hAEC treatment post-ischaemic stroke. Furthermore, to determine the mechanisms by which hAECs contribute to their pro-cognitive effects.

Methods. Male C57Bl/6 mice randomly assigned to undergo either sham or stroke surgery targeting the prefrontal cortex. Saline or hAECs (1 x 10^6 cells IV) was administered 24 h later. Cognition was assessed using the Barnes maze 36 d days later. Brain injury was evaluated using histology and transcriptomic changes relating to synaptic plasticity and cognitive processes was analysed using single-cell RNA sequencing and validated by qPCR.

Results. In the Barnes maze, delayed escape latency (EL) was observed in stroke+saline (day 5 EL=106±20s, $P>0.05$) but not stroke+hAEC (day 5 EL=66±12s, $P>0.05$) compared with sham mice. Infarct volume was significantly reduced following hAEC treatment (1.3±0.2 vs 0.4±0.2mm3, $P<0.05$).

Conclusion. Early hAEC administration following stroke attenuates cognitive impairment and reduces brain injury. The combination of behavioural improvements, reduced infarct pathology, and distinct transcriptomic changes supports hAEC as a promising therapeutic approach for preventing stroke-induced cognitive decline.

P505

Androgen receptor signalling: Does it play a role in cardiac metabolism?

Dr Zenab Dudhwala

Biography:

I am an early career researcher currently working as a Post-doc in the Cardiovascular Pathophysiology and Therapeutics Group at the Basil Hetzel Institute. I completed my PhD in 2022 and now perusing research in cardiovascular health particularly investigating changes in the metabolic pathway that lead to heart diseases such as cardiac hypertrophy and how this may affect cardiovascular health.

Androgen receptor signalling: Does it play a role in cardiac metabolism?

Zenab Dudhwala[1,2], Irene Stafford[2], John D Horowitz[1,2], Cher-Rin Chong [1,2]. Fac of Hlth & Med Sci[1], Univ of Adelaide, Adelaide, Australia; Cardiovasc Pathophysiol & Therapeutics Grp, Basil Hetzel Inst for Transl Hlth Res, The Queen Elizabeth Hosp[2], Woodville South, SA.

Introduction. Cardiac hypertrophy is often accompanied by significant metabolic alterations. Emerging evidence suggests that androgen receptor (AR) signalling plays a critical role in cardiac physiology, influencing both hypertrophic growth and metabolic function. While androgens have been implicated in modulating cardiac hypertrophy, the effect of AR signalling on cardiac metabolism remains unclear.

Aims. In this study, we aim to determine whether androgens independently promote cellular hypertrophy and how androgen receptor antagonists modulate hypertrophy. Additionally, it also investigates the role of androgen signalling in regulating cardiac glucose metabolism.

Methods. Cellular hypertrophy was induced in myocytes (differentiated from H9C2 cells) using either phenylephrine (PE, 100 µM) or dihydrotestosterone (DHT, 0.1 µM) for 48 hours. Inhibition of AR signalling was achieved by bicalutamide (10 or 50 µM). Hypertrophy was assessed by measuring cell surface area using microscopy and image J analysis. Expression of mitochondrial glucose transporter proteins, mitochondrial pyruvate carrier (MPC2) and pyruvate dehydrogenase (PDH) were quantified by western blot.

Results. Treatment with PE significantly increased cell size by 0.8-fold, compared to the control group (n=3, p=0.0004), whereas DHT treatment led to a slight 0.2-fold increase (n=3, p=0.1003). Co-treatment with bicalutamide partially attenuated PE-induced hypertrophy; however, this effect was not dose-dependent. Glucose transporters, MPC2 and PDH were reduced ~0.5-fold by PE-induced hypertrophy group. In contrast, their expression was elevated by bicalutamide co-treatment. Additionally, while bicalutamide co-treatment reduced DHT-induced hypertrophy, it also induced a dose-dependent upregulation of MPC2 and PDH expression.

Discussion. This study shows that inhibition of AR signalling with Bicalutamide may increase mitochondrial glucose metabolism, although the extent of which may depend on the hypertrophic stimuli. It also remains to be determined if such effect may be influenced by the Randle shift, the reciprocal relationship between glucose-fatty acid oxidation.

P506

From aggregation to agglutination: new target for thrombosis regulation

Prof Kazunao Kondo

Biography:

Graduated from Hamamatsu Univ. Sch. Med. in 1990. Worked as physician for 2 years in Kakegawa Municipal Hospital, Post-Doc Fellow for 2 years in Preclinical Study Institute of Sandoz Pharma Basel (CH). Associate Professor in Hamamatsu Univ. (basic Pharmacology). for 8 years. Majoring fields are; arrhythmia, atherosclerosis, thrombosis and clinical pharmacology.

From aggregation to agglutination: new target for thrombosis regulation

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Introduction. Platelets binding in thrombogenesis is usually discussed over their aggregation i.e. Glycoprotein (GP) IIb/IIIa-fibrinogen binding. On the other hand, platelets agglutination i.e. GP Ib-von Willebrand Factor (VWF) binding may also play certain role in clinical thrombosis.

Aims. We evaluate antiplatelet potency of mutated botrocetin derived from snake venom and seek a possibility to develop novel antiplatelet drugs based on GP Ib-VWF binding inhibition.

Methods. Platelet Rich Plasma (PRP) obtained from ICR male mice (6 months old) was stimulated by naïve recombinant botrocetin (B0) or by its mutant (B2:Arg115Glu/Lys117Glu). Platelet agglutination was measured following light-transmission method and the result was described as maximal agglutination ratio (%max) and as Area Under the agglutination Curve (AUC).

Results. Both B0 and B2 similarly induced platelet agglutination in concentration-dependent manner, in spite of a little difference in potency and agglutination pattern. B0 induced maximally 87.0±1.9 % at 1.5 µg/mL (n=4), while B2 did maximally 81.8±14.2 % at 2.0 µg/mL (n=5).

Discussion. B2 is suspected not to be anti-thrombotic but to be pro-thrombotic, following the result of in-vitro supplementation trial. As for the next step, we aim to challenge 3 points mutated botrocetin.

P507

The cardiovascular effects of Rhinella marina toad skin secretion on murine heart

Prof Roselyn Rose'Meyer

Biography:

My research publications are in the fields of pharmacology, pharmaceutical science, genitourinary and cardiovascular research. For most of my career I have studied adenosine receptors in tissues to identify subtypes of receptors and signaling pathways in heart, blood vessels and bladder and how they may change during common chronic disorders including hypertension, diabetes, heart attacks, incontinence and aging in an effort to identify ways to reduce disease burden.

The cardiovascular effects of *Rhinella marina* toad skin secretion on murine heart

Roselyn B Rose'Meyer[1], Jennifer C Wilson[1], I. Darren Grice[1], Joshua Hayton[2], Anthony Carroll[2], Jason N Peart[1], Selvanayagam Nirthanan[3]. School of Pharmacy and Medical Sciences, Griffith University[1], Southport, QLD, Australia;
School of Environment and Science, Griffith University[2], Southport, QLD, Australia; School of Medicine and Dentistry, Griffith University[3], Southport, QLD, Australia.

Introduction. The *Rhinella marina* cane toad from Central and South America is an introduced pest that is now widely distributed throughout Australia. It thrives in temperate environments and produces a milky white toxin-rich skin secretion from parotid glands situated behind its neck, primarily as defence against predators, parasites and microorganisms (Jing et al, 2013). Cane toad secretions also pose a significant hazard to local wildlife and domestic animals (Johnnides et al (2016).
Aims. While the cane toad skin secretions are widely known to contain bufadienolides which are digoxin-like compounds, this research investigated and identified all the cardioactive compounds that are present in the skin secretions.
Methods. Solubilized cane toad skin secretion and HPLC separated fractions of the secretion (1-70) were tested in mouse isolated hearts using the Langendorff method and identified using NMR analysis.
Results. Cane toad secretion, tested as a whole, caused a significant increase in developed pressure, cardiac contraction and heart rate in mouse isolated hearts when compared to digoxin alone ($P<0.05$). HPLC Separated fractions of the toad secretion were observed to have different effects - with early fractions (1-10) causing increased contractility and heart rate while late fractions (40-50) stimulated a mild increase in cardiac contractility only. NMR analysis of early fractions revealed the presence of adrenaline while bufadienolides were observed in later fractions.
Discussion. The results show that multiple cardioactive agents are present in *Rhinella marina* cane toad secretions with the most profound pharmacological effects caused by adrenaline. This provides further insight into the clinical symptoms observed following cane toad poisoning of canines and other animals.

Jing et al (2013) Biomed Chromatography, 27, 685-7
Johnnides et al (2016) J Am Anim Hosp Assoc, 52, 205-11.

P508

Fabrication of microneedle arrays for the dermal delivery of therapeutics

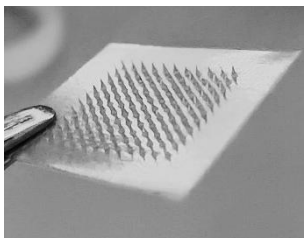
Miss Eleanor Mills

Biography:

Eleanor is a 2nd year PhD candidate in the Department of Pharmacology at Monash University's Biomedical Discovery Institute. After completing her Honours degree in 2022, she commenced her PhD in 2023 under the supervision of Dr Mark Del Borgo, Associate Professor Meredith O'Keeffe and Professor Max Cryle. Combining her background in immunology and pharmacology, she is researching the use of dendritic cell-based extracellular vesicle mimetics for indications in vaccination. In addition, she is exploring the use of microneedles, a novel delivery method targeted to dermal immune cells. She hopes to develop a platform for utilising the innate ability of dendritic cells to transfer antigen to promote an immune response tailored to the target disease.

Fabrication of microneedle arrays for the dermal delivery of therapeutics

Eleanor M Mills[1], Mark P Del Borgo[1]. Dept of Pharmacology, Monash Univ[1], Clayton, VIC, Australia.



Introduction. No one enjoys needles. In fact, hypodermic needles and liquid vaccines struggle with patient compliance, healthcare staff safety, and accessibility in rural communities. Dissolvable microneedles (MNs), which dissolve upon insertion and release drug into the dermis, are an alternative to traditional vaccination that is pain-free as they are not long enough to come into contact with nerves. Additionally, they are self-administrable, sharps and biohazard waste-free, have lower microbial infiltration, do not require cold-chain storage, and deliver cargo directly to dermal immune cells.

Aims. Formulate dissolvable microneedles from carboxymethylcellulose (CMC), with/without a model compound, and assess the ability to perforate and dissolve in artificial and *ex vivo* skin models.

Methods. MN arrays were formed in polydimethylsiloxane moulds from low viscosity CMC. Rhodamine B (RhB MN) was incorporated into the tips as a model compound. For perforation efficiency, MNs were applied to stacked layers of Parafilm, then perforations per layer quantified. To assess dissolution, marmoset skin or parafilm was placed on agarose and warmed PBS (37°C) to emulate physiological conditions, then RhB MNs were applied for up to 60 min. The skin was then fixed and embedded, and sections were taken and imaged on an EVOS microscope. After application to parafilm, RhB MNs were dissolved in Milli-Q water and the amount of rhodamine B remaining quantified by absorbance.

Results. RhB MNs significantly decreased deformation after application to Parafilm by ~20%, compared to CMC alone MNs ($n = 12$, $p<0.0001$). 88% of RhB MNs microprojections perforated one layer of parafilm (127µm), and 27% perforated two (254µm). At 30min post-insertion through parafilm, ~60% of RhB dissolved into agarose. Contrastingly, RhB MNs did not penetrate the stratum corneum of marmoset skin with no observable deposition of RhB.

Discussion. Surprisingly, the incorporation of a model compound into CMC MNs improved the structural integrity, as seen by increased perforation efficiency. 88% of RhB MN microprojections could perforate a depth equivalent to the dermal layer of the skin, and showed effective release of cargo in parafilm-based models. This is the first documentation of the use of excised marmoset skin in this field, but unfortunately perforation was not seen. As this contrasts with the success of the parafilm model, may be attributable to the model chosen rather than the microneedles themselves.

P509

A novel GPCR heteromer demonstrates unique pharmacology revealed with live cell biosensors

Mr Henry Purbrick

Biography:

Henry Purbrick is a CSIRO Industry PhD candidate at the University of Western Australia. His project is linked with Dimerix Bioscience, a Melbourne-based biopharmaceutical company, to investigate the molecular pharmacology of novel G protein-coupled receptor (GPCR) heteromers. Henry is investigating these heteromers in the context of complex inflammatory and fibrotic indications, where current therapeutics are inadequate in controlling progression. He is using live-cell biosensors, predominantly bioluminescence resonance energy transfer, to comprehensively profile the pharmacology of these heteromers. As his project is commercially orientated consideration must be made in how his research may be viably translated through to the clinic.

A novel GPCR heteromer demonstrates unique pharmacology revealed with live cell biosensors.

Henry G Purbrick[1,2,3,4], Elizabeth KM Johnstone[1,2], Carl W White[4], Robert Shepherd[4], Kevin DG Pfleger[1,4]. Molecular Endocrinology and Pharmacology, Harry Perkins Institute of Medical Research[1], Nedlands, WA, Australia. School of Biomedical Sciences, The University of Western Australia[2], Nedlands, WA, Australia. Health & Biosecurity, CSIRO[3], Kensington, WA, Australia. Dimerix Biosciences Pty Ltd[4], Fitzroy, VIC, Australia.

Introduction. Chronic inflammation and organ fibrosis underpins much of the morbidity and mortality of many common diseases, such as chronic obstructive pulmonary disease, stroke, cirrhosis, diabetes and chronic kidney disease. There is clearly an unmet need in controlling the complex pathophysiological inflammatory axes of these diseases effectively. G protein-coupled receptors (GPCRs) are prominent drug targets, due to their cell membrane expression, and ability to modulate physiology. Some GPCRs are shown to form receptor heteromers, complexes composed of two different GPCRs with distinct pharmacology from the component protomers. Given the molecular complexity of these diseases, GPCR heteromer discovery may yield effective targets with profound pharmacology distinct from monomers. This project, linked with an industry partner, aims to discover and profile heteromers with a strong scientific rationale and commercial potential.

Aims. To identify novel GPCR heteromers and elucidate their unique molecular pharmacology.

Methods. Receptor-Heteromer Investigation Technology (HIT) identifies receptor-receptor proximity. The β-arrestin2 recruitment bioluminescence resonance energy transfer (BRET) Receptor-HIT assay was conducted to screen for proximity of GPCR combinations of interest. Positive 'hits' proceeded toward pharmacological characterisation with BRET sensors for intracellular trafficking, G protein activation and second messenger generation.

Results. Receptor-HIT identified multiple novel heteromer candidates, with a selected candidate proceeded toward comprehensive pharmacological profiling. The intracellular trafficking sensor revealed an asymmetrical perturbance to the internalisation of protomers upon their coactivation. The G protein and second messenger sensors revealed complementary effects upon protomer coactivation, observing an asymmetrical loss of agonist potency. A selective antagonist for one protomer rescued the loss of potency induced by protomer coactivation.

Discussion. We have identified a novel candidate, Het-3X, demonstrating pharmacology that satisfies the criteria in classifying a putative GPCR heteromer. This candidate will undergo further scientific and commercial validation.

P510

Astropharmacy: A case study evaluation of medical kits in space analogue missions

Dr Li Shean Toh

Biography:

Li Shean Toh, a pharmacist and a Research Fellow at Monash University learning about deprescribing. Previously, she was a Lecturer at the University of Tasmania, Australia and an Asst Professor at the University of Nottingham. UK. Her area of expertise is in medicines management most notably in osteoporosis and prescribing. Other areas of interest include health literacy and interprofessional collaboration. Her latest and novel research area is in Astropharmacy, exploring medication safety and pharmacy services in space. She utilizes research evidence to inform and shape practice and policy. Toh's research has been funded by the UK Space Agency and the European Space Agency (ESA). She played a key pioneering role in the inclusion of Pharmacological Countermeasures in the ESA 2021 SciSpacE Roadmap. She advises prestigious organizations like the Royal Society and the United Nations. Her exceptional work has been recognized with accolades such as the European Space Leader Award.

Astropharmacy: A case study evaluation of medical kits in space analogue missions

Li Shean Toh[1,2], Marialina Tsinidis[1], Luke Sawyers [1], Myles Harris[3], Laura Backett[1]. School of Pharmacy, University of Nottingham[1], Nottingham, Nottinghamshire, UK; Centre for Medicines Use and Safety, Monash University[2], Melbourne, VIC, Australia; Dept of Risk and Disaster Reduction, University College London[2], London, UK;

Introduction. Since the inception of spaceflight in 1961, over 600 individuals have flown to space. In space, the microgravity environment leads to several physiological changes in the human body. These include muscle atrophy, bone density loss, fluid redistribution, altered cardiovascular function etc. It is crucial to ensure that safe and effective medical and pharmaceutical supplies are provided to our space explorers (1). Analogue space missions are used as a medium to undertake research in conditions simulating various aspects of the extra-terrestrial environment.

Aims. This study explores the user experience of stakeholders (mission control staff and analogue astronauts) towards medication kits used in analogue mission with the aim to input into the redesign of the medication kit for the international space station (ISS).

Methods. Two analogue space missions were used for the case studies (simulating the remoteness of space and the extreme environment of the Lunar South Pole). Six case studies were developed by an expert panel: pelvic fracture, homesickness and anxiety, gastroenteritis, abdominal bleeding, fractured ankle and tension pneumothorax. Purposive samplings were used. Pre and post missions focus groups were conducted both in person and online focusing on the challenges of using the developed medication kits. Focus groups were transcribed verbatim and thematically analysed.

Results. A total of four focus group discussions were conducted with 10 participants from medical backgrounds, 6 from the space sector and 4 analogue astronauts. Participants appreciated the detailed inventory of the medication kit, citing ease of ensuring there were sufficient medications for the mission. However, they noted that because the medications were repackaged to minimise storage it can be difficult to access or identify the correct medications. In terms of recommendations participants would like training specifically on medication use and safety.

Discussion. Overall, this case study provided foundational data on key aspects while using a medication kit in an extreme environment. Future studies are in progress for a 30-country global analogue missions.

[1] Derobertmasure A et al (2025) Eur J Pharm Sci DOI: 10.1016/j.ejps.2025.107063

P511

Development of online medication support tools for older people: a systematic review

Miss Temitope Esther Afolabi

Biography:

With a keen interest in geriatric medicine, research and education, I am currently undertaking my Doctor of Philosophy at The University of Sydney under main supervisor Professor Sarah Hilmer. My research centres round co-designing digital solutions for older people, that optimises medication management and promotes collaboration with health care practitioners.

Development of online medication support tools for older people: a systematic review
Temitope E Afolabi[1], Aili Langford[2], Sarah Hilmer[1], Christopher Etherton-Beer[3], Arpita Das[1], Kevin Winardi[1], Mouna Sawan[2], Lisa Kouladjian O'Donnell[2]. Laboratory of Ageing and Pharmacology, Kolling Institute of Research, Faculty of Medicine and Health, The University of Sydney[1], Sydney, NSW, Australia; School of Pharmacy, The University of Sydney[2], Camperdown, NSW, Australia; School of Medicine, University of Western Australia[3], Crawley, WA, Australia.

Introduction. Success of online medication support tools is contingent on how well they are designed and address the needs of users, especially older people.
Aims. To systematically review and describe existing online medication support tools for older people, their development and how they have been evaluated.
Methods. Five electronic databases (MEDLINE, EMBASE, CINAHL, Scopus and Web of Science) were searched from inception to October 2024 for studies describing the development and/or evaluation of online medication support tools for older people aged ≥65 years, or their informal caregivers. The mixed-methods appraisal tool was used for quality assessment. Two authors completed the screening, data extraction and quality assessments independently and subsequently discussed any conflicts. Extracted data was analysed descriptively in line with PRISMA guidelines.
Results. A total of 1,621 studies were identified, and 29 studies met the inclusion criteria. Over 80% (n=21) of the tools were mobile health apps or websites. The most common development approach involved user-centred design methodologies (comprising user needs assessments, focus groups, interviews, and user experience workshops). Usability testing using questionnaires and surveys (n=13 tools) were the most common evaluation techniques followed by think aloud protocol (n=9 tools), interviews and focus groups (n=9 tools). Findings across 22 studies suggest that user satisfaction of the developed online tools was high. The remaining seven studies did not measure usability of the final prototype or explicitly report on usability.
Discussion. This review summarises online medication support tools for older people and carers and the approaches used to develop and evaluate them. Findings suggest that iterative refinement driven by user feedback may be more influential than any one approach for developing high usability tools. A responsiveness to user feedback and employing development approaches that incorporate iterative prototyping, is essential to ensuring these tools are both effective and satisfactory to their users.

P512

Stakeholder Perceptions on Developing Gabapentinoid Deprescribing Guidelines: A Functional Role Theory Approach

Mr Justin Cheng

Biography:

Justin is a PhD student at the University of Sydney, currently developing a gabapentinoid deprescribing guideline endorsed by the National Health and Medical Research Council (NHMRC). He brings practical experience from working in community pharmacy, which informs his research focus on safe and evidence-based medication management.

Stakeholder Perceptions on Developing Gabapentinoid Deprescribing Guidelines: A Functional Role Theory Approach
Chun Hei Justin Cheng[1], Danijela Gnjidic[1], Stephanie Mathieson[1], Carl R Schneider[1] on behalf of the Working Guideline Group. 1. School of Pharmacy, The University of Sydney[1], Camperdown, NSW.
Introduction. Gabapentinoids (e.g. pregabalin, gabapentin) are indicated for neuropathic pain and increasingly used "off' label" (e.g. fibromyalgia). However, concerns about potential harms have prompted prescribers and consumers to reconsider regular use. **Aims.** To elucidate perceptions of consumer and healthcare professional (HCP) stakeholders on the need and scope of a gabapentinoid deprescribing guideline. **Methods.** A qualitative study with semi-structured interviews was performed. Consumers currently or previously using gabapentinoids, and HCPs caring for such patients were recruited. Inductive thematic analysis was undertaken using Functional Role Theory. **Results.** Twenty-five participants were included (13 consumers, 12 HCPs). The process of deprescribing was described by stakeholders as a holistic, system-wide activity involving not just the prescribes but also allied health professionals. Both stakeholders identified a need for inclusive guidelines that reflect this complexity. Consumers experienced fragmented care, with general practitioners often left to coordinate deprescribing alone. Crucially, consumers expressed a desire to be central to both the process with carers and the development of deprescribing guidelines, not passive recipients but active partners. **Discussion.** Future guideline development should prioritise multidisciplinary targets of guidelines and consumer empowerment to address systemic fragmentation and improve outcomes in deprescribing gabapentinoids.

P513

Co-design approaches to optimise medication safety in people with dementia: Scoping review

Miss Zena El-kadomi

Biography:

Zena is a final year student completing the Bachelor of Pharmacy with Honours at The University of Sydney. Her research focuses on improving medication-safety in people living with dementia and the co-design of resources and tools in medication management.

Co-design approaches to optimise medication safety in people with dementia: Scoping review

Zena El-kadomi[1], Danijela Gnjidic[1], Nicole Werner[2], Mouna Sawan[1]. School of Pharmacy, Faculty of Medicine and Health, The University of Sydney[1], Sydney, NSW, Australia; Center for Research and Innovation in Systems Safety, Department of Anesthesiology, Vanderbilt University Medical Center[2], Nashville, TN, United States

Introduction. People living with dementia are at high risk of medication-related harm due to polypharmacy, complex regimens, and challenges in medication management. Co-designed tools and interventions, which utilise lived experience, are needed to improve medication safety and prevent harm.

Aims. This scoping review describes studies that adopt co-design related approaches to improve medication safety for people living with dementia.

Methods. Seven electronic databases were searched from inception to 15 May 2025. Primary research that used co-design related approaches and involved people living with dementia and/or carers to develop a tool or intervention addressing medication safety were included. We applied the Sanders and Stappers' framework to assess how and at which phase (pre-design, generative, evaluative, and post-design) was co-design implemented.

Results. Of the 5,352 articles screened, eight were included. All studies involved carers, and six studies involved both people with dementia and carers. Most studies involved people with dementia and/or carers in only two phases of co-design (n= 4), the evaluative and generative phases. Evaluative was most common (n=7), followed by generative (n=5), pre-design (n=3), and post-design (n=3). Several studies (n=4) tailored their co-design approaches to accommodate the needs of people with dementia. Elements of medication safety that were addressed included deprescribing (n=4), medication management (n=2), addressing prescribing cascades (n=1) and medication reviews (n=1).

Discussion. This review highlights the need for improved reporting and greater consistency in applying co-design frameworks in the medication safety field. Using recognised frameworks and reporting guidelines would support meaningful co-design and collaborative work with people living with dementia and/or carers, clearer identification of co-design phases, and support wider application of co-design approaches across different vulnerable populations.

P514

Effectiveness of Communication Tools for Deprescribing: A Systematic Review

Miss Carla Haddad

Biography:

My name is Carla Haddad and I am a final year Pharmacy and Management student at the University of Sydney. I am currently undertaking Honours under the supervision of Dr Aili Langford and A/Professor Carl Schneider. My research is focused on deprescribing and how clinicians can approach these conversations with their patients more effectively.

Effectiveness of Communication Tools for Deprescribing: A Systematic Review

Carla Haddad[1], Carl R Schneider[1], Aili V Langford[1,2]. Sydney Pharmacy School, The University of Sydney[1], Sydney, NSW, Australia; Centre for Medicine Use and Safety, Monash University[2], Parkville, VIC, Australia.

Introduction. Deprescribing is a key strategy to improve the safe, effective, and rational use of medicines. However, communication barriers between patients and clinicians often hinder implementation. While communication tools designed to promote shared decision-making may help address these barriers, their effectiveness in supporting deprescribing remains unclear.

Aims. To evaluate the effectiveness of deprescribing communication tools on the proportion of patients who cease or reduce the dose of one or more potentially inappropriate medications, as well as on intermediate outcomes such as self-efficacy for deprescribing, intent to deprescribe, intent to discuss deprescribing, and perceptions of the risks associated with the target medication(s).

Methods. A systematic search of four electronic databases (MEDLINE, Embase, PsycINFO, CENTRAL) was conducted to identify randomised controlled trials (RCTs) evaluating communication tools that facilitated deprescribing discussions between adults (≥18 years) and clinicians. Risk of bias was assessed using the Cochrane RoB 2 tool.

Results. Nineteen RCTs were included, assessing patient-focused (n=16) and clinician-focused (n=3) tools, including brochures (67%), leaflets (8%), booklets (8%), letters (8%) and information sheets (8%). Of ten studies reporting on the primary outcome, eight found greater cessation of at least one target medication in the intervention group compared with usual care (11–30.7% higher), while two showed no difference. Six of thirteen studies reporting on dose reduction reported significant improvements, and three of thirteen found a reduction in total medication count. Five of nineteen studies demonstrated positive effects on intermediate outcomes, including self-efficacy, intention to deprescribe, willingness to discuss deprescribing, and patient risk perception.

Discussion. Communication tools were generally effective in reducing inappropriate medication use and therefore have the potential to support safe and rational deprescribing. Their effectiveness appears greatest when tailored to context, supported by clinicians, and coupled with follow-up mechanisms. These findings highlight the value of integrating communication tools into routine practice, yet a need for further research to evaluate their long-term clinical and behavioural impact remains.

P515

Insomnia treatment preferences in older adults and people with dementia:a qualitative study

Miss Aisling McEvoy

Biography:

Aisling is a PhD candidate from the Centre for Medicine Use and Safety at Monash University. Her research focuses on deprescribing benzodiazepine receptor agonists in people living with dementia. She is excited to find non-pharmacological approaches to assist with sleep as a replacement for benzodiazepines and z-drugs. Before starting as a PhD student, Aisling completed her BPharm and MPharm with Monash University. Aisling continues to work as a clinical pharmacist at The Alfred Hospital while completing her PhD.

Sleep enhancement preferences in older adults and people living with dementia: A qualitative interview study

Aisling M McEvoy,[1] Emily Reeve,[1,2] Jemimah Ride,[3] Aili V Langford,[1,4] Kyung Min Kirsten Lee,[1] Sheryn Loh,[1] Justin P Turner[1,5] Fac Pharm Pharmaceutical Sci, Monash[1], VIC, Aus; Clin Health Sci, UniSA[2], SA, Aus; Sch Public Health, Monash[3]; Fac Medicine and Health, USyd[4], NSW, Aus; Faculty Pharm, Laval University[5], QC, Canada

Introduction. Insomnia is common in people living with dementia and older adults. However, insomnia treatments rarely align with guidelines which may lead to medication-related harm. Benzodiazepine receptor agonists (BZRAs) are commonly prescribed to assist with sleep, but can lead to risk of medication-related harm.
Aims. This research aimed to explore what influences consumer decisions for engaging with insomnia treatments by identifying themes (underlying beliefs and experiences). The secondary aim of this study was to identify factors (as identified by participants in this population) to inform a discrete choice experiment. These factors represent concrete considerations that can be translated into meaningful and realistic hypothetical scenarios within the DCE.
Methods. Semi-structured interviews were conducted with the three populations (older adults, people living with dementia and their carers). The interviews were conducted and transcribed in Zoom. Nvivo was used to thematically analyze the interviews. The factors that influence choice of insomnia treatments were identified during the interviews.
Results. Nineteen interviews with 20 participants were conducted (47% aged between 65-74, 37% female). Five main themes with nine sub-themes were identified. Main themes were external influences, barriers to treatment, treatment expectations, health beliefs, and treatment type. Fourteen factors were identified. The risk of side effects was most commonly selected as the highest-priority factor (n = 10), with effectiveness also rating highly (n = 7). Medication side effects on cognition and daytime sedation were frequent concerns of participants. Effectiveness and side effects were most commonly considered across all participant groups. PLWD noted recommendation from a trusted source (n = 6) more frequently than older adults (n = 2) and carers (n = 0).
Discussion. Decisions about insomnia treatments are influenced not only by expected and experienced treatment effectiveness, but also by perceived risks and health beliefs. Integrating these perspectives into clinical care (including through a future discrete choice experiment) may help reduce inappropriate BZRA use and promote safer, acceptable alternatives.

P516

Ovarian response to follicle-stimulating hormone, luteinizing hormone, and human chorionic gonadotropin: meta-analysis

Ms Toni Michael

Biography:

Toni is a PhD student from the School of Pharmacy at the University of Sydney. Her research is on understanding the pharmacodynamic, pharmacokinetic, and pharmacogenomic properties of commonly prescribed fertility mediations to inform optimal use of medications in practice.

Ovarian response to follicle-stimulating hormone, luteinizing hormone, and human chorionic gonadotropin: meta-analysis

Toni Michael[1], Robin Lu[1], Ranita Kirubakaran[1,2,3], Jonathan Du[1,4], Vinayak Smith[4,5], Beverley Vollenhoven[1,5,6,7], Rui Wang[8], Sophie Stocker[1,3,4,9], Sch. Pharm., Univ. Sydney[1], Sydney, NSW; Dept. Pharm., Seberang Jaya Hosp.[2], Penang, Malaysia; Sch. Clin. Med., Univ. NSW[3], Sydney, NSW; Virtus Health Pty Ltd[4], Melbourne, VIC; Dept. Ob. & Gyn., Monash Univ.[5], Melbourne, VIC; Monash IVF[6], Melbourne, VIC; Monash Health[7], Melbourne, VIC; NHMRC Clinical Trials Centre, Univ. Sydney[7], Sydney, NSW; Dept. Clin. Pharmacol. & Toxicol., St. Vincent's Hosp.[9], Sydney, NSW.

Introduction. Follicle-stimulating hormone (FSH) is often co-administered with luteinizing hormone (LH) for controlled ovarian hyperstimulation (COH). LH activity can be derived from human chorionic gonadotropin (hCG). The impact of the source of LH activity in FSH combination therapy compared to FSH monotherapy for COH remains unclear.
Aims. To compare the ovarian response between FSH + LH, FSH + hCG, and FSH in women undergoing COH.
Methods. Embase, PubMed and Scopus were searched from database inception to 14 July 2025. Studies performed in women administered FSH + LH, FSH + hCG, and/or FSH monotherapy for COH were included. The number of retrieved oocytes and clinical pregnancy rates were measured. Meta-analyses using random-effects models were performed to calculate the mean differences (MD) and risk ratios (RR). Meta-regression assessed the effect of covariates
Results. From 3875 studies screened, 52 (23459 women) were included. Meta-analyses of retrieved oocytes and clinical pregnancy rates for FSH + LH compared to FSH monotherapy were inconclusive. However, longer duration of COH reduced oocyte yield ($p<0.0001$), but increased the likelihood of clinical pregnancy ($p=0.021$) with FSH + LH. FSH + hCG resulted in fewer oocytes (10 studies, 2996 women, MD -1.78, 95% CI -2.90 to -0.67) but higher clinical pregnancy rates (11, studies, 3723 women, RR 1.14, 95% CI 1.03 to 1.26) compared to FSH monotherapy. Older women increased oocyte yield ($p=0.021$), but decreased clinical pregnancy rates ($p=0.017$) with FSH + hCG. FSH + hCG yielded fewer oocytes (6 studies, 1472 women, MD -2.04, 95% CI -3.19 to -0.89) compared to FSH + LH, which was increased in older women ($p=0.010$). The difference in clinical pregnancy rates between these combination therapies was inconclusive. **Discussion.** hCG-driven LH activity may enhance endometrial receptivity early in COH, while FSH monotherapy or FSH + LH combination therapy may be less effective. The composition of LH in combination therapy should be considered when selecting COH medications.

P517

Methods to simplify complex medication regimens in older adults: a scoping review

Miss Amarrah Muker

Biography:

With an interest in research ,Amarrah Muker is a final-year Bachelor of Pharmacy (Honours) student at the University of Sydney under main supervisor Doctor Lisa Kouladjian O'donnell. Her Honours research examines tools to measure and simplify medication regimen complexity in older adults, aiming to support medication management.

Methods to simplify complex medication regimens in older adults: a scoping review

Amarrah K Muker[1], Temitope Esther Afolabi[2], Timothy F Chen[1], Sarah N Hilmer[2], Lisa Kouladjian O'Donnell[1,2]. Sydney Pharmacy School, University of Sydney[1], Camperdown, NSW, Australia; Kolling Institute, Northern Sydney Local Health District and, University of Sydney[2], St. Leonards, NSW, Australia.

Introduction. Older adults are a clinically vulnerable group with a high prevalence of multimorbidity and polypharmacy. Medication regimen complexity (MRC) often accompanies polypharmacy and has been associated with hospitalisation, adverse drug events and treatment burden. Various tools and measures have been developed to measure MRC or guide medication simplification for older adults.

Aims. To identify and describe tools to measure MRC and methods used to simplify medication regimens in older adults.

Methods. Scoping review with a systematic search in three databases (MEDLINE, Embase and International Pharmaceutical Abstracts) conducted from inception to 2nd April 2025. Inclusion criteria: original studies describing the development and/or validation of tools to measure MRC and/or methods of medication regimen simplification. Two authors independently screened abstracts and full texts and extracted data. References of retrieved articles were also scanned to identify relevant papers. Study characteristics and psychometric measures (e.g., validity) were extracted.

Results. Of 2053 studies screened, 48 were included for analysis (measures of complexity (n=19)) and methods of simplification (n=29)). Preliminary results of the review identified 18 distinct tools as measures of complexity in older adults. Core measures of complexity were consistent across MRC tools (e.g. medication count), however more nuanced features were underrepresented (e.g. "splitting or crushing tablet/capsules" and "with or without regard to food"). Only 12 (67%) reported psychometric testing. Of the eighteen MRC tools identified, 6 (33%) of the tools were cross-cultural adaptations of the Medication Regimen Complexity Index. Twenty-two methods of simplification were identified and grouped into eleven categories. Only one simplification tool, the Medication Regimen Simplification Guide for Residential Aged CarE (MRSGRACE) had undergone psychometric evaluation. Most methods of simplification involved pharmacist-led interventions (n=12), multidisciplinary collaboration (n=6) and the use of combination therapies (n=3).

Discussion. This review identified multiple tools and methods to measure or simplify MRC. Future research could evaluate whether the use of MRC tools as an intervention could impact clinical outcomes. Future tools could also incorporate a more person-centred focus.

P518

Assay development to quantify propofol in surgical patients: understanding interpatient response differences

Mr Matthew Ng

Biography:

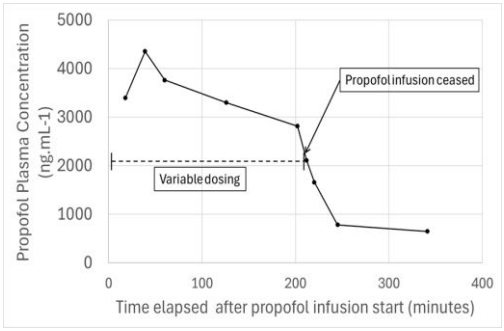
I am a first year PhD student. I completed my Medical Bioscience Degree in 2020. I obtained my Masters in Biotechnology in 2024 and decided to continue my PhD. My research interests centre on elucidating the pharmacokinetics and pharmacodynamics of drugs, particularly in clinical settings, with the aim of improving therapeutic precision and patient outcomes.

Assay development to quantify propofol in surgical patients: understanding interpatient response differences Matthew Ng[1], Stefan Musolino[1], Daniel Barratt[2], Michelle Gerstman[3], Bernhard Riedel[3], Carl Kirkpatrick[4], Andrew Somogyi[1]. Disc of Pharmacol, Univ of Adelaide[1], Adelaide, SA; Disc of Physiol, Univ of Adelaide[2], Adelaide, SA; Dept of Anaesthesia, Peter MacCallum Cancer Centre, Melbourne, VIC[3]; Monash Inst of Pharmaceu Sc, Monash Univ, Melbourne, VIC[4]

Introduction. Propofol is a widely used anaesthetic agent in surgical settings but exhibits high inter-individual response variability. To better understand the reasons, a pharmacokinetic-pharmacodynamic study needs to be undertaken. However, a review of existing literature indicated a lack of suitable liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay for this purpose.

Aims. We developed, optimised, validated, and clinically applied a bioanalytical method using LC-MS/MS quantification.

Methods. We optimised the LC and MS parameters of an electrospray ionisation configuration to detect plasma propofol prepared using methanol precipitation and fully validated this assay using ICH M10 guidelines.



Results. The assay demonstrates intra- and inter-run assay accuracy of 86–114% and 94 – 105%, respectively, across a quantification range of 25 – 5000 ng.mL^{-1}, with a mean extraction recovery of 92%. Intra- and inter-run coefficients of variation(CV) were 2.7 – 15.7% and 1.1 – 5.0%, respectively. It has also demonstrated acceptable dilution integrity, matrix effect and stability. The method has also successfully quantified plasma propofol concentrations (648 – 4356 ng.mL^{-1}) of a surgical patient (see Figure)

Conclusion. A propofol LC-MS/MS assay has been fully validated and is suitable for clinical pharmacokinetic investigations in surgical patients.

P519

Time to pharmacologically justify renal function cut-offs in early-phase clinical trials.

Mr Kushal Paneliya

Biography:

Kushal Paneliya is a clinical research coordinator working in Clinical trials. Kushal's main interest is clinical pharmacology and to improve clinical trials practices whilst broadening personal knowledge.

Time to pharmacologically justify renal function cut-offs in early-phase clinical trials.

Kushal J Paneliya[1], Helena Xu[2], Thomas M Polasek[1,3], Sepehr Shakib[1,2]. CMAX Clinical Research[1], Adelaide, SA, Australia; Discipline of Pharmacology, University of Adelaide[2], Adelaide, SA, Australia; Centre for Medicine Use and Safety, Monash University[3], Melbourne, VIC, Australia

Introduction. Early phase clinical trials require participants with adequate renal function to clear drugs and their metabolites and to minimize the risks of nephrotoxicity.

Aims. To determine whether the renal function cut-offs of early phase clinical trials were pharmacologically justified based on the type of investigational product (IP), IP clearance, and potential for nephrotoxicity.

Methods. A retrospective study of 134 early phase clinical trials was conducted between January 2020 and February 2024 at CMAX Clinical Research. Protocols and investigator brochures were analysed for the methods used to estimate renal function (e.g., Cockcroft-Gault equation), renal function cut-offs (e.g., 90 ml/min), IP type (e.g., small molecule), predominant clearance pathway in non-clinical studies (e.g., renal), and nephrotoxicity in repeat-dose GLP toxicology studies. A de-identified participant database of demographic information and blood test results, including eGFR, at screening and pre-dose (day -1) was used to estimate clinical trial ineligibility rates based on various renal function cut-offs. Data were analysed in Excel and SPSS and presented using simple statistics.

Results. There were 3 major methods to estimate renal function, the Cockcroft-Gault equation (45.5%), serum creatinine (41.8%), and the 2021 CKD-EPI creatinine equation (11.2%). Where calculated, renal function cut-offs at 90, 80 and 60 mL/min/1.73m² were found in 50.7, 15.7, and 27.6% of protocols respectively, whilst a small percentage (6% in total) had various other cut-off values (85, 75, 70, 55, 40, and 15 mL/min/1.73m²). There was a statistically significant relationship between the renal function estimation method and IP type ($p < 0.01$) but not clearance pathway ($p = 0.985$) or nephrotoxicity potential ($p = 0.194$). Predicted clinical ineligibility rates increased as renal function cut-off increased from 60 to 90 mL/min/1.73m², with ~20% of volunteers ineligible at 90 mL/min/1.73m².

Discussion. There is no standardized method to estimate renal function or to set renal function cut-offs in early phase clinical trials, with IP clearance and potential nephrotoxicity rarely considered. Ineligibility rates are directly correlated with renal function cut-offs. A pharmacologically justified approach is recommended when setting renal function cut-offs to avoid unnecessary and costly exclusions in early phase clinical trials (e.g., older participants).

P520

Effect of Renin-Angiotensin System Inhibition on Residual Kidney Function in Peritoneal Dialysis

Ms Jing Xin Goh

Biography:

Jing Xin has recently completed her MPhil at the University of Sydney, where she conducted research on "The Impact of Medication Regimen Complexity on Patient-Centred Outcomes in Kidney Failure." Her passion for clinical pharmacy was ignited during her previous work experience in hospital and health clinic settings. Jing is dedicated to advancing the field of nephrology and improving the care of patients with renal diseases. She is eager to contribute her knowledge and skills to make a meaningful impact in this critical area of healthcare.

Effect of Renin-Angiotensin System Inhibition on Residual Kidney Function in Peritoneal Dialysis

Jing Xin Goh[1], Kamal Sud[2,3], Surjit Tarafdar[4,5], Elvira D'Souza[1], Nazim Bhimani[2], Ronald L Castelino[1,6]. School of Pharmacy, Faculty of Medicine and Health, University of Sydney[1], Sydney, NSW; Sydney Medical School, Faculty of Medicine and Health, University of Sydney[2], Sydney, NSW; Nepean Kidney Research Centre, Department of Renal Medicine, Nepean Hospital[3], Kingswood, NSW; Faculty of Medicine, Western Sydney University[4], Sydney, NSW; Department of Renal Medicine, Blacktown Hospital[5], Blacktown, NSW; Pharmacy Department, Blacktown Hospital[6], Blacktown, NSW.

Introduction. Renin-angiotensin system inhibitors (RASIs) are recommended to maintain residual kidney function (RKF) in peritoneal dialysis (PD) patients; however, studies have shown variable impact on RKF.
Aims. This study aims to assess the effect of RASI on the decline in RKF among patients undergoing PD.
Methods. This retrospective cohort study included patients receiving PD at a large metropolitan dialysis centre in Australia. Patients were stratified into two groups based on RASI use. RKF was assessed using residual Kt/V and urine volume, defined as the time of RASI initiation for patients on therapy, and the last recorded RKF measurement for patients who discontinued RASI during PD treatment. The primary outcome was the comparison of residual urine volume and residual Kt/V between the two groups.
Results. 231 out of 307 PD patients were included in the analysis after excluding patients who lacked comparative RKF data within the required timeframe. Approximately half (n = 111; 48.1%) were receiving RASI. Patients on RASI were younger than those not on therapy [65 years (IQR 56–74) vs. 72 years (IQR 61–77); p = 0.014]. No significant differences were observed between groups in the decline of residual urine volume (288 mL [IQR 106–802] in RASI users vs. 403 mL [IQR 124–813] in non-users; p = 0.392) or residual Kt/V (0.310 [IQR 0.080–0.730] in RASI users vs. 0.420 [IQR 0.113–0.760] in non-users; p = 0.295). Hospitalisation rates and PD-related infections were also similar between groups.
Discussion. RASI therapy was not associated with preservation of RKF in patients undergoing PD in this cohort. While previous studies suggested potential renoprotective effects of RASI, our findings align with the recent evidence supporting mixed efficacy in this population. Larger prospective trials are needed to clarify the role of RASI in improving long-term outcomes in PD.

P521

Antibiotic prescribing for cellulitis in the absence of penicillin-cephalosporin cross-reactivity alerts

Dr Paul Chin

Biography:

Paul Chin is a Senior Lecturer at the University of Otago, Christchurch and Senior Medical Officer at Te Whatu Ora Health New Zealand – Waitaha Canterbury.Research interests include therapeutic drug monitoring (including anticoagulants and antimicrobials), quality use of medicines, electronic prescribing, and clinical decision support.

Antibiotic prescribing for cellulitis in the absence of penicillin-cephalosporin cross-reactivity alerts

Milan Sundermann[1], James Mehrtens[2], Nicholas M Douglas[1,2,3], Sharon Gardiner[2], Matthew Doogue[1,2], and Paul KL Chin[1,2]. Department of Medicine, University of Otago[1], Christchurch, New Zealand; Health New Zealand | Te Whatu Ora Waitaha Canterbury, New Zealand[2], Division of Global and Tropical Health, Menzies School of Health Research, Charles Darwin University, Darwin, NT, Australia[3].

Introduction. Cephalosporins are often avoided in patients with penicillin adverse drug reaction (ADR) labels. Our institution's electronic medication management system is set up not to generate cross-reactive alerts for penicillin and cephalosporin ADR labels. Penicillins and cephalosporins are preferred treatments for cellulitis.

Aims. To describe penicillin, cephalosporin, and non-penicillin, non-cephalosporin (NPNC) prescribing for inpatients with cellulitis in the presence/absence of penicillin and/or cephalosporin ADR labels.

Methods. Index cellulitis admissions were included during 2017-2024 with penicillin and/or cephalosporin ADR labels and at least one penicillin, cephalosporin, or NPNC administered. Index admissions were categorised according to presence/absence of labels to penicillins and/or cephalosporins. Penicillin, cephalosporin, and NPNC prescribing was compared between groups with and without labels using odds ratios (OR).

Results. Of 8,374 index admissions, 7,567 had no penicillin/cephalosporin labels, 729 had penicillin-only labels, 42 had cephalosporin-only labels, and 36 had both labels. Inpatients with penicillin labels were significantly more likely (OR 13.07; 95% CI, 11.05–15.45) to be prescribed cephalosporins than those without labels. There were no differences in penicillin prescribing between those with cephalosporin labels and those without labels (OR 1.04; 95% CI, 0.44–2.47). Inpatients with penicillin and/or cephalosporin labels were 6 to 52 times more likely to receive NPNC antibiotics than those without labels.

Discussion. Absence of cross-reactivity alerts was associated with increased cephalosporin use for cellulitis in inpatients with penicillin ADR labels, sparing NPNC antibiotics that may be less effective. Removal of cross-reactivity alerts may be effective for increasing cephalosporin prescribing for inpatients with penicillin ADR labels.

P522

Deprescribing recommendations: Health professionals' perspectives across 61 countries

Dr Shin Liau

Biography:

Dr Shin Liau is a pharmacist and Research Fellow at the Centre for Medicine Use and Safety, Monash University. She leads work on optimising medication management for older adults living with frailty and dementia in community and residential aged care settings across Australia, Asia and Europe. With a strong commitment to improving medication safety and effectiveness, her current research addresses the unique challenges of appropriate prescribing by incorporating deprescribing recommendations into clinical practice guidelines.

Deprescribing recommendations: Health professionals' perspectives across 61 countries

Shin J Liau,[1] Aili V Langford,[1,2] Wade Thompson,[3] Barbara Farrell,[4] Frank Moriarty,[5] Danijela Gnjidic,[2] Danielle Pollock,[6] Nagham J Ailabouni,[7] Emily Reeve[1]. Fac Pharm Pharmaceutical Sci, Monash U[1], Melbourne, VIC, Aus; Syd Pharm Sch, U Sydney[2], Sydney, NSW, Aus; Depart Anesthesiol Pharmacol Therap, U British Columbia[3], Vancouver, BC, Can; Bruyère Res Inst[4], Ottawa, ON, Can; Sch Pharm Biomolecular Sci, RCSI U Med Health Sci[5], Dublin, Ireland; Health Ev Synthesis Rec Impact, U Adelaide[6], Adelaide, SA, Aus; Sch Pharm, U Queensland[7], Brisbane, QLD, Aus.

Introduction. Fewer than one-third of existing guidelines include deprescribing recommendations, with substantial variability in their format and content.
Aims. To explore the preferences of health professionals (guideline end-users) on the language, content and format of deprescribing recommendations to maximise implementability.
Methods. An online REDCap survey was developed based on a qualitative study and disseminated internationally through professional organisations, personal contacts, social media, and snowball sampling. Medical doctors, pharmacists, and nurses were eligible to participate. Survey responses were analysed descriptively.
Results. A total of 779 survey responses were recorded, representing pharmacists (40%), medical doctors (37%), and nurses (21%) from 61 countries. Responses were from Oceania (34%), Europe (27%), North America (16%), Asia (12%), South America (6%), and Africa (4%). Participants identified 'discontinue' and 'deprescribe' as the most preferred terms for medication discontinuation, in contrast to the less preferred 'cease' and 'withdraw'. More than half of participants considered the following content features as essential to include: medication class, patient population, rationale for deprescribing, and how to deprescribe. Over 80% of respondents preferred a tapering regimen with a specific dose reduction or range (e.g. 5mg or 5-10% every 2 weeks) rather than broad or non-specific guidance.
Discussion. Although health professionals vary in their preferences for the language, content and format of deprescribing recommendations, there was general agreement in certain areas. The majority of health professionals are receptive to comprehensive recommendations – including guidance on when and how to deprescribe – provided the information is clearly presented (e.g. with bullet points or algorithms). These findings highlight the need for further research to build the evidence base for such recommendations and will help establish best practice guidance for guideline developers.

P523

Determination of dolutegravir in dried blood spots and VAMS by LC-MS/MS

Dr Stefan Musolino

Biography:

Stefan Musolino is a biomedical research scientist at The University of Adelaide specializing in neuro-immunopharmacology, chronic and neuropathic pain mechanisms, and behavioural models of pain. His work investigates neuroimmune interactions underlying pain and their implications for therapeutic development. Stefan also has expertise in clinical pharmacogenomics and pharmacokinetic studies, exploring drug interactions and mechanisms of action to improve personalized medicine strategies. He has contributed to multidisciplinary projects advancing the understanding of pain pathways and translating findings into clinical applications.

Determination of dolutegravir in dried blood spots and VAMS by LC-MS/MS

Stefan T Musolino[1], Natália B Andriguetti[1], Daniel T Barratt[1], Joseph Tucci[2], Paul Pumuye[3], Andrew A Somogyi[1]. School of Biomedicine, The University of Adelaide[1], Adelaide, SA, Australia; Department of Pharmacy & Biomedical Sciences, La Trobe University[2], Bendigo, VIC, Australia; School of Medicine and Health Sciences, University of Papua New Guinea[3], PG-NCD, Papua New Guinea.

Introduction. Dolutegravir (DTG) is prescribed worldwide for HIV treatment. Accurate quantification is required to investigate the potential contribution to DTG efficacy and side effects. Conventional sampling can be a challenge for remote places, specifically special transportation requirements (frozen or dry ice) to reference laboratories.

Aims. We aimed to develop and validate a simple method to quantify (DTG) in dried blood spots (DBS) and volumetric absorptive microsampling (VAMS) by LC-MS/MS.

Methods. DTG was extracted from DBS and VAMS using a one-step solvent sample preparation, followed by chromatographic separation using a C18 column. Detection was performed in a LCMS-8040 MS/MS, with a run time of 4.1 min. Validation was performed following official DBS and ICH M10 guidelines. The method was applied to 72 HIV/AIDS patients from Papua New Guinea.

Results. The assay was linear in the range of 25-8000 ng mL^{-1} for both devices. Inter-day and intra-day precision showed a maximum variation of 4.3% and 6.1% for DBS and 4.4% and 2.9% for VAMS, respectively. Accuracy ranged from 98.2-105.4% for DBS, and 93.8-101.4% for VAMS. There was minimum matrix effect, with less than 10% deviation. Mean recovery was 70-71% for both devices. DTG was stable in both devices at room temperature for 14 days, extracted samples were stable in the autosampler for 12 h. Decreased DTG concentrations were observed when kept at 60 ºC for 48 h for both DBS (30%) and VAMS (55%). Volcano effect test showed no difference in accuracy between central and peripheral punch. Haematocrit (HT) 50% increased concentrations between 15-35% higher than nominal. Patients' samples had mean DTG concentrations of 938 ng mL^{-1} for DBS (168-2080 ng mL^{-1}), and 1200 ng mL^{-1} for VAMS. (279-2440 ng mL^{-1}).

Discussion. For the first time, a method for the quantification of DTG in DBS and VAMS was developed and applied to HIV patient samples. DBS and VAMS presented similar results to general validation tests, however as a fixed volume device, VAMS does not require extra HT experiments, simplifying method validation.

P524

Self-sampling for precision dosing in oncology-preliminary data

Dr Mirjana Radovanovic

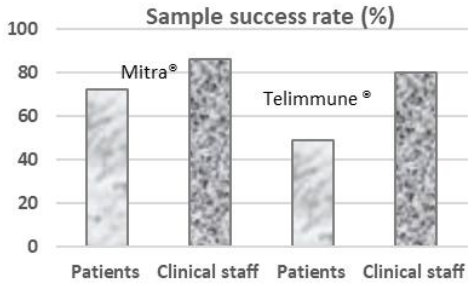
Biography:

Dr Mirjana Radovanovic is a Research Scientist in the Clinical Pharmacology Laboratory at the University of Newcastle. She has extensive experience and expertise in therapeutic drug monitoring as performed in pathology services for routine use and in academic research. This unique blend of expertise has enabled her to contribute to projects that span from laboratory to clinical applications, supporting dose optimisation and improving patient outcomes. Her research interests lie entirely within the field of clinical pharmacology with a particular focus on anti-cancer, anti-infective and immunosuppressive drugs. In her current role, she is involved in developing and validating analytical methods and extraction techniques for measurement of therapeutic drug concentrations using liquid chromatography tandem mass spectrometry (LC-MS/MS). Her work has been substantially focused on investigating less invasive techniques, including the use of microsampling devices and fingerprick blood collection, to support personalised and accessible drug monitoring and therapy optimisation.

Self-sampling for precision dosing in oncology-preliminary data

Mirjana Radovanovic[1], Raina Naik[2], Sarah Glewis[2], May Darwish[2], Jennifer H Martin[1], Marliese Alexander[2].
Centre for Drug Repurposing and Medicines Research, University of Newcastle[1], Callaghan, NSW, Australia; Peter MacCallum Cancer Centre[2], Melbourne, VIC, Australia.

Introduction. Precision dosing using therapeutic drug monitoring (TDM) has demonstrated improved outcomes for patients receiving 5-fluorouracil (5FU), however the optimal testing time is when a patient is usually at home, complicating compliance. Finger-prick microsampling self-collection could improve compliance if adequate sample quality can be achieved.



Aims. To assess the quality of microsampling using a 2-sampler Mitra® device & a Telimmune® UNO card, informed by initial PRECISION trial experience with longitudinal 5FU testing (ACTRN12624000079549).

Methods. Patients (N=26, 48 TDM rounds) receiving a 5FU infusion had finger-prick samples taken both by themselves and by clinical staff, up to four samples per patient. Sample quality was visually assessed by a trained scientist. Mitra® devices were adequate if polymer tips were fully saturated with blood without the white mesh visible, no excess blood present on plastic holders, or dark spots of dried coagulated blood was present on the tips. Telimmune® UNO cards were adequate if the paper disc was evenly covered by a clear liquid smear without excess dried residue. Patients received education via product guides, commercial and in-house videos and instruction leaflets.

Results. Overall sampling success by clinical staff was 86% (38/44; 66% for both samples) with Mitra® and 80% (36/45) with Telimmune®UNO, compared to 72% (30/42; 43% for 2 adequate samples) and 49% (19/39) respectively, for patient-collected samples. The reasons for rejection of both Mitra® samples (18 instances, 36 tips) were due to underfilling (53%) and overfilling (47%). For the Telimmune®UNO devices, sample inadequacy was mainly due to underfilling (45%, 38/84), followed by haemolysis (21%, 17/84) and overfilling (20%, 16/84).

Discussion. Although the success rate of microsampling was higher when clinical staff performed the collection for both devices, poor sample quality produced by patients when using the Telimmune® cards, suggests the need for a comprehensive education programme or a more effective device before it can be implemented in clinical settings. This work was funded by The Australian Medical Research Future Fund (MRFFMMIP000011).

P525

Global systematic review on deprescribing of cholinesterase inhibitors and memantine in dementia

Dr Michelle Tan

Biography:

Dr Michelle Tan is a Research Fellow (National Dementia Clinical Practice Guidelines Development) at the Centre for Medicine Use and Safety (CMUS), Monash University (Parkville Campus), working in close collaboration with the National Centre for Healthy Ageing (NCHA), Cochrane Australia, and the Australian Department of Health and Aged Care on the development of National Clinical Practice Guidelines for Dementia 2026. She also holds ongoing honorary positions as an Affiliate Research Fellow (Global Health) at the Department of Health Service and Population Research, Institute of Psychiatry, Psychology & Neuroscience (IoPPN), King's College London, UK, and as an Adjunct Research Fellow (Health Services) at The Prince Charles Hospital-Northside Clinical Unit, Greater Brisbane Clinical School, Faculty of Health, Medicine and Behavioural Sciences, The University of Queensland (UQ). She has a strong interest and expertise in applying rigorous evidence synthesis methods and leveraging large-scale longitudinal clinical datasets to inform health policies nationally and globally.

Global systematic review on deprescribing of cholinesterase inhibitors and memantine in dementia

Michelle MC Tan[1], J Simon Bell[1], Madeleine SA Tan[1], Alli Patterson[2], Sue Brennan[3], Kelsey Price[2], Max Murano[3], Velandai Srikanth[2], & Emily Reeve[1]. Centre for Medicine Use and Safety, Monash Uni[1], Parkville; National Centre for Healthy Ageing, Monash Uni[2], Frankston; Cochrane Australia, Monash Uni[3], St Kilda Rd, VIC, Australia.

Introduction. Cholinesterase inhibitors (ChEIs) and memantine currently remain the primary symptomatic treatments for dementia. While these medications may offer modest benefits in cognition, function, and behaviour, they are not disease-modifying and carry potential risks, particularly with prolonged use. There is a need for clear evidence-based deprescribing guidance to support the appropriate use of these medications.

Aims. To evaluate the outcomes of withdrawal of ChEIs and/or memantine compared with continuation to inform the development of deprescribing recommendations for inclusion in the update of Australia's National Dementia Clinical Practice Guidelines (CPG) 2026. We conducted an updated systematic review of deprescribing of ChEIs/memantine.

Methods. We systematically searched CENTRAL (Ovid), MEDLINE and Embase databases (July 2016–2025), supplemented by hand-searching. We uniquely include both randomised controlled trials (RCTs) and non-randomised studies of interventions (NRSIs) to balance the strengths and limitations of diverse evidence sources and clinical relevance. For inclusion in the new CPG, additional criteria were explicitly designed to determine the appropriateness of including NRSIs. Risk of bias was assessed using the latest Cochrane RoB and ROBINS-I v2 tools.

Results. Our new search identified 3,039 records, with 74 full texts reviewed and 10 studies included. In the original 2016 systematic review, 5,787 records were screened, 265 full texts assessed and 50 studies included. Therefore, a total of 60 eligible studies were identified (11 RCTs and 49 NRSIs). Applying our NRSI eligibility criteria developed, 30 studies (11 RCTs and 19 NRSIs) were retained. The most common reasons for excluding NRSIs are being at critical risk of bias, mainly due to inadequate comparators and unaddressed confounding.

Discussion. This systematic review represents the most comprehensive and up-to-date global evidence on deprescribing ChEIs/memantine and will inform the development of recommendations for the updated Dementia CPG. These recommendations will support the appropriate deprescribing of ChEIs/memantine. The innovative method of determining eligibility of NRSIs will maximise the utilisation of available evidence to inform deprescribing recommendations, while ensuring methodological robustness and quality of the evidence.

P526

Assessment of ORAI1 Modulators on Prostate Cancer Cells in 3D culture

Miss Magda Abourisha

Biography:

Magda is a fourth-year pharmacy student at The University of Queensland, completing her major research project with the Calcium Signalling in Therapeutics Team (CaSTT), under the supervision of Professor Gregory R. Monteith, Dr Melanie Robitaille, Dr Farzaneh Forouz and Professor Sarah Roberts-Thomson. Her work explores how pharmacological modulators of ORAI1 can influence gene expression in prostate cancer cells grown in 3D culture.

Assessment of ORAI1 Modulators on Prostate Cancer Cells in 3D culture

Magda Abourisha[1], Farzaneh Forouz[1], Sarah Roberts-Thomson[1,2], Gregory R. Monteith[1] and Melanie Robitaille[1], [1]School of Pharmacy and Pharmaceutical Sciences, The University of Queensland, Brisbane, QLD, Australia. [2]Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia.

Introduction. Calcium (Ca^{2+}) signaling regulates diverse cellular functions, and its dysregulation is linked to several diseases, including cancer.[1] Store-operated calcium entry (SOCE), primarily mediated by ORAI1 and STIM1, plays a key role in maintaining calcium homeostasis and regulating gene expression.[2] In prostate cancer cells, altered SOCE is linked to increased survival, highlighting its potential as a therapeutic target. To better model the complex architecture of prostate cancer[3], we used a 3D spheroid model to assess how pharmacological modulation of ORAI1 influences prostate cancer-associated gene expression and compensatory changes in ORAI and STIM paralogs.

Aims. This study aimed to assess cancer-promoting and ORAI1-regulated genes in response to ORAI1 pharmacological modulators (Synta66 inhibitor/IA65 enhancer) in a 3D LNCaP cell model.

Methods. LNCaP prostate cancer cells were cultured in a 3D system and treated with either DMSO, ORAI1 inhibitor Synta66 or ORAI1 enhancer for 72 h. The effects of Synta66 and IA65 on the expression of SOCE components, ORAI1-regulated genes and genes known to promote prostate cancer progression were assessed using qPCR.

Results. Pharmacological inhibition or enhancement of ORAI1 did not induce significant changes in the expression of SOCE components, downstream ORAI1-regulated genes, or genes involved in prostate cancer–promoting pathways in this LNCaP 3D prostate cancer model at the time point assessed.

Discussion. Synta66 or IA65 did not lead to significant changes in the expression of SOCE components, downstream ORAI1-regulated genes, or genes involved in prostate cancer–promoting pathways at the time point assessed. These studies suggest that in 3D culture LNCaP prostate cancer may be insensitive to ORAI1 pharmacological modulation. Future studies should assess the effects of longer exposure periods to ORAI1 modulators and/or their effects concurrent with calcium store depletion.

1. Giorgi et al (2018) Trends in Cell Biology, 28(4), 258-273
2. Kappel et al (2019) Seminars in Cell & Developmental Biology, 94, 66-73
3. Flourakis M et al (2009) Biochimica et Biophysica Acta, 1793(6), 1105–1109

P527

Delineating the signalling pathways of orphan bombesin G protein-coupled receptor, BB3

Miss Olivia Clink

Biography:

Olivia Clink is an Honours student, in her final year of a Bachelor of Advanced Science at UNSW. She majored in both pharmacology and psychology, where she developed a particular interest in molecular pharmacology and G protein-coupled receptors (GPCRs). Olivia is currently completing her honours project under the supervision of Dr. Nicola J. Smith in the Orphan Receptor Laboratory at UNSW, where her project focuses on the biased signalling potential of orphan GPCR, bombesin 3.

Delineating the signalling pathways of orphan bombesin G protein-coupled receptor, BB_3

Olivia A. Clink[1], Mariah R Stavrou[1], Joshua A. Nillama[2], Luke Hunter[2], Nicola J Smith[1]

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Introduction: Lung cancer is deadly, with a five-year survival of only 26% and significant development of drug resistance. Thus, there is an urgent need for new therapeutics. Our lab has identified the orphan G protein-coupled receptor, Bombesin 3 (BB_3), as a novel therapeutic target for lung adenocarcinoma. Though it lacks the characteristics of an oncogenic driver, BB_3 could be used as a conduit for delivering a toxic payload to cancer cells. Identifying appropriate drugs for conjugation requires an accurate understanding of BB_3's signalling profile, including its potential for ligand bias, which has not yet been characterised.

Aims: We sought to elucidate the signalling profile of selective synthetic ligands at BB_3, agonists MK-5046 and Bag-1, and our in-house synthesised antagonist Bantag-1. Pathways of interest are the canonical G protein signalling pathways $G\alpha s$, $G\alpha i$, and $G\alpha q$, as well as β-arrestin recruitment and ERK phosphorylation pathways.

Methods: Human embryonic kidney (HEK293) cells transiently transfected with human BB_3 were stimulated with the selective synthetic ligands across four assays: BRET1 cAMP sensing assay for $G\alpha s$ and $G\alpha i$ signalling; GCaMP5G calcium sensing fluorescent assay for $G\alpha q$; NanoBiT β-arrestin recruitment assay and BRET1-based biosensor for ERK1/2 phosphorylation. The Operational Model of Ligand Bias will be applied to the data.

Results: We report that BB_3 can be activated by Bag-1 and MK-5046 to varying degrees, depending upon the endpoint measured. Our in-house synthesised antagonist, Bantag-1, differed in displaying competitive vs non-competitive antagonism depending upon the assay and the ligand used.

Discussion: Our early results indicate that biased signalling is present at BB_3. Further experiments are needed to understand the extent to which bias may affect development of conjugated BB_3 therapeutics in lung cancer.

P528

Uptake and transport of a vitamin B_{12}-cyanine 5 conjugate in Caco-2 cells

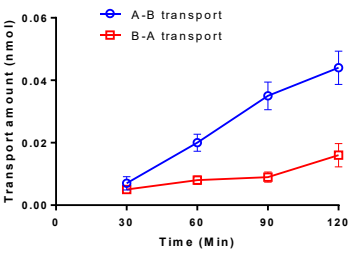
Miss Reem Khalaf

Biography:

I am a pharmacist and a dedicated biomedical scientist and educator. I hold a Master of Medical Science (Pharmacology) and currently pursuing a PhD in Biomedical Sciences at Auckland University of Technology, New Zealand. I am currently exploring absorption, disposition, and cytotoxicity response of antibiotic conjugates of vitamin B_{12}. With a strong background in pharmacology and hands-on experience in teaching and research, I am passionate about student-focused learning and contributing to impactful health science research in a culturally responsive and inclusive environment.

Uptake and transport of a vitamin B_{12}-cyanine 5 conjugate in Caco-2 cells

Reem M Khalaf[1], Jessica M Fredericksen[1], Brent Seale[1], Nicola E Brasch[1], Yan Li[1]
[1]School of Science, Auckland University of Technology, Auckland, NZ



Introduction. Vitamin B_{12} (cobalamin) conjugates have been developed as delivery tools for therapeutic and imaging agents. Emerging evidence suggests these conjugates improve the solubility, stability, and cellular uptake of attached compounds.

Aims. This study aimed to investigate the uptake and directional transport of a fluorescent B_{12}–Cy5 conjugate (BPC5) in a Caco-2 cell model of the intestinal barrier.

Methods. Stability of BPC5 in Hank's balanced salt solution at 37°C over 24 hr was assessed by LC-MS/MS analysis. Time, concentration, and B12-dependent uptake of BPC5 into Caco-2 cells was quantified by using fluorescence microscopy. A typical 21-day protocol was used to prepare Caco-2 monolayers. For transport assays, apical-to-basolateral (A→B) and basolateral-to-apical (B→A) movement of BPC5 was measured over 2 hours. Data were analysed using one-way ANOVA with Dunnett's *post-hoc* test.

Results. BPC5 uptake by Caco-2 cells was rapid and was reduced by 58% ($P < 0.05$) and 86% ($P < 0.01$) in the presence of 0.1 mM and 1 mM B_{12}, respectively. The transport of BPC5 across Caco-2 monolayers appeared to be linear up to 2 hr. Transport assays revealed approximately two-fold higher permeability in the A→B direction compared to B→A.

Discussion. The results suggest that BPC5 uptake occurs via a B_{12}-specific transport mechanism and may serve as a useful probe for studying B_{12} absorption. The polarised transport of BPC5 across Caco-2 monolayers suggests involvement of an active transport system at the apical-to-basolateral direction.

P529

Establishment of a Pseudovirus System for Nipah Virus Research

Miss Jeongin Kim

Biography:

B.S. in Pharmaceutical and Biomedical Engineering, Dong-A University
M.S. Candidate in Bio-Medical Sciences, Gachon University

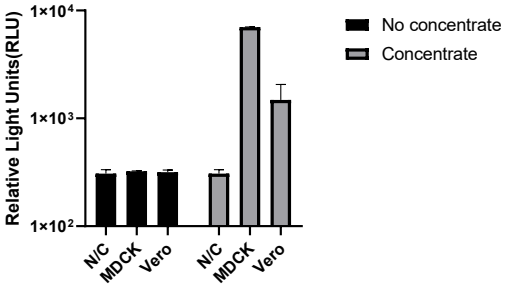
Establishment of a Pseudovirus System for Nipah Virus Research

Jeong-in Kim[1], Timothy An[1], Kee-Jong Hong[1,2,3], Department of Bio-Medical Sciences, Gachon University, GAIST[1], Incheon, Korea; Department of Microbiology, Gachon University College of Medicine[2], Incheon, Korea; Lee Gil Ya Cancer and Diabetes Institute, Gachon University[3], Incheon, Korea

Introduction. Nipah virus causes severe outbreaks with high mortality rates and requires BSL-4 facilities. Since there are no approved vaccines or therapies, establishing a pseudovirus system enables safe evaluation of Nipah virus vaccine candidates.

Aims. This study aimed to develop a VSV-based pseudovirus expressing Nipah virus glycoproteins and to establish a safe and reliable platform for Nipah virus vaccine research.

Methods. MDCK cells were seeded in 100-mm dishes and cultured to ~85% confluency. Cells were transfected with 16 μg of pcDNA3.1 plasmids encoding Nipah virus F and G glycoproteins at a 1:2 ratio using Lipofectamine 2000. At 24h post-transfection, cells were infected with VSV-ΔG-Luc at a multiplicity of infection (MOI) of 4. After 2h, the cells were washed and incubated in DMEM with 5% FBS for 24h. The supernatant was harvested, filtered through 0.45-μm, and concentrated to obtain Nipah pseudoviruses.



Results. Nipah pseudoviruses were generated in MDCK cells, and their infectivity was validated through luciferase assays. In neutralization assays, Nipah Virus-specific antisera markedly reduced infection.

Discussion. These results demonstrate the feasibility of using Nipah pseudoviruses under BSL-2 as a biosafe alternative to virus assays. This system provides a practical platform for assessing vaccine candidates and therapeutic antibodies.

P530

Elucidating human Oligopeptide Transporter 2 (hPepT2) polymyxin interactions for safer antibiotic design

Miss Yining Courtney Luo

Biography:

Yining (Courtney) Luo is a PhD candidate in the Molecular Drug Development Group at the Sydney Pharmacy School, The University of Sydney. Her research focuses on antibiotic pharmacology, investigating the structure-function interactions of the human oligopeptide transporter 2 (hPepT2) and its role in the nephrotoxicity of last-line antibiotics used to treat multidrug-resistant Gram-negative infections. Courtney completed her Bachelor of Pharmacy and has a strong interest in antimicrobial resistance and drug discovery.

Elucidating human Oligopeptide Transporter 2 (hPepT2) polymyxin interactions for safer antibiotic design
Yining Luo[1], Xukai Jiang[2], Jian Li[3], Fanfan Zhou[1,*]. Mol Drug Dev Group, Sydney Pharm Sch[1], Univ of Sydney, Sydney, NSW 2006, Australia; Natl Glycoengineering Res Ctr, Shandong Univ[2], Qingdao 266237, China; Biomedicine Discovery Inst, Infect & Immun Program[3], Monash Univ, Melbourne, VIC 3800, Australia.

Introduction. Multidrug-resistant Gram-negative bacterial infections represent a critical therapeutic challenge. Polymyxins are last-line antibiotics, but nephrotoxicity limits their clinical use. Human Oligopeptide Transporter 2 (hPepT2) has been shown to be involved in the renal reabsorption of polymyxins, contributing to their toxicity.
Aims. This study investigated the structure-interaction relationship of hPepT2 and polymyxins to identify the key residues underlying transporter-drug binding.
Methods. Alanine scanning mutagenesis was applied to generate hPepT2 mutants in predicted polymyxin-binding regions. Uptake of the fluorescent polymyxin probe MIPS-9541 was assessed in HEK293 cells overexpressing wild-type or mutant hPepT2. Kinetic parameters were derived. Biotinylation and immunoblotting were performed to examine cell surface and total protein expression.
Results. Multiple hPepT2 mutants exhibited significantly reduced uptake of MIPS-9541. In particular, the substitution at residue D215 markedly decreased polymyxin binding affinity. Several mutations are associated with impaired transporter protein expression or turnover rate.
Discussion. This study provides the first mechanistic insight into the interaction of hPepT2 and polymyxins. Identification of D215 as a critical residue involved in transporter-substrate binding advances the understanding of hPepT2-mediated polymyxin nephrotoxicity and supports the rational design of novel polymyxin derivatives with reduced renal toxicity.

P531

Dissecting the RXFP1-AT2R interaction reveals functional crosstalk between these receptors

Mrs Deidree Somanader-Livera

Biography:

Mrs Deidree Somanader-Livera, a passionate and aspiring researcher/educator is a final year PhD Candidate who is a part of the Cardiovascular Disease program in the Department of Pharmacology, Monash University, under the supervision of Prof. Chrishan Samuel, Prof. Robert Widdop and Dr Elva Zhao. Her research currently focuses on deciphering the formation of physical heterodimers between the Relaxin Family Peptide Receptor 1 (RXFP1) and the Angiotensin-II type II receptor (AT2R) in the context of fibrosis, given that this receptor interaction has major ramifications for the clinical development of the anti-fibrotic hormone Relaxin. Deidree will be presenting some exciting data from the first 2 aims of her PhD where she has delved into providing some insight into the type and level of molecular interaction between RXFP1 and AT2R, thus solving a mystery in the minds of many cardiovascular researchers.

Dissecting the RXFP1-AT$_2$R interaction reveals functional crosstalk between these receptors.

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Introduction. G protein-coupled receptors (GPCRs) often coexist in tissue microenvironments, which enable the formation of receptor-receptor interactions. The class A GPCRs, relaxin family peptide receptor 1 (RXFP1) and angiotensin II type 2 receptor (AT$_2$R), are both upregulated in myofibroblasts and cardiomyocytes in disease settings, to induce organ protection. Prior studies had identified a potential interaction between these receptors (Chow et al., 2014; Wang et al., 2020), which allowed for antagonists acting at either receptor to inhibit agonist-induced anti-fibrotic responses via the other receptor indirectly. However, the mechanism behind this inhibition remains unknown.

Aims. To mechanistically investigate how co-expression of the AT$_2$R and RXFP1 influences receptor-ligand engagement and transducer (G protein) coupling profiles.

Methods. The human RXFP1 receptor was transiently overexpressed in parental embryonic kidney cells (HEK293) or HEK293 cells stably expressing the AT$_2$R. Increasing concentrations of the RXFP1 agonist (Relaxin) and AT$_2$R agonist (C21) were selected to treat the cells, and ligand-induced dissociation of heterotrimeric G proteins ($G_{\alpha s}$, $G_{\alpha i3}$, $G_{\alpha Ob}$, and $G_{\alpha 11}$) was measured using the TRUPATH system in real-time over 40 minutes. Ligand binding to RXFP1 was measured using both NanoBRET system and HiBiT complementation assays using Fluorescein Amidite (FAM)-labelled RLX.

Results. Activation of RXFP1 led to the dissociation of all four G proteins tested, most robustly with $G_{\alpha s}$, with relatively high potency, which was not significantly altered by AT$_2$R co-expression. On the other hand, the AT$_2$R weakly activated $G_{\alpha s}$ and $G_{\alpha 11}$, but failed to activate $G_{\alpha i3}$ and $G_{\alpha OB}$. Notably, when co-expressed with RXFP1, enhanced AT$_2$R-mediated coupling of both $G_{\alpha i3}$ and $G_{\alpha OB}$ was observed, whereas receptor coupling to $G_{\alpha 11}$ was abolished. However, co-expression of these receptors had limited effects on the binding properties of FAM-RLX to RXFP1.

Discussion. These findings suggested that RXFP1 and the AT$_2$R underwent functional crosstalk when in close proximity, which affected the G protein coupling profile of the AT$_2$R, providing mechanistic insight into the RXFP1-AT$_2$R axis.

[1]Chow BSM et al. (2014) Kidney Int; 86:75-85; [2]Wang C et al. (2020) FASEB Journal; 34:8217-8233.

P532

Targeting the μ opioid receptor with novel β-endorphin (1-13)-based bivalent peptides.

Mr Yifan Wang

Biography:

Yifan Wang is a PhD candidate at the School of Pharmacy and Pharmaceutical Sciences, The University of Queensland. His research explores the design and evaluation of bivalent β-endorphin peptides targeting opioid receptors, with the goal of developing safer and more effective analgesics.

Targeting the μ opioid receptor with novel β-endorphin (1-13)-based bivalent peptides.

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Introduction. Pain is a significant challenge to global public health. According to the World Health Organisation's analgesic ladder, opioids remain the primary therapy for managing moderate to severe pain. Opioid receptors are divided into three principal subtypes: μ-, δ- and κ-opioid receptors (MOPr, DOPr and KOPr). Conventional opioid analgesics exert their effects predominantly through MOPr activation, but their clinical application is limited by severe adverse effects, highlighting the need for safer alternatives. Endogenous opioid peptides (EOPs) provide a promising alternative path to novel analgesics with a reduced side-effect profile. Among these, β-endorphin 1-31 (BE1-31) is a potent MOPr agonist, while the truncated derivative β-endorphin 1-13 (BE1-13) remains functionally active. This work investigates the rational design and pharmacological evaluation of bivalent peptides derived from BE1-13.

Aims. To design, synthesise, and characterise bivalent derivatives of BE1-13 as peptide ligands, and to evaluate their pharmacological efficacy, potency, and selectivity at the MOPr.

Methods. Solid-phase peptide synthesis (SPPS) was employed for peptide generation. The efficacy, potency, and selectivity of peptides were evaluated by cAMP inhibition assays in HEK293 cells overexpressing MOPr, KOPr and DOPr.

Results. The inhibitory potency of BE1-13 (275.1±31.7nM) and BVE13-001 (69.5±8.6nM) was markedly lower than that of fentanyl (9.9±1.1nM, n=3, t-test, $P<0.05$) at the MOPr. BVE13-005 showed significantly higher potency than monovalent, exhibiting no significant difference compared with fentanyl (7.8±0.9 nM, n=3, t-test, $P<0.05$).

Discussion. BVE13-005 demonstrated enhanced potency compared to the parental peptide BE1-13, with activity approaching that of the clinically used agonist, fentanyl. This supports the notion that bivalent design represents a valuable structural modification strategy, consistent with biphalin (Lipkowski et al.,1982). We propose that linking two pharmacophores at a defined distance can increase local drug concentration and promote synergistic interactions, thereby improving receptor targeting. In contrast, BVE13-001 failed to show improvement, likely due to its relatively shorter linker length. These findings underscore the crucial role of linker architecture in determining pharmacological performance and further confirm that the bivalent strategy is a promising approach to enhance opioid peptide potency.

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Bivalent opioid peptides modulate peripheral mu and delta receptors for pain therapy

Mr Junkai Zhang

Biography:

Junkai Zhang is a PhD candidate at The University of Queensland's School of Pharmacy and Pharmaceutical Sciences, specializing in molecular biology, drug discovery, and pharmaceutical formulation. He earned a Bachelor of Pharmacy from Jining Medical University, where he majored in chemistry and pharmacology, and later completed a Master of Pharmaceutical Industry Practice at The University of Queensland, gaining skills in drug development and regulatory affairs. His doctoral research focuses on developing innovative strategies to improve drug formulation, delivery, and quality assurance, with the aim of enhancing therapeutic efficacy and safety. Beyond his core research, Junkai actively engages in scientific communication, conference presentations, and collaborative projects, reflecting his dedication to advancing pharmaceutical sciences. He is committed to addressing key challenges in drug development and healthcare delivery, striving to bridge the gap between laboratory research and clinical application to deliver meaningful improvements in patient outcomes.

Bivalent opioid peptides modulate peripheral mu and delta receptors for pain therapy

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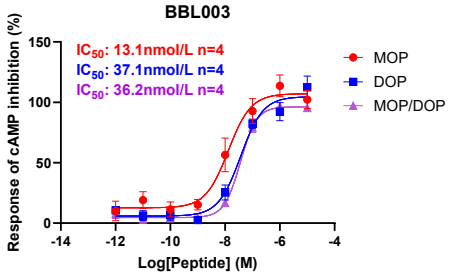
Introduction. Opioids provide effective analgesia through activation of opioid receptors (OPs), a family of G-protein-coupled receptors comprising mu (MOP) and delta (DOP) subtypes (Kieffer and Evans, 2009). Widespread misuse and dependence have resulted in a global opioid epidemic. Endogenous opioid peptides (EOPs), including β-endorphin (BE) and enkephalin (ENK), demonstrate analgesic potential with reduced adverse effects (Stein, 2016). Bivalent opioids synthesised by connecting active fragments of BE and Leu-ENK using linkers of various lengths, such as BBL001, BBL003 and BBL005, have been developed to enhance potency while minimising central side effects. These bivalent peptides are assessed for their modulation of HEK293-MOP, HEK293-DOP, and HEK293-MOP/DOP-expressing cells, evaluating both potency and efficacy.



Aims. To develop MOP- and DOP-selective bivalent opioid peptides and assess their pharmacological activity and efficacy in comparison with controls using established cell lines.

Methods. Bivalent opioid peptides BBL001, BBL003 and BBL005 were synthesised via solid-phase peptide synthesis. cAMP release from HEK293 cells expressing MOP, DOP, or MOP/DOP was measured using the Revvity AlphaScreen kit with forskolin stimulation, with fentanyl and SNC80 as positive controls for MOP and DOP, respectively.

Results. Bivalent peptide BBL003 showed comparable nanomolar potency to the positive controls (fentanyl, SNC80, and the fentanyl-SNC80 combination) in HEK293-MOP, HEK293-DOP, and HEK293-MOP/DOP cell lines based on cAMP inhibition curves.

Discussion. Bivalent peptide BBL003 exhibited comparable efficacy and potency to the control agonist in all three cell lines. BBL003 presumably binds both MOP and DOP receptors, with its precise mechanism still under investigation, and showed superior activity among the tested peptides, making it a candidate for further pharmacological studies.

Kieffer BL, Evans CJ (2009). *Neuropharmacology* 56:205–212. Stein C (2016). *Annu Rev Med* 67:433–451.

P534

Development of HPV mRNA vaccine and evaluation indicators

여사 Hyogyeong Hwang

Biography:

Hyogyeong Hwang is a master's student in the Department of Health Sciences and Technology at Gachon University. Her research focuses on the development of mRNA-based vaccines and evaluation indicators of HPV vaccines.

Development of HPV mRNA vaccine and evaluation indicators

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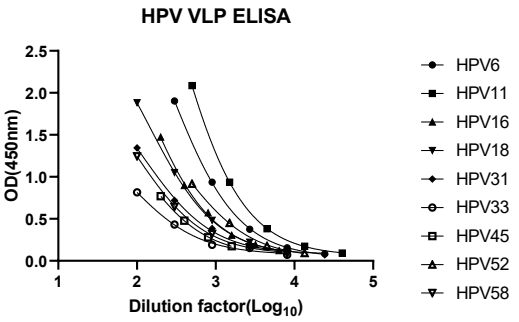
Introduction. HPV (Human Papillomavirus) has over 150 genotypes, with high-risk types 16 and 18 accounting for 70% of cervical cancer cases. Preventive vaccines such as Gardasil (Merck) and Cervarix (GSK) are approved and in use, but in Korea, vaccination coverage remains low due to foreign dependence, unstable supply, and high costs. To address these challenges, we developed an mRNA-based vaccine platform, taking advantage of its safety and rapid large-scale production, and sought to establish evaluation indicators for HPV vaccine efficacy.



Aims. We aimed to develop evaluation indicators for assessing its efficacy and to design an mRNA-based HPV vaccine.

Methods. We produced HPV PsV (Pseudovirus) and VLP (Virus-Like Particle) for nine genotypes. Reference materials and sera from Gardasil-vaccinated humans and mice were utilized to perform VLP ELISA and PBNA (Pseudovirus-based Neutralization Assay). For *in vivo* evaluation, Mice were anesthetized with isoflurane via an inhalation anesthesia system, subjected to vaginal injury, and infected with PsV. Luminescent signals were monitored using IVIS (*in vivo* Imaging system). We designed mRNA constructs. IVT (*in vitro* Transcription) was performed, and the transcribed mRNA was transfected into cells for protein expression analysis by western blot.

Results. We successfully established VLP ELISA, PBNA, and antibody quantification methods for nine HPV genotypes, enabling measurement of binding and neutralizing antibody titers in human sera. Luminescent signals were observed exclusively in PsV-infected mice, and western blotting confirmed protein expression at the expected size.

Discussion. We established an evaluation method and infection model for the HPV vaccine, and demonstrated its potential clinical applicability, which can be applied to mRNA vaccine efficacy assessment.

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Combining SQM2.20 with docking and FEP for finding selective PGK2 inhibitors

Dr Slade Matthews

Biography:

Dr. Slade Matthews is a Senior Lecturer specializing in computational pharmacology and toxicology. His research focuses on predicting chemical properties and bioactivity using Python-based QSAR models and cheminformatic techniques such as molecular fingerprinting, quantum molecular calculations, clustering, and substructure analysis. He earned his PhD in 2007 on machine learning in biomedical data and has published 48 peer-reviewed papers (Scopus h-index: 18). In 2025 Slade published a state-of-the-art graph transformer-based QSAR model for Ames mutagenicity prediction. He serves on the TGA Medical and Scientific Evaluation Services Panel and the NSW Poisons Advisory Committee both since 2010. In 2024, he was elected to the ASCEPT Board and awarded Fellowship of ACTRA in 2025. Based at the University of Sydney, Slade collaborates with academic and regulatory partners to advance public safety through application of in silico toxicology and is passionate about mentoring students and interdisciplinary research bridging chemistry, biology, and data science.

Combining SQM2.20 with docking and FEP for finding selective PGK2 inhibitors

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Introduction. Phosphoglycerate kinase 2 (PGK2) is essential for sperm bioenergetics and male fertility, making it a promising non-hormonal contraceptive target. The running CACHE Challenge 7 seeks selective PGK2 inhibitors over PGK1; participants are provided with structures and unpublished ligands, with adenine-site water networks and subtle PGK2 vs PGK1 side-chain differences informing selectivity

Aims. To develop and demonstrate an integrated computational pipeline combining active-learning docking (AL-Dock), SQM2.20 quantum-mechanical rescoring, and free-energy perturbation (FEP) that identifies selective, non-quinazoline PGK2 inhibitors meeting challenge thresholds (IC50 < 10 µM and ≥20-fold selectivity; primary hits IC50 < 50 µM and ≥5-fold selectivity).

Methods. AL-Dock iteratively trains a surrogate on docking scores to focus library exploration. Candidates are cross-docked to PGK1 (e.g., 4O33/2X15) to penalise non-selective binders, and screened with a SMARTS filter to exclude quinazolines. SQM2.20 rescoring is run on PGK2 and PGK1 poses using PM6-D3H4X with COSMO-like solvation; multiple cofactor states and conserved waters are sampled based on PGK2 (apo 2P9Q, ATP-bound 2PAA, ligand-bound entries) and PGK1 structures. Top series proceed to FEP for rigorous ΔΔG ranking. Throughput from our docking deployment informs cycle sizes and timelines.

Results. Planned outputs during the live challenge include prospective enrichment curves on holdouts, predicted selectivity distributions against PGK1, per-cycle diversity/synthesizability, and a purchase shortlist. Up to 100 compounds meeting pre-specified thresholds will be purchased and submitted for testing

Discussion. By combining scale-efficient AL-Dock with physics-based SQM2.20 and FEP verification, the pipeline aims to deliver selective PGK2 hits under realistic compute budgets. Water-mediated interactions and the enclosed adenine cavity will be explicitly considered to improve selectivity predictions and to prioritise non-quinazoline chemotypes for synthesis during CACHE-7.

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Targeting Lysyl Oxidase to Inhibit Ferroptosis in Epilepsy: Integrated Approach

Prof (dr) Bikash Medhi

Biography:
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Targeting Lysyl Oxidase to Inhibit Ferroptosis in Epilepsy: Integrated Approach

Bikash Medhi[1], Shrajal Kumari[2], Harminder Kaur[3], Gajendra Choudhary[1], Department of Pharmacology[1], PGIMER, Chandigarh, India; Department of Biostatistics[2], Panjab University, Chandigarh, India; Department of Immunopathology[3], PGIMER, Chandigarh, India.

Introduction

Epilepsy is a common neurological disorder marked by recurrent seizures, which, especially when prolonged, lead to significant neuronal damage. Ferroptosis an iron-dependent, lipid peroxidation-driven form of cell death has been increasingly implicated in epilepsy-related neurodegeneration. Lysyl oxidase (LysOX), an extracellular matrix enzyme, is associated with various CNS pathologies, but its role in ferroptosis within the epileptic brain remains underexplored.

Aims

This study aimed to evaluate LysOX as a potential therapeutic target in epilepsy by identifying inhibitors that prevent ferroptosis-mediated neuronal death.

Methods

An *in-silico* screening of FDA-approved drugs was conducted against LysOX, with top candidates selected based on docking scores and blood-brain barrier (BBB) permeability. ADMET profiling assessed pharmacokinetics and safety. Molecular dynamics (MD) simulations evaluated the stability of LysOX-ligand complexes. In vitro validation using SH-SY5Y neuroblastoma cells involved MTT assays for viability and flow cytometry for reactive oxygen species (ROS) quantification.

Results

Top LysOX-binding compounds exhibited strong docking scores, favorable BBB penetration, and drug-like ADMET profiles. MD simulations confirmed complex stability. In vitro, selected compounds significantly improved neuronal viability and reduced ROS levels, indicating effective ferroptosis inhibition.

Discussion

This integrative *in silico–in vitro* approach identified novel LysOX inhibitors with neuroprotective potential in ferroptosis-associated epileptic damage. These compounds represent promising candidates for further preclinical development in epilepsy therapy.

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Modulation of NK1R dependent tachykinin signalling with lipid conjugated small molecule antagonist

Dr Rina Pokhrel

Biography:

I am a passionate and detail-oriented research scientist with a PhD in Biochemistry and Molecular Biology. I've spent over seven years immersed in life sciences research, and currently, I'm working as a Research Fellow at the Monash Institute of Pharmaceutical Sciences, Monash University.

My work focuses on understanding the molecular mechanisms of G Protein-Coupled Receptor, Neurokinin 1 Receptor (NK1R), particularly its roles in pain and inflammation. I use a combination of advanced techniques—including BRET biosensors and high-resolution imaging—to explore cellular signalling and receptor function. I thrive in interdisciplinary environments, collaborating with experts in molecular pharmacology, chemical biology, and imaging to uncover new insights into GPCR signalling and trafficking.

Academically, I hold a PhD from Monash University, an MSc in Medicinal Chemistry from the University of Copenhagen—where I majored in Molecular Pharmacology—and a Bachelor's degree in Pharmacy from Rajiv Gandhi University of Health Sciences.

Modulation of NK1R dependent tachykinin signalling with lipid conjugated small molecule antagonist

Rina Pokhrel[1], Róisín McCague[1], Priyank Shenoy[1], Bernard Flynn[2], Luigi Aurelio[2], Arisbel Batista Gondin[1], Daniel Poole[1] Nicholas Veldhuis[1]. [1]Drug Discovery Biology, [2]Medicinal Chemistry, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, VIC, 3052, Australia

Introduction. GPCRs continue to signal after internalisation into endosomes, creating a sustained and spatially distinct signalling. Neurokinin 1 Receptor (NK1R) is a class A GPCR that mediates nociception and neuropathic pain as well as contributes to pathological processes such as inflammation and cancer. It is stimulated by the tachykinin called Substance P (SP). NK1R endosomal signalling is associated with sustained pain. We have shown that peptide-lipid conjugates improve endosomal targeting and inhibition of signalling, but small molecules haven't been thoroughly explored and may achieve superior efficacy.

Aims. To explore how lipid-conjugated small molecule antagonists fine-tune NK1R-dependent tachykinin signalling by altering receptor compartmentalisation and sustained endosomal signalling.

Methods. Using the FDA-approved small molecule aprepitant (AP), we synthesised a series of aprepitant lipid-conjugates, whereby AP was conjugated to cholestanol as a sterol-based membrane anchor via a flexible polyethylene glycol (PEG) linker. Four AP-Chol conjugates were synthesised with increasing PEG linker length. Initial functional studies using cell-based assays included intracellular Ca^{2+} mobilisation assays and BRET-based G-protein coupling. The analgesic properties of AP and AP-Chol were tested in in vivo pain models; capsaicin injection (acute pain).

Results. Increasing the PEG linker length significantly increased the analgesic effect. Intracellular Ca^{2+} assay showed that increasing the length of the PEG linker from 12 to 36 significantly increased the potency. However, there was no additional benefit using PEG48. In a preclinical model of pain, AP-Chol caused prolonged antinociception (6 h).

Discussion. These findings demonstrate that lipid conjugation markedly improves the pharmacological profile of less potent NK1R antagonist and results in potent and selective inhibition of signalling events associated with central pain transmission. These AP-Chol lipid conjugates lead to >2-fold improvement in analgesia in an acute pain, but further studies are required to determine if this due to altered PK or spatially confined targeting of NK1R.

P538

Development of novel ligands for the short-chain fatty acid receptor 2 (FFA2/GPR43)

Dr Elizabeth Vecchio

Biography:

Dr. Elizabeth Vecchio is a National Health and Medical Research Council (NHMRC) Early Career Fellow in the Hypertension Research Lab with expertise in GPCR molecular pharmacology. She previously worked as a clinical pharmacist prior to completing her PhD at the Monash Institute of Pharmaceutical Science in 2017. Her PhD thesis explored the pharmacology of the adenosine A2B receptor with a focus on constitutive activity and signalling bias.
When not in the lab, her time is spent being a mum to three kids, reading, walking and dreaming of her next holiday.

Development of novel ligands for the short-chain fatty acid receptor 2 (FFA2/GPR43)

Elizabeth Vecchio[1], Naomi Drego[1], Rikeish R. Muralitharan[1], Jessica Holien[2], Francine Z. Marques[1], Department of Pharmacology, Monash University and Victorian Heart Institute[1], Melbourne, VIC, Australia; Department of Biology, STEM College, RMIT University[2], Melbourne, VIC, Australia.

Introduction. Free fatty acid receptor 2 (FFA2, formerly GPR43) is a G protein-coupled receptor (GPCR) that is activated by short-chain fatty acids (SCFAs), generated via microbial fermentation of dietary fibre in the gut. FFA2 is an important modulator of cardiovascular health, with its absence increasing the risk of high blood pressure in experimental models and humans (1). The paucity of high-potency ligands has limited the therapeutic targeting of FFA2 but may provide a novel avenue to treat cardiovascular disease.
Aims. To optimise an *in vitro* semi-high-throughput screening assay to identify novel, small-molecule ligands for FFA2.
Methods. Inhibition of cAMP accumulation (an indicator of FFA2 activation) was measured in CHO cells overexpressing FFA2 using a LANCE® Ultra homogenous time-resolved fluorescence resonance energy transfer assay kit (Revvity). Once assay conditions were optimised, 113 compounds identified during an in-silico screen of our in-house library of 20 million small molecule compounds were tested at a single point concentration (50 µM) to assess potential receptor hits. Ligand activity was normalised to the level of cAMP inhibition elicited by the endogenous ligand, acetate.
Results. Cell suspensions of FFA2-CHO cells (500 cells/well in a 384-well plate), stimulated with 3 µM of the direct adenylate cyclase activator, forskolin at pH 7.4, demonstrated the optimal window for measurement of cAMP inhibition. The 113 lead compounds identified in the in-silico screen displayed varying levels of receptor activation. 12 compounds demonstrated >25% cAMP inhibition relative to 10mM acetate. Some compounds appeared to attenuate cAMP inhibition levels below baseline, which may indicate inverse agonist activity.
Discussion. This study has developed an experimental pipeline for identifying FFA2 ligands. The potential identification of novel ligands contributes to our understanding of FFA2 pharmacology and supports the early-stage development of therapeutic strategies for cardiovascular disease, in particular hypertension.

(1) Muralitharan R et al (2025) Circulation Research 136:e20-e33

P539

Evaluating student engagement and experience in a redesigned third-year pharmacology subject

Ms Monique Stoltz

Biography:

I'm Monique Stoltz - currently studying Honours Education in the Department of Microbiology, Anatomy, Physiology and Pharmacology, La Trobe University. I'm passionate about student-centered learning approaches and understanding what motivates students to engage in a subject. Outside of uni, I love animals and spending time outdoors. I'm also a massive foodie. I'm looking forward to networking with other education academics and sharing my passion for SoTL.

Evaluating student engagement and experience in a redesigned third-year pharmacology subject

Monique Stoltz[1], Ross O'Shea[1], Michael De Silva[1], Elly Djouma[1], Katelyn Mroczek[1], Antony Vinh[1], Rahini Ragavan[1]. Department of Microbiology, Anatomy, Physiology and Pharmacology, La Trobe University[1], Bundoora, VIC, Australia

Introduction. Pharmacology is a core subject in many allied health courses at La Trobe University. Traditionally, it included face-to-face lectures and workshops, with online lectures introduced during the COVID pandemic. In 2025, the subject was redesigned to be more student-centered and interactive, replacing lecture recordings with a digital workbook, practical classes, and interactive workshops to enhance cognitive engagement.

Aims. The goal was to evaluate student engagement and perception of the new subject, particularly the digital workbook, to determine if there is a correlation between online engagement, class attendance, and academic success.

Methods. Online lecture videos were replaced by short, embedded videos, concise online text, and H5P activities optimised for mobile access. Students engaged with the content asynchronously before attending in-person workshops and practicals. Data was collected using qualitative and quantitative methods, including a student survey, student feedback survey, assessment analysis, and engagement metrics.

Results. Sixty-five students completed the survey, with 68% preferring the new digital workbook and 75% finding it more engaging than lecture-based delivery. However, 69% still favored lecture videos for their flexibility, visual learning, and ability to review content at their own pace. Despite high engagement, final exam results were similar to previous years.

Discussion. The findings suggest that while the digital workbook promoted higher engagement and satisfaction, the strong preference for lecture recordings highlights the need for flexible learning modalities to cater to diverse learning needs. The unchanged exam outcomes suggest that engagement strategies may influence student experience more than summative performance. The redesign demonstrates the value of embedding digital interactivity and inclusive pedagogy into pharmacology teaching, while also emphasising the need to balance innovation with flexibility to optimise both student experience and learning outcomes.

Reference: *Kahu, E. R. (2013). Framing student engagement in higher education. Studies in Higher Education, 38(5), 758–773.*

P540

Risk Assessment Tool for the preparation of pharmaceutical and advanced therapeutic products

Ms Kerry Watts

Biography:

Kerry Watts is an expert consultant pharmacist in compounding and research, working in NSW Office for Health and Medical Research as senior officer in training, education and regulatory compliance for health system preparedness to deliver advanced therapeutics as standard of care. Kerry has recently embarked on a PhD with the University of Sydney to explore the impact of collaboration with government and academia to improve knowledge, understanding and compliance to regulation and improve patient access to advanced therapeutics

Risk Assessment Tool for the preparation of pharmaceutical and advanced therapeutic products

Kerry Watts[1,2], Christine Lu[2], Sophie Stocker[,2], Julia Warning[1]. Office for Health and Med Res, NSW Min of Health[1], School of Pharm, Fac Med & Health, The Univ of Sydney[2], Sydney, NSW

Introduction. The increasing number and complexity of registered biological and advanced therapeutics in clinical trials present significant challenges and risks in their preparation, particularly in ready-to-administer dosage forms. To minimise occupational exposure and support informed healthcare decision-making, a structured risk assessment tool was developed and embedded into a state-based policy framework.

Aims. Establish a national working group to validate the risk assessment tool to ensure its applicability across all jurisdictions and support Australian wide harmonisation for the safe preparation of advanced therapeutics and incorporation into national guidelines.

Methods. Nine senior compounding pharmacists and one clinical nurse educator, representing all state health facilities across Australia were invited to participate in the working group to support validation of the risk assessment tool. There are two phases to the study protocol. In each phase, each participant used the risk assessment tool to inform their decision-making process when preparing ten different pharmaceutical or advanced therapeutic products. Each participant then completed and submitted a REDCap survey to document the outcome. The working group reviewed the findings from Phase 1 and updated the tool based on best practice recommendations. Phase 2, a repeat of phase 1, is currently underway.

Results. During Phase 1, a total of 43 products were assessed: 39.4% monoclonal antibodies, 9.1% genetically modified organisms, 3.0% bacteriophages, and 48.5% other advanced therapeutics. The tool effectively supported the best practice decision-making for 88% of products. It has since been refined, with the revised version required to meet a benchmark for informing best practice in at least 90% of cases to be deemed successfully validated.

Discussion. The validated risk assessment tool is expected to standardise the preparation of pharmaceutical and advanced therapeutic products across Australia, serving as the national framework for risk-informed clinical and compounding decision-making.

P541

When students sign-off: Reflections and lessons from inadvertent real-world student electronic prescribing

Ms Amber Zhu

Biography:

Amber Zhu is a final year medical student at University of Otago studying at the Christchurch campus. Her interests include surgery, bananagrams and medical education.

When students sign-off: Reflections and lessons from inadvertent real-world student electronic prescribing

Amber T Zhu[1], Milan Sundermann[1], Paul KL Chin[1,2]. Department of Medicine, University of Otago[1], Christchurch, CAN, NZ; Department of Clinical Pharmacology, Health NZ[2], Christchurch, CAN, NZ.

Introduction. Authentic workplace learning experiences contribute to effective prescribing education. Medical students at Christchurch Hospital are required to create pre-prescriptions in the live inpatient electronic prescribing system (25234 for 3215 patients from 2021 to 2024), for doctors to authorise. However, some have inadvertently created student-authorised prescriptions, which triggered emails from the supervising clinical academic to students.

Aims. To describe student-authorised prescriptions at Christchurch Hospital in terms of clinical impact and educational value. To identify themes from medical students' email responses to the academic's email.

Methods. Prescribing data (2021 to 2024) were extracted, and clinical records were reviewed to inform descriptive statistics (including median and interquartile ranges). Prescriptions in patients ≥ 65 y were examined against START criteria. Deidentified email responses from medical students were subjected to inductive reflexive thematic analysis.

Results. There were 296 student-authorised prescriptions (333 medicines) by 53 students for 69 patients aged 70 y (54-79), and Charlson Comorbidity Index of 3 (1-5). Prescriptions were live for 11.2 h (0.3-46.7) before being ceased by a doctor/medical student (155/296, 52%) or patient discharge (141/296, 48%). The number of doses administered per prescription was 0 (0-2). Of these, 237/333 (71%) medicines were from the Otago Medical School Core Medicines List, 48/333 (14%) medicines met the APINCHS high-risk criteria, and 35 were both. Only 8/333 medicines occurred in ≥ 65-year-old patients with a START criterion clarity score of ≥ 75%; none were considered inappropriate prescriptions. Key themes from 29 medical student emails included: uncertainty and ambiguity in prescribing authority; the role of supervision and responsibility; emotional responses of guilt, caution and professional identity; systemic processes and flaws; and learning from error and seeking clarification.

Discussion. Student-authorised prescriptions reflect system design vulnerabilities rather than individual failures. They had minimal clinical impact but potentially significant learning value, both about medicines and professionalism.

Charles KA et al (2025) BJCP DOI: 10.1002/bcp.70126
Sallevelt et al (2020) BMJ Open DOI: 10.1136/bmjopen-2019-033721

P542

Enhancing pharmacology education with virtual reality (VR): student engagement and conceptual understanding

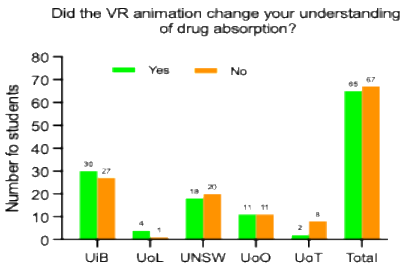
Dr Johnson Liu

Biography:

Dr Johnson Liu is a Senior Lecturer and education-focused academic in the Department of Pharmacology, School of Biomedical Sciences, Faculty of Medicine & Health, UNSW Sydney. He holds a BSc, MSc, and PhD in Pharmacology, and has previously held academic positions at South China Agricultural University, the University of Auckland, AUT University and the University of Tasmania. He teaches pharmacology-related subjects across medicine, biomedicine and pharmaceutical science programs, serving as Course Convenor and Program Academic Coordinator. His research interests span anticancer drug discovery and development, pharmacokinetics, drug transporters, and chemotherapy-induced neuropathy. He also pursues pedagogical research, focusing on core concept mapping and virtual reality application in pharmacology education, supported by funding from reputable organizations. Dr Liu has supervised Honours, Masters and PhD students, and has published over 50 research articles. He also contributes to the academic community as a review editor and expert reviewer for international journals.

Enhancing pharmacology education with virtual reality (VR): student engagement and conceptual understanding

Johnson J Liu[1], Waltraud Binder[1], Jon A Berg[2], Trond T Serkland[2], Monica Kvernenes[2], Steve Gallagher[3], David Reith[3], Ullamari Pesonen[4], Dimitra Mitsa[5], Marit C Strandvik[6], Tiril Mork[2], Silje Skrede[2], Paul White[7]. Faculty of Medicine & Health, University of New South Wales[1], Sydney, NSW, Australia; Faculty of Medicine[2], University of Bergen, Bergen, Norway; School of Medicine, University of Otago[3], New Zealand; Dept Pharmacology, University of Turku[4], Finland; Faculty of Biological Sciences, University of Leeds[5], UK; Dept Game Development, University of Inland Norway[6], Elverum, Norway; Faculty of Pharmacy & Pharmaceutical Sciences, Monash University[7], VIC, Australia



Introduction. Insufficient pharmacological knowledge can often lead to medical errors, underscoring the need for effective educational strategies in healthcare. While VR is gaining traction as an innovative tool, its use in pharmacology education remains limited.

Aims. To explore whether VR technology enhances students' understanding of pharmacological concepts, focusing on oral drug absorption.

Methods. Custom-designed 3D VR animations depicted the journey of an orally administered tablet. A mixed-method approach involved 133 students from five universities with prior pharmacokinetics knowledge. Participants viewed the animation and completed a structured questionnaire. Thematic analysis was also conducted on transcripts from focus group interviews (n=13).

Results. About half of respondents reported improved understanding of drug absorption. No statistically significant difference was found in understanding across students majoring in medicine, biomedicine, or pharmaceutical science ($\chi^2 = 6.36$, $p = 0.095$). Most participants expressed a positive attitude toward the VR application's role in enhancing engagement. The system usability score (SUS) was 80 (max. 100). Thematic analysis revealed specific themes related to the design and effectiveness of the VR aminations.

Discussion. The VR-based learning tool showed technical effectiveness in deepening conceptional understanding, clarifying misconceptions, and increasing engagement. However, challenges were identified in design and implementation, including integrating pharmacology with other health disciplines, balancing immersion with cognitive load, and aligning VR-based learning with assessment frameworks. Kim K et al (2023) Cureus. 15(8): e43411

P543

Education innovation: a drug profile assessment to evaluate integrated pharmacology core concepts

A/Prof Kellie Charles

Biography:

Kellie Charles is a passionate educator and education researcher from the Pharmacology Discipline in the Sydney Pharmacy School at the University of Sydney. She is a Senior Fellow of the Academy of Higher Education in the UK and previous recipient of the ASCEPT Outstanding Teaching Excellence Award. Her recent Churchill Fellowship explored the educator's experience with adapting and integrating AI into teaching practices and assessment. Her ongoing research is about how higher education changes with disruptive paradigms.

Education innovation: a drug profile assessment to evaluate integrated pharmacology core concepts

Kellie A. Charles[1], Slade Matthews[1], Brent McParland[1]. Pharmacology Discipline, Sydney Pharmacy School, University of Sydney[1], Sydney, NSW, Australia.

Introduction. The pharmacology core concepts are a framework for organising the foundational pharmacology knowledge, principles and key relationships needed for students to understand and apply to solve medication-related problems. Traditionally, we teach *and* assess the core concepts in silos – e.g. PK and PD individual assessments or MCQ. However, the pharmacology of a drug is integrated across these concepts. How do we assess student's ability to integrate the knowledge of many pharmacology core concepts in a wholistic assessment?

Aim. To redesign the drug profile assessment to assess student's ability to understand and integrate both PK and PD pharmacology core concepts for Australia's top 100 prescribed medications.

Methods. We re-engineered a previous drug profile assessment from a third-year medicinal chemistry/pharmacology unit to align with the weekly teaching and level of foundational knowledge of pharmacology core concepts in PCOL2021, Foundations in Pharmacology second year unit.

Results. 290 PCOL2021 students were assigned to groups of 4 randomly and allocated one commonly used medication to research weekly core concepts along with the lecture, tutorial and practical content of the week. Each student was expected to complete their own individual research and share with their team every 3 weeks to develop a 10-minute, 5-slide oral presentation for end of semester (final assessment = 10%). Explicit sign posting of relevance of core concepts and guided weekly research questions were delivered in a self-direct Kuracloud module. The rubric included assessing the group's presentation for their pharmacology knowledge integration, teamwork and oral presentation skills as well as each individual student's contribution to the team's research through an upload of the Kuracloud report. 75 group presentations were assessed by marker pairs in two streams held over four days in week 13.

Discussion. We were presently surprised at the high standard of the group presentation, individual research and integration of knowledge across the core concepts. On reflection, inclusion of "drug profile research sessions" would be useful to future timetable to provide students with dedicated time to share learning with group and to gather formative feedback from educators.

P544

Revisiting program-level curriculum alignment with AI assessment changes: The USYD experience

A/Prof Kellie Charles

Biography:

Kellie Charles is a passionate educator and education researcher from the Pharmacology Discipline in the Sydney Pharmacy School at the University of Sydney. She is a Senior Fellow of the Academy of Higher Education in the UK and previous recipient of the ASCEPT Outstanding Teaching Excellence Award. Her recent Churchill Fellowship explored the educator's experience with adapting and integrating AI into teaching practices and assessment. Her ongoing research is about how higher education changes with disruptive paradigms.

Revisiting program-level curriculum alignment with AI assessment changes: The USYD experience.

Kellie A. Charles[1], Tina Hinton[1,] Slade Matthews[1], Brent McParland[1], Bryony Winters[1], Sarasa Mohammadi[1], Mohamed Metwaly[1]. Pharmacology Discipline, Sydney Pharmacy School, University of Sydney[1], Sydney, NSW, Australia.

Introduction. The rapid emergence of AI has led to increased calls from TEQSA for all educators to review their current teaching and assessment practices. USYD DVC-Education Portfolio has requested all programs/ majors conduct a "program-level" review (e.g. across multiple units) to comply with the new AI Assessment Policy.

Aims. To detail and reflect on the curriculum program-level mapping process across the Bachelor of Science, Pharmacology Major and determine which assessments are secure (non-AI) or AI-allowable.

Methods. Following guidance (Bridgemann, et al, 2025), all USYD Pharmacology unit of study coordinators met collectively to review the curriculum across six units of study. Three tasks of this review were; 1) An investigation of the alignment between educator graduate expectations, major learning outcomes, Science Program-level learning outcomes and University undergraduate qualities, 2) An identification of level of learning (acquisition, retainment and application) for each course-level learning outcomes across units and 3) A review and revision of assessments in accordance with the AI assessment Policy to promote a sequential mastery of core pharmacological knowledge and skills (e.g. experimental design and analysis and written and oral communication) across the Pharmacology major.

Results. High alignment between educator expectations and most Science Course, major learning outcomes and graduate qualities was observed. Recent AI assessment adaptions were consistent with policy. Using a whole of major, program-level approach identified key assessment changes; aligning complexity along learner trajectory, reducing overlap and generating ideas for new assessments to address missing course learning outcomes. Co-requisite units across different majors (e.g. medicinal chemistry and neuroscience) required a more nuanced consideration.

Discussion. This approach to program-level curriculum review was universally seen as collaborative, student-focused and informative. Ongoing work to constructively align teaching to assessment needed prior to 2026 implementation.

Bridgeman, A et al (2025) Program level assessment design and the two-lane approach. https://educational-innovation.sydney.edu.au/teaching@sydney/program-level-assessment-two-lane/

P545

Core competencies in pharmaceutical sciences: curriculum mapping and gap analysis

A/Prof Tamara Paravicini

Biography:

Tamara is an Associate Professor and Assistant Associate Dean (Pharmaceutical Sciences) at the School of Health and Biomedical Sciences at RMIT University. She is an experienced academic with expertise in teaching pharmacology and physiology across a wide range of degree programs and to students with diverse backgrounds. She has a strong track record in leading large-scale curriculum reform, including curriculum mapping, review, design and development.

Core competencies in pharmaceutical sciences: curriculum mapping and gap analysis

Tamara M Paravicini[1], Durga Dharmadana[1], Trisha A Jenkins[1]. School of Health and Biomedical Sciences, RMIT University[1], Melbourne, VIC, Australia

Introduction. Competency-based education frameworks are common in accredited health professions and curricula in these programs are explicitly designed to align with these standards. However, competency frameworks are less commonly used in broader disciplines such as biomedical and pharmaceutical sciences. The Pharmaceutical/Medtech sector employs many biomedical/pharmaceutical/health science graduates, and there is scope for new graduates from these disciplines to help meet the acknowledged workforce shortages. However, as a sector with a broad range of professional roles and limited formal accreditation pathways, identifying the preparedness of graduates to meet the required workforce competencies remains difficult to assess.

Aims. This study will use a desktop analysis to examine how degree programs that produce graduates for the Pharmaceutical/Medtech sector map to an established core competency framework, and identify any gaps that may limit the employability of graduates in this sector.

Methods. A desktop analysis of publicly available data will map the Learning Outcomes (LOs) and Graduate Attributes (GAs) from relevant undergraduate and postgraduate degree programs at Australian Universities. A mapping tool will be developed to identify how these LOs and GAs map to an established core competency framework, and the extent to which they align with each competency. A pilot study will assess the validity of this tool, with team members independently using the tool to map different curricula. A consensus-lead approach is used to resolve discrepancies and identify improvements before expanding the study to include a wider variety of degree programs.

Results. The mapping tool and alignment with the core competency framework will be presented along with the findings from the pilot validation study.

Discussion. This study will examine for the first time the extent to which Australian degree program curricula are designed to equip graduates with the skills and attributes that align with an established core competency framework that describes the requirements for effective performance in the Australian Pharmaceutical/MedTech sector. These data will provide valuable insights for the targeted development of curricula in programs aimed at producing graduates with relevant work-ready skills, helping to meet future workforce needs in this growing sector.

P546

Redesigning Pharmacology Practicals and Tutorials: Enhancing Integration, Engagement, and Student Outcomes

Dr Rachael Farrington

Biography:

Dr Rachael Farrington is a pharmacologist with research expertise in complementary and alternative medicines, with a particular focus on the quality and safety of commercialized herbal products. Her work examines the purity and consistency of these preparations, as well as their potential interactions with conventional pharmaceuticals and other herbal medicines, ensuring evidence-based understanding and safer use in clinical practice.

Alongside her research, Dr Farrington is deeply committed to enhancing the student learning experience in pharmacology. She is passionate about creating engaging, active learning environments that foster curiosity, critical thinking, and applied knowledge. Drawing on innovative technologies and interactive teaching methods, she integrates digital resources, scenario-based learning, and problem-solving approaches to support student engagement and success.

Redesigning Pharmacology Practicals and Tutorials: Enhancing Integration, Engagement, and Student Outcomes

Rachael L Farrington[1], Ian F Musgrave[1], Abdallah Salem[1], Susan M Britza[1]. Discipline of Pharmacology, School of Biomedicine, The University of Adelaide[1], Adelaide, SA, Australia.

Introduction. Hands-on practical classes are central to pharmacology education, providing opportunities for students to observe drug effects in biological systems and connect theoretical concepts to applied settings. However, students in a third-year pharmacology course reported poor alignment between lectures and laboratory sessions, overwhelming workload, and disengagement in tutorials, reflected in low student satisfaction scores.

Aims. This project aimed to improve the integration of pharmacology theory and practical application, restructure the delivery of learning material to enhance accessibility and engagement and evaluate the impact of these changes on student satisfaction and learning outcomes.

Methods. A mixed-methods approach was employed. A review of historical course Student Experience of Learning and Teaching (SELT) feedback and staff-student consultations identified key issues in practical and tutorial delivery. Laboratory sessions were redesigned to align more closely with lecture content. Tutorials were replaced with large-class interactive workshops, fostering collaboration and inclusivity, and weekly student-led drop-in sessions. Outcomes were evaluated through SELT satisfaction ratings and grade distributions pre- and post-implementation.

Results. Laboratory redesign, involving simple *in vitro* systems (e.g. organ baths) to whole animals, improved student perceptions of course integration and reduced workload concerns. Overall SELT satisfaction increased from 50% (2022) to 91% (2023), 90% (2024) and 87% (2025). The transition from small-group tutorials to interactive workshops increased participation and engagement, with final grade distributions showing a shift in higher achievement: distinctions and high distinctions rose from 18.4% (2023) to 31.5% (2024) and 26.7% (2025). Student comments highlighted improved support and appreciation for the new workshop format and tailored drop-in sessions.

Discussion. Targeted redesign of pharmacology practicals and tutorials successfully addressed long-standing challenges in student engagement, workload, and theory-practice integration. Scaffolded learning and collaborative, large-class workshops fostered inclusivity, improved student confidence, and enhanced performance. These outcomes align with broader evidence that relationship-rich, and active pedagogies strengthen student education. This model may be transferable to other laboratory-based disciplines seeking to improve alignment, engagement, and outcomes.

P547

Educator perceptions of teamwork implementation in undergraduate bioscience units

Dr Jennifer Irvine

Biography:

Jennifer Irvine is an education-focused lecturer in the Department of Pharmacology at Monash University.

Educator perceptions of teamwork implementation in undergraduate bioscience units
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Introduction. Teamwork is increasingly valued during hiring processes for supporting both career success and positive workplace dynamics. Our recent unpublished study involving third-year undergraduate pharmacology students revealed that while students unanimously acknowledge the necessity of teamwork, the vast majority still prefer to work individually due to a number of teamwork challenges. Thus, assessing how teamwork is being implemented by educators is crucial to understanding how student experiences of teamwork in their tertiary studies can be improved.
Aims. To explore how educators implement teamwork in their bioscience curriculum and their perceptions of how students are supported in this process.
Methods. An anonymous online survey was completed by 28 Monash University unit coordinators and/or chief examiners from the Biomedical Discovery Institute, the Department of Immunology, and first-year prerequisite units from the Faculty of Science.
Results. Formative in-class activities (93% of survey respondents) and presentations (86%) were the most common approaches to fostering teamwork skills in students. Of the tasks nominated as fostering teamwork, presentations (82%) were the most often to include summative assessment of the final product of teamwork, followed by written assignments (43%). The summative assessment of individual students' contributions to these team tasks was much less common, with presentations (50%) again being the most frequently used modality. With regards to student support, 64% of survey respondents nominated that they consciously employed teamwork skills training, yet thematic analysis of free text responses indicated that approximately half of these nominated approaches actually contained no formal skills training. Nonetheless, 93% of respondents felt confident in supporting students when there was a team dispute, and 75% intervened if approached by students with a teamwork problem.
Discussion. This study suggests there remains a disconnect between how students and educators perceive the delivery of teamwork tasks. Addressing this mismatch could ultimately lead to an improved experience for both students and educators.

P548

Education Innovation: A Cogniti agent to develop critical analysis of AI

Dr Eryn Werry

Biography:

Eryn Werry is a Senior Lecturer in Brain and Mind Sciences (Central Clinical School, Faculty of Medicine and Health) and Research Associate in the Drug Discovery Lab (School of Chemistry, Faculty of Science). She completed her PhD at the University of Sydney, studying glial cells, and then took up a Brain Sciences Postdoctoral Fellowship at UNSW, studying neurogenesis. Since 2012, she has been researching new therapeutics for brain diseases at the University of Sydney. She is also Program Director for the Master of Brain and Mind Sciences at the University of Sydney.

Education Innovation: A Cogniti agent to develop critical analysis of AI

Samuel D. Lane[1], Charleigh Agius[1,2] and Eryn L. Werry[1,2] Central Clinical School, Faculty of Medicine and Health[1], School of Chemistry, Faculty of Science[2], The University of Sydney, NSW, Australia

Introduction. Educating students for future success now involves facilitating the development of skills relating to critical analysis of artificial intelligence (AI) output[1], in addition to development of traditional skills such as scientific writing. Cogniti is a tailorable generative AI agent that allows educators to design custom chatbots which respond according to rules constructed by the educator, using sources specified by the educator and hosted on a secure server.

Aims. We aimed to develop an assessment requiring students to use a custom-made Cogniti chatbot to develop students' ability to critically analyse AI output and also develop their scientific writing skills.

Methods. As part of this assessment within the Master of Brain and Mind Sciences at the University of Sydney, students were required to write a draft literature review. They were then asked to submit a paragraph of that draft to the Cogniti agent for feedback. The Cogniti agent was programmed to give 4 pieces of tailored accurate feedback and one piece of tailored inaccurate feedback on the scientific writing style and content of the paragraph. Students then had to submit the draft paragraph, the feedback received from Cogniti, an appraisal of whether they agreed with each point of the feedback or not and why. They also had to outline how they changed their draft paragraph in response to the feedback and were required to submit the final literature review.

Results. The agent correctly gave both valid and erroneous feedback. Through marking this assessment, we learned about both the students' ability to appraise AI and the common mistakes students make in academic writing, which will inform training we will introduce in these 2 areas.

Discussion. In the future, we plan to evaluate the impact of this assessment on the scientific writing of students by getting external evaluators to rate the quality of scientific writing in the draft literature review paragraph compared to the final paragraph. We also plan to evaluate the impact on AI critical appraisal skills by comparing performance on a future AI critical appraisal assessment between those who have done this current assessment and those who haven't.

1. Dumitru & Halpern (2023) J Intell 11:194

P549

Electronic pre-prescribing by final year medical students as a potential workplace-based assessment

Dr Paul Chin

Biography:

Paul Chin is a Senior Lecturer at the University of Otago, Christchurch and Senior Medical Officer at Te Whatu Ora Health New Zealand – Waitaha Canterbury.
Research interests include therapeutic drug monitoring (including anticoagulants and antimicrobials), quality use of medicines, electronic prescribing, and clinical decision support.

Electronic pre-prescribing by final year medical students as a potential workplace-based assessment

Kellie Charles[1], Lorna Pairman[2], Emily Moon[2], Matt Doogue[2], Tim Wilkinson[2], Paul Chin[2]. University of Sydney[1], Sydney, NSW, Australia; University of Otago[2], Christchurch, CAN, NZ.

Introduction. The development of effective prescribing skills requires a learning environment that provides medical students with practical experience without risking patient harm. There is very limited information on student use of live electronic prescribing and administration systems (ePA).
Aims. We examined the educational and clinical utility of a formative assessment model where final year medical students embedded in hospital teams in Christchurch, were permitted to create pre-prescriptions in the ePA, which doctors could then activate to live prescriptions.
Methods. Current students, post-graduate year 1 doctors and supervisors (senior doctors) were interviewed. We conducted inductive reflexive thematic analysis on the audio transcripts. ePA prescribing data were extracted from the local health district's data warehouse spanning four years (2021-2024). Patient clinical records were interrogated to identify potentially inappropriate live student prescriptions. These were analysed with descriptive statistics.
Results. Five interpretative themes were generated from 10 interviews about the educational benefits of the formative assessment: 'Practice, practice, practice' (repeatedly performing the prescribing process facilitated students' clinical mastery of therapeutic decision-making and technical ePA mastery); "Finding my place in work" (developed students' social-professional relationships with clinical team); "Conquering time" (appreciation of time saving from students reducing doctors' prescribing tim0065); "Safety protected" (embedded ePA-related safety mechanisms enhanced engagement with using it for learning); "Becoming a real doctor" (student formation of an authentic professional identity was fostered). The live ePA was used by 355/370 students. They completed 25,324 pre-prescriptions in 3,268 patients (median 63 pre-prescriptions in 8 patients per student). Supervising doctors activated 58% to live prescriptions. Students mistakenly generated 296 live prescriptions; 33% (97/296) had doses administered, and 3% (8/296) were potentially inappropriate (no adverse drug reactions against these were documented).
Discussion. Medical student use of a live electronic prescribing system enabled learning about safe prescribing, facilitate the transition from student to doctor, and fits the definition for formative workplace-based assessment.
Charles K et al (2025) Brit J Clin Pharmacol DOI:10.1002/bcp.70126

P550

Evolution of a clinical trials practical class for 3rd year pharmacology students

A/Prof Nicole Jones

Biography:

Associate Professor Nicole Jones is the head of the Neuropharmacology and Brain Injury group in School of Biomedical Sciences (SBMS) and Associate Dean of Postgraduate Research Training in Faculty of Medicine and Health at UNSW, Sydney. She completed her PhD in Pharmacology at Monash University (Melbourne), and postdoctoral fellowships at Eli Lilly (UK and USA) and the Howard Florey Institute (Melbourne). Since 2008, she has been a leading Neuroscience and Pharmacology educator across different programs in SBMS (Neuropharmacology, Drug Discovery, Design and Development), demonstrating impact through the design and implementation of innovative teaching initiatives to motivate and engage students, resulting in enhanced student outcomes.

Evolution of a clinical trials practical class for 3rd year pharmacology students

Nicole M Jones[1], Matthew D Perry[1], Angela M Finch[1].
Department of Pharmacology, School of Biomedical Sciences, UNSW Sydney[1], Sydney, NSW, Australia.

Introduction. Drug Discovery, Design and Development (PHAR3202), is a third-year pharmacology course at UNSW Sydney, with 56-70 students (2017-2025). This course follows the stages of drug discovery including project and target selection through lead identification, pre-clinical studies, clinical trials, registration and commercialization processes.
Aims. To design a clinical trial to assess the effects of a drug in a practical class. The class has evolved over several years, where students consider trial design, comparison groups; blinding; randomisation; inclusion and exclusion criteria; ethics; sample size; endpoint(s), data analysis and presentation of the data collected.
Methods. Class 1 (2017-2019) involved a small trial being performed in the class where students assessed the influence of colour on the ability of subjects to detect the sweetness of a liquid and ways to avoid bias. Class 2 (2020-2021) was performed in a virtual manner due to Covid-19 restrictions preventing on-campus attendance. Students designed and conducted a Phase I clinical trial on a virtual subject population (using "The Islands") where they assessed the effects of a drug (or control) on key physiological variables. Class 3 (2022-present) involved students developing a design plan and then performing a pilot study for a Phase I or Phase II clinical trial and assess the effect of a drug using "The Islands" virtual subject population.
Results. Over the evolution of this practical class, students have developed a robust understanding of the clinical trials process by integrating hands-on findings with the key principles of clinical trials presented in lectures. Anonymous course feedback consistently highlights the practical components as a key strength of the course.
Discussion. By engaging students in the design and execution of clinical trials—both in-person and virtually—this unique class has fostered a deep understanding of the complex considerations inherent throughout this late stage of drug development. Moving into the future (2025), we have removed the final exam from the course and instead students will submit a technical report on their clinical trial as part of a portfolio during the exam period.

"The Islands" - https://islands.smp.uq.edu.au/login.php

P551

Performance in concept mapping: a better match to exams than quizzes?

Dr Sheila Doggrell

Biography:

Sheila joined ASCEPT in 1978 after taking up a lectureship in Auckland. She has presented at many scientific meetings of ASCEPT in NZ and Australia (and organised a few). Sheila is presently a Life Member of ASCEPT. Sheila was awarded a DSc for her research in experimental pharmacology in 1997. Sheila has received both the IUPHAR Education Section Teaching Excellence award and the ASCEPT Teaching Excellence award. In retirement, Sheila has an Adjunct position at Griffith University. She continues with scholarly writing (mostly opinions on recent clinical trials) and the education research.

Performance in concept mapping: a better match to exams than quizzes?

Sheila A Doggrell[1], Matthew Barton[2]. School of Pharmacy and Medical Science[1] and School of Nursing and Midwifery[2], Griffith University, Gold Coast, QLD, Australia

Introduction. In courses where it is not compulsory to pass the exam/s, students can fail the exam/s but pass the course based on their coursework assessment marks. This is not ideal, but occurs because marks for coursework assessments (e.g., quizzes, practicals, or group projects) are generally higher, than for examination. This finding includes students in nursing undertaking a pharmacology course with tutorials and a case study assignment as coursework (Doggrell 2020). To avoid students passing, who have failed the exam, the marks for coursework and exams need to be similar. One way to do this would be to use coursework that better differentiates students with different abilities, and concept maps may do this and have similar marks to exams.

Aims. In a second-year pathophysiology/pharmacology course for 307 students in nursing, 50% of the marks were allocated to the exam, 20% to online quizzes, and 30% to a concept map-based assignment. Our aim was to test whether concept mapping better matches with examination marks and failure rates compared to quizzes.

Methods. We determined the marks (as a percentage of 100%) and failure rates for the concept mapping, quizzes, and final exam. We then conducted regression analysis between concept mapping or quiz marks and exam marks.

Results. The overall marks and marks in the concept mapping, quizzes, and final exam were 58% ± 14 (mean ± SD), 58% ± 16, 68% ± 16, and 54% ± 14, and the failure rates were 32%, 23%, 13%, and 41%, respectively. Thus, there were smaller percentage points difference in the marks between the concept mapping and exams than with quizzes, 4% vs 14% pts, and between the failure rate with concept maps than quizzes 18% and 28% pts, respectively. Regression line analysis showed a moderate relationship between marks for concept mapping and the exam, r = 0.48.

Discussion. Concept mapping marks and failure rates corresponded more closely with final exam outcomes than quiz marks did. Comparing this with previous studies (Doggrell, 2020) revealed that the lower coursework marks using concept map in this study led to a lower overall mark and higher student failure rates. Concept maps, with their effectiveness in differentiating students of different abilities, may be the key to a fairer assessment method.

Doggrell SA (2020) BMC Nursing 19:112

P552

Making the disciplinary assessment literacy of pharmacology explicit

Assoc Prof Lynette Fernandes

Biography:

Lynette was part of a nation-wide team that secured funding from the Australian Learning and Teaching Council (ALTC) for a project entitled "Ensuring quality graduates of Pharmacology". She has developed a program in responsible conduct in learning and research that is now embedded within Pharmacology and Medical Research Honours curricula. Lynette led the development and implementation of the multi-disciplinary ethics unit, Social Responsibility in Action SCIE2100 and a Minor in Applied Ethics. Lynette developed the ASCEPT Mentoring Program and has received the ASCEPT Teaching Excellence Award. She is an active member of the ASCEPT Education Forum, having previously served as Chair. Lynette collaborated with ASCEPT colleagues to define the core concepts in Pharmacology. She is a Senior Fellow of the Higher Education Academy. Lynette is an active member of the IUPHAR-Education Section, where she is a Councillor, core concepts of pharmacology expert group member, and Online Meetings Steering Group Member-at-Large.

Making the disciplinary assessment literacy of pharmacology explicit

Lynette B Fernandes[1], Anna-Marie Babey[2], Órla P Barry[3]. School of Biomedical Sciences, University of Western Australia[1], Perth, WA, Australia; School of Science & Technology, University of New England[2], Armidale, NSW, Australia; School of Medicine, University College Cork[3], Cork, Ireland.

Introduction. Assessment is essential for driving student learning. However, unless students understand what is being asked of them, learning may be steered in the wrong direction. While students readily address knowledge demands of assessment questions, they often handle processing demands either inappropriately or not at all. Our research is a continuation of an international assessment project initiated in University College Cork.

Aims. To identify the most frequent action words / phrases used in pharmacology assessments. To determine the meaning pharmacology academics attribute to the most commonly used action words / phrases.

Methods. Summative exam papers over a 5-year period were collated from four core pharmacology units that contribute to the Major in the Bachelor of Biomedical Science at The University of Western Australia. A frequency analysis of action words was performed on short answer questions. Pharmacology academics were invited to participate in a focus group to discuss the meaning they attribute to the most commonly used action words (UWA Approval No. 2024/ET000208).

Results. Across all four core pharmacology units, the most frequently used action words in exams were: describe, explain, discuss, provide, highlight, and interpret. Example meanings attributed to these words that arose from the focus group were: "describe" – "implies a bit of depth" / "pretty peripheral" / "a definition"; "explain" – "address … why and how" / "more depth"; "discuss – "implies … breadth … or depth" / "a lot more information"; "provide" – "provide your reasoning" / "justify"; "highlight" – "this is a concept, give examples that highlight it"; "interpret" – "demonstrating their ability to analyse" / "given them some data and you want them to interpret the findings". Participants ascribed similar meanings to "interpret" and "discuss" as well as to "highlight" and "provide". However, participants agreed on the following sequence of action words, arranged by increasing depth of information required: "describe", "explain", and "discuss".

Conclusion. Findings from this project could be used to guide the development of literacy guidelines aimed at supporting student learning and success in pharmacology.

P553

Implementing OSPEs in large pharmacology cohorts: logistics, challenges, successes, lessons learned

Dr Nilushi Karunaratne

Biography:

Nilushi Karunaratne is a dynamic Education-focused academic specialising in skill-based instruction and innovative teaching practices in physiology and pharmacology. Her education research spans building core pharmacology knowledge and essential skills, as well as exploring teamwork and resilience skill-based instruction to support students in contemporary educational landscapes.

Implementing OSPEs in large pharmacology cohorts: logistics, challenges, successes, lessons learned

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Introduction. Scaling authentic assessments such as Objective Structured Practical Examinations (OSPEs) presents significant logistical challenges, particularly in large science cohorts.
Aims. To describe the design, coordination, and implementation of an OSPE for ~220 students in a 2nd-year pharmacology unit, highlighting practical considerations and lessons learned.
Methods. The OSPE comprised 3 stations covering laboratory techniques, data analysis, and oral justification tasks. Logistics involved timetabling rotations, training 15 examiners, developing consistent rubrics, and ensuring equitable student experience. A pilot trial informed refinement in station timing, examiner calibration, and resource allocation.
Results. The OSPE was delivered successfully within a single day. Timetable modelling ensured manageable student flow, while examiner training reduced variability in marking. Key challenges included venue availability, resource duplication, and staff workload. Solutions included early station prototyping, deployment of sessional staff, and staggered student scheduling. Feedback from staff and students indicated the assessment was demanding but authentic and fair.
Discussion. Implementing OSPEs at scale requires careful planning of staff, space, and resources, alongside clear communication with students. Building on lessons learned, refinements for 2026 include running separate days for laboratory and verbal stations, clustering consulting rooms to streamline transitions, enforcing clearer protocols for academic integrity, and strengthening examiner-student identification and marking calibration. While resource-intensive, the process has proven feasible and transferable, providing a blueprint for other science disciplines considering authentic, AI-resilient assessment models.

P554

Development of Online Assessment Database to Improve Quality, Consistency and Efficiency

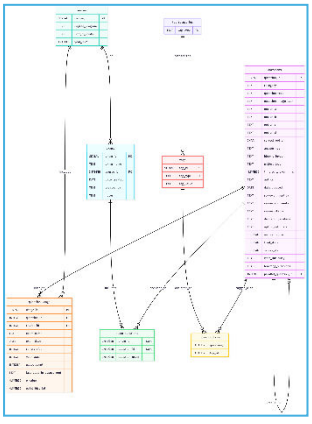
Dr Slade Matthews

Biography:

Slade is a researcher and educator in both pharmacology and toxicology at the University of Sydney School of Pharmacy. His BmedSci (Hons), 1995, included an investigation of copperhead snake venom using classical pharmacological bioassays, chromatography, and electrophysiology. His doctoral research (PhD 2007) focused on the integration of machine learning techniques for cell classification tasks and modelling clinical outcomes in clinical data. He also holds two educational qualifications: a DipEd and a GradCertEd (HigherEd). Slade's primary research focus is computational toxicology – a fusion of experimental design, statistical analysis, and machine learning. He serves as representative pharmacologist on NSW Health, Poisons Advisory (statutory) Committee and is also an external assessor for TGA Therapeutic Goods Evaluation Panel and also collaborates with AICIS on computational Ames-assay models for mutagenicity chemical assessment. He is Deputy Chair of the ASCEPT Toxicology Special Interest Group and contributes to ASCEPT's official responses to TGA requests for consultation.

Development of Online Assessment Database to Improve Quality, Consistency and Efficiency

Slade Matthews, Megan Anakin, Andrew Bartlett, Tina Hinton, Kellie Charles, Rebecca Roubin
Sydney Pharmacy School, The University of Sydney, Sydney, NSW, Australia



Introduction. Manual management of assessment data is time-consuming and limits the ability to track item performance or maintain accessible historical records. An online assessment database can address these limitations by enabling item anaylsis[1], streamlining workflows, and supporting standard-setting processes. However, the database must also be designed for the specific needs of educators. Currently, there is no affordable, commercially available database tailored for pharmacy and pharmacology education.

Aims. To design and develop an online assessment database to automate creation, storage, administration, and retrieval of multiple-choice questions in pharmacy and pharmacology education.

Methods. The database was designed and developed following stakeholder consultations and SWOT analysis to identify essential features. Key functionalities included question management and tagging, reporting functions, and a wish list including role-based access and logging. The technical architecture was based on cptlab.au design stack.

Results. The database design is represented by an Entity-Relationship Diagram (ERD, Fig. 1) showing flags and metadata necessary for item evaluation and cataloguing. The tech stack includes PostgreSQL database, Flask backend, and Bootstrap frontend, with deployment via Nginx (web traffic) and Gunicorn (Python application server).

Discussion. The database will provide a secure, centralised repository for MCQs, enabling metadata-driven organisation to support educators to compile balanced assessments efficiently. The next step is to pilot test with a limited number of educators to evaluate usability and searchability. Further training about MCQ construction and evaluation is planned.

[1]Szyjewski, G. (2025) In: Hernes, M., Wątróbski, J., Rot, A. (eds) ECAI 2024. Lecture Notes in Networks and Systems, vol 1217. Springer, Cham.

P555

Using multiple-choice questions to develop evaluative judgement in students and educators

Dr Slade Matthews

Biography:

Slade Matthews is a researcher and educator whose career has been marked by his dedication to the intersection of biomedical science and machine learning. He is committed to fostering mathematical literacy among students and has made contributions to both research and education in the field. He holds two teaching awards for university teaching. Recognizing the importance of effective pedagogy, Slade completed a Graduate Certificate in Higher Education in 2011. He has a Bachelor of Medical Science, Honours (1995) which included an investigation into the venom of the Australian copperhead snake using classical pharmacological bioassays, chromatography, and electrophysiology. His doctoral research (PhD 2007) focussed on the integration of machine learning techniques for cell classification tasks and modelling relationships in clinical data. Slade's primary research focus centres on the fusion of experimental design, statistical analysis, and machine learning to investigate biomedical problems, especially in toxicology. He has published 43 publications in peer-reviewed journals and has been cited 1275 times.

Using Multiple-Choice Questions to Develop Evaluative Judgement in Students and Educators

Rebecca Roubin, Slade Matthews, Tina Hinton, Andrew Bartlett, Kellie Charles, Megan Anakin
Sydney Pharmacy School, The University of Sydney, Sydney, NSW, Australia

Introduction. Multiple-choice questions (MCQs) are widely used to assess student knowledge, yet they also offer opportunities to foster critical thinking. Time constraints, however, often limit educators' capacity to write and review high-quality MCQs, which can compromise assessment integrity and hinder students' ability to demonstrate deeper learning. Engaging students in the creation and evaluation of MCQs can help them—and their educators—develop evaluative judgement: the ability to discern the quality of assessment items and reflect on learning depth.

Aims. This project aims to engage both students and educators in the collaborative development of MCQs to enhance evaluative judgement and improve assessment quality.

Methods. Evaluative judgement will be cultivated through interactive workshops where participants co-create MCQs aligned with learning outcomes and designed to elicit higher-order thinking. These sessions will also introduce practical techniques for writing, critiquing and refining MCQs.

Results. Preliminary workshops provided early insights into the collaborative process and its impact on assessment literacy. These workshops are producing a bank of outcome-aligned MCQs and equipping participants with skills to critically assess question quality. Student-generated MCQs are being used as formative assessments to support learning, reflection, and feedback.

Discussion. Anticipated outcomes include a structured, systematic process for generating, storing, and evaluating MCQs. This approach will promote consistency across assessments, support curriculum alignment, and foster deeper engagement with assessment design. By involving students in question creation, the project aims to build their evaluative judgement and enhance their understanding of assessment standards. Further findings and reflections from the workshops will be shared.

P556

Integrating Scientific Inquiry and Transferable Skills in a Pharmacology Capstone Subject

Dr Rahini Ragavan

Biography:

I am a Lecturer (Teaching Focused) in the Department of Physiology and Pharmacology at La Trobe University. I completed my PhD in the Department of Pharmacology at Monash University, where I investigated the cardiovascular effects of animal venoms. I have over eight years of experience delivering workshops, tutorials, and wet practicals to undergraduate science, allied health, and biomedical students. More recently, I have been involved in curriculum development for third-year pharmacology subjects, with a strong focus on creating student-centered content and embedding transferrable skills and knowledge. My passion is inspiring the next generation of STEM students to continue their education and explore research and STEM-related careers. I am also interested in lifelong learning and collaborating with colleagues on education research, particularly around how to retain student engagement and support long-term involvement in STEM courses.

Integrating Scientific Inquiry and Transferable Skills in a Pharmacology Capstone Subject

Rahini Ragavan, Elly Djouma, Ross O'Shea, Antony Vinh, Michael De Silva
Department of Microbiology, Anatomy, Physiology and Pharmacology, La Trobe University, Bundoora, VIC, Australia

Introduction. *Drug Discovery and Development* (PCY3002) is a new capstone subject in the Physiology and Pharmacology major of the Bachelor of Biomedicine at La Trobe University. It consolidates discipline knowledge while developing transferable skills, offering students an immersive experience of the drug development pipeline—from identifying a lead compound to considering translation to market. Delivered over 12 weeks, the subject integrates workshops, practicals, industry guest lectures, and an asynchronous digital workbook to simulate authentic scientific inquiry.

Aims. To develop student knowledge and transferable skills through authentic learning activities that mirror the drug development pipeline.

Methods. Designed collaboratively by discipline and education experts, the subject includes eight unique practicals (one per group) where students investigate the mechanism of action of a disease drug target. Guest lecturers provide specialist expertise and career insights. Assessments, aligned with active learning principles (Bonwell & Eison, 1991) and Vygotsky's scaffolding theory (Vygotsky, 1978; Taber, 2018), progressively build higher-order thinking, communication, and teamwork skills. Student engagement will be evaluated through surveys, assessment outcomes, and thematic analysis of feedback.

Results. Students collaborated to analyse pharmacological data and communicated findings through diverse assessments: a "check your knowledge" quiz, individual laboratory report, "shark tank"–style group pitch to investors, and a final oral presentation synthesising the drug development process. Analysis of student perceptions of skill development is ongoing.

Discussion. Embedding authenticity, industry relevance, and active learning in capstone subjects can enhance engagement, integrate disciplinary and transferable skills, and better prepare graduates for STEM careers.

References: Bonwell, C. C., & Eison, J. A. (1991). Active Learning: Creating Excitement in the Classroom. ASHE-ERIC Higher Education Report No. 1.
Taber, K. S. (2018). Scaffolding learning: Principles for effective teaching and the design of classroom resources. Effective teaching and learning: Perspectives, strategies and implementation, 1-43.
Vygotsky, L. S. (1978). Mind in Society: The Development of Higher Psychological Processes. Harvard University Press.

P557

Bidirectional transport of beta-amyloid1-40 through CLEFF4 cells. Evidence of P-glycoprotein mediated efflux.

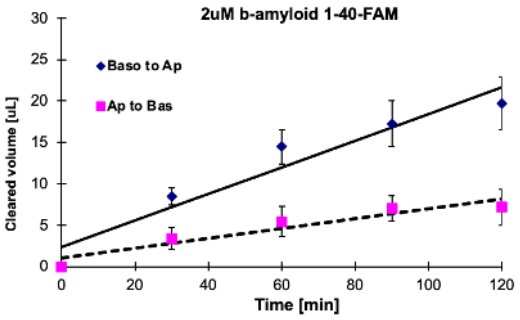
A/Prof Andrew Crowe

Biography:

Course Coordinator for the Bachelor of Pharmacy(Honours) course at Curtin University in Western Australia, teaching physiology, biochemistry and pharmacology to Pharmacy and Biomedical Science students, while having a research program in understanding multi drug efflux systems using polarised rapid in vitro human models such as Caco-2 and CLEFF4, while also working on Iron and Copper depletion in cancer, infectious disease treatment, and drug distribution.

Bidirectional transport of beta-amyloid1-40 through CLEFF4 cells. Evidence of P-glycoprotein mediated efflux.

Andrew Crowe[1], Curtin Medical School, Cutin University[1], Perth, WA, Australia.



Introduction. There is much interest in the role of β-amyloid in the manifestation of Alzheimer's disease. β-amyloid is a metabolite formed from enzymic degradation of the much larger amyloid precursor protein, which can be cleaved into either a 42 or 40 amino acid peptide. We know that these smaller proteins leave the brain by slow transcytosis processes and a small body of evidence suggested P-gp plays a role [1, 2]. **Aims**. Previous suggestions for P-gp's involvement in β-amyloid's removal has only been associative, with no direct efflux evidence. Our aim was to measure β-amyloid transport directly using FAM linked β-amyloid and our human *in vitro* monolayer system to discover the rate of P-gp involvement in its efflux. **Methods**. A human Caco-2 sub clone with rapid differentiation characteristics allowing transport studies in 6 days, called CLEFF4, was chosen for bi-directional transport studies using PSC-833 as our dedicated P-gp inhibitor and Rh123 as our positive control for active P-gp mediated transport. **Results.** 2μM FAM labelled β-amyloid 1-40 [4.7 kDa MW] was transported through CLEFF4 cells with an apparent permeability (Papp) of 4.47×10^{-6} (±0.75) cm/sec in the efflux direction (Basolateral (Bas) to apical (Ap)) while Ap to Bas direction was only 1.67×10^{-6} (±0.42) cm/sec with a p value of 0.03. This being a significant 2.7 fold efflux ratio. This ratio dropped to 0.96 fold, essentially equivalence in both directions, once 4μM PSC-833 was included in the transport buffer. **Discussion.** Even though β-amyloid is over 4 kDa and larger than any previously known P-gp substrate, evidence here is that such a large endogenous peptide is effluxed by P-gp, and work is ongoing to compare this peptide to the more plaque forming 1-42 derivative.

1. Cirrito, J.R., et al. J Clin Invest, 2005. **115**(11): p. 3285-90.

2. Hartz, A.M., D.S. Miller, and B. Bauer. Mol Pharmacol, 2010. **77**(5): p. 715-23.

P558

Investigating the Efficacy of Cannabis-Derived Compounds for Treatment of Parkinson's Disease

Mr Eric Okrah

Biography:

Eric Okrah obtained his master's degree in Pharmaceutical Science from Jiangsu University, China, where his research focused on the discovery and development of anticancer agents targeting breast cancer. He later joined the Annesley Lab at La Trobe University, Australia, to pursue his PhD. Now in his third year of doctoral research, he is investigating the therapeutic potential of cannabis-derived compounds for the treatment of Parkinson's disease. His work focuses on drug discovery, aiming to identify novel biological pathways involved in disease progression, with a particular emphasis on developing innovative therapeutics for neurological and neuropsychiatric disorders. He is especially interested in strategies that alleviate multiple pathophysiological processes and selectively target receptors and ion channels to improve drug design and efficacy.

Investigating the Efficacy of Cannabis-Derived Compounds for Treatment of Parkinson's Disease

Eric A. Okrah[1,2], Claire Allan[1], Monika S. Doblin[2*] and Sarah J. Annesley[1,2*] [1]Department of MAPP, LTU, Bundoora, Vic 3086, Australia; [2]Australian Research Council Research Hub for Medicinal Agriculture, Bundoora, Vic 3086, Australia

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder characterized by death of dopaminergic neurons in the substantia nigra and the accumulation of protein aggregates called Lewy bodies. Although PD primarily affects the brain, its pathology is systemic, with manifestations in peripheral non-neural tissues such as blood and skin. Despite recent preclinical advances proposing therapeutic approaches, there is no cure, and current treatments are ineffective long-term. Cannabinoids have emerged as promising therapeutic agents due to their antioxidant, neuroprotective, anxiolytic, analgesic and anti-inflammatory properties. Accumulating evidence suggest cannabinoids mitigate PD symptoms by modulating signalling pathways, but exact mechanisms remain poorly defined. Our laboratory detected mitochondrial dysfunction and calcium signalling abnormalities in PD blood-derived cell lines.

Aims: This study aimed to investigate the therapeutic potential and efficacy of cannabidiol (CBD) and its propyl analogue cannabidivarin (CBDV) on mitochondrial function and calcium signalling in PD patient-derived cells.

Methods: Immortalised lymphoblastoid cell lines (LCLs) from PD (n = 35) and healthy controls (n = 22) were treated for 24 hours with 10-20 µM CBD, 10-20 µM CBDV, or a 1:1 combination of 10-20 µM CBD and 10–20 µM CBDV dissolved in 0.1% DMSO. Untreated controls were included for PD and healthy groups. Following treatment, mitochondrial energy production and cytosolic calcium signalling were assessed using fluorescence-plate-based measurements to evaluate cannabinoid therapeutic efficacy.

Results: In our LCLs, we observed elevated ATP levels and increased calcium signaling in PD compared to healthy controls. CBD treatment (20 µM) rescued elevated mitochondrial energy production in PD lines by reducing ATP steady-state levels to those observed in healthy controls. The increase in mitochondrial energy production in PD was not due to increased mitochondrial mass, and other parameters of mitochondrial function remained unaltered. CBD also did not alter mitochondrial mass, suggesting the balance between biogenesis and degradation was unaltered. Mitochondrial membrane potential, reactive oxygen species production, and removal were unaffected. CBD treatment (10 µM and 20 µM) also rescued elevated cytosolic calcium levels in PD cell lines. CBDV produced similar, though less pronounced, effects.

P559

The in vitro neuroprotective effects of α adrenergic ligands

Mr Aari Oliphant-Hand

Biography:

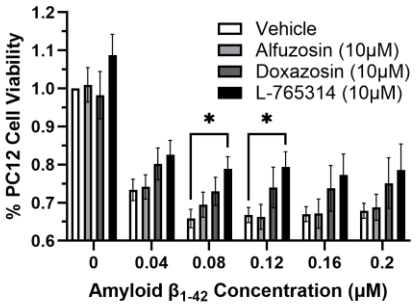
Having moved from Darwin to study at the University of Adelaide, Aari graduated from his Bachelor of Health and Medical Sciences (Advanced) in late 2022 and its associated Honours in 2023 before commencing his PhD in Pharmacology in 2024. Aari has a broad passion for the field of pharmacology, with special interest in neuropharmacology, particularly neurodegenerative diseases and the search for disease-modifying treatments.

The *in vitro* neuroprotective effects of α adrenergic ligands

Aari Oliphant-Hand[1], Scott Smid[1]. Discipline of Pharmacol, Univ of Adelaide[1], Adelaide, SA, Australia.

Introduction. A group of α adrenergic ligands demonstrate neuroprotective bioactivity, potentially applicable in the treatment of neurodegenerative diseases (NDs) related to misfolding and aggregating proteins such as amyloid β. We assessed neuroprotective and anti-aggregatory properties of quinazoline-based α_1 adrenergic antagonists alfuzosin, doxazosin, terazosin and L-765314, in addition to the imidazoline/α_2 agonist rilmenidine, against amyloid β 1-42 ($A\beta_{1\text{-}42}$) or rotenone exposure in PC12 neuronal cells.

Methods. PC12 neuronal viability was assessed via MTT assay. Cells pretreated with each drug were incubated with $A\beta_{1\text{-}42}$ (0-0.2μM, 0-1uM) or rotenone (0-0.25uM) for 48hrs. Direct ligand effects on $A\beta_{1\text{-}42}$ fibrillisation were assessed using Thioflavin T (ThT) assay.



Results. $A\beta_{1\text{-}42}$ (0-0.2μM, 0-1μM) toxicity was significantly reduced with L-765314 (1μM: vs 0.2*, 1μM* $A\beta_{1\text{-}42}$, n=3; 10μM: vs 0.08*, 0.12μM* $A\beta_{1\text{-}42}$, n=9; *p<0.05). Rotenone (0-0.25μM) toxicity was significantly reduced with 1μM alfuzosin (vs 0.1**, 0.15μM** rotenone; **p<0.01, n=3), rilmenidine (vs 0.1*, 0.15*, 0.2μM* rotenone; n=3) and L-765314 (vs 0.15**, 0.2μM* rotenone; n=3). Doxazosin and L-765314 also significantly inhibited $A\beta_{1\text{-}42}$ fibrillisation as measured via ThT assay (20μM* vs 10μM $A\beta_{1\text{-}42}$; n=3) .

Discussion. These findings highlight a neuroprotective role of L-765314 against $A\beta_{1\text{-}42}$ neurotoxicity and of alfuzosin, rilmenidine and L-765314 against rotenone toxicity, warranting characterisation in additional ND models. The inhibitory action of L-765314 on $A\beta_{1\text{-}42}$ fibrillisation suggests anti-aggregatory mechanisms may contribute to the neuroprotective effect of this ligand against $A\beta_{1\text{-}42}$. The protective effects observed of alfuzosin, rilmenidine and L-765314 against rotenone may indicate the presence of mechanisms capable of remediating mitochondrial dysfunction. These in vitro findings provide impetus to further investigations into the potential clinical repurposing of selected α adrenergic ligands in Alzheimer's disease.

P560

Single target-dual therapy at M4 muscarinic receptors for the treatment of schizophrenia

Dr Celine Valant

Biography:

A/Prof Celine Valant is the co-leader of the Analytical and Structural Neuropharmacology group at Monash Institute of Pharmaceutical Sciences. She is internationally recognised for advancing the mechanistic understanding and therapeutic exploitation of G protein-coupled receptors (GPCRs), the largest family of drug targets. Her research focuses on 3 major innovations in receptor pharmacology: allosteric modulation, biased signalling, and bitopic ligand design. Together, these concepts have reshaped approaches to GPCR drug discovery, led to structural breakthroughs, enabled successful commercial translation, and informed international pharmacological standards. Her contributions span foundational science through to industry uptake and regulatory implementation. She is an associate editor of npj Drug Discovery (Nature portfolio journal), a member of the board of the mAChR Nomenclature subcommittee for the International Union of Basic and Clinical Pharmacology, and co-chair of the Neuropharmacology SIG of Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists.

Single target-dual therapy at M4 muscarinic receptors for the treatment of schizophrenia

Jasmin (Chendi) Li, Vi Pham, Michaela Kaoullas, Arthur Christopoulos, Jesse Mobbs, David Thal, Christopher Choy, and Celine Valant. Drug Discovery Biology, Monash Institute of Pharmaceutical Sciences, Parkville, VIC, Australia

Introduction. Since Sept. 2024, xanomeline, a muscarinic M_4 receptor (mAChR) agonist, has emerged as a first-in-class treatment for schizophrenia[1,2]. However, xanomeline's therapeutic utility is limited by significant peripheral off-target effects, primarily due to activation of M_2/M_3 mAChRs. Currently, these side effects are mitigated by co-formulating xanomeline with trospium, a peripherally restricted non-selective mAChR antagonist, which dampens gastrointestinal adverse effects. Here, we propose an alternative co-formulation strategy involving xanomeline and a highly selective M_4 positive allosteric modulator (PAM)[3,4]. We hypothesize that low-dose xanomeline alone would elicit minimal activation of both central (M_4) and peripheral (M_2/M_3) mAChRs. However, in the presence of a M_4 PAM, xanomeline's efficacy would be selectively amplified at central M_4 mAChRs, without potentiating activity at peripheral M_2/M_3 mAChRs. This highly targeted "single target-dual therapy" offers a more refined pharmacological approach, preserving the antipsychotic efficacy of xanomeline while circumventing peripheral side effects altogether.

Aims. To validate our proof-of-concept "single target-dual therapy" strategy through a broad range of methodologies.

Methods. We performed cell-based *in vitro* pharmacology, cryo Electron Microscopy (cryo-EM) structural determination, and utilised several *in vivo* models (incl. locomotor activity (LMA) and prepulse inhibition (PPI)).

Results. The cryo-EM structure of the M_4 mAChR bound to xanomeline and novel M_4 PAMs demonstrates co-binding of the two drugs. In all *in vitro* signalling pathways investigated, M_4 PAMs significantly enhance xanomeline agonist properties at both human and mouse M_4 mAChRs. In our *in vivo* models, we confirmed that M_4 PAMs can "boost" xanomeline's antipsychotic activity (LMA) and reversal of impaired gating mechanisms (PPI) in a synergistic manner, and that side effects remained minimal when only M_4 mAChR is engaged.

Conclusion. We demonstrated that co-administration of an M_4 mAChR preferring agonist and an M_4 PAM has the potential to become the next *best-in-class* antipsychotic medications for the treatment of schizophrenia.

[1] Kaul et al., JAMA Psychiatry 2024;81(8):749-756. [2] Liu at al., J Med Chem 2025;68(8):7932-7954; [3] Clinical trial ID: NCT05227690. [4] Tong et al., J Med Chem 2020;63(5):2411-2425.

P561

Safety and efficacy of gabapentinoids for non-pain indications in adults

Mr William Forrest

Biography:

Fourth year Bachelor of Pharmacy student at Sydney University. Academic awards include Year 12 HSC Dux at Champagnat Catholic College, the 2024 University of Sydney Academic Merit Award, and current enrollment in honours. Clinical pharmacy experience includes currently employment as a pre-intern (student) pharmacist at a hybrid community and clinical hospital role.

Safety and efficacy of gabapentinoids for non-pain indications in adults

William B Forrest[1], Danijela Gnjidic[1], Stephanie Mathieson[1], Justin Cheng[1], Carl R Schneider[1]. 1. School of Pharmacy, Univ of Sydney, Camperdown, NSW.

Introduction. Gabapentinoids are increasingly prescribed for the treatment of a wide range of conditions, despite limited evidence of their efficacy. This growth in use has raised concerns regarding their safety profile, especially for indications with little evidence supporting their benefits.

Aims. To evaluate and systematically review the safety and efficacy of gabapentinoids for non-pain indications.

Methods. An overview of reviews was conducted by systematically searching electronic databases from 2015 to April 2025 for systematic reviews of randomised, placebo-controlled studies on the safety and/or efficacy of gabapentinoids in adults published in the last 10 years. Two reviewers independently screened the resulting articles against predefined inclusion criteria. Included studies were independently assessed for bias using A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR-2) (PROSPERO: CRD420251033113).

Results. Forty-seven systematic reviews encompassing 326 primary studies across 34 unique conditions were included. Risk of bias ranged from critically low (55%), to low (17%), moderate (19%) and high (9%). Preliminary results suggest that gabapentinoids are associated with a higher rate of discontinuation due to adverse effects compared to placebo (n=92 studies, 29,494 participants), as well an increase in the incidence of dizziness (n=41, 7356) and somnolence (n=23, 6036). Evidence supports potential efficacy in treating generalised anxiety disorder (n=32, 9810), some forms of sleep disturbance and insomnia (n=42, 9787), restless legs syndrome (n=17, 3764) and menopausal hot flashes (n=26, 3578). However, for other conditions, the evidence remains limited and of low quality.

Discussion. Gabapentinoids may be effective for limited conditions, however, clinicians should consider whether there is high quality evidence for broader off-label prescribing, given the significant increase in serious adverse effects. Understanding of the role of these agents would be improved by further research into common off-label uses, such as alcohol withdrawal and bipolar disorder, which currently lack enough evidence to make a strong recommendation.

P562

Antihyperglycemics and dementia at end-of-life in Australia and the United Kingdom

Ms Darshna Goordeen

Biography:

Darshna is a clinical pharmacist and final year PhD candidate at the Centre for Medicine Use and Safety at Monash University, Faculty of Pharmacy and Pharmaceutical Sciences. Her PhD explores optimising appropriate medication use in type 2 diabetes for older adults, focused on those living with dementia, frailty or receiving end of life care. Her work includes pharmacoepidemiology studies using linked hospital and administrative data to observe diabetes medication use populations often excluded from clinical trials.

Antihyperglycemics and dementia at end-of-life in Australia and the United Kingdom.

Darshna Goordeen[1], Olivia Bryant[2], Emily Reeve[1], Joshua D Niznik[3], Wallis Lau[2,4,5], Li Wei[2], J Simon Bell[1]. Centre for Medicine Use and Safety, Fac Pharm Pharmaceutical Sci, Monash U[1], Parkville, VIC, Australia; Sch Pharm, U College London[2], London, UK; Eshelman Sch Pharm, U North Carolina[3], Chapel Hill, NC, USA; Centre for Medicines Optimisation Research and Education, U College London, Hosp NHS Foundation Trust[4], London, UK; Centre for Safe Medication Practice and Research, Dept of Pharm and Pharmacy, Li Ka Shing Faculty of Medicine, U Hong Kong[5], PKL, Hong Kong;

Introduction. People living with dementia and Type 2 Diabetes (T2D) are predisposed to an increased risk of adverse drug events (ADEs) from T2D treatment. Deprescribing antihyperglycemics or de-intensifying antihyperglycemic regimens in this population could reduce the risk of ADEs and is often recommended in those approaching end-of-life.
Aims. To investigate the prevalence of T2D medication use in the last year of life in people living with dementia and to explore patient-level factors associated with likelihood of discontinuation in the 6-months prior to death.
Methods. We used linked hospital and administrative data for individuals in the United Kingdom (UK) and Victoria, Australia. The cohort included individuals with data available for at least 12-months prior to death between July 2012 and June 2018. Logistic regression estimated the association of co-variates such as age, sex, cardiovascular disease, chronic kidney disease (CKD) and cancer with discontinuation of antihyperglycemics.
Results. 10,016 (UK) and 6,436 (Australia) individuals were identified. Those aged 85+ made up 55.8% of the UK and 37.7% of the Australia cohort. In both datasets overall discontinuation was observed at minimal rates, the largest change was observed in prevalence of insulin supply with a 25.6% (UK) and 43.5% (Australia) absolute reduction in use in the last 3-months-of-life compared to use at 12-months. CKD was associated with higher odds of discontinuing metformin in the UK (OR 1.05, 95% CI 1.03–1.07) and Australia (OR 1.60, 95% CI 1.15–2.12).
Discussion. Despite observing some discontinuation of T2D medications, over half of individuals were supplied one or more of these mediations in the final 3-months-of-life. To increase comfort and minimize potential ADEs, strategies to facilitate deprescribing of antihyperglycemics near end-of-life need to be explored.

P563

Authority to Access: National Rituximab prescribing after PBS General Schedule listing

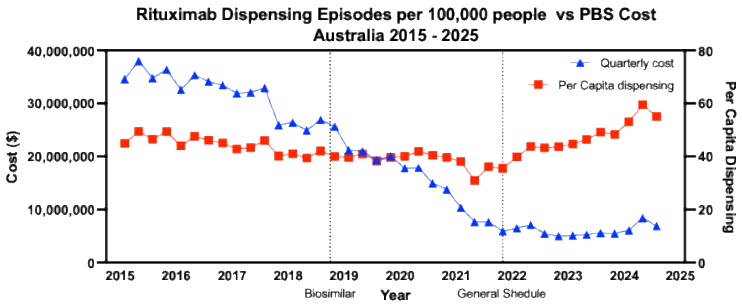
Mr Mitchel Hurlbert

Biography:

Dr. Mitchel Hurlbert is a Canadian/Australian physician and first year Clinical Pharmacology advanced trainee at St Vincent's Hospital, Sydney. He obtained his MD at the University of Sydney after completing a Bachelor of Science with Honours in evolutionary biology at Queen's University in Kingston, Ontario, Canada. He previously contributed to multiple sclerosis research in a basic science laboratory in Calgary, Alberta, Canada. His academic interests include biologic therapies, small molecule inhibitors, and drug development for systemic inflammatory conditions, with a strong focus on reducing health inequalities in access to medicines and clinical trials. Dr. Hurlbert's long-term goal is dual training in Clinical Pharmacology and Rheumatology, integrating the foundations of clinical pharmacology into his future rheumatology practice to advance safe and cost-effective treatment strategies.

Authority to Access: National Rituximab prescribing after PBS General Schedule listing

Mitchel G Hurlbert, Jonathan Brett, Bridin Murnion. Clinical Pharmacology and Toxicology, St. Vincent's Hospital, Sydney, NSW, Australia



Introduction. Rituximab, an anti-CD20 monoclonal antibody, is approved by the Therapeutic Goods Administration for five conditions, with more than 350 off-label indications reported in Australia (O'Connor et al., 2013). Biosimilars entered the Australian market in 2019, and in 2022 the Pharmaceutical Benefits Scheme (PBS) subsidy was extended from written authority to General Schedule.

Aims. We aim to quantify quarterly changes in rituximab dispensing rates and government expenditure across Australia from 2015-2025 and evaluate equity of access by comparing per-capita dispensing across Australia. Finally, we will compare PBS trends with in-hospital rates of Individual Patient Use (IPU) approvals and costs at St Vincent's Hospital, Sydney.

Methods. An interrupted time-series analysis will be performed on PBS and IPU data to compare trends at local, state and national levels.

Results. The interrupted time-series analysis suggests a post-intervention change in slope, indicating a upward shift in prescribing of rituximab post intervention

Discussion. Rituximab costs have declined since its PBS listing, with biosimilars further reducing government expenditure. Per capita dispensing has risen following its general schedule listing. While broader access may reduce health inequities, it also raises risks of non-evidence-based use and may compromise the quality use of medicines.

O'Connor K, Liddle C. Prospective data collection of off-label use of rituximab in Australian public hospitals. Intern Med J. 2013 Aug;43(8):863-70. doi: 10. 1111/imj.12206. PMID: 23735074.

P564

Real-world comparative safety of immune checkpoint inhibitors in small cell lung cancer

Miss Juhee Koo

Biography:

Juhee Koo is a final-year Bachelor of Pharmacy student at the University of Sydney and is completing her Honours research at the Kolling Institute. Her research focuses on pharmacoepidemiology and oncology, using real-world data to investigate medicine safety and effectiveness in clinical practice.

Real-world comparative safety of immune checkpoint inhibitors in small cell lung cancer

Juhee Koo[1,2], Chin Hang Yiu[1,2], Hieu T Le[1], Edwin CK Tan[1,2], Christine Y Lu[1,2,3]. Sydney Pharmacy School, The Univ of Sydney[1], Camperdown, NSW, Australia; Kolling Institute, The Univ of Sydney and Northern Sydney Local Health District[2], St Leonards, NSW, Australia; Dept of Pharmacy, Royal North Shore Hosp[3], St Leonards, NSW, Australia.

Introduction. Immune checkpoint inhibitors (ICIs) have shown significant improvements in survival and prognosis for advanced small cell lung cancer (SCLC) patients. However, ICIs are associated with treatment-related adverse events (TRAEs), particularly immune-related adverse events (irAEs) which can diminish ICI efficacy and patient quality of life. Most safety data on ICIs are obtained from clinical trials, which do not accurately reflect large-scale real-world populations. Hence, real-world data can help address this gap and facilitate better-informed clinical decisions.

Aims. This systematic review aimed to compare the real-world safety of ICIs against other therapies in SCLC patients.

Methods. A comprehensive search was conducted using four online databases (MEDLINE, Embase, Scopus, and CINAHL) from inception date to 21st July 2025. Real-world observational cohort studies comparing any safety outcome between ICI-regimens and other cancer therapies (e.g., chemotherapy, targeted therapy) in SCLC were included. The quality of studies were assessed using the Newcastle-Ottawa Scale, and a narrative synthesis was conducted to summarise key findings.

Results. A total of 20 retrospective cohort studies were included, with all studies obtaining safety data from electronic health records. Data was provided for 14–188 patients per cohort. Majority of the studies (n=19) were rated as poor quality due to limited confounder adjustments. The incidence of TRAEs did not differ significantly between the combination of an ICI and chemotherapy (ICI+Chemo) against chemotherapy alone. Moreover, the incidence of TRAEs was also comparable between different ICIs used in ICI+Chemo combinations. The comparison of TRAEs was less well-defined for targeted therapy, due to the lack of studies (n=2). Moreover, the incidence of irAEs was similar between different ICI+Chemo combinations.

Discussion. The addition of ICIs to chemotherapy does not significantly increase the risk of TRAEs. Furthermore, different ICIs tend to exhibit a similar safety profile. This study calls for more large-scale and good-quality studies to strengthen the evidence on the comparative safety of ICI-based therapies as well as enhance the utility of these key findings in clinical settings.

P565

Clusters of psychotropic and health service use in people with dementia

Mr Edward Chun Yin Lau

Biography:

Edward is a community pharmacist in Australia and PhD student at the University of Sydney with a research interest in pharmacoepidemiology in older people, especially people living with dementia in community settings in Australia. He is particularly interested in the prevalence, risk factors and outcomes of high-risk prescribing in this population. His research is aimed at improving the safety and effectiveness of medication use in people living with dementia.

Clusters of psychotropic and health service use in people with dementia living

Edward C.Y. Lau[1], Sarah Hilmer[2], Yun-Hee Jeon[3], Christine Y. Lu[1,2], Chin Hang Yiu[1,2], Edwin C.K. Tan[1]. Sydney Pharmacy School, The University of Sydney[1], Sydney, NSW, Australia; Kolling Institute, The University of Sydney [2], Sydney, NSW, Australia, Susan Wakil School of Nursing and Midwifery, The University of Sydney [3], Sydney, NSW, Australia.

Introduction. Psychotropics are commonly used in people with dementia. Health service utilisation is important in managing both dementia-related symptoms and multimorbidity. However, patterns and clusters of psychotropic and health service utilisation among people with dementia remain poorly understood in the Australian context.

Aims. To identify prevalence of and factors associated with different clusters of psychotropic and health service use, and assess their association with mortality in Australians with dementia.

Methods. This cohort study utilised linked 2021 Census, death registration, Pharmaceutical Benefits Scheme (PBS) and Medicare Benefits Schedule data. People with dementia aged ≥65 years in Australia in 2021 were included in the study. Latent class analysis involving 16 variables, including different classes of psychotropics (antipsychotics, opioids, antidepressants, antiepileptics and benzodiazepines), chronic health service use (such as chronic disease management plans and medication review), mental and physical healthcare (such as allied health and psychiatrist visits). Logistic regression was used to identify factors associated with class assignment. Association with 12-month mortality was assessed using inverse probability of treatment weighting adjusted Kaplan-Meier curves and Cox regression.

Results. Overall, 165,655 people with dementia were included. A five-class model was selected using data-driven approach. Groups were described as (1) low-risk psychotropic & high chronic disease management use (35.3%); (2) low-risk psychotropic & low health services use (36.0%); (3) high-risk psychotropic & high chronic disease management use (12.6%); (4) high-risk psychotropic & low health service use (13.2%); and (5) moderate-risk psychotropic & high mental health service use (2.8%). People with dementia residing in remote/regional areas were less likely to be in high health service utilisation classes. Compared to those in the low-risk psychotropic use group, mortality risk was higher among those in high-risk psychotropic use groups (adjusted hazard ratio [aHR]: 1.35, 95% confidence interval [CI] 1.30-1.40). In contrast, those with high mental health services use had a lower mortality risk (aHR: 0.84, 95% CI 0.72-0.97).

Discussion. Health services may mitigate mortality risk in individuals with dementia but disparities in access to these services highlight the need for more equitable service delivery across Australia.

P566

Treatment Modifiers and Predictors of Risperidone in Dementia: An Individual Participant Meta-Analysis

Mr Harry Le

Biography:

Trong Hieu (Harry) Le is a recent Master of Philosophy graduate from the School of Pharmacy, The University of Sydney. His research focuses on pharmacoepidemiology, dementia, and the quality use of medicines. Harry has experience working with a range of large-scale datasets, including the Person Level Integrated Data Asset (PLIDA), The National Health Data Hub (NHDH), and individual participant data from clinical trials. His research applies advanced pharmacoepidemiological methods and machine learning approach to evaluate medicine use, safety, and treatment outcomes in older adults and people living with dementia."

Treatment Modifiers and Predictors of Risperidone in Dementia: An Individual Participant Meta-Analysis
Hieu T. Le[1], Edward C.Y. Lau[1], Sarah N Hilmer[2], Yun-Hee Jeon[1], Christine Y. Lu[1,2], Tuan A. Nguyen[3], Lee-Fay Low[1], and Edwin C.K. Tan[1,2]. Faculty of Medicine and Health, The University of Sydney, Sydney, NSW[1]; Kolling Institute, Royal North Shore Hospital, St Leonards, NSW[2]; National Aging Research Institute, Parkville, VIC[3].

Introduction. Risperidone is the only antipsychotic approved in some countries for behaviours and psychological symptoms of dementia (BPSD). Its benefits appear modest and vary by symptom, while risks remain a concern. Identifying responsive symptoms and predictors may support more individualised use.
Aims. To determine BPSD symptoms most responsive to risperidone, assess subgroup differences, and identify predictors of therapeutic response.
Methods. A one-stage individual participant data meta-analysis of six randomised controlled trials (Risperidone: N=1009; Placebo: N=712) was conducted. Symptoms were assessed with the Behavioural Pathology in Alzheimer's Disease (BEHAVE-AD) scale across seven domains. Therapeutic response was defined as a ≥30% reduction in total scores. Mixed-effects logistic and linear regression were used to evaluate treatment effects, modifiers, and predictors.
Results. Risperidone did not significantly improve overall response (OR: 1.26; 95% CI: 0.97–1.63; p=0.08) but showed modest 8-week benefits for aggression (SMD: -0.22; 95% CI: -0.34 to -0.10; p<0.001), psychosis (SMD: -0.23; 95% CI: -0.37 to -0.09; p=0.001), and anxiety/phobias (SMD: -0.19; 95% CI: -0.35 to -0.04; p=0.014), with no effect on activity, affective, or sleep disturbances. Subgroup analyses suggested that pharmacokinetic and pharmacodynamic factors (e.g., BMI, endocrine disease, race/ethnicity) may modify treatment effects. Early response at week 2 strongly predicted sustained improvement at week 4 (OR: 9.04; 95% CI: 6.10–13.39; p<0.001) and week 8 (OR: 4.46; 95% CI: 3.00–6.62; p<0.001).
Discussion. Risperidone showed potential symptom-specific benefits in different time points, particularly for aggression, psychosis, and sleep disturbances. Subgroup analyses identified specific baseline characteristics influencing treatment efficacy, while early response and baseline cognitive function predicted sustained improvement. This study provides potential evidence for individualised treatment in people with BPSD; however, further research is needed to balance risks and benefits across subgroups.

P567

Trends and costs of potentially inappropriate medications

Miss Yannee Liu

Biography:

Yannee Liu is a PhD student from the Centre for Medicine Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University in Melbourne. Yannee is a clinical pharmacist. Yannee's research areas of interest include potentially inappropriate medication use, health economics and sustainability.

Trends and costs of potentially inappropriate medications

Yannee Liu[1], Zanfina Ademi[1], Emily Reeve[1], Justin P Turner[1]. Centre for Medicine Use and Safety, Monash University[1], Parkville, VIC, Australia

Introduction. Potentially inappropriate medications (PIMs) are defined as medications where the potential for harm outweigh the potential for clinical benefits, particularly when used in older adults.
Aims. To identify trends in utilisation and costs of commonly dispensed PIMs in Australia.
Methods. This is a retrospective analysis of publicly available Pharmaceutical Benefits Scheme (PBS) data. The dataset captures all Australians who received medications dispensed under the PBS from 2014 and 2024. Variables include the top fifty medications dispensed by volume for all ages, top ten medications dispensed for older adults (≥60 years, age and sex breakdown) and top 10 PBS medications dispensed for residents of aged care facilities. Government and patient costs were extracted. PIMs were defined using the American Geriatrics Society Beers and STOPP criteria.
Results. In 2024, the majority (67%) of medications dispensed via the PBS were to people aged 60 years or older. In 2014, thirteen of the top fifty highest volume PBS medications were considered PIMs. In comparison, eight of the top fifty higher volume medications were categorised as PIMs in 2024. The cumulative cost of these eight PIMs was more than $400 million for the Australian Government. The cumulative patient contribution was greater than $110 million. In 2024, two of the top ten medications dispensed to both older males and females were PIMs, being pantoprazole and esomeprazole. In residential aged care facilities, two of the top ten PBS medications dispensed by highest prescription count are PIMs in 2024. These are pantoprazole and buprenorphine. In both years, frequently dispensed PIMs included proton pump inhibitors, gabapentin, opioids, NSAIDs, benzodiazepines and sulfonylureas.
Discussion. Nationally, of the top fifty highest volume PBS subsidised medications, 26% are classified as PIMs in 2014, reducing to 16% in 2024. Proton pump inhibitors are the most common PIM. One strength of this data is the use of national dispensing data. The term “potentially” inappropriate is used because the data does not contain duration of use or patients’ clinical data. Additionally, PIMs lists are designed specifically for older adults, however, the top fifty high volume PBS medication list reflects prescribing across all age groups. This study demonstrates that PIMs are becoming less prevalent in the top fifty high volume dataset. However, a more detailed analysis of pharmacy claims data is required to assess the trends in utilisation and costs of PIMs in older Australians.

P568

Long-term off-label antipsychotic therapy and cardiometabolic outcomes in adults: a systematic review

Ms Ramya Padmavathy Radha Krishnan

Biography:

Ramya is a PhD candidate at the University of Sydney in the Faculty of Medicine and Health. With a Masters in Bio-Technology, her prior experience of working in the drug discovery and pharmacovigilance field has inculcated a passion for Pharmacoepidemiology and drug safety. Her research utilises population-based health data to generate real-world evidence on medicine use and safety in the mental health space. She has further undergone training in Epidemiological methods and Health economic evaluations. Ramya's PhD is focussed on the investigation of cardiometabolic adverse effects associated with antipsychotic treatments given at low doses in off-label disorders, using Australian administrative datasets. Her aim is to improve patient health and well-being through the quality use of medicines.

Long-term off-label antipsychotic therapy and cardiometabolic outcomes in adults: a systematic review

Ramya Padmavathy Radha Krishnan[1], Monika Dzidowska[1], Danni Zheng[1], Danielle J Russell[2], Ebony Quintrell[2], Amina Rhaman[2], Chun Hong Chan[1], Nicholas A Buckley[1], Jacques Eugene Raubenheimer[1] Faculty of Medicine and Health, The University of Sydney[1], Sydney, NSW, Australia; School of Population and Global Health, University of Western Australia[2], Perth, WA, Australia.

Introduction. Antipsychotic use for non-psychotic conditions is rising, often at low doses and long durations. There is a lack of evidence on the resulting safety issues.

Aims. To review cardiometabolic safety of antipsychotics used for ≥1 year in adults with non-psychotic disorders.

Methods. Systematic review of randomised and observational studies. Due to high heterogeneity, data was synthesised through vote counting (using studies with comparison to untreated patients) and estimates depicted in forest plots without overall estimate.

Outcome (number of studies/participants)	Vote counting (% of studies [95% CI], P value, n)
Weight gain (4/88,322)	Increase (100% [39.8–100], P=0.125)
Hyperglycaemia (3/119,617)	Increase (100% [29.2–100], P=0.250)
Dyslipidaemia (3/87,480)	Increase (100% [29.2–100], P=0.250)

Results. There were 13 observational studies with 663,718 participants (mean age 44.7 years, 46% males) and no clinical trials. Mean treatment duration was 3 years and nearly 50% of the studies reported low antipsychotic doses. Through vote counting, prolonged antipsychotic treatment was associated with weight gain, hyperglycaemia and dyslipidaemia among individuals with non-psychotic disorders compared with untreated patients or general population controls. A weak association was found for ischaemic heart disease and cardiometabolic mortality. Longer treatment duration was negatively linked to ischaemic heart disease and positively associated with cardiometabolic mortality, while higher treatment doses were positively correlated with hyperglycaemia, ischaemic heart disease, and cardiometabolic mortality. All studies had moderate-high methodological quality.

Discussion. Long-term antipsychotic use in adults, even at low doses, can disrupt metabolic processes that may have physical health impacts. It is crucial that healthcare providers consider safety issues carefully in their approach to antipsychotic prescription in non-psychotic conditions.

P569

Influence of patient characteristics on effects of anti-amyloid therapies for Alzheimer's Disease

Ms Grace Shim

Biography:

Grace is an Honours student in her final year of her Bachelor of Pharmacy at the University of Sydney. As a student who is at the beginning of her research journey, Grace holds a keen interest in research, particularly in the field of pharmacoepidemiology, geriatrics and dementia. Her Honours projects involved the exploration of novel antidementia therapies and antipsychotic drug-drug interactions in people with dementia. With a growing passion for research, Grace aspires to develop her skills and knowledge, and is looking forward to learn from world class experts.

Influence of patient characteristics on efficacy and safety of anti-amyloid monoclonal antibodies for Alzheimer's Disease: A systematic review and meta-analysis.

Grace H Shim[1], Edward C.Y. Lau[1], Christine Y Lu[1,2], Edwin C.K. Tan[1,2]. The University of Sydney School of Pharmacy, The University of Sydney[1], Sydney, NSW, Australia; Kolling Institute, The University of Sydney and the Northern Local Health District[2], Sydney, NSW, Australia.

Introduction. Lecanemab and donanemab are the first anti-amyloid monoclonal antibodies (mAbs) clinically available as disease-modifying therapies for Alzheimer's disease. While their efficacy in slowing cognitive decline and general safety profiles have been evaluated, whether these treatment effects vary across demographic, clinical and genetic subgroups have not yet been summarised.

Aims. This systematic review aimed to examine how patient characteristics modify the efficacy, safety and humanistic outcomes of lecanemab and donanemab in patients with early Alzheimer's disease.

Methods. Five databases (MEDLINE, Embase, Scopus, Web of Science, Cochrane Library) were searched from inception to July 30th, 2025, using a combination of keywords and Medical Subject Heading terms relating to lecanemab and donanemab. Meta-analyses were conducted for safety outcomes where sufficient data were available.

Results. Sixteen studies were included relating to six randomised clinical trials (Total N = 5633). The most commonly reported cognitive outcome was the Clinical Dementia Rating – Sum of Boxes (CDR-SB) score (n=8). Both mAbs demonstrated the greatest slowing of cognitive decline in White/Caucasian patients and apolipoprotein E4 (ApoE4) allele non-carriers. Lecanemab was more beneficial for male patients and those aged ≥75 years, while donanemab showed greater efficacy in females and those aged 65-74 years. Amyloid-related imaging abnormalities (ARIA) (ARIA-E: 17%, ARIA-H: 21%) and headache (13%) were the most frequently reported adverse events in treated patients. Among ApoE4 carriers, the risk of ARIA-E was 2.19 times higher (95% CI: 1.91-2.50) and the risk of ARIA-H was 3.45 times higher (95% CI: 1.36-8.72) compared to non-carriers. Statistically significant improvements in health-related quality of life were observed with lecanemab in ApoE4 heterozygous participants and in those aged 65-74 years.

Discussion. These findings highlight the potential for personalised treatment strategies and inform national drug policy development regarding anti-amyloid mAb use in Alzheimer's disease. However, further research is needed to evaluate long-term outcomes and to address under-represented patient populations.

P570

Characteristics and Nature of Digital Tools to Improve Uptake of Deprescribing Recommendations

Miss Mia Tesoriero

Biography:

Mia Tesoriero is a 4th year Bachelor of Pharmacy (Honours) student at the University of Sydney. She was the recipient of the University of Sydney Academic Merit Prize for 2024, and in 2022 was awarded the Dean's List of Excellence in Academic Performance. She has extensive experience in community pharmacy, with particular interest in the field of deprescribing. In 2023, Mia began work as an undergraduate research assistant, and is a published academic author.

Characteristics and Nature of Digital Deprescribing Tools to Improve the Uptake of Deprescribing Recommendations: A Scoping Review

Mia A Tesoriero[1], Carl R Schneider[1], Aili V Langford[1], Jiefei Yu[1], Mouna J Sawan[1], Danijela Gnjidic[1]. School of Pharmacy, The University of Sydney[1], Sydney, NSW, Australia.

Introduction. While deprescribing is widely recommended to improve patient outcomes, it is often challenging to implement in clinical practice. Digital tools may improve deprescribing uptake for patients and clinicians, however the characteristics of these tools are not well-documented.

Aims. The aim of the scoping review was to characterise the nature and purpose of digital deprescribing tools available for healthcare professionals (HCPs) and patients.

Methods. We conducted a search in three databases including Medline, Embase and PsycINFO, complemented by a search of the grey literature to identify digital tools to facilitate the deprescribing process. We defined a digital deprescribing tool as any interactive software that supports healthcare professionals or patients at any point in the deprescribing process. Tools were categorised according to their target user, purpose and format.

Results. A total of 49 digital deprescribing tools were identified, with most being published in the last 5 years. Most tools targeted HCPs (76%, n = 37), with 46% of these being pharmacists (n = 17) compared with patients (27%, n = 13). One tool was usable by either patients or HCPs . The purpose of tools was primarily to identify deprescribing opportunities (82%, n = 40). Tools typically adopted a potentially inappropriate medication set of criteria (65%, n = 32) to guide deprescribing activities. Tools utilising web-based platforms were the predominant format (41%, n = 20), and only two tools (4%) included the use of artificial intelligence.

Discussion. The preliminary findings highlight the growing number of digital tools to facilitate deprescribing and underscores the need to address gaps in patient engagement with tools. Interaction with tools was vastly segregated, allowing interaction by only one of either HCPs or patients. This feature may limit the utility of digital tools for shared decision making. There is also a need for further evaluation of tools' effectiveness in translating guideline recommendations into improved clinical outcomes.

P571

Frequency of CYP2C19 genetic variants in clopidogrel-indicated populations: a scoping review

Miss Teoni Antonopoulos

Biography:

Teoni Antonopoulos is a fourth-year Bachelor of Pharmacy (Honours) student at the University of Sydney. She is currently undertaking her honours research which focuses on the influence of pharmacogenomics on antiplatelet therapy, in particular its impact on patient outcomes. This research contributes to the movement towards precision medicine by highlighting how genetic variation can guide safer and more effective treatments.

Frequency of *CYP2C19* genetic variants in clopidogrel-indicated populations: a scoping review.

Teoni C Antonopoulos[1], Josephine J Hughes[2], Sam Mostafa[1,3,4], Asad E Patanwala[1], Stephen Hughes[1], Sophie L Stocker[1]. Sch of Pharm, Univ of Sydney[1], NSW; Sch of Medical Science, Univ of Sydney[2], NSW; Centre for Medicine Use and Safety, Monash Univ[3], VIC; MyDNA Life[4], Australia Limited, VIC.

Introduction. Clopidogrel, an antiplatelet prodrug, is metabolised by CYP2C19 into its active metabolite. *CYP2C19* loss of function (*2 and *3) and gain of function (*17) alleles are highly prevalent in the general population and have implications for the safety and efficacy of clopidogrel. Genotype-predicted intermediate and poor metabolisers have reduced clopidogrel active metabolite concentrations and are at risk of secondary cardiovascular events. To date, the global prevalence of *CYP2C19* genetic variants in clopidogrel-indicated populations has not been reported.

Aims. To summarise the frequency of *CYP2C19* diplotypes and metaboliser phenotypes in clopidogrel-indicated populations by geographic region.

Methods. Scopus (from database inception to 29th April 2025), Ovid MEDLINE and Ovid Embase (both from database inception to 6th May 2025) were searched. Included studies tested for *CYP2C19* *2, *3 and *17 alleles at a minimum, to comply with the Association for Molecular Pathology Tier 1 recommendation for pharmacogenomic (PGx) testing and to ensure detection of multi-variant diplotypes (e.g. *2/*3). Diplotype and phenotype frequencies were recorded per country and aggregated by geographic regions (East Asia, South Asia, Southeast Asia, Middle East and North Africa (MENA), Europe and the Americas). Data were analysed using descriptive statistics (range, median).

Results. 45 studies were included in the review. East Asia (20 studies, n=10691) had the highest frequency of intermediate and poor metabolisers (range: 54%-77%, median: 61%), followed by South Asia (3 studies, n=904, 47%-71%, 55%) and Southeast Asia (3 studies, n=1269, 46%-58%, 55%). *1/*2 was the most common intermediate metaboliser diplotype while *2/*2 was the most common poor metaboliser diplotype in all regions. MENA (7 studies, n=1072) had the highest frequency of rapid (*1/*17) and ultra-rapid (*17/*17) metabolisers (27%-44%, 30%), followed by Europe (4 studies, n=607, 29%-37%, 32%). In the Americas (8 studies, n=5721), both intermediate and poor metabolisers (14%-49%, 28%) and rapid and ultra-rapid metabolisers (14%-36%, 31%) were common.

Discussion. There is a high prevalence of CYP2C19 poor and intermediate metabolisers, especially in Asia, highlighting regions where PGx-guided antiplatelet therapy has the greatest potential to improve patient outcomes.

P572

Antiplatelet prescribing patterns following percutaneous coronary intervention: is CYP2C19 testing of value?

Ms Josephine Hughes

Biography:

Josephine Hughes is an Honours student at The University of Sydney, within the School of Medical Sciences. Her research focuses on determining the value of CYP2C19-informed antiplatelet prescribing, to advance personalised approaches to cardiovascular treatment within Australia.
Josephine is completing her Honours thesis under the supervision of A/Prof Sophie Stocker and is excited to present her work at the 2025 ASCEPT conference and have the opportunity to connect with peers and experts in clinical pharmacology.

Antiplatelet prescribing patterns following percutaneous coronary intervention: is CYP2C19 testing of value?

Josephine J Hughes[1], Tark J Patel[2], Teoni C Antonopoulos[2], Ruby Soueid[2], Asad E Patanwala[2], Stephen Hughes[2], Leonard Kritharides[3], Sophie L Stocker[2]. Sch of Medical Science, Univ of Sydney, NSW[1]; Sch of Pharm, Univ of Sydney, NSW[2]; Concord Repat Hosp, Sydney NSW[3].

Introduction. CYP2C19-guided clopidogrel therapy in patients following percutaneous coronary intervention (PCI) reduces recurrent ischaemic events (Ingraham et al, 2023). Given clopidogrel is second-line therapy, with ticagrelor and prasugrel being first-line, it is unclear if prescribing is sufficient to warrant a CYP2C19 genotyping service.
Aims. To identify current P2Y12 inhibitor prescribing patterns in patients post PCI and assess switches in antiplatelet therapy amongst patients with a previous myocardial infarction.
Methods. Medical records of patients receiving a PCI for cardiovascular disease at a large Australian hospital between 01/06/2023 – 01/06/2025 and were commenced or continued on dual antiplatelet therapy (DAPT) at discharge were reviewed. Clinical data collected included PCI indication, DAPT prescribed, patient demographics, concomitant medications and medical history. Relative risk ratios were calculated for certain comparisons.
Results. Patients (n = 680) were predominantly male (76%, 518/680) with a mean age of 67 (12.6) years. Clopidogrel was more commonly prescribed (72%, 491/680) than ticagrelor (28%, 189/680). No patients were prescribed prasugrel. Clopidogrel was prescribed in a higher proportion to those 65 and over (82%, 343/418) and to those taking concomitant anticoagulants (81%, 61/75). ST-segment elevation myocardial infarction (STEMI) patients were 3.4 times more likely (95% CI 2.77 to 4.23) to be prescribed ticagrelor compared to clopidogrel. Twenty-two patients (3%, 22/680) had a myocardial infarction in the preceding 12 months to their PCI. Of these, thirteen (59%, 13/22) remained on clopidogrel, seven remained on ticagrelor (32%, 7/22), and two were switched from aspirin only or aspirin and ticagrelor to DAPT with clopidogrel (9%, 2/22).
Discussion. Although clopidogrel is considered second-line therapy, it remains the preferred P2Y12 inhibitor, particularly in older patients and/or those on anticoagulants. Only in patients who had a STEMI-indicated PCI (i.e. more high-risk) was ticagrelor preferred. Recurrent cardiovascular events within 12 months did not lead to switching from clopidogrel. These findings suggests that a CYP2C19 genotyping service to guide antiplatelet therapy is of value.
Ingraham BS et al (2023) JACC Cardiovasc Interv 16:816-825.

P573

Antidepressant treatment outcomes of patients receiving pharmacogenomics-guided therapy

Mr Mihin Meegasdeniya

Biography:

Mihin Meegasdeniya is a medical student at UNSW with research interests in psychiatry, pharmacogenomics, and primary care. He has clinical and academic experience in mental health, with a focus on personalised approaches to improving treatment outcomes in mental health disorders.

Antidepressant treatment outcomes of patients receiving pharmacogenomics-guided therapy

Mihin H. Meegasdeniya[1,2] Rosalind Moxham[1,2], Kathy H. C. Wu[1-4]
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Introduction. Major depressive disorder (MDD) and anxiety disorder are leading causes of disability, yet many patients fail to achieve remission due to suboptimal, trial-and-error treatment (Rush et al, 2006). Pharmacogenomic (PG) testing may optimise treatment by identifying antidepressants with minimal drug–gene interactions (DGIs).
Aims. To evaluate whether PG-guided pharmacotherapy improves response, remission, and adherence in people with MDD ± anxiety.
Methods. Participants (n=80) were prospectively recruited from St Vincent's Hospital Sydney and the community via self-referral to receive PG-guided pharmacotherapy. Symptoms were assessed at baseline and weeks 4, 8, 12 and 24 using the Quick Inventory of Depressive Symptomology (QIDS-SR16) and Depression Anxiety Stress Scale (DASS-21). Medication adherence was self-reported. Comparisons were made between those taking congruent (minimal/moderate DGIs) vs incongruent (major DGIs) antidepressants.
Results. QIDS-SR16 showed no significant difference in response (17.5% vs 21.0%, p=0.48) or remission (12.3% vs 14.0%, p=1.00). DASS-21 demonstrated significant improvements in those taking congruent vs incongruent medications, including reduced anxiety (p=0.023) and higher remission rates in depression (p=0.014), anxiety (p<0.001) and stress (p<0.001). Medication adherence was high across groups (mean=5.24/6). Patients valued PG testing, citing reduced trial-and-error prescribing.
Discussion. PG-guided therapy was associated with significant improvements for congruent medications measured on DASS-21 and a positive but non-significant trend on QIDS-SR16, with high adherence and positive patient experience. These findings suggest PG testing may support engagement and improve outcomes, warranting further study.
Rush AJ, Trivedi MH, Wisniewski SR, et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: A STAR*D report. American Journal of Psychiatry. 2006:163(11):p1905–p1917. Doi: 10.1176/ajp.2006.163.11.1905

P574

High-throughput mutagenesis towards a comprehensive AGTR1 missense variant library

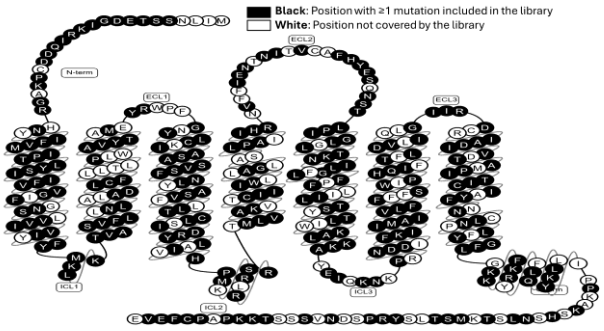
Mr Felipe De Jesus Navarro Vela

Biography:

Mr. Felipe de Jesus Navarro Vela is a Master's student in Biotechnology at Flinders University. His research, conducted at Flinders Health and Medical Research, employs a high-throughput approach to systematically analyze and characterize the functional effects of missense variants in the AGTR1 gene. This project aims to create an arrayed plasmid library of over 400 variants for downstream cell-based functional analyses. Felipe is developing expertise in molecular mutagenesis and variant analysis techniques. His work contributes to advancing precision medicine approaches in hypertension treatment by improving understanding of genetic influences on blood pressure regulation.

High-throughput mutagenesis towards a comprehensive *AGTR1* missense variant library

Felipe de J. Navarro Vela,[1] Harald Janovjak,[1] Joshua G. Dubowsky[1]. Flinders Health and Medical Research Institute, Flinders University[1], Adelaide, SA, Australia.



Introduction. Over 400 million individuals worldwide require antihypertensive drugs (AHD), with an estimated 600,000 carrying a missense variant in AGTR1, the primary target of these therapies. Hundreds of *AGTR1* missense variants have been documented in the global population, yet most remain uncharacterised regarding their impact on AHD effectiveness. A significant obstacle for pharmacogenomic research is the time and resource intensive production of large mutant libraries. The high-throughput, discretely arrayed method of site-directed mutagenesis utilised here allows rapid, reproducible and precise dissection of mutations.

Aims. To develop an arrayed plasmid library of more than 400 *AGTR1* missense variants for downstream cell based functional analysis.

Methods. All *AGTR1* missense variants reported in gnomAD were compiled and mutagenesis primers were designed accordingly. Leveraging an in-house, high-throughput cloning pipeline, 405 arrayed mutant constructs were generated in less than two weeks. The presence of the intended missense mutations was confirmed through long-read sequencing and bioinformatic analysis of the open reading frames.

Results. A single round of mutagenesis yielded 99.7% of *AGTR1* missense variants reported in gnomAD. Functional screening of selected variants is underway to evaluate receptor responsiveness to angiotensin II and antihypertensive drugs using Ca^{2+} assays.

Discussion. This high-throughput approach enables rapid, systematic functional analysis of missense variants, facilitating pharmacogenomic studies of *AGTR1* and other genes. These advances support translational outcomes for precision medicine through systematic characterisation of genetic variants.

P575

Comparing Australian Prescribing and International Pharmacogenomic Guidelines: A Consideration for Clinical Practice

Ms Ruby Soueid

Biography:

Ruby Soueid is a registered pharmacist and PhD student at The University of Sydney, specialising in the implementation of pharmacogenomics in clinical practice, with a particular focus on cardiovascular medicine. Her research examines how pharmacogenomic services can be integrated into routine healthcare to optimise prescribing, improve patient safety, and enhance treatment outcomes. With a foundation in pharmacy and patient care, Ruby is passionate about bridging the gap between emerging pharmacogenomic innovations and their practical application in everyday clinical settings. Ruby is committed to advancing precision medicine in Australia and contributing to its integration into healthcare systems, ensuring that patients benefit from personalised approaches to treatment.

Comparing Australian Prescribing and International Pharmacogenomic Guidelines: A Consideration for Clinical Practice

Ruby Soueid[1], Jackson Thomas[1], Stephen Hughes[1], Sophie L Stocker[1]. School of Pharm, Fac Med & Health, The Univ of Syd[1], Sydney, NSW;

Introduction. Pharmacogenomic (PGx) guided medication management underpins precision medicine by optimising therapy and enhancing patient outcomes. However, implementation of PGx services in Australian clinical practice remains limited, notably due to the lack of PGx testing indications for drugs with actionable PGx variants in key national prescribing guidelines and, when present, their inconsistency with international PGx guidelines.

Aims. To evaluate the alignment of key Australian prescribing guidelines with established international guidelines regarding PGx testing indications.

Methods. Drugs available in Australia with the highest evidence of clinical utility (e.g. Clinical Pharmacogenetics Implementation Consortium level A) were included. PGx testing indications (e.g. 'recommended', 'considered' or 'not recommended') were compared between key Australian prescribing guidelines (Royal College of Pathologists of Australasia (RCPA), Australian Medicines Handbook (AMH), Therapeutic Guidelines (TG), Therapeutic Goods Australia (TGA) and eviQ), and established international guidelines (Dutch Pharmacogenetics Working Group (DPWG)).

Results. Of the 36 drugs included, PGx testing indications were provided for 20 (DPWG) and 2–21 (Australian) guidelines, respectively. Among the 18 drugs with PGx testing indications in both DPWG and RCPA, the strength of recommendation was discordant for 33% (6/18) of the drugs (e.g. strength of testing for allopurinol 'considered' by DPWG vs 'recommended' by RCPA). For the 13 drugs with an indication in both RCPA and at least one other Australian resource, the strength was concordant for only 38% (5/13), 8% (1/13), 23% (3/13) and 15% (2/13) of drugs in AMH, TG, TGA and eviQ, respectively.

Discussion. PGx testing indications in key Australian prescribing guidelines, when provided, differ from established international consensus. The absence of clear and consistent representation of PGx testing indications in guidelines developed for Australian practice is a major barrier to its acceptance and utilisation by Australian healthcare professionals. To support clinical implementation, healthcare professionals require the inclusion of PGx testing indications for drugs with actionable PGx variants that also align with established international recommendations.

P576

Implementation of a pharmacogenomic testing service in residential aged care: Preliminary findings

Miss Eman Wehbe

Biography:

A higher degree by research student at the University of Sydney under the supervision of A/Prof Sophie Stocker (School of Pharmacy). My work focuses on the implementation of pharmacogenomics into clinical practice.

Implementation of a pharmacogenomic testing service in residential aged care: Preliminary findings

Eman Wehbe[1], Jennifer Hewitt[2], Michael Scalley[3], Alyson Jarrett[2], Zanfina Ademi[4], Stephen Hughes[1], Sam Mostafa[1,4,5], Carl Kirkpatrick[4], Sophie L Stocker[1]. Sch of Pharm, Univ of Sydney[1], Sydney, NSW; Whiddon[2], Glenfield, NSW; Choice Aged Care[3], Sydney, NSW; Cent for Med Use & Safety, Monash Uni[4], Parkville, VIC; myDNA Life[5], South Yarra, VIC.

Introduction. Pharmacogenomics (PGx) as an emerging tool for precision medicine is particularly relevant for older adults at risk of medication-related harm due to polypharmacy. Despite its potential, PGx-guided medication management has not yet been implemented in Australian residential aged care, and its feasibility remains uncertain.

Aims. To evaluate the feasibility, clinical utility and value for money of implementing PGx-guided medication management in Australian residential aged care.

Methods. An observational study was conducted across five NSW aged care homes, where clinical staff collected buccal swabs from residents for analysis using an 11-gene PGx panel (myDNA, NATA-accredited laboratory; CYP1A2, CYP2B6, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, OPRM1, SLCO1B1, VKORC1, ABCG2). Pharmacists reviewed PGx reports and made prescribing recommendations during routine residential medication management reviews. Service evaluation was guided by the RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) framework.

Results. Three of five aged care homes have completed recruitment, with 76 of 168 residents (45%) consenting to participate; 74% self-consented and 26% via their Registered Supporter. Fourteen residents were excluded due to palliative care or behavioural concerns. Common reasons for refusal to participate included satisfaction with current medications or lack of interest. Of the 63 PGx reports generated to date, 22 identified major prescribing considerations (dose change or alternative medication recommended), and 49 identified minor ones (possible altered medication response but no specific dose change).

Discussion. Preliminary data demonstrates the feasibility of implementing a PGx testing service in residential aged care, with moderate resident participation and successful integration into existing workflows. The PGx reports revealed clinically relevant prescribing considerations, supporting the potential utility of PGx-guided medication management in this population. While prescribing adjustments and economic impact data are pending, early findings suggest potential value; however, challenges with Registered Supporter consent and inclusion of residents with cognitive impairment may limit broader reach and sustainability.

P577

Targeting brevican improves key disease features in experimental chronic obstructive pulmonary disease.

Miss Cory Butlin

Biography:

Cory Butlin is an Honours student at the University of Technology Sydney under the supervision of Dr Chantal Donovan and Dr Richard Kim.

Targeting brevican improves key disease features in experimental chronic obstructive pulmonary disease.

Cory Butlin, Richard Y Kim, Madison L Coward-Smith, William Dewar, Jessica Tolentino, Hudson Taylor-Blair, Brian GG Oliver, Chantal Donovan. School of Life Sciences, Univ of Technology Sydney, Sydney, NSW; Respiratory Cell and Molecular Biology, Woolcock Institute of Medical Research, Sydney, NSW.

Introduction. Chronic Obstructive Pulmonary Disease (COPD) is a progressive lung disease characterised by a reduction in respiratory airflow, destruction of the small airways, excess mucous secretion and chronic inflammation. The extracellular matrix (ECM) proteins play a critical role in maintaining lung structure and repair in COPD and disruption of homeostasis of these proteins can lead to tissue remodelling. Brevican is an ECM protein that has been previously unstudied in COPD, however, emerging evidence suggests that it may have a critical role in COPD pathology.

Aims. To analyse the effects of targeting *Bcan* (the gene for brevican) on key features of experimental COPD including lung function and structure.

Methods. Male BALB/c mice (n=8/group, 8 weeks of age) were administered porcine pancreatic elastase (PPE; 0.25IU) i.n. (day 0; or saline control) to induce pulmonary emphysema. On day 7, some mice were treated with *Bcan*-siRNA or scrambled-siRNA control (2.5mg/kg; 3x per week) i.n. for two weeks. Endpoint analyses (day 21) included lung function measurements and airway inflammation measured in bronchoalveolar lavage fluid. Alveolar enlargement/emphysema was measured in lung sections stained with haematoxylin and eosin.

Results. PPE treated mice (PPE/scr-siRNA) had increased inspiratory capacity compared to control treated mice (Saline/scr-siRNA). *Bcan*-siRNA treatment in PPE-treated mice (PPE/*Bcan*) significantly improved tissue elastance back to control levels. PPE/scr-siRNA and PPE/*Bcan* had minimal effects on airway inflammation. PPE/scr-siRNA treatment increased alveolar enlargement/emphysema, and this was significantly reduced in *Bcan*-siRNA treated mice.

Discussion. Inhibiting Brevican using *Bcan*-siRNA improved PPE-induced experimental COPD, including improving lung function and reducing alveolar enlargement/emphysema. These data suggest that targeting brevican may be a novel treatment approach in COPD.

P578

Targeting C-C motif chemokine receptor 6 with PF-07054894 in COPD

Mr William Dewar

Biography:

William Dewar is a Bachelor of Medical Science (Honours) student at the University of Technology Sydney under the primary supervision of Dr Richard Kim and co-supervision of Dr Chantal Donovan.

Targeting C-C motif chemokine receptor 6 with PF-07054894 in COPD

William F Dewar[1], Chantal Donovan[1,2], Madison L Coward-Smith[1,2], Cory Butlin[1], Jessica R Tolentino[1], Hudson C Taylor-Blair[1], Brian GG Oliver[1,2], Richard Y Kim[1,2]. School of Life Sciences, Univ of Technology Sydney[1], Sydney, NSW, Australia; Respiratory Cellular and Molecular Biology, Woolcock Institute of Medical Research[2], Sydney, NSW, Australia.

Introduction. Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death globally with approximately 480 million reported cases in 2020. Current COPD therapies fail to reduce airway obstruction in most patients and cause adverse effects, necessitating the need for better therapies. C-C motif chemokine receptor 6 (CCR6) is implicated in several inflammatory diseases and is detected in the airways of COPD patients. However, no *in vivo* studies of CCR6 in COPD have assessed changes in lung function or explored the potential for therapeutic targeting of CCR6 in COPD.

Aims. To determine the effects of administering the novel CCR6 inhibitor, PF-07054894, to the lungs in a porcine pancreatic elastase (PPE)-induced model of COPD, and to characterise the roles of CCR6 in inflammation and airway obstruction.

Methods. Six-week-old, male, wild type, BALB/c mice (*n*=8/group) were treated with 50µL of PPE (0.25IU) or PBS intranasally. Mice were treated with PF-07054894 (5mg/kg) or vehicle (PBS [2% dimethyl sulfoxide]) intranasally from day 7, 3 times per week, for 2 weeks. Intranasal treatments were administered under isoflurane anaesthesia (3% isoflurane, 2.0L/min O^2). At the endpoint (day 21), several lung function parameters were measured using a FlexiVent FX1 apparatus (SCIREQ), airway inflammation assessed in bronchoalveolar lavage fluid, and immune cells analysed in lung and bone marrow cell suspensions by flow cytometry.

Results. Treatment with PF-07054894 had no effects on airway and tissue inflammation, however, it robustly reduced PPE-induced increases in hysteresis (P = 0.0019) back to baseline levels. PF-07054894 treatment also resulted in close to statistically significant reductions in Newtonian resistance (P = 0.0813), respiratory system resistance (P = 0.0693) and elastance (P = 0.0723).

Discussion. Targeting CCR6 with PF-07054894 improved lung function in PPE-induced COPD but had no effects on inflammation in the airways, lungs, and bone marrow. These data highlight the need for greater exploration of the potential of CCR6 inhibition in the treatment of COPD.

P579

FPR2 agonist attenuates pulmonary arterial hypertension and right ventricular dysfunction in mice

Miss Ting Fu

Biography:

Ting is a third-year PhD student at the Monash Institute of Pharmaceutical Sciences, where she has the privilege of working under the esteemed guidance of a dynamic team of researchers, including Dr. Chengxue Helena Qin, Professor Rebecca Ritchie, Associate Professor Barbara Kemp-Harper, and Dr. Peishen Elva Zhao. Her research focus is centred on unravelling the intricate regulation of formylpeptide receptors, with a particular emphasis on their role in Cardiopulmonary diseases.

FPR2 agonist attenuates pulmonary arterial hypertension and right ventricular dysfunction in mice

Ting Fu[1], Chloe Landy[1], Yuchi Sun[1], Miles J De Blasio[1], Jaideep Singh[1], Anida Velagic[1], Owen L Woodman[1], Barbara Kemp-Harper[2], Peishen Zhao[1], Rebecca H Ritchie[1,2], Chengxue Qin[1*].[1]Drug Discovery Biology and [2]Department of Pharmacology, Monash Univ, VIC; Australia.

Introduction. Pulmonary arterial hypertension (PAH) is characterised by vascular remodelling, including intimal hyperplasia, fibrosis, and inflammation, which progressively increase pulmonary vascular resistance and vasoconstriction. The selective FPR2 agonist BMS-986235 enhances pro-resolving macrophage activity and improves cardiac remodelling post-myocardial infarction[1], but its therapeutic potential in PAH remains unknown.

Aim. To investigate the therapeutic effects of FPR2 agonist in preventing PAH progression.

Methods. Male C57BL/6J mice (9 weeks old) were allocated to normoxia (21% O_2) or sugen/hypoxia (SuHx, 10% O_2 plus weekly sugen 5416, 20 mg/kg) for 4 weeks. The SuHx cohort was randomly divided into three groups: (i) treatment-vehicle, (ii) BMS-986235 (3mg/kg/day), or standard clinical treatment (iii) sildenafil (0.3mg/kg/day). The normoxia cohort received the treatment-vehicle (10% DMSO in 0.8% Tween 80 in saline). At experimental endpoint, haemodynamics were assessed, and lungs and hearts were collected for histological and molecular analyses.

Results. SuHx mice displayed elevated right ventricular systolic pressure (RVSP), decreased tricuspid annular plane systolic excursion (TAPSE), complete muscularisation of small pulmonary arteries, and upregulated pro-inflammatory gene expression (*mIl-6*) in the lungs. BMS-986235 treatment reduced RVSP, increased TAPSE, limited pulmonary arterial muscularisation, and downregulated *mIl-6* and *mTnf-α* expression, comparable to or exceeding the effects of sildenafil.

Discussion. Our study demonstrates that BMS-986235 lowers RVSP and limits vascular remodelling, similar to current clinical therapies, while additionally reducing inflammation and preserving RV function, highlighting its potential advantages beyond haemodynamic improvement.

	Normoxia + Vehicle	SuHx + Vehicle	SuHx + BMS-986235	SuHx + Sildenafil
RVSP (mmHg)	25±1 (n=12)	40±2**** (n=12)	34±2$$$ (n=16)	30±1$ (n=13)
TPASE (mm)	1.03±0.06 (n=16)	0.56±0.06*** (n=19)	0.78±0.04 (n=15)	0.69±0.05 (n=13)
PA muscularisation (%)	15.0±4.2 (n=5)	57.0±7.5*** (n=5)	26.0±7.0$$ (n=5)	33.1±5.2$ (n=6)
m*Il-6* (fold increase)	1.0±0.2 (n=11)	1.9±0.3* (n=13)	0.9±0.3$ (n=11)	1.0±0.3 (n=10)
m*Tnf-α* (fold increase)	1.0±0.2 (n=11)	1.8±0.5 (n=13)	0.8±0.2$ (n=11)	1.0±0.1 (n=10)

*P<0.05, ***P<0.001, ****P<0.0001 vs Normoxia + vehicle;$P<0.05, $$P<0.01,$$$P<0.001 vs SuHx + vehicle, (One-way ANOVA with Šídák's multiple comparisons test). RVSP: Right ventricular systolic pressure, TAPSE: Tricuspid annular plane systolic excursion, PA: Pulmonary arteries, m*Il-6*: Interleukin6, m*Tnf-α*: Tumour necrosis factor-α.

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P580

Low-dose Australian air pollution promotes neutrophilic, steroid-insensitive, experimental asthma

Mr Hudson Taylor-Blair

Biography:

Hudson is an emerging researcher who is currently an Honours student at the University of Technology Sydney under the supervision of Distinguished Professor Brian Oliver.

Low-dose Australian air pollution promotes neutrophilic, steroid-insensitive, experimental asthma

Hudson C. Taylor-Blair[1,2], Chantal Donovan[1,2], Madison Coward-Smith[1,2], Jessica Tolentino[1,2], William Dewar[1], Cory Butlin[1], Meng Wang[1,2], Alexia Defrancesco[1], Andrew E. Thorpe[1,2], Hongdan Wang[2], Baoming Wang[1,2], David D. Cohen[3], Armand Atanacio[3], Richard Y. Kim[1,2], Brian G. Oliver[1,2]. School of Life Sciences, UTS[1], Sydney, NSW, Australia; Woolcock Institute of Medical Research[2], Sydney, NSW, Australia. ANSTO[3], Menai, NSW, Australia.

Introduction. Particulate matter <2.5 µm ($PM_{2.5}$) is an airborne pollutant and a critical global health threat. Epidemiological studies show that $PM_{2.5}$ exposure is associated with the development and increased severity (including reduced symptom control with corticosteroids) of asthma. However, the pathobiology of $PM_{2.5}$ exposure at levels present in Australia is relatively unexplored.

Aims. To investigate how chronic Sydney $PM_{2.5}$ exposure influences the phenotype of experimental asthma and response to corticosteroids.

Methods. Mice (n=12/group) were exposed daily to $PM_{2.5}$ (i.n.; 10 µg) or Sham (PBS) control. In some groups, experimental asthma was superimposed by sensitising with ovalbumin, (Ova; i.p.; 50 µg; day 21) or saline, followed by challenge (i.n; 20 µg Ova; days 33, 34, 54, 55) and corticosteroid treatment (i.n.; 2 mg/kg dexamethasone; days 53-55) or vehicle control. At endpoint (day 56), we measured lung function and airway hyperresponsiveness (AHR), airway inflammation (bronchoalveolar lavage fluid), and lung leukocytes (flow cytometry).

Results. In Ova-sensitised mice, PM exposure resulted in an 18% reduction in inspiratory pulmonary capacity compared to sham (n=8/group; p<0.05), although no changes in the magnitude of AHR or total airway leukocyte numbers occurred. Analysis of bronchoalveolar lavage fluid revealed that Ova-sensitised, sham-exposed mice had airway eosinophilia; however, Ova-sensitisation with PM exposure caused a significant shift to airway neutrophilia (n=12/group; p<0.001), but a >40% and >70% increase in both eosinophils and neutrophils in lung tissue (n=8/group; p<0.01). In Ova-sensitised mice, PM-exposure reduced the ability of corticosteroid treatment to suppress AHR and inflammation back down to baseline levels observed in corticosteroid-treated, sham-exposed groups, indicating steroid insensitive disease.

Discussion. Our data show that PM exposure promotes a neutrophilic inflammatory phenotype and reduced responsiveness to corticosteroid treatment in experimental asthma. Next, characterising cytokine, chemokine, and histopathological changes will help elucidate our findings and determine the potential relevance to other diseases.

P581

Targeting the alpha-chemokine receptor, CXCR3, with SCH546738 in asthma and severe asthma

Ms Jessica Tolentino

Biography:

Jessica is a first-year PhD student at the University of Technology Sydney under the supervision of Dr Chantal Donovan and Dr Richard Kim as part of the ImmunoPharmacology Research Group.

Targeting the alpha-chemokine receptor, CXCR3, with SCH546738 in asthma and severe asthma

Jessica Tolentino[1], Richard Y Kim[1,2], Eyla Oxborrow[1], Madison L Coward-Smith[1], Andrew E Thorpe[1,2,] Brian GG Oliver[1,2], Chantal Donovan[1,2]. School of Life Sciences, Univ of Technology Sydney[1], Sydney, NSW; Respiratory Cell and Molecular Biology, Woolcock Institute of Medical Research[2], Sydney

Introduction. Asthma is a chronic inflammatory disease characterised by airway hyperresponsiveness (AHR), inflammation, and remodelling. CXCR3, a chemokine receptor, plays key roles in inflammation, and targeting CXCR3 with selective antagonists like SCH546738 may have therapeutic potential in asthma and severe asthma.
Aims. To characterise the roles of targeting CXCR3 on lung inflammation and AHR in asthma and severe asthma.
Methods. Mice (n=8/group) were administered ovalbumin (Ova; 50µg) i.p. (day 0; or saline control) then challenged with Ova i.n. (or saline control) (days 12-15) to induce allergic asthma. For severe asthma models, mice were sensitised with Ova i.p. (day 0), challenged with Ova i.n. (day 12,13), infected with *Chlamydia Muridarum* i.n. (day 14), and Ova i.n. (day 33, 34). In some groups, mice were treated with SCH546738 (10mg/kg) or vehicle (veh) (days 11-15 asthma model, days 32-24 severe asthma model). Endpoint analysis (day 16 for asthma, day 35 for severe asthma) included lung function measurements to assess AHR and airway inflammation measured in bronchoalveolar lavage fluid.
Results. Ova-treated mice (Ova/veh; experimental asthma) had AHR compared to Sal controls (Sal/veh). Administration of SCH in Ova-treated mice (SCH/Ova) significantly decreased AHR compared to Ova/veh (vehicle-treated control). Ova-treated mice had increased airway inflammation compared to Sal/veh reflected by a significant increase in the total leukocytes. Administration of SCH in Ova-treated mice (SCH/Ova) had decreased airway inflammation compared to Ova/veh. Ova/Cmu-treated mice (experimental severe asthma) had AHR compared to Sal/veh. Administration with SCH in Ova/Cmu-treated mice (Ova/Cmu/SCH) had reduced AHR compared to Ova/Cmu. Ova/Cmu/SCH-treated mice also had decreased airway inflammation compared to Ova/Cmu (severe asthma controls).
Discussion. Inhibiting the alpha-chemokine receptor, CXCR3, with SCH546738 reduces AHR, decreases airway inflammation in both asthma and severe asthma. These data highlight the need for further exploration of its potential therapeutic application in the treatment and management of asthma.

P582

Novel informatics approaches for the regulatory management of UVCB substances

Ms Hannah Gerstmyer

Biography:

Hannah Gerstmyer is an undergraduate student at the University of Sydney, currently pursuing a Bachelor of Science and Advanced Studies majoring in Chemistry and Pharmacology. Her academic interests include span materials chemistry, drug design, and cheminformatics.

Hannah's current research focuses on the cheminformatics challenges posed by substances of unknown or variable composition, complex reaction products, and biological materials (UVCBs). This work aims to assist regulatory bodies such as AICIS in linking chemical structure to bioactivity.

Hannah has previously contributed to the University of Sydney's Education Innovation program, aiding in the development and implementation of a chemical biology laboratory activity designed to foster collaborative learning and student engagement. She is passionate about bridging supramolecular chemistry, data science and drug discovery and hopes to continue exploring these areas in postgraduate research.

Novel informatics approaches for the regulatory management of UVCB substances

Hannah Gerstmyer[1], Raymond Lui[2], Slade Matthews[1]. Computational Pharmacology and Toxicology Laboratory, Sydney Pharmacy School, The University of Sydney[1], Sydney, NSW, Australia; Australian Industrial Chemicals Introduction Scheme, Department of Health, Disability and Ageing, Australian Government[2], Sydney, NSW, Australia.

Introduction. Common chemical entities such as petroleum products, botanical extracts, and resins frequently have large numbers of constituents whose identities and concentrations fluctuate with source material and manufacturing processes. These entities, 'substances of unknown or variable composition, complex reaction products and biological materials' (UVCBs) evade precise structural representation [1]. This poses an ongoing cheminformatics challenge for federal regulators like AICIS who rely on accurate substance characterisation to manage hazard data for public safety.

Aims. This project aims to establish a new *uvcbfile* format to encode UVCB constituent data in a manner that: (1) accounts for structural variability and (2) facilitates the transformation of structural data for modelling and analysis.

Methods. A literature review of international regulatory requirements for UVCB nomenclature and current methods of encoding UVCB substance data was completed. Potential UVCB datasets were investigated and will be used to populate *uvcbfiles* with constituent information collated by semi-automated data-scraping. Markush structures and associated fingerprints that capture structural variability will be generated from *uvcbfiles.* Structure-based clustering of fingerprints will be performed and compared with manufacturing and hazard classifications.

Results. The *uvcbfile* format has been developed using a JSON-based structure to encode five levels of constituent structural representation [2]. A new dataset of *uvcbfiles* is being generated for 141 petroleum UVCBs [3] and a workflow for augmenting structural information from PubChem has been developed.

Discussion. It is expected that further chemical structure-based clustering of this petroleum dataset will align with existing manufacturing and bioactivity-based groupings, thereby linking structure and hazard classification, and aiding AICIS in its management of UVCB data. Once finalised, this methodology should also be applicable to other UVCBs.

[1] Prussia et al. (2024) Front. Toxicol. 6:1452838; Salvito et al. (2022) Environ. Toxicol. Chem. 41:2649-2657
[2] Lai et al. (2022) Environ. Sci. Technol. 56:7448-7466; Clark et al. (2019) J. Cheminform. 11:33.
[3] House et al. (2020) ALTEX. 1:123-137; House et al. (2022) ALTEX. 3:388-404.

P583

In-Vitro investigation of cytotoxic effects and potential metabolic pathway of Isopsoralen

Mr Yeow Li Png

Biography:

A student at University of Adelaide, undergoing Honours of Bachelor of Health and Medical Science studies. Currently working on project regarding hepatoxicity effect and metabolic pathway of isopsoralen. Graduated from University of Adelaide, with a Bachelor of Health and Medical Science, Majoring in Medical Sciences.

In-Vitro investigation of cytotoxic effects and potential metabolic pathway of Isopsoralen

Yeow Li Png[1], Susan M Britza[1], Rachael L Farrington[1], Ian F Musgrave[1]. Discipline of Pharmacology, School of Biomedicine, The University of Adelaide[1], Adelaide, SA, Australia.

Introduction. Complementary and Alternative Medicines (CAM) are seeing increased usage worldwide, with an estimated 70% of the world's population using herbal products[1]. Studies have shown that people may use CAM in combination with other medications. This increases the dangers of herb-drug interactions, which can result in organ damage. *Psoralen corylifolia* (PC) has been found to cause liver toxicity, potentially from the phytochemicals present, including psoralen and isopsoralen. A previous study investigated the toxicity of psoralen, and its interaction with paracetamol on liver cell viability. This study examined the toxicity of isopsoralen and psoralen with paracetamol.

Aims. This study aims to elucidate the hepatoxic effects and metabolic pathway of isopsoralen, compared to psoralen.

Methods. A human liver carcinoma cell line (HepG2) was used for determining hepatotoxicity. Paracetamol (10- 50mM), psoralen and isopsoralen (200-1000µM) were tested for individual toxicity. The combination of paracetamol and psoralen or isopsoralen were then tested to assess their combined toxicity. The role of CYP3A4 enzymes in meditating toxicity in HepG2 cells was investigated using rifampicin (2mM) (CYP3A4 inducer). Cell viability is assessed through MTT colorimetric assays.

Results. Psoralen (600 µM) significantly decreased HepG2 cell viability to 73.24% ($p<0.0208$), while isopsoralen was significantly toxic across all the concentrations ($p<0.0001$). The combination of paracetamol and isopsoralen showed increased toxicity, with cell viability reduced to 61.5% ($p=0.005$) with the combination of 200µM of isopsoralen and 10mM of paracetamol, in comparison to paracetamol alone at 10mM (96.03%; $p=0.8108$). Data shows no significant difference between rifampicin and paracetamol, psoralen, and isopsoralen interactions individual concentrations.

Discussion. Results have shown that isopsoralen is considerably more toxic compared to psoralen. Induction of CYP3A4 by rifampicin shows little effect on phytochemical toxicity. However, it may be noted that rifampicin may induce other P450 enzymes that may metabolize psoralen and isopsoralen to an even more toxic byproduct. However, further testing is required to be sure that that is the case.

1. Byard RW, Musgrave I, Maker G & Bunce M (2017). What risks do herbal products pose to the Australian community? Med J Aust 206, 86-90.

P584

Bakuchiol Exacerbation Of Paracetamol Hepatotoxicity And Potential Metabolic Mechanisms

Mr Henry Williams

Biography:

Bachelor of Health and Medical Sciences(Honours) student. In 4th year of university currently and at the University of Adelaide. Currently doing a Honours project in the school of biomedicine in the discipline of pharmacology as part of University of Adelaide.

Bakuchiol exacerbation of paracetamol hepatotoxicity and potential metabolic mechanisms

Henry Williams[1], Susan M Britza[1], Rachael L Farrington[1], Ian F Musgrave[1], Discipline of Pharmacology, School of Biomedicine, University of Adelaide[1], Adelaide, SA, Australia.

Introduction: Up to 70% of Australians use complimentary medicines (CM), often used to compliment conventional medicine such as paracetamol. Herbal extracts, a type of CM, are often seen as natural and therefore safe. However, recent studies show potential toxicity concerns particularly with herbal extracts of *Psoralea corylifolia* potentially lowering threshold of paracetamol hepatotoxicity. *Psoralea corylifolia* has 163 phytochemicals; two of the most common are bakuchiol and psoralen which have been associated with hepatotoxicity.

Aim: To examine individual and combined toxicity of paracetamol, bakuchiol and psoralen in a human liver cell line (HepG2) was tested. The interactions of bakuchiol with paracetamol were examined for potential additive or synergistic interactions. To evaluate the role of key liver metabolic enzyme pathways, itraconazole (CYP inhibitor), rifampicin (CYP inducer), and zafirlukast (UGT inhibitor) were used.

Method: HepG2 cells were exposed to increasing concentrations of paracetamol (0-50mM), bakuchiol (0-400µM), psoralen (0-1000µM) and a fixed concentration of bakuchiol (150µM) with increasing concentrations of paracetamol (0-50mM). HepG2 liver cells were also exposed to paracetamol (0-50mM) with fixed concentrations of rifampicin (36µM), itraconazole (200nM), and zafirlukast (50µM). Cell viability was determined with the MTT colorimetric assay.

Results: Paracetamol caused 22% drop in cell viability ($p=0.26$) at 50mM ($n=4$). Bakuchiol caused a 53% drop in HepG2 cell viability at 400 µM ($p=0.07$). Psoralen showed a significant 77% reduction at 1000µM ($n=4$) ($p<0.0001$). Bakuchiol (150µM) has shown to enhance paracetamol toxicity to 66% cell viability at 50mM ($n=2$). Enzymatic modulators including itraconazole have shown to enhance paracetamol toxicity with 56% drop in cell viability at 50mM, with significant reduction in cell viability at 50mM paracetamol concentration ($p=0.0059$). Rifampicin has shown to drop cell viability to 55% at 50mM ($n=2$). Zafirlukast has also shown to drop cell viability to 57% at 50mM ($n=3$).

Discussion: Bakuchiol is more toxic than psoralen and paracetamol. CYP and UGT modulators that impact detoxification pathways have shown to enhance paracetamol toxicity. This is important as these herbal medicines are popular in society today, so therefore may offer consumers valuable insight into the potential health risks these medicines pose when used both individually and in combination with paracetamol.

P585

Frailty, polypharmacy, deprescribing and 23-hour activity: insights from a mouse model

Mr Kevin Winardi

Biography:

Kevin is a scientific officer at the Laboratory of Ageing and Pharmacology, Kolling Institute and the University of Sydney, led by Prof Sarah Hilmer. He leads the bioinformatics analyses of omics data to investigate the molecular mechanisms of drug-related harms in old age, aiming to understand the impact of polypharmacy whether medication cessation (deprescribing) offers any molecular reversibility benefits.

Title: Frailty, polypharmacy, deprescribing and 23-hour activity: insights from a mouse model

John Mach[1,2], Kevin Winardi[1,2], and Sarah N Hilmer[1,2]
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2 Departments of Clinical Pharmacology and Aged Care, Royal North Shore Hospital, St Leonards, NSW, Australia

Introduction. Management of older people with frailty commonly includes polypharmacy and deprescribing. Functional activity is an important outcome that is a key component of healthy ageing. The impacts of frailty on the outcomes of medication use and deprescribing are poorly understood, as are the effects of medication use on frailty.
Aims. Here, using aged C57BL/6 male mice, we explore the effects of different chronic drug regimens; polypharmacy and monotherapy, and deprescribing on daily activities using an automated recognition cage, and explore the relationship of frailty and trajectories.
Methods. At 12 months, male C57BL/6 mice were chronically administered control diet, one of 5 monotherapy diets or one of 3 polypharmacy diets with an increasing Drug Burden Index (measure of total exposure to sedative and anticholinergic medications). At 21 months of age, mice were stratified to continue treatment or to have treatment withdrawn (deprescribed). At 24 months, mice were assessed using the LABORAS automated recording system for 23 hours. Mouse clinical frailty index was measured at 5 timepoints (12, 15, 18, 21, and 24 months) and used for trajectory cluster analysis.
Results. We found that polypharmacy substantially altered activity over 23 hours (LABORAS), could not be extrapolated from monotherapy response and was partially reversed with deprescribing. Frailty score did not contribute to treatment or deprescribing response when added to the model. However, unique correlations were found between frailty at 24 months and LABORAS for each intervention. We identified 4 main frailty trajectory clusters, each with different deficit attributes and each influenced specific LABORAS outcomes.
Conclusion. This preclinical study demonstrates that medications can impact activity and frailty. Interventions targeting frailty should consider testing in the context of polypharmacy to enhance translation.

P586

hERG blockade prediction using docking and SQM2.20 rescoring

Dr Slade Matthews

Biography:

Dr. Slade Matthews is a Senior Lecturer specializing in computational pharmacology and toxicology. His research focuses on predicting chemical properties and bioactivity using Python-based QSAR models and cheminformatic techniques such as molecular fingerprinting, quantum molecular calculations, clustering, and substructure analysis. He earned his PhD in 2007 on machine learning in biomedical data and has published 48 peer-reviewed papers (Scopus h-index: 18). In 2025 Slade published a state-of-the-art graph transformer-based QSAR model for Ames mutagenicity prediction. He serves on the TGA Medical and Scientific Evaluation Services Panel and the NSW Poisons Advisory Committee both since 2010. In 2024, he was elected to the ASCEPT Board and awarded Fellowship of ACTRA in 2025. Based at the University of Sydney, Slade collaborates with academic and regulatory partners to advance public safety through application of in silico toxicology and is passionate about mentoring students and interdisciplinary research bridging chemistry, biology, and data science.

hERG blockade prediction using docking and SQM2.20 rescoring

Davy Guan[1], Daniella James-New[2], Slade Matthews[2]. Decisions & Statistical Learning, CSIRO's Data61[1], Sydney, NSW, Australia; Computational Pharmacology and Toxicology Laboratory, Sydney Pharmacy School, The University of Sydney[2], Sydney, NSW, Australia

Introduction. Drug-induced block of the cardiac hERG channel can prolong QT and precipitate torsades, making early *in silico* triage essential alongside ICH S7B/E14 best-practice assays. Recent cryo-EM structures of hERG with bound blockers reveal a well-defined cavity and key aromatic determinants (Y652, F656), enabling structure-based workflows beyond ligand-only QSAR.

Aims. To evaluate whether docking followed by SQM2.20 rescoring improves rank-ordering of hERG blockers versus docking alone, and to benchmark against ligand-based ML baselines.

Methods. We will dock curated reference ligands and candidates into cryo-EM hERG models (e.g., 7CN1 astemizole-bound and matched open/inactivated-state models), retaining K^+ and conserved waters. Top poses are rescored using SQM2.20 (PM6-D3H4X with implicit solvation and entropic proxy), explicitly sampling protomer/tautomer states and alternative poses. Performance will be assessed by enrichment, ROC/PR-AUC and rank correlations; uncertainty is reported as mean±SEM (n specified).

Results. Planned interim analyses will compare docking, docking+SQM2.20, and ligand-only ML QSAR (RF/XGB), quantify sensitivity to protonation/pose/state, and report prospective enrichment on held-out compounds. Success criteria: ΔSpearman $\rho \geq 0.15$ over docking; PR-AUC ≥ 0.70 on the reference panel.

Discussion. This study aims to deliver a robust, mechanistic triage for hERG liability that complements regulatory assays by combining structure-informed docking with SQM2.20 rescoring that addresses applicability-domain limits of purely ligand-based models.

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. (2022). E14/S7B Q&As, (ICH E14/S7B). Retrieved from https://database.ich.org/sites/default/files/E14-S7B_Qas_Step4_2022_0221.pdf

P587

Compliance of Herbal Medicines with the Therapeutic Goods Administration labelling requirements

Dr Ian Musgrave

Biography:

Dr Musgrave is a molecular pharmacologist/toxicologist. He obtained his PhD from the University of Melbourne in 1989, postdoctoral work in the Institute of Pharmacology at the Free University of Berlin in 1991-1994, returning to Australia in 1994 on a CJ Martin Fellowship. He was appointed as Senior Lecturer in Pharmacology at the University of Adelaide in 2001.

He has a broad interest in neuronal function and survival, natural product pharmacology and drug design. Current research focuses on the safety of herbal medicines and natural products as potential anti-amyloid medications. Ian has consulted with the State Health and the TGA on the safety of herbal medicine.

Compliance of Herbal Medicines with the Therapeutic Goods Administration labelling requirements

Eton Williams [1], Sophie Dunow[1], Eden Klos[1], Ian Musgrave[1]. Pharmacology, The University of Adelaide[1], Adelaide, SA, Australia.

Introduction. Complementary medicines are widely used as alternatives to conventional drugs, with many consumers falsely believing their natural ingredients to be without risk. Herbal medicines sold in Australia must comply with the Therapeutic Goods Administration's (TGA) regulations on listed medicines to be included on the Australian Register of Therapeutic Goods (ARTG).

Aims. To determine if listed complementary medicines comply with ARTG requirements. This study specifically assesses four ingredients with known health concerns: Andrographis, Echinacea, Glucosamine & Chondroitin, and St John's Wort

Methods. All medicines registered since 2015 containing Andrographis, Echinacea, Glucosamine & Chondroitin, and St John's Wort were recorded from the ARTG online database. The label requirements were cross-referenced with online and in-store dispensaries to assess compliance with regulatory guidelines.

Results. 88.9% of in-store St John's Wort medications did not comply with the TGA required label. Andrographis can cause anaphylaxis and taste disturbances; only 72% of the reviewed medications included both warnings. Significantly, 93.6% of the online medications containing Echinacea did not disclose its potential to trigger asthma. 43.75% of Glucosamine/Chondroitin in-store medications did not correctly label its anaphylaxis warning.

Discussion. The results of this study indicated that complementary medicines are frequently incorrectly labeled to inform of associated risks of use. This was particularly apparent with inaccurate label ordering on medicines sold in-store and insufficient warning information for online medicines.

P588

Effect of the TGA's labelling requirements on reporting of andrographis/echinacea adverse reactions

Dr Ian Musgrave

Biography:

Dr Musgrave is a molecular pharmacologist/toxicologist. He obtained his PhD from the University of Melbourne in 1989, postdoctoral work in the Institute of Pharmacology at the Free University of Berlin in 1991-1994, returning to Australia in 1994 on a CJ Martin Fellowship. He was appointed as Senior Lecturer in Pharmacology at the University of Adelaide in 2001.

He has a broad interest in neuronal function and survival, natural product pharmacology and drug design. Current research focuses on the safety of herbal medicines and natural products as potential anti-amyloid medications. Ian has consulted with the State Health and the TGA on the safety of herbal medicine.

The effect of the TGA's labelling requirements on reporting of *andrographis/echinacea* adverse reactions

Charlotte Beven, Mehrin Hasan, Tara Hislop, Ian Musgrave[1]. Pharmacology, The University of Adelaide[1], Adelaide, SA, Australia.

Introduction. *Andrographis paniculata* and *echinacea* containg herbal medicines used to treat cold symptoms have increased in popularity due to COVID-19. These medicines can elicit hypersensitivity adverse drug reactions (ADRs), such as anaphylaxis, in susceptible individuals. The Therapeutic Goods Administration (TGA) legislated new warning labels for *andrographis* and *echinacea* containing medicines in Dec-2019, in effect by May-2020.

Aims. To determine the effectiveness of these new warning labels in ADR prevention in the context of COVID-19 and influenza-like illnesses

Methods. Data from the TGA Database of Adverse Event Notifications (DAEN) was exported to Excel. Reports from 2015-2024 with hypersensitivity symptoms, defined by the Brown Scale[1], were included (n=513). ADR reports of glucosamine and chondroitin were used as a control since their usage should not have increased during COVID (n=25). Data was analysed alongside Australian influenza and COVID statistics and sales data of Andographis/Echinacea from IQVIA.

Results. Five years before legislation change in May 2020, there was an average of 2.3 ADRs reported per month, compared to 7.3 per month after legislation, revealing an increase in hypersensitivity ADRs despite legislation changes. The ADR rates were not constant but formed distinct peaks that mostly correlated with both preceding increases in sales of *Andographis/Echinacea* and influenza-like illnesses with a lag phase. *Andographis/Echinacea* use was not particularly associated with COVID. Average ADR reports for glucosamine and chondroitin remain stable.

Discussion. Despite the TGA's new warning label requirements, spread of influenza-like illnesses is associated with an increase in *andrographis* and *echinacea* hypersensitivity ADRs. Awareness of COVID-19 may also have an effect. This indicates the need for a review of TGA warning label sizing and placement, and to educate the public of possible ADRs associated with *andrographis* and *echinacea* use.

[1] Brown, S. G. J Allergy Clin Immunol, 114, 317-6, 2004

Acknowledgement: IQVIA for provision of complementary medicine sales data for Australia

P589

Female mice exhibit reduced hallmarks of MASH in the GAN DIO model

Miss Isabella Simon

Biography:

Isabella Simon is a highly motivated 2nd year PhD Candidate who has an immense passion for liver disease research following her own lived-experience. Following her diagnosis of autoimmune hepatitis in 2015 at age 16, and subsequent liver transplant in 2019 at 20 years of age, Isabella pursued a Bachelor of Science and Bachelor of Arts, where she was awarded First-Class Honours in Pharmacology and commenced her PhD in 2023 at Monash University. Her PhD investigates novel therapeutic avenues for metabolic dysfunction-associated steatohepatitis.

Female mice exhibit reduced hallmarks of MASH in the GAN DIO model

Isabella A. Simon[1], Timothy S. Fitchett[1], Yu-Anne Yap[2], Khashayar Asadi[3], Remy Robert[2], Robert Jones[3], Avik Majumdar[3], Robert E. Widdop[1], Mark P. Del Borgo[1]. Department of Pharmacology, Monash University[1], Clayton, VIC, Australia; Department of Physiology, Monash University[2], Clayton, VIC, Australia; Liver Transplant Unit, Austin Hospital[3], Heidelberg, VIC, Australia

Introduction. Metabolic dysfunction-associated steatohepatitis (MASH) is the progressive form of steatotic liver disease. There are suggested sex differences in disease prevalence, with lower risk seen in premenopausal women compared to men (Younossi et al, 2023). However, preclinical studies are predominantly male-biased, resulting in limited understanding of sex-specific disease mechanisms.

Aims. This study aimed to investigate sex differences in MASH development using the gold standard Gubra Amylin NASH (GAN) diet-induced obesogenic (DIO) mouse model.

Methods. Five-week-old male and female C57BL/6 mice were fed standard chow or the GAN diet for up to 36 weeks prior to euthanasia. Immunohistochemistry and immunofluorescence were performed on excised liver tissue to conduct integrated MASH Activity Score (MAS, 0-8) and fibrosis (F, 0-4) scoring, as well as individual measures of steatosis and inflammation. Second harmonic generation (SHG) was also conducted on fixed liver tissue to analyse levels of fibrillar collagen deposition and architecture.

Results. Male mice developed definitive MASH (MAS≥5) by 26 weeks, with all exhibiting clinically significant fibrosis (F≥2). In contrast, female mice showed delayed and reduced MAS scores with one-third remaining below diagnostic threshold at 36 weeks. Fibrosis severity was markedly lower in females, with only 8% reaching advanced fibrosis (F3–4) at 36 weeks versus 68% of males ($P<0.01$). Based on SHG analysis, females had significantly lower collagen deposition with shorter and fewer fibers, consistent with histological findings.

Discussion. Female C57BL/6 mice show delayed onset of MASH and fibrosis compared to males in the GAN DIO model, mirroring clinical sex differences seen in premenopausal women. These findings highlight the need for sex-balanced preclinical studies to investigate mechanisms of disease susceptibility and identify opportunities for targeted therapy.

Younossi ZM et al (2023) Hepatol Baltim Md 77:1335-1347

P590

Post-translational insights into gastrointestinal tract ligand-gated ion channels

Prof Helen Irving

Biography:

Helen Irving is a Professor in Biomedical Sciences and leads a theme in the Holsworth Biomedical Research Centre and is member of the La Trobe Institute for Molecular Sciences (LIMS). Helen's current research focusses on understanding moonlighting ligand-gated ion channels, cryptic enzymes and inflammatory signals at the molecular level to develop new and improved approaches to managing inflammatory conditions.

Post-translational insights into gastrointestinal tract ligand-gated ion channels.

Helen R Irving[1], Santosh T R B Rao[1], Amy Li[2], Holsworth Biomedical Research Centre, La Trobe Institute for Molecular Science, La Trobe University[1], Bendigo, VIC, Australia; Centre for Healthy Futures, Torrens University Australia[2], Surrey Hills, NSW, Australia.

Introduction. Ligand-gated ion channels (LGICs) are important components of membranes enabling specific signaling ligands to modulate ion transport of cells and cellular compartments. LGICs are important in maintaining gastrointestinal motility. Both 5-HT3 and nACh receptors (R) are implicated in dysregulation of gut function and other organs including the heart. Surprisingly, both 5-HT3R and nAChR have recently been reported in mitochondrial membranes where they modify its function. Signal peptides (Rao et al 2023) or glycosylation states (Skok 2022) enable the receptor subunits to enter mitochondria. Whether other LGICs can enter mitochondria is unknown.

Aims. To systematically analyse LGIC sequences to identify mitochondrial location signals and post-translational modifications.

Methods. Sequences of LGIC subunits were retrieved from NCBI data base and analyzed for the presence of predicted organelle localization signals, conserved phosphorylation and glycosylation sites using various web-based software.

Results. No nuclear localization signal was detected in any of the LGIC subunits while 5HT3A and 5HT3E subunits and $GABA_A$ subunit theta precursor possess mitochondria localization signals. Most phosphorylation sites occur at intracellular serine, threonine or tyrosine residues. However, various ASIC, GL, P2X, nACh, $GABA_A$ and glutamate receptor subunits contain predicted sites in extracellular domains and occasionally transmembrane regions. As expected, glycosylation sites largely occur in the extracellular domain. However, several subtypes of glycine, P2X, $GABA_A$, nACh and ionotrophic glutamate receptors contain cytoplasmic facing N glycosylation sites.

Discussion. Together these findings raise the possibility that other LGICs normally associated with the plasma membrane contribute to mitochondrial function. Determining when and how these subunits enter mitochondria may develop our understanding of mitochondrial dysbiosis in chronic disease states including gastrointestinal mobility.

Rao S T R B et al (2023) Int J Mol Sci 24: 8301
Skok M (2022) Int J Biochem Cell Biol 143: 106138

P591

The role of intracellular calcium and Rho-kinase in porcine urethral mucosa contractions

Asst Prof Iris Lim

Biography:

Dr Iris Lim's research spans urogenital pharmacology and physiology, focusing on the urethra and ureter. She also investigates innovative educational approaches, particularly the use of educational escape rooms to enhance student engagement.

The role of intracellular calcium and Rho-kinase in porcine urethral mucosa contractions

Eriq Burovski[1], Donna Sellers[1], Russ Chess-Williams[1], Iris Lim[1]. Centre for Urology Research, Faculty of Health Sciences and Medicine, Bond University[1], Gold Coast, QLD, Australia.

Introduction. Contraction of urethral smooth muscle is mediated not only by rises in intracellular calcium but also by calcium sensitisation pathways that maintain contraction without further calcium elevation (Rembetski et al., 2020). However, whether similar mechanisms operate in the urethral mucosa has not been investigated.

Aims. The present study aimed to determine the role of intracellular signalling pathways on 5-HT-mediated contraction of the urethral mucosa.

Methods. Using an organ bath setup, contractile responses of isolated porcine urethral mucosal strips to cumulative concentrations of 5-HT (10 nmol/L – 100 µmol/L) were recorded. Experiments were conducted in the absence and presence of inhibitors targeting calcium influx (nifedipine), intracellular calcium release (cyclopiazonic acid (CPA) and ryanodine), and Rho-kinase (fasudil and Y-27632). Paired Student's *t*-tests were performed, with *p*-values <0.05 considered statistically significant.

Results. In the presence of nifedipine (1 µmol/L) the 5-HT-mediated tonic contractions were significantly attenuated in the urethral mucosa ($p<0.05$). Additionally, the spontaneous contractions of the urethral mucosa were also completely abolished. When subjected to ryanodine (10 µmol/L) or CPA (10 µmol/L), there was no effect on either tonic or phasic 5-HT-induced contractions of the urethral mucosa. In the presence of fasudil (10 µm) and Y-27632 (10 µmol/L), there was a significant decrease in 5-HT mediated tonic contractions ($p<0.05$) at higher concentrations of the agonist (100 µmol/L) while spontaneous contraction rate also decreased.

Discussion. The present findings indicate that 5-HT–mediated contraction of the urethral mucosa depends on calcium influx through L-type channels and is modulated by Rho-kinase–mediated calcium sensitisation, whereas release from intracellular calcium stores does not appear to contribute.

Rembetski B et al (2020) Am J Physiol Renal Rhysiol 318:496-505

P592

Mas-related G protein-coupled receptors X2 and β-defensin-1 in UPEC-Infected bladder urothelium

Assoc Prof Lu Liu

Biography:

Associate Professor Liu is a pharmacologist whose research centres on the causes and treatment of gastrointestinal and urinary bladder diseases. She brings over 20 years of experience investigating conditions such as inflammatory bowel disease, constipation, diverticular disease, bladder urothelium function, overactive bladder, and urinary tract infections.

She earned her PhD in Pharmacology from Monash University in 1998, receiving the prestigious Mollie Holman Medal. She subsequently held NHMRC-funded research positions at UNSW, where she garnered both national and international recognition through multiple awards. Since 2006, she has served as an academic in the School of Biomedical Sciences at UNSW, integrating her research with teaching responsibilities.

As Chief or Sole Investigator, A/Prof Liu has secured over $3 million in competitive and collaborative research funding, including four NHMRC project grants. Her work has led to extensive national and international collaborations and has produced numerous publications on gastrointestinal and bladder physiology and disease.

Mas-related G protein-coupled receptors X2 and β-defensin-1 in UPEC-Infected bladder urothelium

Lu Liu[1], Abhiniti Negi[1], Irit Markus[1], Zhuoran Chen[2], Kylie J Mansfield[3]. School of Biomedical Sciences, UNSW Sydney[1], Sydney, NSW, Australia; St George Hospital, UNSW Sydney[2], Sydney, NSW, Australia; Graduate School of Medicine, University of Wollongong[3], Wollongong, NSW, Australia

Introduction. Urinary tract infections, predominantly caused by uropathogenic *Escherichia coli* (UPEC), are among the most common bacterial infections worldwide. Mas-related G protein-coupled receptors (MRGPRs), particularly MRGPRX2, and antimicrobial peptides such as β-defensin-1 (BD1), have been implicated in mucosal immune responses. However, their roles in bladder immunity remain poorly defined.

Aims. This study aims to characterize the expression of MRGPRX2 and BD1 in porcine bladder tissue under normal and UPEC-infected conditions, and to determine whether MRGPRX2 activation modulates BD1 expression *in vitro.*

Methods. Porcine bladder tissues were exposed *ex vivo* to the UPEC strain UTI89 and processed for immunohistochemistry to assess MRGPRX2 and BD1 expression. In parallel, human urothelial RT4 and UROTSA cells were infected with UPEC in the presence or absence of the MRGPRX2 agonist compound 48/80. BD1 levels were quantified using ELISA, and mRNA expression of MRGPRs and BD1 was analysed via RT-PCR.

Results. UPEC caused significant damage to urothelial integrity, barrier function, and permeability, as evidenced by the loss of uroplakins and tight junction protein ZO-1 expression. However, there were no significant differences in the density of MRGPRX2 and BD1 immunoreactivity in the urothelial layer between control and UPEC-infected bladder tissues. Similarly, mRNA expression levels of MRGPRX2 or BD1 did not show significant changes across treatment conditions. Basal BD1 levels in RT4 cells were approximately 20 pg/ml and nearly undetectable in UROTSA cells. Treatment with compound 48/80, however, significantly increased BD1 levels to 150–200 pg/ml in both cell types.

Discussion. UPEC induced substantial damage to the urothelium and uroplakin layer. Despite this, MRGPRX2 and BD1 immunoreactivity remained unchanged in porcine bladder tissues. Although mRNA expression of MRGPRX2 and BD1 was unaffected by UPEC infection and compound 48/80 treatment, compound 48/80 significantly enhanced BD1 production and secretion in both RT4 and UROTSA cells. These findings provide valuable insight into the potential interaction between MRGPRX2 and BD1, suggesting that MRGPRX2 may play a role in modulating bladder immune responses during infection.

P593

SNPs in 5-HT3 receptors alter structure, function, and impact clinical disorders.

Dr Santosh Rama Bhadra Rao Tata

Biography:

Dr. Santosh Rama Bhadra Rao Tata is a biomedical researcher specializing in serotonin receptor neurobiology, particularly the 5-HT₃ receptor. He earned his PhD from La Trobe University's Rural Health School in Bendigo, Australia, in 2023. His doctoral research combined in-silico modeling and experimental techniques to explore 5-HT₃ receptor expression and function, with implications for gastrointestinal and psychiatric disorders. Dr. Tata has co-authored several publications, including studies on mitochondrial localization of 5-HT₃ receptors and receptor subunit interactions. He currently collaborates with Prof. Helen Irving on cancer immunology projects and teaches microbiology, biochemistry, and molecular biology as a casual academic at La Trobe University.

SNPs in 5-HT3 receptors alter structure, function, and impact clinical disorders.
Santosh T R B Rao [1], Helen R Irving [1]Holsworth Biomedical Research Centre, La Trobe Institute for Molecular Science, La Trobe University[1], Bendigo, VIC.

Introduction. 5-HT₃ receptors are ligand-gated ion channels (LGICs) composed of five distinct subunits A, B, C, D, and E. Functional receptors can form either as homomers (comprising only the 5HT3A subunit) or as heteromers, in which 5HT3A subunits combine with one or more other subunits. These receptors are expressed in the central and peripheral nervous systems including the gastrointestinal tract, where they modulate many physiological functions. Single nucleotide polymorphisms (SNPs) in genes encoding the 5-HT₃ receptor subunits have been linked to clinically significant neurological and gastrointestinal disorders, including anxiety, schizophrenia, obsessive-compulsive disorder, and irritable bowel syndrome. Nonsynonymous SNPs can result in structurally or functionally altered receptor proteins, potentially contributing to disease pathogenesis. In this study, we investigate how the 5HT3D subunit and SNP-derived variants affect the conformational dynamics and functional properties of heteromeric 5-HT₃ receptors.
Methods. Homology models of the full-length human 5HT3D subunit were constructed in AlphaFold and SWISS-MODEL based on available crystal and cryo-EM structures of the mouse 5HT3A subunit. Heteromeric 5-HT₃ receptor models with A3D2 (A-A-D-A-D) and A3BD (A-A-B-A-D) stoichiometries were assembled. The receptor models were compared in their ligand-free (apo) states, and with either the endogenous agonist serotonin or the anti-emetic antagonist granisetron.
Results. Serotonin-bound models of the 5-HT₃AD receptor complex exhibit similar conformational arrangements across the transmembrane and intracellular domains. Granisetron-bound models closely resemble the ligand-free (apo) state, with the transmembrane domains of the 5HT3D subunit undergoing conformational changes analogous to those observed in the 5HT3A subunits. Notably, nonsynonymous SNP substitutions at position Gly110 (rs6443930: Gly → Ala/Val/Asp) in the 5HT3D subunit resulted in substantial structural alterations within the extracellular domain.
Discussion. Homology modeling reveals that rs6443930 SNPs in the 5HT3D subunit cause conformational changes in the extracellular domain, potentially affecting ligand binding and receptor activation. These alterations may underlie clinical associations with neurological and gastrointestinal disorders, emphasizing the functional impact of genetic variation on 5-HT₃ receptor behavior and therapeutic responsiveness.

P594

Barriers and enablers to high quality blood pressure measurement in primary care

Dr Ritu Trivedi

Biography:

Ritu is a Postdoctoral Research Fellow at the University of Sydney. Her PhD explored digital health technologies for supporting patients with atrial fibrillation and her postdoctoral research work is focused on the accuracy of devices used by Australians to measure their blood pressure at home. Ritu's research interests are in optimising self-management for those with cardiovascular diseases.

Barriers and enablers to high quality blood pressure measurement in primary care

Ritu Trivedi[1], Eleanor Clapham[2], Dean S Picone[1,2], Gautam Satheesh[1,3], Aletta E Schutte[3,4], Kaylee Slater[1], Niamh Chapman[1,2]. School of Health Sciences, USYD[1], Camperdown, NSW, Australia; Menzies Institute for Medical Research, UTAS[2], TAS, Australia; UNSW[3], Sydney, Australia; The George Institute for Global Health[4], Sydney, NSW, Australia.

Introduction. High-quality blood pressure (BP) measurement is the cornerstone of hypertension diagnosis and management. Yet, healthcare providers (HCPs) face many barriers that compromise the quality of measurement in primary care.

Aims. Understand barriers and enablers to high-quality measurement in primary care from the perspective of HCPs.

Methods. We conducted 50 semi-structed interviews with primary care doctors (n=24), nurses (n=15) and community pharmacists (n=14) according to an interview schedule (based on the Theoretical Domains Framework) that included recall of BP measurement method and prompts to explore workflow barriers. Analysis followed thematic principles, using inductive then deductive coding, with themes mapped to the Capacity, Opportunity and Motivation – Behaviour (COM-B) model to explore behavioural mechanisms underlying BP measurement practices among HCPs.

Results. A preliminary analysis of 12 interviews (4 of each HCP type) revealed several gaps and misconceptions about guideline-recommended BP measurement. While HCPs generally assumed competency in conducting BP measurements, many acknowledged a lack of recent formal training. Measurement practices were more rigorously applied in patients with a known diagnosis or suspected hypertension, indicating a prioritisation of technique in these patients. Medical practices were generally well-resourced with appropriate equipment; however, pharmacists predominantly relied on home BP monitors and reported challenges in securing dedicated space for measurements. Workflow and system-level constraints, including limited time and competing priorities, were commonly mentioned. Additionally, system and policy-related barriers, such as the absence of funding incentives for BP measurements outside of care plans and health checks, were noted. Participants also highlighted issues with documentation and communication of BP readings across HCPs, which further impeded coordinated BP management.

Discussion. Various barriers, including workflow challenges and resources constraints, impede high-quality BP measurement, which need to be addressed through targeted approaches. Next steps include mapping these barriers to existing implementation frameworks to identify proven strategies to address these challenges.

P595

Gut Regulated Associations of Neuronal Signalling in high BP (GRAiNS-BP): RCT Protocol

Miss Malindi Welathanthree

Biography:

Currently pursuing a PhD in Medicine at Monash University, I am a First Class Honours graduate in Science with a background in industrial laboratory research. My work centers on genetics and genome biology, with a particular focus on advancing our understanding of cardiovascular health. I bring a strong work ethic, adaptability, and a collaborative mindset to every research endeavor, and I thrive in multidisciplinary environments. My commitment to impactful science is reflected in my first-author publication, and I continue to explore novel genomic mechanisms that may inform future therapeutic strategies. Through my academic and professional journey, I aim to contribute meaningful insights to the scientific community and foster innovation in medical research.

Gut Regulated Associations of Neuronal Signalling in high BP (GRAiNS-BP): A Randomised Controlled Trial Protocol

Malindi Welathanthree[1], Vaughan Macefield[2], Francine Z. Marques[1], Rikeish R. Muralitharan[1], on behalf of GRAiNS-BP Investigators. [1]Hypertension Research Laboratory, Victorian Heart Institute; [2]Human Neurophysiology Lab, Department of Neuroscience, Monash University

Introduction. Hypertension affects one in three Australian adults and is the leading cause of death globally. Despite the range of available medications, more than half of patients do not have their BP under control due to poor adherence, difficulty finding the right treatment due to side effects, or avoiding medication altogether. Diet plays a crucial role in cardiovascular health, with high-fibre intake shown to lower BP through the production of short-chain fatty acids (SCFAs), formed during fibre fermentation. A clinical trial found that a chemically modified resistant starch that releases SCFAs in the colon (HAMSA/B) significantly reduced BP in hypertensive patients via the gut-brain axis. Although the exact mechanism is still unclear, SCFAs may influence BP.

Aims. To investigate the effects of SCFA supplementation on the gut-brain-immune axis of BP regulation.

Methods. The GRAINS-BP trial will recruit 29 adults with untreated hypertension (≥140/90 mmHg) for a randomised double-blinded, placebo-controlled, cross-over study using the non-commercially available HAMSA/B shakes taken twice daily. Over 48 days including a 20-day washout period, participants will attend four visits at Alfred Hospital, Melbourne. Measurements will include muscle sympathetic nerve activity (MSNA), heart rate variability as an indirect measure of vagal activity using continuous heart rate monitoring, 24-hr ambulatory BP, cognitive and mental wellbeing tests, and gastrointestinal transit time. Faecal, urine, and blood samples will be collected at each visit to assess microbiome, cardiometabolic, renal, and immune markers. Mediation analyses will be performed to determine causation.

Expected Results. The primary outcome of this study is the effect of SCFA supplementation on the autonomic nervous system. Secondary outcomes include changes in 24-hour BP, plasma SCFA levels, immune cell profiles, gut microbiome profiles, cognitive function, quality of life, and gastrointestinal transit time.

Discussion. The GRAiNS-BP trial will help confirm and uncover how SCFA supplementation lowers BP, including whether it acts through the gut–brain axis. By clarifying these mechanisms, the study will strengthen evidence for SCFA supplementation as a viable non-pharmacological treatment for hypertension.

P596

Arterial Stiffness May Limit Functional Improvement in Frail Aortic Stenosis Patients

Dr Audrey Adji

Biography:

Dr. Audrey Adji is a research scientist at the Victor Chang Cardiac Research Institute and a research fellow at St Vincent's Hospital, Sydney. Her work explores pulsatile function in cardiovascular and pulmonary diseases, including mechanical circulatory support devices in heart failure. She has authored >80 peer-reviewed publications, presented at international conferences, and fostered collaborative research networks. Dr. Adji has received multiple scientific awards and serves on editorial boards of hypertension journals. She mentors postdoctoral fellows and supervises higher degree students across medicine and engineering. As Chair of the Women in Hypertension (Research) Committee at Hypertension Australia and the Early Career Research Network of Pulse of Asia, she advocates for equity and emerging researchers. She is a member of the Hypertension Australia Taskforce and a Fellow of both the International Society of Hypertension and the Cardiac Society of Australia and New Zealand. Dr. Adji actively cultivates national and global research partnerships.

Arterial Stiffness May Limit Functional Improvement in Frail Aortic Stenosis Patients

Ning Song[1,2], Georgio Salloum[1], Audrey Adji[1,2,3]. [1]St Vincent's School of Clinical Medicine, University of New South Wales, Sydney, NSW, Australia. [2]Department of Cardiology, St Vincent's Hospital, Sydney, NSW, Australia. [3]Victor Chang Cardiac Research Institute, Sydney, NSW, Australia.

Introduction. Patients with severe aortic stenosis (AS) requiring transcatheter aortic valve replacement (TAVR) are elderly and often have co-existing frailty and elevated arterial stiffness, both of which may limit functional improvement post TAVR.

Aims. We investigated the effect of baseline arterial stiffness and frailty on the medium-term functional status severe AS patients post TAVR.

Methods. We enrolled severe AS patients planned for TAVR between November 2023-September 2024. Haemodynamic and arterial stiffness measures were obtained using echocardiogram, non-invasive blood pressure, carotid-femoral pulse wave velocity (PWV), and central systolic pressure (CSP) derived from radial applanation tonometry with the Sphygmocor® system. The Rockwood clinical frailty score and Kansas City Cardiomyopathy Questionnaire 12-item (KCCQ-12) assessed frailty and functional status respectively.

Variable	Mean±SD or Median (Range)	As Predictor for Follow Up KCCQ	
		Beta	P Value
Frailty	3.8±1.2	-9.502	**0.007**
Heart Rate (bpm)	66.5±11.6	0.024	0.946
CSP (mmHg)	134.1±15.3	-0.098	0.685
Ejection Fraction (%)	50.1±15.1	0.255	0.304
SVi (ml/m^2)	38.6±14.1	-0.747	**0.012**
PWV (m/s)	10.2±2.6	-3.930	**0.017**
Baseline KCCQ	64.8±25.6	0.385	**0.015**

Results. Total of 47 patients (82±8 years, 22 (47%) females) underwent comprehensive baseline measures with repeated KCCQ-12 obtained at 243±76 days post TAVR. The median baseline frailty score was 4. Twenty-seven (57%) patients experienced improvement in their follow-up KCCQ (baseline 64.8±25.6, follow up 69.2±26.9, delta 4.3±30.1). After correcting for age, sex and mean transvalvular gradient, the strongest predictor of follow-up KCCQ score was frailty, with stroke volume index (SVi), baseline KCCQ score and PWV also being significant predictors (see table).

Discussion. In AS patient undergoing TAVR, lower KCCQ on medium-term follow up is associated with higher baseline frailty and arterial stiffness measured by PWV. This finding suggests that elevated pulsatile arterial load is a potential contributor to poorer functional improvement of frail AS patients independent to blood pressure.

P597

Longitudinal validity of the Indian diabetes risk score in an Indian population

Ms Duc Nguyen

Longitudinal validity of the Indian diabetes risk score in an Indian population

Duc Nguyen[1,2], Quan Huynh[1,2], Tilahun Haregu[2], Brian Oldenburg[2] (1) School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia (2) Baker Heart & Diabetes Institute, Melbourne, Victoria, Australia.

Introduction. Type 2 diabetes (T2D), a comorbidity of hypertension, is the fastest growing non-communicable disease (NCD) globally with high risks of micro- and macro-vascular complications. It is a major public health crisis in low- and middle-income countries particularly India, where laboratory diagnostic tests are not feasible in low-resource areas and approximately 50% of cases remain undiagnosed. The Indian diabetes risk score (IDRS) was developed as a simple self-assessment questionnaire based on 4 known risk factors including age, waist circumference, physical activity and family history. Proposed to be a more cost-effective method for screening for individuals at high risk of T2D, IDRS has shown slightly above average sensitivity when validated in numerous cross-sectional studies. However, there has been no studies to date evaluating the longitudinal performance of IDRS to determine its predictive validity.

Aims. This is the very first longitudinal study to evaluate the validity of IDRS in predicting future T2D incidence.

Methods and proposed analysis. This is a secondary analysis of the Kerala Diabetes Prevention Program (K-DPP) where the 'baseline' IDRS formed the basis of participant recruitment. The 'high-risk' individuals as identified by IDRS screening (IDRS score ≥60) was recruited to the intervention trial. The 'low-risk' individuals (IDRS<60) were excluded from the main trial however were randomly selected for separate follow-up. Both groups were followed for 9 years. For my study, data from the high- and low-IDRS groups were pooled together to assemble a single-cohort prospective study. The primary outcomes are diabetes incidence (binary) and glycaemic indicators including fasting plasma glucose and HbA1c (continuous) at 9-year. Univariable and multivariable linear and logistic regression models will be applied to assess the longitudinal relationship between IDRS at baseline and glycaemic outcomes at future timepoint. Validity metrics (sensitivity, specificity, AUC ROC analysis) will be applied to evaluate the predictive validity of IDRS.

Discussion. Given that a lack of T2D awareness and timely intervention are major barriers to effective disease management, the findings of this study will confirm the validity of IDRS as a prediction tool. If successfully implemented in a primary healthcare setting, IDRS can significantly facilitate early detection and timely tight glycaemic control, which are essential to reduce the burden of diabetes-related complications including hypertension and cardiovascular disease. The study can also provide insights into potential areas for recalibration of the risk score.

P598

Arterial hypertension and outcomes after transcatheter aortic valve implantation for aortic stenosis

Mr. Grzegorz Procyk

Biography:

Grzegorz Procyk, MD, is a third-year PhD candidate at the 1st Chair and Department of Cardiology, Medical University of Warsaw. His research focuses on lipoprotein(a) and biomarker-based risk prediction in aortic stenosis/TAVI and arrhythmias. He is a multi-time recipient of Poland's Minister of Health Scholarship (2022/23–2024/25), Rector's awards and scholarships, and the "Talenty Jutra" grant. As PI, he has secured competitive funding for projects on lipoprotein(a) in TAVI and in young adults. He has authored or co-authored papers in the Journal of Molecular Medicine, Polish Archives of Internal Medicine, Cardiology Journal, and Journal of Clinical Medicine. Grzegorz has presented at ACC.25 (Chicago), APSCC 2025 (Busan), EAS 2024–2025, and the European Lipoprotein Club. He trained in the Cath Lab at San Giovanni Bosco Hospital (Turin) and is active in ESC and PTK.

Arterial hypertension and outcomes after transcatheter aortic valve implantation for aortic stenosis

Grzegorz Procyk[1], Paweł Tyrna[2], Janusz Kochman[1], Aleksandra Gąsecka[1]. 1st Chair & Dept Cardiol, Med Univ Warsaw[1], Warsaw, Poland; Dept Histol & Embryol, Med Univ Warsaw[2], Warsaw, Poland.

Introduction. Severe aortic stenosis (AS) can be treated with either surgical aortic valve replacement (SAVR) or transcatheter aortic valve implantation (TAVI). TAVI is recommended mainly for older patients and those with higher surgical risk. However, in the case of some patients, both SAVR and TAVI can be considered. The final decision should consider individual patient characteristics. Outcome predictors for both treatment options would facilitate this decision. Arterial hypertension (AH) is a well-known risk factor for multiple cardiovascular diseases and may impact the course of many conditions.

Aims. Our study aimed to assess whether AH influences the long-term survival of AS patients undergoing TAVI.

Methods. In this prospective multicentre study, we included and analysed 82 patients with severe AS who underwent TAVI in any of the three participating centres between November 2018 and September 2021. Patients were divided into AH and non-AH groups based on the presence of chronic AH at baseline. The demographic and clinical data were collected during hospitalization. The survival follow-up was ended on 12.11.2023. Statistical analysis was performed with GraphPad Prism Version 10.3.1 using the Shapiro-Wilk test, Student's t-test or Mann–Whitney U test, Fisher's exact test or Chi-square test, and Cox proportional hazards regression.

Results. Sixty-seven patients had AH at baseline, and 15 patients did not have AH. AH patients, compared to non-AH patients, had lower creatinine concentration (median 1.13 mg/dL [IQR 0.92-1.41] vs. 1.36 mg/dL [1.13-1.61]; P = 0.022), higher GFR (mean ± SD: 57.70 ± 19.60 mL/min/1.73m^2 vs. 43.13 ± 15.71 mL/min/1.73m^2; P = 0.009), and higher NT-proBNP levels (median 3527 pg/mL [IQR 2032-10733] vs. 1777 pg/mL [771-3573]; P = 0.041). The groups had no differences in other baseline characteristics, echocardiographic parameters, and comorbidities. Survival probability adjusted for GFR did not differ between the AH groups (HR: 0.76, 95% CI 0.30-2.35; P = 0.601) over a median follow-up of 1096 days (IQR 786-1492).

Discussion. Despite observed differences in creatinine concentration and GFR levels, baseline AH was not associated with long-term survival in AS patients after TAVI. Therefore, AH alone has limited utility in predicting patient outcomes and is of secondary importance for making treatment choices.

P599

Simultaneous blood pressure and atrial fibrillation screening in May Measurement Month

Mr Gianni Sesa-ashton

Biography:

Gianni is a research assistant in the Cardiometabolic Health and Exercise Physiology laboratory exploring the role of the sympathetic nervous system in health and disease. Overactivity of this system contributes strongly to the development and maintenance of cardiovascular diseases such as hypertension and heart failure. Gianni's work has looked at therapies that target this system in the form of renal denervation — a surgical approach to lowering blood pressure by 'silencing' the nerves which control the kidneys and consequently drive-up blood pressure. They continue to work on projects investigating the role of the microbiome in the development of a hyperactive sympathetic nervous system in patients with hypertension and understanding which brain regions controls blood pressure.

Simultaneous blood pressure and atrial fibrillation screening in May Measurement Month

Gianni Sesa-Ashton[1], Revathy Carnagarin[2,3], , Thomas Beaney[4], Gabriele Kerr[4], Aletta E Schutte[5], George Stergiou[6], Ben Freedman[7], Neil Poulter[8], Markus P Schlaich[1,2]. Baker Heart and Diabetes Institute[1], Melbourne, VIC, Australia; Dobney Hypertension Centre, Medical School, University of Western Australia[2], and Departments of Cardiology and Nephrology, Royal Perth Hospital[3] Perth, WA, Australia; Department of Primary Care and Public Health[4], Imperial College London, UK; School of Population Health, University of New South Wales[5], Sydney, NSW, Australia; School of Medicine, Hypertension Center STRIDE-7 National and Kapodistrian University of Athens[6], Athens, Greece; Heart Research Institute, Charles Perkins Centre, University of Sydney[7], NSW, Australia; Imperial Clinical Trials Unit, Imperial College London[8], W12 7RH, UK.

Introduction. May Measurement Month (MMM) is an annual global blood pressure (BP) screening campaign. Given the strong association between hypertension and atrial fibrillation (AF), in two campaigns, simultaneous AF and BP screening was conducted in some MMM centres.

Aims. Here we report AF detection rates and associated risk factors.

Methods. In 2022 and 2023, adults were screened opportunistically in 17 countries for BP and AF using a single standardised protocol. Three seated BP measurements were taken with concurrent AF screening during each automated BP measurement using OMRON Complete or M7 devices. Of those detected to have AF, 'known' AF was defined as having a previous diagnosis of either AF or irregular heartbeat, or taking oral anticoagulants.

Results. 135,434 participants had joint screening (mean age: 50.2 years; 56.3% female). Overall, 2,639 (1.9%) had AF detected, of whom 57.9% had known AF and 42.1% were newly diagnosed. AF detection was more common in those ≥60 years (3.3%) than <60 (1.2%), in those with a history of heart failure (11.7%), previous stroke (7.9%), myocardial infarction (7.2%), or diabetes (4.0%) ($p<0.0001$ for all). After age and sex standardisation, 44.5% and 32.3% of those with and without AF, respectively, had co-existing hypertension ($p<0.0001$). Of participants with 'known' AF, 31.3%, 25.2% and 43.6% were taking anticoagulants, aspirin, or either, respectively. Adjusted higher odds of AF detection were observed in those with fewer years of education, established CVD or diabetes, and an increased alcohol intake.

Discussion. Simultaneous BP and AF screening in MMM 2022 and 2023 detected AF in 1.9% of participants with 42.1% new cases (untreated). AF detection was more common with increasing age and with cardiometabolic conditions.

P600

Neuroinflammation without Hypoxia, and Brain Injury Biomarkers after Cardiopulmonary Bypass in Sheep

Dr. Taku Furukawa

Biography:

Dr. Taku Furukawa is a PhD candidate at the Florey Institute of Neuroscience and Mental Health, University of Melbourne and a dual-trained intensivist and anaesthetist. He is completing his PhD under the supervision of Prof. Yugeesh Lankadeva, Prof. Clive May, Dr. Connie Ow, and the late Prof. Rinaldo Bellomo. His research focuses on the mechanisms of acute kidney and brain injury arising from cardiac surgery and sepsis, aiming to develop novel diagnostics and therapeutics. He received the Best Oral Presentation Award at the Hypertension Australia ASM 2023 and represented the society at the British and Irish Hypertension Society meeting in 2024.

Neuroinflammation without Hypoxia and Brain Injury Biomarkers after Cardiopulmonary Bypass

Taku Furukawa[1], Alemayehu H Jufar[1], Anton Trask-Marino[1], Clive N May[1], Sally G Hood[1], Pei Chen Connie Ow[1], Lindsea Booth[1], Yugeesh R Lankadeva[1], 1. Trans Cardiovasc Renal Res, The Florey, The Univ of Melb, Parkville, VIC, Australia.

Introduction. Delirium occurs in ~50% of patients undergoing cardiopulmonary bypass (CPB) in the first 48-h postoperative period. Cerebral hypoxia and neuroinflammation have been proposed as important contributing factors, but their duration and severity after CPB remain unclear. Furthermore, blood biomarkers for early detection or prognostication are not yet established, and their direct relationship with histological injury remains unknown.

Aims. To investigate the effects of CPB on cerebral microcirculation, neuroinflammation, and blood biomarkers of neurological injury over a postoperative period of up to 4 weeks in a clinically relevant sheep model

Methods. Healthy adult merino ewes underwent CPB for 2 h and were recovered for either 48 h (n=8) or 4 weeks (n=8). Frontal cortical tissue oxygen tension (PO_2) was monitored before, during, and after CPB. Neuroinflammation was quantified by morphometric analyses of microglia and astrocytes in the frontal cortex in both CPB groups and healthy naïve controls (n = 5). Plasma neurofilament light chain (NfL; neuronal injury marker) and glial fibrillary acidic protein (GFAP; astrocyte injury marker) were measured at baseline, 2-h of CPB, and 24 h and 48 h post-CPB.

Results. Compared with baseline, cerebral PO_2 did not change at 48-h or over 4-weeks post-CPB. Compared with controls, at 48 h post-CPB, there was microglial activation characterised by increased number of microglia (mean ± SD, 54 ± 3 vs 71 ± 3 cells, $P < 0.001$) and reduced sphericity (0.83 ± 0.01 vs 0.79 ± 0.02, $P < 0.05$). Astrocyte reactivity was characterised by increased GFAP-stained area (17 ± 2 % vs 10 ± 2 %, $P = 0.026$). At 4-weeks post-CPB, these measures did not differ from controls. Peak elevations in NfL levels (median [IQR]) occurred from 138 [96, 185] pg/mL at baseline to 198 [149, 265] pg/mL at 48 h CPB ($P = 0.0007$), while GFAP rose from 3.0 [1.3, 4.5] pg/mL at baseline to a peak at 2-h of CPB (14.4 [4.7, 32.4] pg/mL, $P < 0.0001$).

Discussion. Even in absence of tissue hypoxia, neuroinflammation in the frontal cortex was evident 48 h after CPB, which coincides with the clinical window in which cardiac surgery-associated delirium occurs. This neuroinflammatory response was accompanied by elevated blood biomarkers of neurodegeneration. Therapeutic strategies targeting neuroinflammation may help prevent CPB-related brain injury, and blood-based biomarkers such as NfL and GFAP show promise as surrogate markers for monitoring treatment efficacy in future clinical trials.

P601

Human amnion epithelial cell therapy modulates brain cell heterogeneity in experimental stroke

Mr Yeshwanth Reddy Yeraddu

Biography:

I am a final-year PhD candidate at the Centre for Cardiovascular Biology and Disease Research, led by Prof. Chris Sobey and Prof. Grant Drummond. I completed my Master's in Biomedical and Health Sciences at Monash University in 2020. My research uses single-cell and spatial transcriptomics to investigate the role of human amnionic epithelial cells (hAECs) in stroke, focusing on their neuroprotective effects and impact on cognition. I aim to investigate the effects of stroke on transcriptional changes in brain cell populations and characterize how hAECs influence recovery processes. My work incorporates advanced techniques such as the photothrombotic stroke model, neurobehavioral testing, transcriptomics, and bioinformatics tools to better understand the mechanisms underlying stroke recovery.

Human amnion epithelial cell therapy modulates brain cell heterogeneity in experimental stroke.

Yeshwanth R Yeraddu[1], David E Whong Zhang[1], Malathi I Dona[1,2], Grant R Drummond[1], Christopher G Sobey[1], Maria Jelinic[1,2] & T. Michael De Silva[1],

[1]Department of Microbiology, Anatomy, Physiology and Pharmacology, Centre for Cardiovascular Biology and Disease Research, La Trobe University[1], Melbourne, VIC, Australia. [2]Baker Heart and Diabetes Research Institute, Prahran, VIC, Australia.

Introduction. Stroke is a leading cause of death and disability worldwide. Current treatment options have a narrow therapeutic window and do not address secondary injury. Human amnion epithelial cells (hAECs) have several properties that make them a promising cell-based therapy. Ischaemic injury leads to loss of brain cells within minutes, but the transcriptional changes that occur during the delayed phase after stroke in response to hAEC therapy are unknown.

Aim. To investigate the effects of stroke and hAEC therapy on transcriptional changes in brain cell populations using single-cell transcriptomics.

Methods. Male and female C57Bl6 mice (14-18 weeks, *n*=3 per group) underwent sham or photothrombotic stroke surgery targeting the prefrontal cortex and received saline or 1×10^6 hAECs intravenously 24 hours post-stroke. Five weeks after stroke, brains were collected. A 3 mm section from the infarct region was prepared for single-cell RNA sequencing. Data were quality filtered, clustered, and analysed for differential gene expression and gene ontology to identify treatment-associated molecular changes.

Results. Single-cell analysis identified 12 brain cell populations. Additionally, we identified multiple clusters in saline- or hAEC-treated mice. hAEC therapy modulated cell transcriptional profiles, with upregulation of genes related to survival, and neuroprotection, and downregulation of pro-apoptotic and inflammatory pathways. Unique cell subpopulations in the hAEC group displayed enhanced repair signatures and reduced injury markers. Gene ontology analysis supported these findings, suggesting a shift towards a reparative phenotype with hAEC treatment.

Discussion. The modulation of gene expression by hAEC treatment suggests a potential role in promoting brain repair mechanisms after stroke. Further investigation of additional brain cell populations and their interactions will be important to fully elucidate the therapeutic effects of hAECs.

P602

Cardiac surgery with cardiopulmonary bypass depletes brain ascorbate: implications for neuroprotection

Dr Alemayehu Jufar

Biography:

Dr Jufar is a postdoctoral researcher in the Translational and Cardiovascular Research at the Florey Institute of Neuroscience and Mental Health. He completed his PhD in Physiology at Monash University in 2024, where his work focused on the pathophysiology of cardiac surgery–associated acute kidney injury (CSA-AKI) and brain injury, as well as potential therapeutic approaches to reverse injury in these vital organs.

His current research investigates the safety and efficacy of sodium ascorbate as a novel therapy to mitigate cardiac surgery–associated acute brain injury and acute kidney injury. Dr Jufar has published more than 16 papers in high-quality peer-reviewed journals.

Cardiac surgery with cardiopulmonary bypass depletes ascorbate in the brain: Implications for neuroprotection

Alemayehu H. Jufar[1], Clive N. May[1], Taku Furukawa[1], Roger G. Evans[1], Andrew D. Cochrane[1], Jaishankar Raman[2], Peter R. McCall,[2] Sally G. Hood,[1] Lachlan F. Miles[2], Yugeesh R. Lankadeva[1]. 1. Trans Cardiovasc Renal Res, Florey Inst 2. Dept of Crit Care, The Univ of Melbourne, Melbourne, VIC, Australia

Introduction. Cardiac surgery requiring cardiopulmonary bypass (CPB) is frequently complicated by postoperative acute brain injury. Intraoperative cerebral neuroinflammation, driven by microglial activation, has been proposed as a key mediator of cardiac surgery associated brain injury. Vitamin C (ascorbate) plays a critical neuroprotective role in the brain by acting as a potent antioxidant, reducing oxidative stress, regulating microglial activation, preserving blood–brain barrier integrity, and supporting neurotransmitter synthesis. However, the effects of CPB on the temporal kinetics of cerebrospinal fluid (CSF) and plasma ascorbate concentrations remain unclear.

Aims. To investigate the temporal kinetics of CSF and plasma ascorbate concentrations in a clinically relevant ovine model of CPB before, during, and after surgery.

Methods. Eight sheep were anesthetized and instrumented with a lateral ventricle guide tube for serial CSF sampling, and the carotid artery was cannulated for blood collection. CSF and plasma ascorbate concentrations were measured at baseline (conscious, pre-CPB), after 2 h of CPB (median duration in humans), and at 24 h and 48 h postoperatively (clinical window for brain injury development in humans).

Results. CSF concentrations of ascorbate were markedly higher at baseline compared with plasma ascorbate levels (166.1 ± 2.3 µmol/L vs. 20.6 ± 2.4 µmol/L; $p < 0.001$). Compared with baseline, CSF ascorbate concentrations were significantly reduced after 2 h of CPB (166.1 ± 2.3 vs. 132.1 ± 7.7 µmol/L, n = 5, $p = 0.04$), following which it returned back to baseline levels at 24-h (to 155.0 ± 14.5 µmol/L; $p = 0.77$) and 48-h (to 150.2 ± 9.6 µmol/L; $p = 0.42$) postoperatively. In contrast, plasma ascorbate concentrations remained unchanged during CPB and throughout the postoperative period.

Discussion. In a clinically relevant large animal model of CPB, the ascorbate concentrations in CSF were 8-fold higher than in circulating blood. CSF ascorbate levels were depleted after CPB while plasma levels were preserved. Reduced CSF ascorbate may reflect enhanced utilisation and turnover in response to neuroinflammation in the brain. These findings highlight a potential therapeutic role for intravenous sodium ascorbate in mitigating CPB-associated neuroinflammation and postoperative brain injury.

P603

Long-term outcomes with RDN in ESC-guideline recommended patients from the Global SYMPLICITY-Registry

Professor Markus Schlaich

Biography:

Prof Markus Schlaich is a renal physician and a European Society of Hypertension (ESH) accredited hypertension specialist. Markus is Chair of Hypertension Australia and Co-Chair of the National Hypertension Taskforce. He has a strong background in clinical research with a focus on the pathophysiology of hypertension, the role of the sympathetic nervous system, involvement of the kidneys, and hypertension mediated organ damage. He has a specific interest in treatment modalities targeting the sympathetic nervous system and has been a pioneer of renal denervation and other interventional and pharmacological approaches to treat hypertension. He has authored more than 500 articles in peer reviewed journals and serves on the Editorial Board of Hypertension, Journal of Hypertension, and Hypertension Research.

Long-term outcomes with RDN in ESC-guideline recommended patients from the Global SYMPLICITY-Registry

Markus P Schlaich[1,2], Gianni Sesa-Ashton[3], Felix Mahfoud[4], Roland Schmieder[5], Krzysztof Narkiewicz[6], Bryan Williams[7], Michael Böhm[8]. Dobney Hypertension Centre, Medical School, The University of Western Australia[1] and Departments of Cardiology and Nephrology, Royal Perth Hospital[2], Perth, WA, Australia; Baker Heart and Diabetes Institute[3], Melbourne, VIC, Australia; Department of Cardiology, University Hospital Basel[4], Basel, Switzerland; University Hospital Erlangen[5], Erlangen, Germany; Medical University of Gdansk[6], Gdansk, Poland; University College London[7], London, United Kingdom; Saarland University Hospital[9], Homburg, Germany

Introduction. Recent ESC guidelines recommend that renal denervation (RDN) should be considered in 2 groups of patients: 1) those with an elevated office (BP) ≥140/90 mmHg despite using 3+ antihypertensive (AH) medications or 2) in HTN patients on <3 AH medications but with high CV disease risk.

Aims. To investigate 3-year outcomes in ESC guideline-recommended patients from the Global SYMPLICITY Registry.

Methods. Enrolled patients (n=3,615) underwent radiofrequency (RF) RDN using either the first-generation Symplicity Flex or latest-generation Spyral catheter. Office blood pressure (BP), 24-h ambulatory BP, medications, and adverse events were recorded at each follow-up.

Results. Among patients with an elevated BP and taking 3+ AH medications (n=2,703), the mean age was 60±12y, 41.9% were female, mean BMI was 31±6 kg/m^2, 11.8% had AF, 42.2% had diabetes mellitus, and 47.6% had cardiac disease. They were prescribed an average of 4.9±1.3 AH medications. Mean baseline office systolic BP was 170.3±21.6 mmHg (n=2,703), whereas baseline 24-h ambulatory systolic BP was 155.7±18.4 mmHg (n=1,886). Mean baseline eGFR was 76.3±25.7 mL/min/1.73m^2. At 3 years (y), an office systolic BP change of -20.6±26.8 mmHg (n=1,132; p<0.0001 from baseline) and a 24-h ambulatory systolic BP change of –10.0±20.9 mmHg (n=452; p<0.0001) was evident. These patients were prescribed an average of 4.7±1.6 antihypertensive (AH) medications by 3 y. Mean eGFR at 3 y was 68.5±26.2 mL/min/1.73m^2. At 3 y, the adverse event rates were 5.8% for death, 3.0% for CV death, 2.5% for myocardial infarction. Further results will be presented from data collected through August 2025, as well as in ESC-guideline recommended patients at high CVD risk but taking <3 AH medications.

Discussion. Long-term results from GSR DEFINE continue to support the durable efficacy and safety of RDN in ESC-guideline recommended patients. The efficacy of RDN in reducing CV events needs further investigation.

P604

Effect of a Novel Triple Single-Pill Combination on Systolic Blood Pressure Variability

Dr Tian Wang

Biography:

Dr Wang is a Research Fellow at The George Institute for Global Health and an Accredited Practising Dietitian. She holds Conjoint Senior Lecturer and Adjunct Senior Lecturer positions at UNSW and the University of Sydney. Her PhD investigated plant-based diets and cardiovascular health, and her research has since broadened to scalable, multidisciplinary interventions combining nutrition and blood pressure–lowering therapies.

Her current work focuses on reducing blood pressure variability through novel approaches, including single-pill combination therapies and potassium-enriched salt. She has published in leading journals such as the European Heart Journal and was recently named a Prize Finalist at the Cardiac Society of Australia and New Zealand 2025.

At this conference, Dr Wang will present findings on the effect of a novel triple-pill combination compared with dual therapies on blood pressure variability.

Effect of a Novel Triple Single-Pill Combination on Systolic Blood Pressure Variability

Tian Wang[1], Stephen Van Der Hoorn[1], Sonali Gnanenthiran[1], Anthony Rodgers[1], Aletta E. Schutte[1]. [1]The George Institute for Global Health, Sydney, NSW, Australia

Introduction. The effect of which BP lowering therapies are most effective in reducing systolic BP variability (SBPV) remains unclear.

Aims. To evaluate the effect of a novel triple single-pill combination (SPC), Widaplik (containing telmisartan [T], amlodipine [A], and indapamide [I]), compared with placebo and dual therapies (TI, TA, AI) on SBPV.

Methods. Individual patient data from two randomized controlled trials were analysed: (1) a placebo-controlled trial (PCT, n=295) investigated the efficacy of two doses of Widaplik (¼ and ½) versus placebo over 4 weeks; and (2) an active-controlled trial (ACT, n=1385) compared standard-dose Widaplik with dual therapies over 12 weeks. BPV was assessed from home BP (HBP) measurements using the coefficient of variation (CV).

Results. A total of 1584 participants (mean age: 58 years; 52% female) with ≥2 HBP readings were included. In the PCT, no difference in CV was observed between Widaplik ½ dose and placebo, but Widaplik ¼ dose showed a higher CV (+1.11, CI: 0.01, 2.21) compared with placebo at Week 4. In the ACT, no significant between-group differences were observed between Widaplik, AI, TI and TA.

Discussion. In patients with mild-to-moderate BP elevation, no significant between-group differences were observed between Widaplik ½ and placebo, or between standard-dose Widaplik and dual therapies (AI, TA, TI).

Comparison	Between group difference (95% CIs), p-value
Widaplik ¼ Placebo	1.11 (0.01, 2.21), p=0.047
Widaplik ½ Placebo	0.12 (-0.98, 1.22), p=0.83
Widaplik AI	0.05 (-0.47, 0.57), p=0.85
Widaplik TA	-0.19 (-0.70, 0.33), p=0.48
Widaplik TI	0.02 (-0.49, 0.54), p=0.92

P605

Left ventricular mass regression following transcatheter aortic valve implantation: the arterial link

Dr Audrey Adji

Biography:

Dr. Audrey Adji is a research scientist at the Victor Chang Cardiac Research Institute and a research fellow at St Vincent's Hospital, Sydney. Her work explores pulsatile function in cardiovascular and pulmonary diseases, including mechanical circulatory support devices in heart failure. She has authored >80 peer-reviewed publications, presented at international conferences, and fostered collaborative research networks. Dr. Adji has received multiple scientific awards and serves on editorial boards of hypertension journals. She mentors postdoctoral fellows and supervises higher degree students across medicine and engineering. As Chair of the Women in Hypertension (Research) Committee at Hypertension Australia and the Early Career Research Network of Pulse of Asia, she advocates for equity and emerging researchers. She is a member of the Hypertension Australia Taskforce and a Fellow of both the International Society of Hypertension and the Cardiac Society of Australia and New Zealand. Dr. Adji actively cultivates national and global research partnerships.

Left ventricular mass regression following transcatheter aortic valve implantation: the arterial link

Jack Hall[1], Ning Song[1,2], Audrey Adji[1,2,3] St Vincent's Centre for Applied Medical Research[1], Sydney, NSW; Faculty of Medicine[2], UNSW, Sydney, NSW; Victor Chang Cardiac Research Institute[3], Sydney, NSW

Introduction. Left ventricular mass index (LVMi) regression following transcatheter aortic valve implantation (TAVI) for aortic stenosis (AS) predicts improved outcomes. The arterial contribution to LVMi reverse remodelling post-TAVI remains poorly characterised.

Parameter	Regressors (n=9)			Non-regressors (n=11)			p-value* (between group change)
	Baseline	Post-TAVI	Change	Baseline	Post-TAVI	Change	
LVMi (g/m²)	83±20	66±13	-17±7	73±17	76±22	+3±5	<0.001
Zva-INS (dynes·s·cm⁻⁵)	194±58	138±46	-56±35	183±61	188±103	+5±59	0.012
Zc (dynes·s·cm⁻⁵)	138±60	107±36	-31±24	105±30	109±45	+4±15	0.086
Zva (mmHg·mL⁻¹·m²)	4.5±2.4	3.0±0.37	-1.5±2.0	4.3±1.3	3.0±1.0	-1.3±0.3	0.783
PP (mmHg)	58±21	55±12	-3.5±18	48±17	62±19	+14±16	0.032

Aims. To determine whether persistent arterial impedance may limit LVMi reverse remodelling post-TAVI.

Methods. We assessed severe AS patients using simultaneous cardiac MRI and radial applanation tonometry derived aortic pressure with same day echocardiography at baseline (BL) and follow up. Reverse remodelling was defined as a ≥10% LVMi reduction on MRI. Parameters assessed were aortic characteristic impedance (Zc), echocardiographic valvulo-arterial impedance (Zva), MRI derived instantaneous valvulo-arterial impedance (Zva-INS) and aortic pulse pressure (PP) from radial applanation tonometry. All values are mean±SD.

Results. Twenty patients (80±7years, 40% female) were followed up at a median 60 days (IQR 40-119) post TAVI. Nine (45%) achieved relevant reverse remodelling. BL age, BMI, sex, and HR were well matched between groups, as were improvements in valve area, mean gradient and stroke volume on echocardiography (all p>0.10). Despite comparable BL values, post-TAVI Zva-INS diverged significantly: those with LVMi regression showed substantial reductions (p<0.01); non-regressors rose. Zc also showed opposing trajectories between groups, falling from an elevated BL in regressors but rising in non-regressors. PP decreased in regressors but increased significantly in non-regressors (BL vs post TAVI p=0.01). Echocardiographic Zva improved similarly in both groups.

Discussion. Persistent arterial impedance may prevent LVMi regression post-TAVI. Arterial assessment beyond valvular evaluation alone may identify patients requiring adjunctive vascular therapy for optimal myocardial recovery.

P606

The Role of Arterial Stiffness in Hypertensive Post Heart Transplantation Patients

Dr Audrey Adji

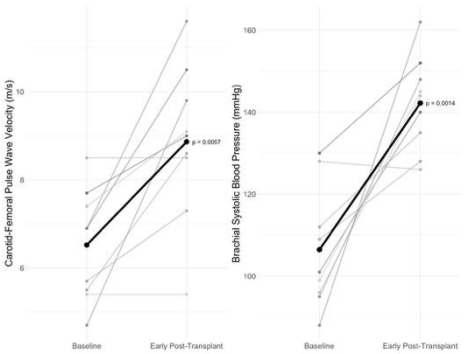
Biography:

Dr. Audrey Adji is a research scientist at the Victor Chang Cardiac Research Institute and a research fellow at St Vincent's Hospital, Sydney. Her work explores pulsatile function in cardiovascular and pulmonary diseases, including mechanical circulatory support devices in heart failure. She has authored >80 peer-reviewed publications, presented at international conferences, and fostered collaborative research networks. Dr. Adji has received multiple scientific awards and serves on editorial boards of hypertension journals. She mentors postdoctoral fellows and supervises higher degree students across medicine and engineering. As Chair of the Women in Hypertension (Research) Committee at Hypertension Australia and the Early Career Research Network of Pulse of Asia, she advocates for equity and emerging researchers. She is a member of the Hypertension Australia Taskforce and a Fellow of both the International Society of Hypertension and the Cardiac Society of Australia and New Zealand. Dr. Adji actively cultivates national and global research partnerships.

The Role of Arterial Stiffness in Hypertensive Post Heart Transplantation Patients

Ezra Ng[1], Ning Song[1,2], Audrey Adji[1,2,3]

1. St Vincent's School of Clinical Medicine, UNSW; 2. St Vincent's Hospital; 3. Victor Chang Cardiac Research Institute, Sydney, NSW



Introduction. Arterial stiffness predicts cardiovascular mortality, but its role in post heart transplant hypertension is unclear.

Aims. To assess whether baseline arterial stiffness predicts blood pressure post-transplant response by evaluating pre-transplant carotid-femoral pulse wave velocity (cf-PWV) and pulse wave analysis (PWA).

Methods. From March-August 2025, we performed paired PWA and cf-PWV measurements in end-stage heart failure patients pre- and post-transplant using the Sphygmocor XCEL®. Paired t-tests and linear regression were used for statistical analysis.

Results. Of 26 participants that underwent baseline measurements, 9 participants (56.4±6.3 years, 8 males/1 female) had post-transplant measurement at median 6.0 days (IQR:6.0–9.0). At post-transplant, mean brachial systolic pressure (BSP) was 142.2±11.5mmHg (standard deviation - SD) and mean cf-PWV 8.87±1.79m/s (SD). The post-transplant BSP increased by 35.8mmHg (95%CI: 18.4–53.1mmHg, p=0.001), and cf-PWV increased by 2.34m/s (95%CI: 0.90–3.79m/s, p=0.006) (see figure). While no association was found with post-transplant change in BSP (r=-0.32, p=0.44), higher baseline cf-PWV predicted a smaller increase in central systolic pressure (CSP) (β=–10.9mmHg per 1 m/s, r=–0.67, p=0.047), and smaller increases in mean pressure (β=–10.1mmHg per 1 m/s, r=–0.83, p=0.006). Similarly, higher brachial baseline systolic pressures were associated with smaller increases in systolic pressure post-transplant for both brachial (β=–1.4mmHg per 1mmHg BSP, r=–0.90, p=0.001) and central measures (β=–1.2mmHg per 1mmHg BSP, r=–0.89, p=0.001).

Discussion. Higher baseline cf-PWV values predicted smaller increases in central systolic pressure post-transplant, suggesting patients with increased arterial stiffness pre-transplant may have less hypertension response post-transplant. The study was limited by small sample size, and recruitment is ongoing.

P607

Impact of dialysis on cardiovascular, cerebrovascular and renovascular hemodynamics in sepsis

Dr Munenori Kusunoki

Biography:

Dr. Munenori Kusunoki is a dual-trained anaesthesiologist and intensive care physician. He earned his medical degree in 2010 and completed a PhD at Kansai Medical University in 2020, studying the effects of hypoxia on organ injury and metabolism, and the impact of anaesthetics on insulin secretion. He currently serves as an Assistant Professor at Kansai Medical University Hospital, teaching medical students and fellows, and providing anaesthesia and intensive care for approximately 2,500 patients annually. He has published 16 peer-reviewed articles and received multiple awards and research grants.

In May 2024, he joined the Translational Cardiovascular and Renal Research Group at the Florey Institute of Neuroscience and Mental Health in Australia as a Clinician Research Fellow. His research focuses on haemodynamics and organ injury in sepsis-associated acute kidney injury requiring continuous renal replacement therapy. His overarching goal is to improve cardiovascular, brain, and kidney outcomes in critically ill patients.

Impact of dialysis on cardiovascular, cerebrovascular and renovascular hemodynamics in sepsis

Munenori Kusunoki[1], Taku Furukawa[1], Jonathan Nübel[1,2], Connie P C Ow[1], Clive N May[1], Yugeesh R Lankadeva[1]. 1. Translational Cardiovascular and Renal Research Group, Florey Institute of Neuroscience and Mental Health, Univ of Melbourne, Parkville, VIC, Australia. 2. Dept of Intensive Care, Austin Hosp, Heidelberg, VIC, Australia.

Introduction. Sepsis is a life-threatening condition that often leads to cardiovascular failure and sepsis-associated acute kidney injury (SA-AKI), which is associated with high mortality and prolonged hospitalisation. Continuous renal replacement therapy (CRRT), a form of dialysis, is widely used to support renal function for SA-AKI in intensive care units. However, the effects of CRRT on cardiovascular, cerebrovascular and renovascular hemodynamics are unclear.

Aims. To assess the effects of CRRT on cardiovascular function and on microcirculation in the brain and kidneys in a sheep model of SA-AKI.

Methods. Adult female sheep (n = 16) were induced with sepsis with intravenous (iv) infusion of live *Escherichia coli* for 31-h. At 23-h of established SA-AKI, sheep were randomised into two groups: sedation only or sedation with CRRT (n = 8 each). All sheep were sedated with fentanyl (5 µg/kg/h, iv), propofol (20 mg/kg/h, iv), and midazolam (0.5 mg/kg/h, iv), followed by intubation and mechanical ventilation. CRRT was applied for 4-h in the CRRT group. Systemic haemodynamics and microcirculatory perfusion and oxygenation in the frontal cortex, renal cortex and renal medulla were recorded. Noradrenaline was titrated to maintain a mean arterial pressure (MAP) of 70 mmHg after sedation.

Results. At 23 h following *Escherichia coli* infusion, SA-AKI was characterised by reduced MAP (91.47 ± 2.34 to 77.98 ± 2.96 mmHg; $P < 0.001$), increased arterial blood lactate (0.54 ± 0.05 to 1.56 ± 0.34 mmol/L; P=0.0389) and increased serum creatinine levels (70.50 ± 5.63 to 129.5 ± 19.67 µmol/L; P=0.0994). CRRT did not alter perfusion or oxygenation in the frontal cortex, renal cortex and renal medulla. Following sedation, septic sheep undergoing CRRT required higher doses of noradrenaline to maintain target MAP of 70 mmHg compared with those who underwent sedation alone (0.28 ± 0.02 vs. 0.54 ± 0.04 µg/kg/min, p=0.0309).

Discussion. In a clinically relevant sheep model of SA-AKI, CRRT did not enhance cerebral or renal perfusion or oxygenation but was associated with increased vasopressor requirements. These findings suggest that, in the acute phase of septic AKI, the cardiovascular hemodynamic instability of CRRT may offset potential benefits, emphasizing the importance of optimizing timing and patient selection when initiating CRRT in critically ill patients.

P608

Willingness to take preventive medication for cardiovascular disease relates to self-perceived risk

Prof James Sharman

Biography:

James is a professor of medical research at the Menzies Institute for Medical Research, Hobart. He heads the Blood Pressure Research Group and is former Deputy Director of the Institute.

Willingness to take preventive medication for cardiovascular disease relates to self-perceived risk

James E Sharman[1], Katherine Chappell[1], Niamh Chapman PhD[1,2], Alison J. Venn[1], Mark R. Nelson[1]. Menzies Institute for Medical Research, University of Tasmania, Hobart, TAS, Australia.[1] School of Health Sciences, University of Sydney, Sydney, NSW, Australia.[2]

Introduction. Guidelines recommend using preventive medications (cholesterol-lowering and antihypertensives) for cardiovascular disease (CVD) in high-risk patients. However, this does not routinely occur for many reasons, including patient attitudes to taking medication. Little is known on willingness to take medication based on self-perceived risk before detailed information on risks and benefits is provided.

Aims. To determine whether patient attitudes on willingness to take preventive medication for CVD is related to self-perceived CVD risk.

Methods. Study participants were 1577 treatment naive adults (61% females; mean (SD) age 60.6 (8.9) years) enrolled in a CVD-related trial who had their 5-year absolute CVD risk (Framingham) calculated at baseline and were followed over 12 months to determine adherence to guideline-recommended treatment (dispensing of both cholesterol-lowering and antihypertensive medications) in people at high CVD risk. All participants completed a baseline survey in which they rated their self-perceived 5-year risk of a heart attack or stroke (low, moderate, high) and willingness to take a daily pill recommended by their doctor to reduce their risk of heart attack or stroke (not-, maybe-, probably-, almost certainly-willing). At the time of the survey, participants were not aware of their calculated 5-year CVD risk.

Results. Participants who perceived themselves to be at high-risk of heart attack or stroke had a higher prevalence of willingness (probably- or almost certainly-willing) to take a daily pill compared to those with self-perceived moderate or low risk (78% vs 56% and 46%, respectively). This baseline intention was corroborated in the 12-month follow up of 162 participants at high-risk, in which there was a higher prevalence of taking both cholesterol-lowering and antihypertensive medications in those expressing higher baseline willingness (probably- or almost certainly-willing) to take a daily pill compared to those not willing or unsure about taking a daily pill (25% vs 9%, RR=2.6, p=0.008).

Discussion. People who perceive themselves to be at high-risk for CVD may be more willing and more likely to take preventive medication for CVD. This emphasises the importance of patient education on the benefits of preventive medication for CVD in high-risk people.

P609

Creating evidence-based personas to illuminate hypertension journeys and guide education strategies

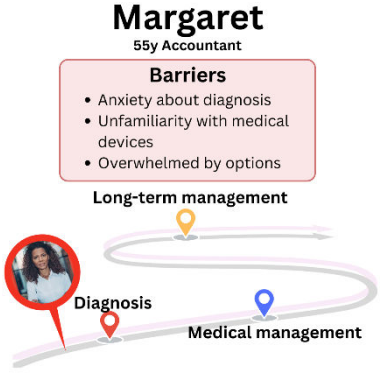
Dr Kaylee Slater

Biography:

Dr Kaylee Slater is a Postdoctoral Research Fellow and at the University of Sydney, with a strong focus on cardiovascular disease prevention and blood pressure management. Kaylee has led and contributed to numerous co-design and consumer involvement projects, developing patient education strategies tailored to diverse populations. Her research spans the care continuum, exploring hypertension management from both patient and healthcare professional perspectives. Kaylee uses qualitative methods to understand lived experiences and systemic barriers, informing evidence-based interventions. Her work integrates patient voices into clinical and educational frameworks, aiming to improve outcomes and engagement in primary care. Additionally, her current research includes a randomised controlled trial to improve blood pressure care in pharmacies and sex-specific blood pressure education for high risk women. She is also an Accredited Practising Dietitian with clinical experience in fertility and pregnancy nutrition.

Creating evidence-based personas to illuminate hypertension journeys and guide education strategies

Kaylee Slater[1], Eleanor Clapham[2], Elizabeth Halcomb[3], Ben Kostyrka[4], Lisa Kouladjian O'Donnell[1], Florence Lopez[1], Mitchell Sarkies[1], Gautam Satheesh[1, 4], Mouna Sawan[1], Aletta E Schutte[4,5], Catherine Stephen[3], Ritu Trivedi[1], Niamh Chapman[1,2]. [1]Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia; [2]Menzies Institute for Medical Research, University of Tasmania, Australia; [3]Faculty of Science, Medicine and Health, University of Wollongong, Wollongong, NSW, Australia; [4]The George Institute of Global Health, Sydney, NSW, Australia; [5]School of Population Health, UNSW Sydney, Sydney, NSW, Australia.



Introduction: Effective hypertension management relies on patient education, yet it is often poorly delivered. Understanding patient preferences is critical to developing timely, tailored, and person-centred education.

Aim: Identify leverage points and behavioural and cultural factors that influence the delivery and uptake of patient education for primary hypertension in primary care.

Methods: Qualitative study using semi-structured interviews with adults in Australia who self-monitor blood pressure (n=27), and with general practitioners, nurses, and pharmacists involved in hypertension care (n=12). Initial inductive coding identified themes related to the hypertension journey, including key time points, behavioural barriers, and enablers. Themes were then mapped to the capability, opportunity, motivation (COM-B) framework. Patient personas were developed by synthesising behavioural patterns across COM-B domains, informed by insights from both patient and practitioner interviews.

Results: Unique behavioural barriers and enablers to patient education emerged across key stages of hypertension management including diagnosis, treatment initiation, and long-term care. Barriers included feeling overwhelmed, inconsistent guidance, and clinician assumptions about motivation, while a strong desire to self-manage was a consistent enabler. Six distinct patient personas were developed, each reflecting different responses to these barriers and enablers, highlighting diverse needs and opportunities for tailored education strategies.

Discussion: These personas reflect the complexity of hypertension management and highlight gaps in education. They offer a practical tool for designing person-centred interventions to reduce disparities in primary care.

P610

Developing implementation strategies to improve patient education for blood pressure in Australian

Dr Kaylee Slater

Biography:

Dr Kaylee Slater is a Postdoctoral Research Fellow and at the University of Sydney, with a strong focus on cardiovascular disease prevention and blood pressure management. Kaylee has led and contributed to numerous co-design and consumer involvement projects, developing patient education strategies tailored to diverse populations. Her research spans the care continuum, exploring hypertension management from both patient and healthcare professional perspectives. Kaylee uses qualitative methods to understand lived experiences and systemic barriers, informing evidence-based interventions. Her work integrates patient voices into clinical and educational frameworks, aiming to improve outcomes and engagement in primary care. Additionally, her current research includes a randomised controlled trial to improve blood pressure care in pharmacies and sex-specific blood pressure education for high risk women. She is also an Accredited Practising Dietitian with clinical experience in fertility and pregnancy nutrition.

Developing implementation strategies to improve patient education for blood pressure in Australian

Kaylee Slater[1], Eleanor Clapham[2], Elizabeth Halcomb[3], Ben Kostyrka[4], Lisa Kouladjian O'Donnell[1], Liliana Laranjo[1], Mitchell Sarkies[1], Gautam Satheesh[1, 4], Mouna Sawan[1], Aletta E Schutte[4,5], Catherine Stephen[3], Ritu Trivedi[1], Niamh Chapman[1,2]. [1]Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia; [2]Menzies Institute for Medical Research, University of Tasmania, Australia; [3]Faculty of Science, Medicine and Health, University of Wollongong, Wollongong, NSW, Australia; [4]The George Institute of Global Health, Sydney, NSW, Australia; [5]School of Population Health, UNSW Sydney, Sydney, NSW, Australia.

Introduction: Hypertension affects over 6.8 million Australians, yet patient education in primary care remains inconsistent and opportunistic. While effective education improves hypertension management, it is not routinely delivered, and there is limited guidance to support its implementation in practice.
Aim: Develop and prioritise implementation strategies for the delivery of patient education to support BP management.
Methods: Initial implementation strategies were developed using the Expert Recommendations for Implementing Change framework to address common barriers and enablers to patient education for hypertension management. These were refined during a three-hour in-person action-learning workshop with primary care professionals and industry representatives (n=21). Participants were grouped by profession and assigned a patient persona and scenario. Through structured activities, they identified implementation barriers, refined strategies using guided prompts, presented and received group feedback, and delivered final refined pitches. Strategies were then ranked by feasibility, impact, and cost-effectiveness using participatory voting. Qualitative data were analysed thematically and voting data descriptively.
Results: Six implementation strategies were refined, each targeting a different stage of hypertension management: (1) pharmacist-led education at device purchase using a structured protocol; (2) general practitioner consultations using a digital BP education platform with nurse follow-up; (3) nurse-led drop-in group sessions with home BP monitors; (4) nurse-led group education on interpreting readings with general practitioner follow-up; (5) nurse-led lifestyle planning with allied health referrals; and (6) pharmacist-delivered BP measurement and medication review. Pharmacy-based strategies (1) ranked highest for feasibility and impact, and (6) for cost-effectiveness.
Discussion: This study identified strategies that show promise for improving hypertension education in primary care and will inform practical guidance, with further research needed to assess their impact on BP outcomes.

P612

Aus-Can Do It: A framework for hypertension guidelines collaboration between Hypertension Canada&Australia

Prof Ross Tsuyuki

Biography:

Dr. Ross Tsuyuki is a Professor of Medicine (Cardiology) and Director of the EPICORE Centre (a health research coordinating centre) at the University of Alberta and is the Editor-in-Chief of the Canadian Pharmacists Journal. Having previously served on Hypertension Canada's Board of Directors, Dr. Tsuyuki was elected in 2019 and appointed Vice-President. He also serves as a Chair of the Education & Implementation Committee and is a member of the Hypertension Canada Guidelines Committee. Dr. Tsuyuki's interests are in clinical trials design and execution, hypertension, heart failure, community practice-based research, cardiovascular risk factors, and in the provision of support for clinical researchers through the EPIRCORE Centre. Dr. Tsuyuki has received several awards for teaching, as well as an appointment as a Fellow of the Canadian Society of Hospital Pharmacists, the American College of Cardiology and the Canadian Academy of Health Sciences. In 2005, he was recognized as the Canadian Pharmacist of the Year by the Canadian Pharmacists Association and the International Society of Hypertension.

Aus-Can Do It: A framework for hypertension guidelines collaboration between Hypertension Canada and Hypertension Australia

Ross T. Tsuyuki[1,2], Remi Goupil[1,3], Gregory Hundemer[1,4], Garry Jennings[5,6], Markus Schlaich[5,7]. [1]Hypertension Canada; [2]Dept of Medicine, University of Alberta, Edmonton, AB, Canada, [3]Dept of Medicine, Hôpital du Sacré-Coeur de Montréal, Université de Montréal, Montréal, QC, Canada; [4]Dept of Medicine, University of Ottawa, Inflammation and Chronic Disease Program, Ottawa Hospital Research Institute, Ottawa, ON, Canada; [5]Hypertension Australia; [6]Heart Foundation; [7]University of Western Australia, Dobney Hypertension Centre Royal Perth Hospital.

Introduction: Hypertension guidelines are important to guide clinical care, but proper guideline preparation is very resource intensive. And, does each country need to duplicate efforts? Australia and Canada share similar population demographics, culture and core values and it makes sense to work together on hypertension guidelines.

Aims: To develop a framework for countries to share resources and work together towards unified hypertension guidelines.

Methods: Several meetings were held between Hypertension Australia (HA) and Hypertension Canada (HC). Our principles of collaboration included:

- We will use the latest guidelines for guidelines, e.g., GRADE. ADAPTE, and AGREE II
- Shared effort and costs of evidence syntheses
- Ultimate goal of creating unified guidelines, with the understanding that HA and HC might have some different needs. As such, it is possible that not all guidelines topics will be jointly done.
- Incorporate patients' voices
- Promote team-based care

Process: We created a priority setting exercise wherein we surveyed our stakeholders to identify the most important topics for review. HA and HC steering committee members met in June to review the results and plan the next steps.

Results: Both countries identified an immediate need for some foundational work. For HC, that was in the form of a Primary Care Guideline. For HA, this will be guidance on diagnostic and treatment thresholds, targets, first-line therapies and behavioural/lifestyle interventions.

The results of the priority setting exercise identified resistant hypertension as a common priority and this will be the first joint guideline exercise. Both countries will appoint an expert lead for resistant hypertension. To encourage consistency and efficiently drive the processes, we will develop terms of reference for the guidelines committees, and templates for creating focused evidence synthesis questions and guidelines documents. Once completed, the guidelines will be posted on the HA and HC websites, as well as jointly published.

Discussion: This represents a new, novel, and efficient model for collaboration between countries. Given the challenges of resource constraints and the urgency to improve hypertension care, it makes sense to work together.

P613

Global Gaps in Hypertension Care Across 199 Countries: Advancing Task-Sharing and Innovation

Dr Shiva Raj Mishra

Biography:

Dr. Shiva Raj Mishra is a global health researcher and epidemiologist specializing in cardiovascular health, health equity, and implementation science. Currently a Senior Research Fellow at the School of Medicine, Western Sydney University, he focuses on cardiovascular prevention and management at the primary care and community settings. Dr. Mishra earned his PhD in Epidemiology from the University of Queensland, where he was a Global Change Scholar. His research integrates causal inference, health data science, and policy evaluation, with a focus on low-income settings. Dr. Mishra has held positions at the University of Melbourne and served as a visiting scholar at Harvard Medical School. He is also affiliated with the Nepal Development Society and the World Heart Federation. Driven by personal experiences with non-communicable diseases in his family, Dr. Mishra is committed to advancing equitable healthcare solutions globally.

Global Gaps in Hypertension Care Across 199 Countries and Territories: Advancing Task-Sharing and Innovation

Shiva Raj Mishra PhD[1], Gautam Satheesh PharmD[2,3], Dean S. Picone PhD[3], Niamh Chapman PhD[3], Aletta E. Schutte PhD[2,4]. School of Medicine, Western Sydney University[1];The George Institute of Global Health, NSW, Australia[2];School of Health Sciences, The University of Sydney, NSW, Australia[3]; School of Population Health, The University of New South Wales, NSW, Australia[4]

Background: This study estimates the overall gaps between health system capacity provided by physician and non-physician providers (nurses, pharmacists, community health workers) and patients' needs for hypertension. management, with stratification based on the regional economy.
Methods: We extracted data on population, physician and non-physician provider density (nurses, pharmacists, community health workers) per 10,000 people from the World Bank Databases for 199 countries and territories in 2021. We estimated three scenarios for patient need to visit a clinic for hypertension management: 12, 6 and 3 visits per patient per year, and two scenarios based on health worker capacity to provide clinic services: 20, and 10 patients per provider.
Results: The overall prevalence of hypertension was 37.5 (SD=6.6%): 36.2 (7.0%) in HIC, 40.3 (6.7) in UMIC, 36.1 (5.7%) in LMIC, and 36.7(4.8%) in LIC. Physicians (mean±SD=19.2±17.4), nurses (47.3±54.1), pharmacists (3.9±4.7) per 10,000 were higher in high income countries, while. CHWs (3.4±SD=7.3) were higher in low- and middle-income countries. All countries and territories and CHWs showed deficits in the base scenario, with deficits decreasing when switching to intermediate and minimal scenarios. In low-income countries (LICs) and LMICs, deficits persisted even with a single visit per year. Incorporating non-physicians into the hypertension workforce under the same scenario reduced these deficits, resulting in 36 countries achieving net surpluses. The largest surplus was observed in the United States (0.7 billion visits).
Conclusions: Our analysis highlights significant disparities in health service capacity for hypertension management due to physician shortages globally. Addressing these gaps requires targeted interventions, involving non-physician health workers into team-based care and leveraging innovative technologies, improving training and enhancing healthcare infrastructure, to meet the growing demand for hypertension services.

P614

Gender disparities in community-dwelling hypertensive elderly: sociodemographic and health-related factors

Dr Riana Rahmawati

Biography:

Dr. Riana Rahmawati, PhD, is a lecturer at the Faculty of Medicine, Universitas Islam Indonesia, Yogyakarta, Indonesia. She earned her medical degree and a master's degree in Drug Management and Policy from Universitas Gadjah Mada and completed her PhD in Pharmacy at the University of Technology Sydney. Her research focuses on medication adherence among hypertensive older adults and on community-based programs supporting chronic disease management, with numerous publications in esteemed journals and books. She is actively committed to enhancing medication literacy, adherence, and hypertension management in Indonesia, especially among the older adult population.

Gender disparities in community-dwelling hypertensive elderly: sociodemographic and health-related factors

Riana Rahmawati[1,2]. Pharmacology Dept, Fac of Medicine, Univ Islam Indonesia[1], Yogyakarta, Indonesia; Centre for Gender Studies, Univ Islam Indonesia[2], Yogyakarta, Indonesia

Introduction. Hypertension is highly prevalent among older adults and represents a significant public health challenge. Gender differences may influence sociodemographic profiles, comorbidities, and health behaviours (Song et al, 2020; Rezaianzadeh et al, 2024); however, evidence from community-based settings in Indonesia remains limited.
Aims. This study aimed to examine gender disparities in sociodemographic and health-related characteristics among community-dwelling older adults with hypertension.
Methods. A cross-sectional survey was conducted involving 1,147 individuals aged >60 years, of whom 434 were diagnosed with hypertension. Data were collected on sociodemographic factors (age, education, income, occupation), comorbidities, medication use, participation in elderly health posts (*posyandu lansia*), and perceived loneliness. Gender-based differences were assessed using chi-square tests.
Results. Among the 434 hypertensive older adults, 168 (38.7%) were male and 266 (61.3%) female, with a mean age of 68.3 years (SD = 6.3; range: 59–89 years). Significant gender differences were found in education (p=0.006), income status (p<0.001), occupation (p<0.001), comorbid hypercholesterolemia (p<0.001), and participation in *posyandu* activities (p<0.001). No significant differences were observed in age distribution, comorbid diabetes mellitus, comorbid heart disease, medication use, or perceived loneliness.
Discussion. Gender disparities were identified in several sociodemographic and health-related factors among hypertensive elderly in the community. These findings underscore the importance of incorporating gender-sensitive approaches into elderly health programs, particularly in enhancing participation in community-based program and addressing comorbid conditions.

Rezaianzadeh, A., et al. (2024). Sex differences in hypertension incidence and risk factors: a population-based cohort study in Southern Iran. BMC Public Health, *24*(1), 3575.
Song, J. J., et al. (2020). Gender differences in hypertension. J. of Cardiovasc. Trans. Res., *13*(1), 47-54.

P615

Team-based hypertension care in Australia: A qualitative study among primary care providers

Dr Gautam Satheesh

Biography:

Gautam Satheesh is a PhD candidate at the Faculty of Medicine and Health, University of Sydney, and a researcher at The George Institute for Global Health in Sydney. His doctoral research focuses on strengthening team-based care for hypertension in Australia, with particular emphasis on enhancing the roles of nurses and pharmacists in supporting evidence-based blood pressure management. His work applies mixed methods and implementation science approaches to explore provider perspectives, workforce modelling, and system-level reforms that can expand access and equity in hypertension care. Gautam has also contributed to global policy efforts, including the World Heart Federation's efforts on Single Pill Combinations and the WHO HEARTS technical package on hypertension control. His broader research interests span cardiovascular disease prevention, access to essential medicines, and innovative service delivery models in low- and middle-income countries. He is passionate about building evidence that bridges clinical practice, health systems, and policy for population-level impact.

Team-based hypertension care in Australia: A qualitative study among primary care providers

Gautam Satheesh[1,2], Kaylee Slater[1], Ritu Trivedi[1], Eleanor Clapham[3], Florence Lopez[1], Aletta E Schutte [2,4], J. Jaime Miranda[1], Brendan McCormack[1], Niamh Chapman[1,3]. [1]Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia; [2]The George Institute of Global Health, Sydney, NSW, Australia; [3]Menzies Institute for Medical Research, University of Tasmania, Australia; [4]School of Population Health, UNSW, Sydney, NSW, Australia

Introduction. Hypertension care in Australia is burdened by poor BP control (32%) and a projected shortage of 5,000 general practitioners (GPs) by 2030, underscoring the need to expand team-based care with pharmacists and nurses.
Aims. To explore barriers and attitudes among primary care providers towards team-based hypertension care.
Methods. We conducted 43 semi-structured interviews with GPs (N=21), nurses (N=11), and pharmacists (N=11), purposively recruited from diverse primary care settings. We employed framework analysis, combining deductive analysis, based on Theoretical Domains Framework embedded within COM-B (Capability, Opportunity, Motivation–Behaviour), with inductive analysis to identify emergent themes across individual and system levels.
Results. Hypertension management remained GP-centred, with nurses and pharmacists confined to supporting roles for BP measurement, follow-up, and counselling. Contributions of nurses and pharmacists were constrained by barriers at both individual/practice (e.g., mistrust among GPs) and system levels. Nurses described being "hamstrung" by workload and absence of direct funding for hypertension services, despite being critical in care planning. Pharmacists reported that unreimbursed BP checks and capped MedsChecks hindered sustainability. Communication across providers was largely fragmented, with pharmacists noting almost no referral pathways to GPs. Role ambiguity and absence of protocols on shared workflow further limited collaboration, with concerns about overstepping professional boundaries. Attitudes towards team-based care ranged from active disregard (outright rejection), through more passive/conditional acceptance, to active uptake (strong endorsement).
Discussion. Hypertension care in Australia remains largely GP-centred, despite demonstrated willingness and potential among nurses and pharmacists to alleviate burden on GPs and provide quality care. Addressing provider-level barriers of workload and trust, alongside system-level barriers of funding and authority, is critical for sustainable workforce planning, task sharing and team-based care.

P616

Blood pressure reduction is attained through nurturing colonic short-chain fatty acid producers

Ms Phoebe Cheong

Biography:

Phoebe Tsin Tse Cheong is a second-year PhD student at the Biomedicine Discovery Institute of Monash University, and the Victorian Heart Institute (VHI) of the Victorian Heart Hospital in Clayton, VIC. She holds a Masters degree in Microbiome in Health and Disease from King's College London, UK, and Bachelor's degree in Food Science and Nutrition, Universiti Malaysia Sabah.

Phoebe's academic journey has compelled her to integrate methodologies from interdisciplinary aspects to uncover the potential of the gut microbiome for biotherapies. Her keen interest is in the modulation of the gut microbiome in health and diseases, particularly in blood pressure regulation. Phoebe's dedication to research has been recognized with the VHI travel grant, which has enabled her to present her findings at the Human Microbiome Symposium, in EMBL Heidelberg, Germany. Phoebe aspires to contribute to the growing field of microbiome research and its translational potential in precision and personalised nutrition.

Blood pressure reduction is attained through nurturing colonic short-chain fatty acid producers

Phoebe TT Cheong[1], Leticia C Tavares[1], Dakota Rhys-Jones[1], Jane Muir[1], Charles Mackay[2], Simone Li[1], Francine Z Marques[1*] [1]Monash Univ, VIC; [2]Qilu Univ of Technology, Jinan, China

Introduction: Manipulation of the gut microbiome via fermentation of dietary fibre and production of metabolites called short-chain fatty acids (SCFA) has emerged as a non-pharmacological treatment for hypertension. SCFA, delivered as acetylated and butyrylated high amylose maize starch (HAMSAB), reduced 24-h systolic blood pressure (BP) by 6.1mmHg.[1] How fast these changes occur and the specific microorganisms contributing to lower BP remain unknown.
Aim: To identify gut microbiome changes associated with HAMSAB treatment across six timepoints of the trial.
Methods: Shotgun metagenome sequencing was performed at 3M reads on stool samples at baseline, 7 and 21 days per study arm per participant (n=118). MetaPhlAn4 and the *phyloseq* R package were used for species-specific taxonomic profiling. Permutational multivariate analysis of variance was used for diversity analysis. Differentially abundant microbial species were identified using random effects linear regression (MaAsLin2).
Results: HAMSAB significantly shifted β-diversity by the first week of intake (p=0.001) and persisted till end of the trial (p=0.001). β-diversity remained constant in the placebo arm (p=0.43). Relative to placebo arm, the SCFA arm significantly changed the prevalence of 10 taxa (FDR-adjusted q<0.05), including increased *Parabacteroides distasonis* (log2 fold change(FC)=2.05, q=3.9×10^{-7}). Abundances of *Alistipes finegoldii* (log2FC=0.49, p=0.005) and *Roseburia intestinalis* (log2FC=0.002, p=0.014) correlated with plasma butyrate.
Discussion: High SCFA intake resulted in dynamic and distinct microbial profiles in mere seven days. This shows that microbiota changes associated with improvement of chronic conditions such as hypertension need long-term dietary commitment. The species identified may be used in the future as a probiotic to reduce BP.

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The relationship between the cortisol awakening response and blood pressure in late-life

Dr Daria Gutteridge

Biography:

Dr. Daria Gutteridge is a postdoctoral Research Fellow at the University of South Australia (UniSA) where she focuses on the quality use of medicines in Australian aged care facilities, working on the MRFF-funded PHarmacists Actioning Rational use of Medicines in Aged Care (PHARMA-Care) project. At the end of 2023, Daria completed her PhD in the field of Psychology (Cognitive Neuroscience) at UniSA, at the Cognitive Ageing and Impairment Neuroscience Lab. Her PhD focused on the relationship between blood pressure variability, cognitive functioning and cerebrovascular health in older adults. Daria is an early career researcher who is passionate about improving cardiovascular health, cognitive functioning and aged care services to advance the quality of life and health outcomes in older adults.

The relationship between the cortisol awakening response and blood pressure in late-life

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Introduction The role of the hypothalamic–pituitary–adrenal axis (HPA) functioning in blood pressure (BP) and BP variability is not well understood. Investigating the link between the cortisol awakening response (CAR), a distinct circadian marker that can assess HPA axis activity, and BP may help clarify factors contributing to hypertension and increased BP variability.
Aims This cross-sectional observation study aimed to investigate the relationship between the CAR, and both BP and BP variability in community dwelling older adults.
Methods The CAR and BP were assessed in 53 adults (68% female, 32% male) aged between 60 to 78 years (median age=70.5 years). BP and BP variability were assessed via 24-hour ambulatory BP monitoring and home-based measures in the morning for 5 days. Saliva samples for CAR assessment were collected by the participants at home immediately after awakening (S1) and at 15, 30 and 45 min thereafter, over two consecutive mornings. The CAR was assessed using the increased area under the curve across the 4 samples, and cortisol levels from S1 were computed. Correlation analyses and generalized addictive models were conducted to investigate associations.
Results The CAR at the second sampling day was significantly positively associated with systolic (p=0.013, edf=6.8) and diastolic (p= 0.028, edf =6.4) BP levels during sleep, after controlling for age and sex. No significant relationships were present between the CAR and systolic or diastolic BP variability, or between S1 cortisol levels and BP outcomes.
Discussion Our preliminary findings suggest a potential link between the CAR and night-time BP in older adults, but not with BP variability, though the strength of associations varied across days. Further research is needed to understand the role of HPA functioning in relation to increased cardiovascular risk.

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Differential effects of hormone therapies for advanced prostate cancer on cardiovascular health

Dr Katrina Mirabito Colafella

Biography:

Dr Katrina Mirabito Colafella leads the Molecular and Integrative Mechanisms of Vascular Biology Laboratory at Monash University's Biomedicine Discovery Institute (BDI), where she also serves as the inaugural Monash BDI Anita Castan Fellow. Her research vision is to transform the treatment of hypertension and cardiovascular disease through precision medicine, with a focus on sex-specific mechanisms in blood pressure regulation. She is also at the forefront of research into the cardiovascular side effects of cancer therapies, aiming to develop innovative strategies that prevent or reverse these complications. Through her work, Dr Mirabito Colafella is redefining how we understand and treat cardiovascular disease in vulnerable populations, with the ultimate goal of improving long-term health outcomes.

Differential effects of hormone therapies for advanced prostate cancer on cardiovascular health

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Introduction: The standard-of-care for advanced prostate cancer is continuous suppression of androgen receptor (AR) signaling using androgen deprivation therapy (ADT) combined with AR signaling inhibitors (ARSI). While effective, this approach often leads to treatment resistance and cardiovascular disease. We hypothesize that newer hormone therapies, such as bipolar androgen therapy (BAT), which uses cycles of high-dose testosterone instead of constant hormone suppression, may pose fewer risks to cardiovascular health compared to the standard treatment.
Aims: To determine the impact of standard-of-care versus BAT on cardiovascular and kidney health.
Methods: Male C57Bl/6 mice were randomised to 1 of 5 groups: intact, intact with testosterone (eugonadal model (intact+T)), 3) castrated (ADT model), 4) castrated with enzalutamide (ARSI model) or 5) castration plus BAT. Two cohorts were studied over 6 weeks: cohort 1 underwent continuous mean arterial pressure (MAP) monitoring via radiotelemetry; cohort 2 was assessed for cardiac (echocardiography) and kidney (transcutaneous measurement of glomerular filtration rate (GFR)) function, body composition (DEXA scan) and proteinuria pre- and post-treatment. Blood and tissues were collected to evaluate hormone levels, cardiometabolic markers and end-organ damage.
Results: MAP remained stable in the intact and intact+T groups. Castration, with or without BAT, significantly reduced MAP from weeks 2 to 6, while castration+ARSI increased MAP by ~15 mmHg in the final week of treatment. Castration alone did not impair cardiac function. However, when combined with ARSI, it led to mild cardiac disfunction, reflected by a reduction in global longitudinal strain (-17.1±1.3 vs -15.2±0.7; P=0.05) and an increase in myocardial performance index (0.45±0.05 vs 0.60±0.03; P=0.002). These adverse effects were abrogated by BAT. Proteinuria was 1.6±0.4. 1.9±0.2 and 2.4±0.5 mg/24h in the intact, intact+T and castration+BAT groups, respectively. Castration alone and in combination with ARSI significantly reduced proteinuria to 0.4±0.1 mg/24h in both groups (P=0.02 versus intact+T). No significant differences in GFR were detected between the groups.
Discussion: This study confirms that BAT has distinct impacts on cardiovascular health compared to standard-of-care, warranting further investigation into the implications for overall cardiovascular health.