

ANNUAL REPORT Year 3 (2023/2024)

May 2024 From the Glukhova lab at our WEHI Node: "Shining a light on PORCN". In this ribbon diagram, the structure of Porcupine (PORCN), the membrane bound Oacyltransferase is shown with it's potent inhibitor, C59, highlighted in the binding pocket.

Image Credit Dr. Sarah Piper

Centre for Cryo-electron Microscopy of Membrane Proteins

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Centre for Cryo-electron Microscopy of Membrane Proteins

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Image credit: Dr. Sarah Piper

ccemmp.org



Centre Overview











MOLECULAR HORIZONS









Centre Overview

The Centre for Cryo-electron Microscopy of Membrane Proteins (CCeMMP) is funded by the Australian Government through the Australian Research Council (ARC) Industrial Translation Research Program (ITRP). The Centre is an academic-industry partnership supported by the Industrial Transformation Training Centre arm of the scheme. Our core academic partners are Monash University (Administering Institution), The University of Melbourne, the Walter and Eliza Hall Institute of Medical Research (WEHI), and the University of Wollongong. Key goals of the Centre include training industry-ready, world-class graduates in cryo-electron microscopy of membrane proteins, and providing leadership and innovation in the application of cryo-EM to advance industrial expansion in structure-enhanced drug design. Expected outcomes include world-first structural biology knowledge and techniques, and the generation of next-generation cryo-EM researchers with entrepreneurial and technical skills desired by industry.

Vision

The Centre will provide a world-leading workforce that can advance Australia's biotechnological capability and to build strong linkages with the drug discovery and development industries. Our Centre will train industry-ready, world class graduates in cryo-electron microscopy of membrane proteins. The Centre's graduates and research results will enable tomorrow's industrial expansion in structure-enhanced drug design.





Director's Report

Prof. Patrick Sexton, ARC CCeMMP Director

As we farewell the third year of the Centre, I am pleased to provide my reflections on the last 12 months of operations and the activities of the Centre. The Centre saw significant growth with 56 new members joining, and with this, an increase in activities and member participation. This year was smooth sailing for our CCeMMP Doctoral Program, and we expanded participation in our training rotations beyond students enrolled in the Centre to other Centre members and affiliates. We are excited that 2024 has also marked the first of our CCeMMP students embarking on industry placements and getting "real-world" industry hands-on experience, and release of the first publication led by an ICHDR.



Research Success: 2023-2024 has been a particularly strong year for members in the cryo-EM field, with multiple high-quality publications, research grants and awards, and promotions of Centre members. These included papers in Nat Methods, Commun Biol, Sci Rep, Structure, Nat Genetics, eLife, Blood, Angewandte Chemie Int Ed, and multiple papers in Nat Commun. Multiple researchers received prestigious NHMRC Early Leader and Leadership Investigator grants as well as ARC and various international grants. We were particularly excited by the number of major awards and Honors received by members that included an Order of Australia, Eureka award for Outstanding Mentoring of Young Researchers and an International Award from the Biochemical Society (Prof. Ryan), a Commonwealth Health Minister's Award for Excellence in Health and Medical Research (Dr. Stewart), NHMRC Peter Doherty (Prof. Sexton) and Elizabeth Blackburn (Prof. Wootten) Investigator grant awards, as well as recognition Prof. Christopoulos and Prof. Sexton as 2023 Clarivate Highly Cited Researchers. Congratulations to these awardees and to the many others that are detailed in this report.

Comings and goings: Dr. Jackie How returned from maternity leave in September 2023 to take the Centre Manager reins from the diligent interim Centre Manager Dr. Tracie Pierce, who continues to support committees and activities of the Centre. Our Wollongong Node Leader, Assoc. Prof. Gökhan Tolun went on sabbatical early 2024 and the interim Node Leader position is being filled by Prof. Lezanne Ooi. Our second student representative for Executive Committee and Graduate Research Committee, Qinghao Ou, completed his role in January 2024 and has passed the baton to Minakshi Baruah. We thank Qinghao for all his contributions to the committees during this time. We also thank Alok Pradhan and Bindu Paul for their student representative roles in the Seminar Committee as we welcome Marialena Georgopoulou and Shubha Udupa as the 2024 student representatives.

Ins and Outs: We are pleased to have finalised and executed our Project Agreement with founding industry partner, Dimerix.



Director's Report (cont.)

External Engagement: The Outreach and Engagement Committee and Graduate Research Committee have been busy this year with numerous outreach and training activities and communications. Multiple technical training workshops were delivered by trainers within the Centre to members and the community. Our seminar series continues its impact with providing the community with exciting international and domestic speakers presenting cutting-edge research and techniques in the field.

Overall, another strong year for the Centre. I thank the Centre members for their contributions and support for the Centre and its activities, and I look forward to Year 4 of the Centre.

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Patrick Sexton ARC CCeMMP Director



CCeMMP Snapshot

Centre Operational Timeline



Current Partners





Key Data



Our People

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Expanding CCeMMP Membership

As part of its strategic plan the Centre continues to reach out to scientists, inside and outside of the founding academic institutions, who are involved in cryo-EM and membrane protein research to provide opportunities for them to become members or affiliates of the Centre and to participate in Centre activities.

Over the last 12 months, we have seen a substantial increase in membership and have welcomed a total of 56 new members and affiliates, including 28 new affiliate members outside of the foundational Nodes, from institutions around the country and New Zealand.



- Prof. Brett Collins (Group Leader), The University of Queensland
- **Dr. Evelyne Deplazes** (Group Leader), The University of Queensland
- Prof. Renwick Dobson (Group Leader), The University of Canterbury, NZ
- Dr. Matthew Doyle (Group Leader), The University of Sydney
- Assoc. Prof. Chris French (Group Leader), The University of Melbourne (Royal Melbourne Hospital)
- Dr. Rhys Grinter (Group Leader), The University of Melbourne
- Assoc. Prof. Michael Landsberg (Group Leader), The University of Queensland
- Dr. Jacob Lewis (Group Leader), The University of Wollongong
- **Prof. Trevor Lithgow** (Group Leader), Monash University (BDI)
- Dr. Rachel North (Group Leader), The University of Sydney
- Assoc. Prof. Tracy Putoczki (Group Leader), Walter and Eliza Hall Institute of Medical Research
- Prof. Wai-hong Tham (Group Leader), Walter and Eliza Hall Institute of Medical Research
- Dr. Celine Valant (Group Leader), Monash University
- Dr. Ben Gully (Team Leader), Monash University (BDI)
- Dr. Hamish Brown (PostDoc), The University of Melbourne
- Dr. Tyler Chang (PostDoc), Monash University
- Dr. Kevin Chen (PostDoc), The University of Queensland
- Dr. Kelsi Hall (PostDoc), The University of Canterbury, NZ
- Dr. Brooke Hayes (PostDoc), Monash University
- Dr. Matthew Johnson (PostDoc), The University of Melbourne
- Dr. Manasi Arcot Anil Kumar (PostDoc), The University of Melbourne
- Dr. Yan Li (PostDoc), Monash University
- Dr. Shadi Maghool (PostDoc), The University of Melbourne



- Dr. Biswa Mishra (PostDoc), Griffith University
- Dr. Sarah Mueller (PostDoc), Australian National University
- Dr. Natsumi Murata (PostDoc), The University of Queensland
- Dr. Andrew Thompson (PostDoc), Walter and Eliza Hall Institute of Medical Research
- Dr. Phuc Trinh (PostDoc), Monash University
- Dr. Naveen Vankadari (PostDoc), The University of Melbourne
- Dr. Mai Vu (PostDoc), The Doherty Institute for Infection and Immunity
- Dr. Shan Zhen (PostDoc), The University of Queensland
- James Lingford (Research Assistant), Monash University (BDI)
- Zubair Jashim (Research Assistant), The University of Melbourne
- Nadezhda Aleksandrova (Student Affiliate), The University of Queensland
- Irene Antony (Student Affiliate), The University of Canterbury, NZ
- Yunzhi (Anastasia) Chen (ICHDR), The University of Melbourne
- Amy Cheng (Student Affiliate), The University of Sydney
- Lyn Deng (Student Affiliate), Walter and Eliza Hall Institute of Medical Research
- Thomas Ficker (ICHDR), The University of Wollongong
- Daniel Fox (Student Affiliate), The University of Melbourne
- Stephanie Hedditch (Student Affiliate), The University of Wollongong
- Kenta Ishii (Student Affiliate), Monash University
- Vignesh Kamath (ICHDR), The University of Melbourne
- Firoz Khan (Student Affiliate), Monash University
- Ashleigh Kropp (Student Affiliate), Monash University
- Meihan Lu (Student Affiliate), The University of Queensland
- Fabian Munder (Student Affiliate), Monash University
- Michael Newton-Vesty (Student Affiliate), The University of Canterbury, NZ
- Ada Quinn (Student Affiliate), The University of Queensland
- Solace Roche (Student Affiliate), The University of Queensland
- Alexandra Shanahan (Student Affiliate), The University of Wollongong
- Monica Suehiro (Student Affiliate), Monash University
- Patrick Sutton (Student Affiliate), The University of Queensland
- Mahmuda Yeasmin (Student Affiliate), Monash University
- Yi (Jack) Zeng (Student Affiliate), Victor Chang Cardiac Research Institute
- Ruosang Zhang (Student Affiliate), The University of Canterbury, NZ



Education and Training



Education Overview

The CCeMMP Doctoral training program is a 4-year degree, inclusive of specialist training in cryo-EM of membrane proteins (3 x practical rotations in Year 1), an experiential, embedded, industry placement and a series of vocational workshops and advanced coursework. We provide updates on each of these training opportunities. In this report, we also hear from one of our students who has completed their experiential, embedded industry placement with industry partner AstraZeneca.



ICHDR Recruitment

In Year 3 we welcomed 3 new ICHDRs, bringing the number of students currently enrolled in the Centre's HDR program to 18. Their background and projects are outlined below. Anastasia, Thomas and Vignesh will join our current ICHDRs Isabella Russell, Jack Tovey, Qinghao Ou, Dongju Lee, Riya Joseph, Marialena Georgopoulou, Minakshi Baruah, Alok Pradhan, Maria Katarina Lambourne, Mayada Mazher, Ania Beyger, Xiaomin Wang, David Safadi, Bhavika Rana and Inamur Rahman.

Our ICHDRs



Anastasia Chen



Vignesh Kamath

Anastasia is a PhD candidate supervised by Assoc. Prof. Michael Griffin at The University of Melbourne/Bio21 Node. In her PhD, she will use cryo-EM and X-ray crystallography, combined with biophysical analysis to study the structures and dynamics of interleukin 11 in complex with its receptors. Anastasia completed her Masters of Research in Structural Biology at the Imperial College London, UK. Outside of research, she enjoys hiking and exploring various places in nature.

Supervisors: Assoc. Prof. Michael Griffin, Dr. Tracy Putoczki.

Thomas is a PhD candidate supervised by Assoc. Prof. Gökhan Tolun at the University of Wollongong Node. His project will investigate the structure and function of the Kv7.5 potassium ion channel, which plays an important role in the regulation of neuronal excitability. Thomas grew up in Munich, Germany and completed his MSc in Molecular and Applied Biotechnology at RWTH Aachen University, Aachen, Germany. He enjoys hiking, football and skiing to clear his head in between research.

Supervisors: Assoc. Prof. Gökhan Tolun, Prof. Lezanne Ooi, Dr. Aidan Grosas.

Vignesh is undertaking his doctoral studies in Assoc. Prof. Michael Griffin's lab at The University of Melbourne/Bio21 Node. His PhD will involve understanding structure and signalling of the IL6 family cytokines, developing inhibitors, and exploring their therapeutic modality. When Vignesh clocks out of work, he loves to watch movies. He is a bike enthusiast who loves to ride in nature, and he loves to have biryani for breakfast, lunch and dinner.

Supervisors: Assoc. Prof. Michael Griffin, Dr. Tracy Putoczki.





Rotational Training

The Centre ICHDRs undertake approximately 5 months of intensive hands-on foundational training through three practical rotations: Rotation 1, Biochemistry; Rotation 2, The Theory and Operation of Cryo-EM Instruments; Rotation 3, Data Processing and Analysis. These rotations are completed in Year 1 of the program and provide an introduction to, and core skills in, biochemical approaches to study membrane proteins, cryo-EM preparation and imaging, and data processing for 3D map reconstruction and protein modelling. The biochemistry rotation is completed soon after commencement and is Node-specific, focussing on the particular membrane proteins and techniques that their thesis projects will use.

This year, for the first time, we invited CCeMMP members and affiliates to participate, via Zoom, in the theoretical component of Rotation 2, The Theory and Operation of Cryo-EM Instruments. We were also able to offer a limited number of in-person places in Rotation 3, Data Processing and Analysis. In the coming years we expect that more places in this unit will be available to members and affiliates. We now have a total of 16 students (5 in this past year) who have completed all their training rotations.

Rotation 2: Theory and Operation of Cryo-EM Instruments

Five CCeMMP ICHDRs participated in this cryo-EM training rotation. With lectures co-ordinated by Dr. Matthew Belousoff and presented in person and via zoom by Centre members (Assoc. Prof. Isabelle Rouiller, Dr. Debnath Ghosal, Dr. Alisa Glukhova, Dr. James Bouwer, Dr. Matthew Belousoff) and our partner organisation (Dr. Lingbo Yu, Thermo Fisher Scientific). The topics covered included: Introduction to transmission electron microscopy; Negative stain and its application; Sample preparation & vitrification for SPA of membrane proteins; Introduction to image formation; General considerations for microscope set up (SPA); Electron detector technology. For our ICHDRs, the lectures were interspersed with hands-on training at their respective Nodes, organised and instructed by our Centre ICPDs, Dr. Sepideh Valimehr (UoM/Bio21 Node), Dr. Aidan Grosas (UoW Node) and Dr. Matthew Belousoff (Monash Node).

This year, an additional 32 zoom attendees registered for the theory lectures including members and affiliates from within our Nodes (Monash, UoM/Bio21, UoW), external affiliates (ANU, The University of Sydney) and partner organisations (Dimerix, Pfizer and Boehringer Ingelheim).

Rotation 3: Data Processing and Analysis

This rotation was a two-week intensive in-person, hands-on training in data processing of cryo-EM data, co-ordinated by Dr. Matthew Belousoff (Monash Node), followed by self-directed learning supported by Dr. Belousoff. Five CCeMMP ICHDRs attended the Monash Node to take part in the training. They were joined by an additional 6 student affiliates from within our foundational nodes who successfully applied to attend (one even securing a travel grant to come to Melbourne); Monash (1), UoM/Bio21 (3), WEHI (1), UoW (1). Dr. Matthew Belousoff (Monash Node) and Dr. Sepideh Valimehr (UoM/Bio21 Node) delivered most of the components of this rotation. Dr. Joshua Hardy (WEHI Node) and Dr. Andrew Thompson (WEHI Node) presented on point group symmetry and protein construct



design choices for structural biology analysis. Dr. Sarah Piper (Monash Node) and Dr. Cindy Zhang (Monash Node) ended the program with PDB validation and final steps for ensuring your data is ready for publication.

We will continue to provide access to this valuable training opportunity to affiliate student members. In subsequent years, as our current ICHDRs complete their training, our training will evolve and more places will be available to Centre members/affiliates who would like to attend.



Advanced technical training in CryoEM, 2023

The Process of Drug Discovery

Drug discovery scientists in academia and industry must appreciate how different facets of discovery science are integrated into the discovery pipeline. The Centre, in collaboration with the Drug Discovery Biology Theme at the Monash Node provides advanced coursework that gives an indepth understanding of the different stages of the drug discovery process, including target validation, drug screening methods, computational modelling, drug design and physicochemical optimisation, preclinical development, clinical development, and pharmacoepidemiology. The unit concludes with students designing their own drug discovery program. Centre students join PhD students in the Drug Discovery Biology Theme at the Monash Node for this unit.

EduWeek 2023

We were pleased to continue our professional development series, "EduWeek", in 2023. These sessions were held in-person with all ICHDRs of the Centre attending at the Monash Node.



All sessions were also open to other members and affiliates of the Centre and were well attended

ICHDRs EduWeek 2023. From left: Jack, Alok, Dongju, Bhavika, David, Minakshi, Ania, Marialena, Riya, Inamur, Xiaomin, Mayada, Isabella and Qinghao and highly valued by members. These workshops were presented by partner organisations, ICPDs or external facilitators.

For EduWeek 2023, sessions included:

- Research and Industry Engagement
- Mastering Research and Industry Engagement: Business Development
- Safe Conversations in Research Candidate Student Supervisor Relationships - separate workshops for both PhD students and supervisors
- Consistent and Interpretable Visual Design Language for Scientific Communication
- Mindfulness





- Scientific Writing: Literature Reviews
- Scientific Writing: Clarity and Impact
- Succinct and Clear Oral Presentation

This year we also offered a series of optional workshops in the week following EduWeek. These were designed to further enhance specific cryo-EM related knowledge and technical skills for those keen to know more. These included:

- Introduction to BASH Scripting
- Theoretical Basis for Image Formation in a Transmission Electron Microscope
- How to Set Up Imaging Conditions for SPA Cryo-EM
- Blender3D Workshop (two days)

BASH and Blender workshops were both zoom-enabled to allow our interstate (UoW, USyd, UQ and Griffith) members and affiliates to participate. All workshops were well attended by our members and affiliates; we hope to continue to provide these additional deep-dive workshops in future years.

Research & Industry Engagement

This workshop was presented by Dr. Cathy Drinkwater from our partner organisation, BioCurate. Cathy has experience in a range of therapeutic areas from neurobiology to oncology and brings а deep understanding of industry perspectives on collaborative research. In this workshop, Cathy covered topics such as: Understanding the requirements of industry and investors (what do they want to see in your research?); What's involved in getting a drug/product to market?; How to get Industry interested in your research (making a pitch). The students completed the workshop by making an impromptu elevator pitch of their project.



Research & Industry Engagement



Mastering Research & Industry Engagement

Mastering Research & Industry Engagement: Business Development

This workshop was presented by the Business Development Manager at Monash Institute of Pharmaceutical Sciences (MIPS), Dr. Cameron McDonald. At the time, Cameron led MIPS business industrv development, engagement, and commercialisation in collaboration with Monash Innovation. In this workshop, Cameron discussed the role of business development in the context of the pharmaceutical sector; Understanding contractual obligations including confidentiality, IP, restrictions, and deliverables; How to properly cost projects - why it's important not to under-price (it's not just a postdoc



salary); valuing your expertise and the value of relationships – why they are important (tips on how to engage professionally).

Safe Conversations in Research Candidate Student-Supervisor Relationships

We had two separate workshops; one for the PhD students and a second for supervisors. Both were delivered by consulting psychologist Andrew Carnegie, of Carnegie Consulting Group. In these workshops, participants explored the importance of building an effective and supportive relationship with their student/supervisor; explored the principles of shared responsibility in building respectful, congenial and productive relationships that supports HDR success;



built awareness on their relationships with others; gained strategies to constructively manage differences of opinion and interpersonal conflict; learnt how to approach and manage difficult conversations; worked through case scenarios to translate their learning into practice.



Consistent & Interpretable Visual Design Language for Scientific Communication

Consistent & Interpretable Visual Design Language for Scientific Communication

This workshop was delivered by ICPDs from the Monash Node, Dr. Matthew Belousoff and Dr. Sarah Piper. In it they covered what makes a good scientific figure, how to best convey your results. The students critiqued example figures then worked on making their own from their data.

Mindfulness

This workshop was run in conjunction with the ARC Centre for Fragment-Based Design. It was facilitated by Prof. Craig Hassed, founding Director of Education at the Monash Centre for Consciousness and Contemplative Studies. The topics covered included: Science, philosophy and practice of mindfulness; Managing stress; Work-life balance; Enhancing mental and physical health; Communication; Dealing with imposter syndrome.







Scientific Writing: Literature Reviews

Scientific Writing: Literature Reviews

The scientific writing workshops were presented by Student Academic Success, Monash University. The Literature Reviews workshop provided the students with strategies to create a logical and coherent structure to their literature review that reflects their understanding of the research area; to argue for the significance of their project while building on the ideas of others.

Scientific Writing: Clarity & Impact

Also presented by Student Academic Success, Monash University, this workshop was designed to show the students writing skills to improve the clarity and impact of their scientific writing. The session's focus was "clarity in scientific writing" and "impactful writing strategies for different audiences".



Scientific Writing: Clarity & Impact



Succinct & Clear Oral Presentation

Succinct & Clear Oral Presentation

A large part of what constitutes an excellent public speaker is someone who has a sense of empathy to their audience and can adjust their presentation style and language in order to be fully understood and engaging. This was a practical workshop presented by ICPD, Dr. Matthew Belousoff (Monash Node), which required everyone to participate in both a public speaking exercise and provide constructive feedback to their peers. Topics were chosen from a list provided, and the target "audience" for the exercise was "latestage high school students."

Other EduWEEK Workshops

Introduction to BASH Scripting

This was the first of our optional, 'delve a little deeper' workshops, to enhance skills required for cryo-EM data processing. Bourne Again Shell (BASH), is a Unix shell and command language that also has the ability to be a potent scripting programming language, a feature which is very useful for



everything from text file manipulations, file handling and program automation. Dr. Joshua Hardy (WEHI Node) and Dr. Matthew Belousoff (Monash Node) presented a hands-on scripting masterclass which involved solving a series of Bash exercises to introduce common concepts such as how to write "for" loops, how to write "if/then" statements and how variables work in BASH. There were 21 in-person and 4 zoom attendees for this workshop.



Introduction to BASH scripting



Theoretical basis for image formation in a transmission electron microscope

Theoretical Basis for Image Formation in a Transmission Electron Microscope (TEM)

The aim of this workshop was to further theoretical understanding of how an image is formed and the physical effect of objective defocus on image contrast. Dr. Matthew Belousoff (Monash Node) discussed the physical underpinnings for how contrast is formed in a TEM experiment and derived the contrast transfer function from first principles. There were 18 in-person attendees; this was a "whiteboard" lecture so was not zoom enabled.

Blender3D Two-Day Workshop

Blender3D workshops are becoming a regular feature at CCeMMP. Blender3D is a free and opensource 3D computer graphics suite used for creating 3D animation movies and video games, and lately has become a useful tool to create engaging scientific renders. Dr. Sarah Piper (Monash Node) organised a two-day Blender3D workshop led by Dr. Brady Johnston (University of Western Australia), biochemist and Blender-in-Science expert. In this workshop, Brady demonstrated how

to use the software interface Blender3D as well as presenting his Molecular Nodes add-on, which makes it easy to load structural data, such as PDB files, into Blender3D. There were 23 in-person and 10 zoom attendees from University of Wollongong, University of Queensland, University of Sydney and Griffith University. Due to the large number of participants, we also had six able assistants (Dr. Sarah Piper, Dr. Jesse Mobbs, Dr. Brian Cary, Dr. Jason Cao, Monash Node; Dr. Sepideh Valimehr, UoM/Bio21 Node; Dr. Joshua Hardy, WEHI Node), who helped to facilitate training across the two days.





Other Workshops

Blender 3D Workshops

Further to the EduWeek 2023 Blender workshop, the Monash Node also hosted two additional Blender workshops in January 2024, ahead of the Single Particle cryo-EM analysis workshop and the Lorne Proteins 2024 meeting. Led by Dr. Sarah Piper (Monash Node) with expert support from Dr. Sepideh Valimehr (UoM/Bio21Node) and Dr. Joshua Hardy (WEHI Node), they presented both a beginners and an advanced session. In these ½-day workshops, participants were guided through the preparation of an image, including demonstration of tips and tricks on structure visualisation in the Blender package. There were 13 in-person attendees, from Monash University, ANU, University of Queensland and WEHI comprising members/affiliates or PhD students from the labs of our external affiliates. Sarah plans to run these in-person workshops on a regular basis, but also aims to hold a dedicated online only session for interstate members and affiliates.



2024



Blender3D Workshop, session 2, Jan 2024



Blender image of the glycine transporter, GlyT2, interacting with membrane lipids, by PhD student, Ada Quinn (UQ)





SPA Workshops

Single Particle Analysis (SPA) workshops regularly occur throughout the year, usually two in our reporting year. This year however there were four workshops to meet popular demand, highlighting the high value that these workshops have for the national cryo-EM community. Sponsored by Thermo Fisher Scientific, two were held in June and October, followed by another just prior to Lorne Proteins 2024, catering to international and interstate attendees of that conference. Due to high volume of applications for the latter workshop, an additional workshop was held in March to accommodate the high local interest. These latter workshops were supported by CCeMMP and the Monash MASSIVE High Performance Computing Centre.





Dr. Sepideh Valimehr (ICPD, UoM/Bio21 Node) organised two hands-on Cryo EM SPA workshops at the lan Homes Imaging Centre (IHIC), sponsored by our industry partner, Thermo Fisher Scientific.The first in June (21-23 June, 2024), with the help of Dr. Hamish Brown (IHIC; UoM/Bio21 Node), Dr. Matthew Belousoff (Monash Node) and Dr. Joshua Hardy (WEHI Node), had 10 attendees from various regions across Australia, including Griffith University, Charles Sturt University, Monash University, The Royal Melbourne Hospital, University of New South Wales, and Peter Doherty Institute. The second in October (23-25, October 2024), with the assistance of Dr. Hamish Brown (IHIC; UoM/Bio21 Node) and Dr. Matthew Belousoff (Monash Node), had 8 attendees from various regions across Australia: University of Sydney, Griffith University, WEHI, Monash University and The University of Melbourne.

MASSIVE



SPA Workshop, 21-23 June 2023



SPA Workshop, 23-25 October 2023

A consistent factor throughout both these workshops is that participants really enjoyed the handson aspect and some would have liked the course to run longer, to enable a couple of days dedicated to data processing alone.







The Monash Node also hosted a cryo-EM data processing workshop just prior to the Lorne Proteins 2024 conference, January 31st-February 2nd, supported by CCeMMP and the MASSIVE High Performance Computing Centre. Organised by Dr. Matthew Belousoff (Monash Node) with expert support from Dr. Sepideh Valimehr (UoM/Bio21 Node), Assoc. Prof. Michael Landsberg (University of Queensland) and Dr. Brian Cary (Monash Node) this workshop covered both fundamental theoretical and practical aspects of SPA cryo-EM. Over the three days the entire image processing workflow was covered from collection of micrographs to 3D map calculation. Facilitators were assisted by PhD students Theodore Nettleton (Monash Node) and Qinghao Ou (Monash Node). There were 17 attendees, coming from New Zealand and most of the universities from the East coast of Australia.

Due to popular demand, Dr. Matthew Belousoff (Monash Node), Dr. Sepideh Vahlimer (UoM/Bio21 Node), Dr. Aidan Grosas (UoW Node) and Dr. Hamish Brown (IHIC; UoM/Bio21 Node), ran another SPA workshop in March (21-23 March, 2024), this time at the IHIC. There were 16 attendees; 2 from The University of Queensland, the remaining 14 were from various institutes around Melbourne (The University of Melbourne, The Florey Institute of Neuroscience and Mental Health, WEHI and Monash University).





SPA Workshop Jan/Feb, 2024

This workshop was also supported by CCeMMP and the Monash MASSIVE High Performance Computing Centre.

The overall consensus was that these are very worthwhile workshops, even for the experienced user, with a good mix of theory and practice.

The ongoing high demand for the SPA workshops emphasises the growing integration of cryo-EM into academic and industrial research.

Media Engagement Workshop

During the Centre Retreat, December 2023, centre ICHDRs and PhD student affiliates participated in two workshops designed to build their skills in communicating their research; "Meet the Media" and "Present your Science" with both workshops led by Tanya Ha (Catalyst). The Meet the Media session was delivered as a discussion and Q&A moderated by Tanya with panel members, Lana Murphy (Channel 9), James Lake (Triple M), and Bridget O'Connell (Herald Sun). The principal subject of the discussion was "what makes science newsworthy?" Topics included: "How do you



Media Workshop Dec 2023





ensure your research is reported accurately?" "What do journalists look for in a story?" "Where do they find their stories?" and "What makes some stories work and others go wrong?".



The Present your Science workshop was a 90 minute session where the students explored how to present their research quickly and clearly to anyone. Following an introduction from Tanya, including key tips on how to break down complex research into meaningful concepts for a lay audience, students broke into groups to present to each other and get feedback and then a member from each of the smaller groups presented to the larger group.

3D Printing Workshop

The Outreach and Public Engagement committee organised a 3D printing workshop for its members 8 April, 2024. Led by Dr. Sarah Piper (Committee



Drs. Sepideh Valimehr, Joshua Hardy, Jason Cao & Sarah Piper

Chair, Monash Node), with participants, Dr. Joshua Hardy (WEHI Node), Dr. Sepideh Valimehr (UoM/Bio21 Node) and Dr. Jason Cao (Monash Node). In the workshop they learned how to use the softwares ChimeraX and Blender to prepare files for 3D prints of protein structures. These 3D structure prints are approximately 10 *million* times larger than the actual molecules that they



represent, and are very 'handy' for displaying how different protein subunits interact.

Joint ITTC Careers Day

The Centre joined forces with five other local ITTC's to hold a Careers Day, 12 April, 2024, Swinburne University, Hawthorn Campus, for their respective members and students. With interstate members and students, the presentations were available both in person and via zoom. This was an all day event that included a training workshop on the best way to present and write your CV/resume, a Q & A session with a panel of experts (industry, academia and entrepreneurs) and a 'speeddating' mentoring session with mentors from different backgrounds. As some of our students are approaching



their final year, we will begin to include more workshops like this that will prepare them to enter the job market.





Industry Placements



The first of our ICHDR's has completed their industry placement. Isabella Russell, has just returned from Cambridge (UK), with project partner organisation AstraZeneca. Isabella undertook a fully embedded 3 months experience with her industry partner before returning in April, 2024. Jack Tovey commenced a 3 month placement with partner organisation Astex, Cambridge UK, April 2024. Alok Pradhan also started placement in April 2024 with local partner, Dimerix. Alok will be onsite with his project partner organisation one day a week for twelve months. In the coming 12 months, many students from our early HDR cohorts will be taking part in industry placements, both locally and overseas.

Isabella was kind enough to share reflections of her industry experience with us.

It's hard to imagine that 3 months ago I arrived in the UK, in the middle of a cold snap, fresh out of the blistering Australian summer. I spent 10 days exploring London, a brief jaunt in Edinburgh, then caught the train 1 hour north from London to Cambridge. From day 11 was fully embedded in the AZ structural and biophysics team, working on a variety of different targets using cryo-EM, and to my shock, crystallography, which was entirely new to me. I was guided through the maze of industry by 2 amazing researchers, Dr. Fiona Shilliday for cryo-EM and Dr. Gavin Collie for crystallography, who were both incredibly generous with sharing their time and expertise. There were plenty of meetings and slides (as I had been promised), but there was a really amazing collaborative environment both within and between teams. The scientific rigour and knowledge around me were incredible: everyone on my team had something different and unique to teach me, and it was an invaluable experience. In particular, it was really interesting to see the impact structure had on drug discovery and development which was an awe inspiring process. In the end, I solved 2 cryo-EM structures and 10 crystal structures! It's an achievement I'm incredibly proud of, but I'm even more proud of everything I've learnt along the way about asking for help and sharing thoughts and opinions with others. Overall the experience has inspired me to look beyond academia for my future, and shown me that moving to industry definitely does not mean giving up on scientific exploration and publishing – quite the opposite! 3 months flew by in no time at all and I wish I could have stayed longer! -- Isabella Russell



n. PDB: 8U18; complex with thr From the WEHI Node: Cryo-EM structure of the extracellular domain of murin thrombopoietin recepto EMD-41805. Nature Communications, 15: 11345, 2024 https://www.nature.com/articles/s41467-024

Image credit : Dr. Joshua Hardy



Research



Research Overview

The Centre has 3 major program areas that address Key Objectives (KO) of the ARC Industrial Transformation Training Centre Scheme. These key objectives and activities against the 3 program areas are described below.

Centre objectives: Key objective 1. Industry-ready, world-class graduates with critical and highly-sort after expertise in the application of cryo-EM to drug discovery. **Key objective 2.** Innovation in membrane protein cryo-EM that advances robustness, resolution and cycle times that will be internationally leading. **Key objective 3.** Solution of novel membrane protein structures that are relevant to drug development. **Key objective 4.** Advancement of Australian biotechnological capacity and improved linkages with major pharmaceutical partners.



Research Programs

Program Area 1. Advanced Training in Single Particle Cryo-EM of Membrane Proteins



Details of the bespoke 4-year Doctoral Training Program were outlined in the Year 1 report (K01; core ITTC subprogram objective).

In 2023, 5 ICHDRs completed the 3 technical rotations (biochemistry; microscopy; data processing and structure determination) comprising ~5 months of intensive hands-on training in the core disciplines for the field. This year marked the first time that Rotations 2 and 3 were open to other members and students within in the Centre (not formally enrolled). A total of 32 members and students joined the ICHDRs for Rotation 2. Attendance to Rotation 3 outside of ICHDRs was by application and we admitted 6 students into the Rotation.







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Program Area 2. Innovative Research for Implementation of Cryo-EM in Membrane Protein Structure-Based Drug Design.

Academic and academic-industry partnered research across membrane protein targets to deliver on KO2, KO3 and KO4 of the Centre (aligned to the core objective of the ITTC subprogram). We have included reference to publications formally published in 2023 or which were deposited into a publicly accessible pre-print server during 2023.

Theme 1: Technological Advancements

Subproject 1. Integrated Methods to Study Membrane Protein Dynamics

To understand membrane protein conformational dynamics and mechanism of drug action, ARC CCeMMP researchers are continuing to apply integrated approaches that describe the intrinsic conformational dynamics of membrane (and other) proteins and how these are influenced in a ligand-specific (natural ligands and/or drugs), including conformational variance information that can be directly extracted from cryo-EM data. Complementary techniques include molecular dynamics simulations (e.g. Burger et al, Nat Commun 2023; Vuckovic et al, eLife 2023), NMR (e.g. Bumbak et al, Nat Commun 2023), & HDX-MS (e.g. Fernando et al, Cell Rep 2023). In ongoing work, CCeMMP researchers are also expanding the integrated application of hydrogen-deuterium exchange-mass spectrometry (continuous and pulsed) to interrogate differential and sequential conformational changes upon membrane protein engagement with different ligands that further supports understanding of protein structure derived from cryo-EM. Centre researchers continue to assess and apply new algorithms and latest versions thereof for analyses of conformational information within cryo-EM data, including CryoDRGN, a neural network for continuous heterogeneous reconstruction developed at MIT, and 3DVA & 3DFlex (cryoSPARC) (e.g. Cao et al, Nat Chem Biol 2024; Burger et al, Nat Commun 2023, Mobbs et al, Blood 2023; Cary et al, Structure 2023), as well as new graphical tools for visualisation of 3D variance data (e.g. "Wiggle", manuscript in preparation, collaboration with Novo Nordisk).

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Subproject 2. Structural Utility of 200kV Cryo-EM

With the expense, and limited access to high-end 300kV instruments, CCeMMP researchers continue to investigate the structural resolutions that can be achieved with 200kV imaging on membrane protein samples of differing complexity (yield, dynamics, heterogeneity), and also how this can support commercial and academic drug discovery and development at lower cost. Our researchers continue to illustrate a routine ability to achieve resolutions suitable for many structural questions, including identification of drug binding (Cao et al, Nat Chem Biol 2024 – collaboration with Sanofi; Cary et al, Structure 2023; Russell et al, Biochemistry 2024 – collaboration with Astra Zeneca; >20 conference presentations; Commentary in Walsh et al, Structure 2023) and are using the data to develop processes that prioritise the best samples for more expensive, higher resolution, 300kV imaging.

Subproject 3. General Advances in Cryo-EM



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Work is continuing on development of new cryo-EM sample preparation devices (noted in the Year 1 & 2 reports). The second iteration, with a simpler design and a 2-fold speed increase has completed its testing phase and small numbers of units are being built for CCeMMP members. In parallel, optimisation of sample vitrification is continually pursued (e.g. presentation by ICPD Valihmer). CCeMMP researchers, in collaboration with Thermo Fisher Scientific have demonstrated improvements to cryo-EM imaging with a new "square condenser" (Brown et al, Nat Methods, 2024), while others are involved in improvements in analysis of single particle and tomographic cryo-EM data (Vuillemot et al, Science Rep 2023, Vuillemot et al, J Mol Biol 2023). Centre members also continue to apply their learning to cryo-EM of soluble and peripheral membrane proteins, and more complex samples using both single particle and tomographic imaging (Mobbs et al, Blood 2023; Shepherd et al, iScience 2023; Xu et al, bioRxiv preprint 2023; Meng et al, Nat Commun 2023; Roy et al, Nat Commun 2023).







Theme 2. Cell Surface Receptors (GPCRs)







GPCRs are a major membrane protein family studied by many researchers within the Centre. Of note, while we have divided the research into subproject areas, in many instances publications and collaborative partnerships cross over between subprojects. As such, outputs may appear in more than one subproject research update.

Subproject 1. Understanding Receptor Activation and Transducer Coupling

We have continued to determine structures of different agonist-receptor complexes to support understanding of how individual ligands control efficacy and selectivity. Within this subproject area are collaborative projects with our Industry partners Novo Nordisk, Boehringer Ingelheim, Sanofi, AstraZeneca and Dimerix. In addition to determination of novel ligand-receptor complexes (e.g. Burger et al, Nat Commun 2023, with Karuna collaborators; Cary et al, Structure 2023; Vuckovic et al, eLife 2023; Cao et al, Nat Chem Biol 2023, with Sanofi collaborators), we have been exploring the relationship between constitutive activity at different receptor subtypes, and different transducer proteins, and stability of agonist-receptor complexes to support structure determination as part of our collaborations with Astra Zeneca and Boehringer Ingelheim.

Our structural work also continues to inform (and is being informed by) *in vitro* and *in vivo* studies on the mechanism and consequences of GPCR activation (e.g. Pham et al, Mol Pharmacol 2023; Ubhayarathna et al, Br J Pharmacol in press 2023; Chandrashekar et al, Bioconj Chem 2023; Tibrewal et al, Mol Psychiatry 2023; Lu et al, Br J Pharmacol in press 2023; Diao et al, Am J Resp Cell Mol Biol 2023; Baltos et al, Br J Pharmacol in press 2023; Muraleetharan et al, Mol Pharmacol 2023). More recently, Centre researchers have collaborated with bioinformatic groups to combine structural insights into understanding of genetic variation in GPCRs (Lagou et al, Nat Genetics 2023; Schneider et al, Am J Med Genet A 2023).

Subproject 2. Molecular Mechanism for Biased Agonism

Understanding efficacy and biased agonism (the ability of individual ligands acting at the same receptor to generate different profiles of transducer and regulatory protein binding and activation) remains a major area of research within Theme 2. This continues to be a productive area of research with multiple papers exploring the structure and function of GPCRs in complex with different agonist ligands (e.g. Cary et al, Structure 2023; Cao et al, Nat Chem Biol 2023 – with Sanofi; Vuckovic et al, eLife 2023). Within this subproject area, we have active industry collaborations with Boehringer Ingelheim, Servier, Novo Nordisk and Septerna, where multiple manuscripts are now in preparation.

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Subproject 3. Allosteric and Bitopic Regulation of GPCRs

We are continuing our pharmacological and structural research across two fronts.

(i) small molecule modulation of receptors, with ongoing work on muscarinic structures (Burger et al, Nat Commun 2023 - collaboration with Karuna Therapeutics) and pharmacology, as well as collaborative research with Boehringer Ingelheim investigating the allosteric modulation of class B GPCRs (Yuliantie et al, in review).

(ii) protein-protein modulation of receptors by other GPCRs and by accessory proteins (Cao et al, Nat Chem Biol 2023 – collaboration with Sanofi; Cao et al, manuscript in preparation – collaboration with Novo Nordisk), and have additional collaborative projects with Dimerix and Novo Nordisk in this research area.

Subproject 4. Inhibitor-Bound GPCR Structures

We continue investigating methods for generation of novel receptor constructs that can potentially improve particle alignment and resolution. This includes correlative assessment of chimeric receptors and the ability of software such as AlphaFold to predict optimal constructs. These constructs have been investigated via pharmacological and biochemical approaches and we are currently determining how different constructs behave in cryo-EM imaging. This has provided insight into parameters associated with stable biochemistry and improving resolution. We currently have several inhibitor-bound receptor complexes at moderate resolution (conference presentations from Baruah – collaboration with Pfizer) and expect to achieve resolutions capable of understanding inhibitor binding in the next 6 months.

Subproject 5. Orphan Receptor Structures

Work has progressed well on the collaborative projects with our industry partners AstraZeneca and Boehringer Ingelheim. Multiple constructs have been generated and the ability of receptor constructs to potentially form a transducer bound complex with different G proteins has been performed. In parallel, pharmacological evaluation of the extent of constitutive activity for each construct with different G proteins is being assessed (presentations from Lee and from Russell). In one of the projects, stable complex formation of the target orphan GPCR has been achieved (Russell et al, Biochemistry 2024 – with AstraZeneca). With our partner organisation, Servier, we have solved structures of the orphan receptor, GPR88 (manuscript in preparation), and also structures of GPR52, in collaboration with the local biotechnology company, Phrenix (a potential new Partner Organisation in 2024; manuscript in preparation).

Theme 3. Other Membrane Proteins

Subproject 1. Applying Cryo-EM to Understand Receptor Tyrosine Kinase Structure and Function

Work is ongoing to develop best methodology to express and purify the full-length membrane receptor tyrosine pseudokinase, EphA10 in its native state. To facilitate our structural studies, we have now established a robust expression system to produce truncated constructs of the ectodomain and intracellular domains of EphA10 and generated in collaboration with the Centre for Biologics Therapies, 14 high affinity EphA10 selective nanobodies and 22 high affinity EphA10 selective antibodies. Importantly, we have implemented a cell-based approach using fluorescently labelled full-length EphA10 to validate the impact of these high affinities nanobodies/antibodies on EphA10 signalling. One primary aim of the PhD student will be to employ a structural biology approach to determine epitope mapping to further enhance our understanding of EphA10's interaction and signalling mechanisms.



Subproject 2. Structural and Functional Studies of Potassium Ion Channels Linked to Epilepsy

Progress on this project has been limited in 2023 due to maternity leave for most of the year of the ICHDR undertaking the project.

Subproject 3. Cryo-EM on Membrane Proteins Involved in Chronic Pain

Progress on this project has been limited due to chronic illness of the ICHDR on the project. Unfortunately, the nature of the illness has now required the student to withdraw from the HDR program.

Other Projects

Centre researchers recently published their cryo-EM data examining the structure and dynamics of interleukin 11 signalling complexes (Metcalfe et al, Nat Commun 2023), and have solved the structure of the thrombopoietin receptor bound to cytokine that is involved in platelet level regulation (Sarson-Lawrence et al, Nat Commun 2024). Centre researchers continue to be involved in a range of academic collaborative projects on structure of various additional membrane proteins. Recent publications on this structural work include: Zeng et al, Nat Commun 2023; Di Cesare et al, J Biol Chem 2024; Tran et al, Int J Mol Sci 2023. An exemplar is the recent work, now published, on bacterial secretion systems noted in the 2022 report that revealed stoichiometric protein-phospholipid assembly (Kreida et al, Structure 2023). We have also made good progress on the project studying the interaction of the single-pass membrane protein, neuropilin-1, with SARS-CoV-2 virus (Vankadari et al, J Phys Chem Lett 2024).









Program Area 3. Joint Research Projects with Industry Partners and Embedded Industrial Training

Industry-partnered research to deliver on KO4 of the Centre (aligned to Linkage Program objectives (a) – (c), and the core objective of the ITTC subprogram).

The Centre continues its active engagement with Industry, both through our founding and new partner organisations and via other industry partnerships. This includes commencement of a new project in 2023 with our partner Novo Nordisk. As in previous years, the Centre was also visited by investigators from Industry. Dr. Claudio Ciferri (Genentech), held a mentoring sessions with Centre members during his stay.

We currently have multiple ongoing collaborative projects with our industry partners (detailed below), inclusive of regular joint meetings that provide important experiential training for the project participants.











Investigation of factors driving resolution of receptor structures and interactions with low affinity ligands. Astex is currently hosting one of our ICHDRs for their industry placement (April - July 2024). Dedicated project members: 1xICHDR, 1xICPD; additional support from the Monash ARC ICPD [monthly joint meetings].

Methods for orphan receptor structure determination. AstraZeneca has hosted one of our ICHDRs for their industry placement (Jan - April 2024). Dedicated project members: 1xICHDR; additional support from the Monash ARC ICPD [monthly joint meetings].

Investigation of molecular mechanisms for biased agonism at incretin receptors. Structure determination for orphan receptors. Boehringer Ingelheim will be hosting two of our ICHDRs for their industry placement (May - August 2024). Dedicated project members: 2xICHDR, 2xICPD additional support from the Monash ARC ICPD [monthly joint meetings].

Structure and allosteric regulation across GPCR oligomers. We are pleased to announce that we have finalised our project agreement with Dimerix Pty Ltd, one of our original Partner Organisations. Dimerix is a partner with the Monash Node of the Centre and is conducting collaborative research on GPCR dimers. Dimerix is also currently hosting one of our ICHDRs for their industry placement. Dedicated project members: 1xICHDR [monthly joint meetings], industry experiential training commenced in late 2023.

Structure and pharmacology of peptide obesity therapeutics. Dedicated project members: 1xICPD in 2023; additional support from the Monash ICPD [minimally monthly joint meetings, additional *ad hoc* meetings]; New project commencing in 2023 structure of novel peptide-incretin receptor structures. Dedicated project members: 1xICPD; additional support from the Monash ICPD [monthly joint project meetings].



Research



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Methods for determination of inhibitor-bound structure determination. Dedicated project members: 1xICHDR [monthly joint meetings].

An additional 3 ICPDs in 2023 were involved in collaborative research on GPCR drug discovery funded by Septerna [weekly meetings until September 2023].

Structural mechanisms for activation and inhibition of chemokine receptors. 1xICHDR [monthly meetings].



The Centre continues its broad partnership with Thermo Fisher Scientific in the areas of innovations in cryo-EM, improving workflows for drug discovery and implementation of training in cryo-EM.





From the Bio21/UoM Node: inward facing conformation of the multidrug ABC transporter, BmrA . PDB: 8CHB; EMD-16659. Journal of Biological Chemistry, 300(1): 105546, January 2024. doi: 10.1016/j.jbc.2023.105546

Image credit: Dr. Sepideh Valimehr


Engagement

CCeMMP Social Media



External facing events



- 1 Conference sponsorship
- 14 CCeMMP seminars
- 4 SPA workshops
- 1 Joint ITTC IWD event



- 1 Centre retreat
- 2 Blender workshops
- 13 EduWeek workshops
- 2 Professional workshops
- 1 3D Print workshop

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4 Newsletters



Academic and Public Engagement



Prof. José María Carazo Visit

With the IUCr meeting being held in Melbourne, August 2023, we were fortunate to have a visit from Prof. José-María Carazo. Prof. Carazo is Head of the Biocomputing Unit at the National Center of Biotechnology (Spain). His laboratory was selected as the Instruct Center for Image Processing in Structural Biology. He has extensive experience in cryo-EM, particularly in methods development and his lab also develops and supports software packages and web services; Xmipp, Scipion and 3DBionotes. Prof. Carazo presented a CCeMMP seminar on August

29 at our University of Melbourne/Bio21 Node (in person and via zoom), followed by a networking session. He also took the time to meet with individual CCeMMP members and spoke with a group of our CCeMMP ICHDRs.

Prof. Renae Ryan visits MIPS

During Prof. Renae Ryan's visit to MIPS as a seminar speaker, our Melbourne-based ICHDRs were fortunate enough to meet with her. We had an impromptu mentoring session covering the path Renae took to get to her current position, as well as gender equity and diversity, inclusive and supportive environments and the postdoc experience. Renae was very generous with her time, knowledge and experience.



Prof. Renae Ryan visits MIPS, Aug 2023



Charcot-Marie-Tooth Australia

September 1, 2023, Dr. Winnie Tan hosted a lab tour with philanthropic partner, Charcot-Marie-Tooth Australia, to mark Charcot-Marie-Tooth (CMT) disease awareness month. Twelve members from CMT Australia were hosted at WEHI where they were given a tour of the laboratory and heard updates on Winnie's work and the cryo-EM research conducted at WFHI.



In the Spotlight

To promote members of the CCeMMP, the Outreach and Public Engagement Committee instigated a publicity initiative called "In the Spotlight" that has a primary (but not exclusive) focus on newer members of the Centre. These took the form of feature articles that highlighted recent members and affiliates in our newsletter and social media platforms, and included information about their scientific background, current research, and hobbies. Thus far, we have had two newsletters featuring "In the Spotlight", showcasing four of our affiliates: Prof. Lezanne Ooi, acting Node leader at UoW Node; Doulin Shepherd, a student affiliate from the Bio21/UoM Node; Dr. Winnie Tan, a PostDoc at WEHI; ICHDR Qinghao Ou from the Monash Node.







MPGPCR at MIPS, 15-17 November, 2023

The 11th International Molecular Pharmacology of G Protein Coupled Receptors (MPGPCR) meeting took place at MIPS, 15-17 November, 2023. CCeMMP was a major sponsor for this meeting, which was cochaired by the Monash Node leader, Prof. Denise Wootten (together with Dr. Lauren May) with many CCeMMP members being part of the local organising committee (Assoc. Prof. Karen Gregory, Dr. David



Thal, Dr. Elva Zhao, Dr. Tracy Josephs and Dr. Cindy Zhang). In addition to the Centre, the meeting was co-sponsored by some of our industry partner organisations, including Thermo Fisher Scientific (principal sponsor), NovoNordisk and industry collaborator, Karuna.



The meeting included presentations from leading international researchers and provided a relaxed atmosphere for interaction between students, postdocs and academic and industrial scientists.

MPGPCR runs every two years and focuses on novel concepts in GPCR pharmacology and drug discovery encompassing structural biology and biophysical studies, receptor pharmacology

(ligand bias and allostery), chemical biology, cell signalling and systems biology. The opening keynote lecture was delivered by our Centre Director, Prof. Patrick Sexton.

Many CCeMMP members were present at the meeting, and it was exciting to see the recognition of the quality of their research. Highlights included ICHDR Isabella Russell winning the Thermo Fisher Scientific Oral Presentation Prize for her talk titled "Lipid-



Dr. Jason Cao wins CCeMMP Best Postdoctoral Poster Prize

dependent activation of the orphan G protein-coupled receptor, GPR3."

Another highlight was centre member, Dr. Jason Cao, winning the CCeMMP sponsored Best Postdoctoral Poster Prize for his



ICHDR Isabella Russell wins Thermo Fisher Scientific Oral Presentation Prize

work titled "Structural understanding of amylin of amylin receptor targeted therapeutics for obesity. While Jason was awarded the poster prize, three of the other four shortlisted posters were from Centre members: Dr. Brian Cary, Dr. Wessel Burger and Dr. Cindy Zhang.





CCeMMP Retreat, 4-5 December, 2023

On December 4th and 5th 2023, the Centre held their annual retreat, at the Treacy Centre in Parkville; 61 members and affiliates registered to attend. We heard various scientific presentations from PhD students, and more senior members and affiliates.



Ten ICHDRs who have been working on their

PhD's for more than 12 months presented their research: Jack Tovey, Ania Beyger, Riya Joseph, Isabella Russell, Minakshi Barauh, Alok Pradhan, Marialena Georgopoulou, Xiaomin Wang, Qinghao Ou and Dongju Lee. These talks were delivered across two sessions, each chaired by Centre ICHDRs (Qinghao Ou and Xiaomin Wang; Jack Tovey and Isabella Russell). There were also two science presentation sessions from various CCeMMP members and affiliates. These included: Dr. Sarah Piper (Monash Node), Dr. Alisa Glukhova (WEHI Node), Susovan Das (WEHI Node), Dr. Aidan Grosas (UoW Node), Dr. Brian Cary (Monash Node), Dr. Jesse Mobbs (Monash Node), Dr. Joshua Hardy (WEHI Node), Yi (Jack) Zheng (Victor Chang Cardiac Research Institute), Assoc. Prof. Michael Landsberg (University of Queensland), Dr. Debnath Ghosal (UoM/Bio21 Node) and Dr. Winnie Tan (WEHI Node).



The talks were followed by a series of strategic planning sessions. Following an update on our current performance, Centre members worked in small breakout groups to discuss topics that ranged from new initiatives, funding, longevity, leadership and transition and brought their ideas back to the larger group. The Centre will move to implement as many of these ideas and initiatives in 2024 to improve Centre activities, collaboration, education and community outreach.

CCeMMP 2024 Calendar

A limited run of a 2024 CCeMMP calendar was printed that showcased structures determined by Centre members and affiliates. This was the brainchild of Dr. Sarah Piper and the Outreach & Public Engagement Committee, with image contributions across all our nodes: Monash University, University of Melbourne, WEHI and University of Wollongong, including external affiliates Alastair Stewart (VCCRI) and Emily Furlong (ANU).

All images were rendered by our Blender-Render-Masters: Dr. Sarah Piper, Dr. Jesse Mobbs, Dr. Joshua Hardy, Dr. Brian Cary and Dr. Sepideh Valimehr.

We aim to continue to produce these calendars in future years, showcasing structures from each of our Nodes and external affiliates that have been released from the previous calendar year.



A selection of images from the 2024 CCeMMP calendar





International Women's Day, 8 March, 2024

CCeMMP celebrated many of the brilliant women we have in our Centre by posting their highlights to our socials (twitter/X and LinkedIn) during the week of International Women's Day (IWD). Members and affiliates, who wanted to take part, were asked to provide a sentence or two about themselves along the lines of; What inspired them to be in STEM?; How would they like to see emerging women in the field supported?; What is their research?

In all, 12 profiles were posted on social media (twitter/X and LinkedIn) across all career stages: Marialena Georgopoulou, Riya Joseph, Mayada Mazher, Xiaomin Wang, Bhavika Rana,



Dr. Shadi Maghool, Dr. Natalie Diepenhorst, Dr. Isabella, Lambert-Smith, Dr. Winnie Tan, Assoc. Prof. Isabelle Rouiller, Prof. Isabelle Lucet, Prof. Lezanne Ooi.



On March 5th, CCeMMP, along with 7 other ARC ITTCs, joined to throw a IWD Panel event on 'Inspiring Inclusion' and discussing topics such as women's representation in the STEM workforce and the major challenges they still face with workplace prejudice. The panel was made up of women in STEM from different walks of life and cultural backgrounds: (pictured left to right) Dr. Indu Chandrashekaran, Dr. Bhavna Middha, PhD student Alka Batra, Assoc.Prof. Harriet Whiley, Prof. Jia-Yee Lee, Vesna Stefanovski (MC) and PhD student Jana Zielinski. They discussed their individual journeys and how they

were able to face these challenges, including where they gained their support from.

Newsletters



July 2023



October 2023



January 2024



We continued our quarterly newsletters that keep our members and stakeholders abreast of current research and achievements of the Centre. All newsletters can be accessed via the Centre website. We rotate the covers of the newsletters between our Nodes so that each newsletter cover image is of a membrane protein structure determined from the laboratory of a member or affiliate within that Node. We are particularly proud of our most recent cover (April 2024) being of a structure deposited by third year ICHDR, Isabella Russell; this is also the cover of the current annual report.

CCeMMP Seminar Series

In Year 3 of operation, the Centre continued its seminar series focussed on the advancement of research on cryo-EM and membrane proteins. Speakers were selected and invited by the CCeMMP Seminar Subcommittee. The committee aims to choose a diverse range of international and domestic speakers across academic, industry, including those with different career paths and strives for gender balance. The scheduled monthly seminars are open to the scientific and public communities and highlight leading researchers and research in the field. The seminars are routinely recorded and posted on our webpage (and YouTube channel). Since our last annual report, we have had 11 speakers in our regular program, and 3 special seminars, as detailed below. Seminars run from February to December, inclusive.





Dr. Joseph Brock Australian National University - The Structural basis of multi-drug transport: A story of a SynBio curious structural biologist. (May 9, 2023)



Prof. Renae Ryan The University of Sydney – The twisted link between a dual function glutamate transporter and episodic ataxia. (June 13, 2023)

Dr. Alisa Glukhova The Walter and Eliza Hall Institute of Medical Research - Using cryo-electron microscopy to understand the biology and drug binding at clinically relevant targets, Porcupine and 12-lipoxygenase. (August 8, 2023)



Dr. Marc Kschonsak Genentech/Roche, California, USA – From basic research to structure-based drug design: Using cryoEM to target voltage-gated ion channels. (July 11, 2023)



Engagement



Prof. José-María Carazo Spanish National Center for Biotechnology, CNB-CSIC Madrid, Spain - CryoEM conformational landscapes: Directly accessing macromolecular flexibility. (Extra Seminar Aug 29, 2023)



Dr. Steve Reichow Oregon Health and Science University, Portland, Oregon, USA - Mechanistic insights into gap junction cell-to-cell communication enabled by cryo-EM. (Oct 10, 2023)





Dr. Max Clabbers

University of California, Los Angeles, USA - Recent advances in MicroED: Membrane protein structure determination, direct electron detection, and ab initio phasing. (Sept 12, 2023)

Assoc. Prof. Tian Hua ShanghiTech University, Shanghi, China - Structure biology studies on cannabinoid receptors and putative cannabinoid receptor GPR12. (Special Seminar Oct 17, 2023)

Prof. Ariane Briegel Leiden University, Netherlands - Cryo-Electron Tomography contributes to our understanding of bacterial interactions with their environment. (Special Seminar Nov 28, 2023)



Dr. Susan Buchanan NIH, Bethesda, Marlyland, USA - Structural insight into outer membrane protein folding in bacteria and mitochondria. (Nov 14, 2023)





Prof. Scott Prosser

University of Toronto, Toronto, Canada- Allosteric activation networks in GPCRs (what you don't see by cryoEM). (Dec 12, 2023)





Dr. Xin (Cindy) Zhang MIPS, Monash University – Structural insights into the activation and modulation of a class B1 GPCR by small molecule ligands. (Feb 13, 2024)



Dr. Lisanne Spenkelink Molecular Horizons, University of Wollongong – Revealing biological stochasticity: Insights from single-molecule visualisation. (Mar 12, 2024)





Engagement



Prof. Brett Collins

Institute for Molecular Bioscience, University of Queensland - Structure of the endosomal Commander complex mutated in Ritscher-Schinzel syndrome: Combining crystallography, cryoEM & AlphaFold2. (Apr 9, 2024)

Industry Engagement

Visit to Boehringer Ingelheim

Prof. Patrick Sexton and Prof. Denise Wootten visited Boehringer Ingelheim, Biberach, Germany, for collaborator meetings, 8th-9th June, 2023. During the visit, Prof. Denise Wootten presented a talk "Linking structure to function - GLP-1R biased agonism and allosteric modulation."

Genentech Visit

With the IUCr meeting being held in Melbourne, August 2023, we were fortunate to have one of our industry partners, Dr. Claudio Ciferri from Genentech, take time to visit the Monash Node. During his visit, he ran an impromptu mentoring session with Centre students and Postdocs and student affiliates; there were 11 in-person and 5 on zoom. Dr. Ciferri provided valuable insight to industry and the different career pathways available within the pharmaceutical industry. His time was immensely appreciated.



Dr. Claudio Ciferri, Genentech, mentoring session, Aug 2023

Industry Placement

Isabella Russell - 3 month industry placement, AstraZeneca, Cambridge, UK (Jan - April 2024). During this time Isabella also participated in a Cambridge Cryo-EM consortium, presenting "Lessons in constitutive activity from the orphan receptor GPR3", 20 January 2024. At the conclusion of her placement, she was able to visit AstraZeneca, Gothenburg, Sweden where she participated in a drug discovery workshop, Challenges in GPCR Drug Discovery Workshop, April 18, 2024, presenting "Lessons in constitutive activity from the orphan receptor GPR3". Isabella's reflections on her time at AstraZeneca are on page 25.

Jack Tovey - 3 month industry placement, Astex, Cambridge, UK, commenced April 2024.

Alok Pradhan - Industry placement (1 day/week for 12 months), Dimerix, Fitzroy, commenced April 2024.



Media Engagement

Journal Highlights

Blood, Commentary. October 5, 2023: "Pass the 12-LOX!" Commentary on **Mobbs** et al., Blood, 42(14):1233, 2023. https://ashpublications.org/blood/article/142/14/1180/498142/Pass-the-12-LOX

eLife magazine insight. Dr David Thal "Drug Discovery: Decoding the mechanisms of allostery." https://elifesciences.org/articles/88749

Nature Review Drug Discovery, News In Brief. October 6, 2023: 'Novel schizophrenia therapy filed for FDA approval' [Article refers to **Burger** et al., Nat Commun 14(1): 5440, 2023. doi: 10.1038/s41467-023-41199-5. "Xanomeline binds and acts at both the orthosteric and an allosteric site on M4 mAChR, researchers recently reported."]https://www.nature.com/articles/d41573-023-00164-z

Nature Reviews Drug Discovery, Research Highlight. September 26, 2023: 'Antipsychotic displays dual GPCR binding mode' [Highlighting **Burger** et al., Nat Commun 14(1): 5440, 2023. doi: 10.1038/s41467-023-41199-5.] https://www.nature.com/articles/d41573-023-00154-1

CCeMMP Members in the News

Prof. Renae Ryan, August 11, 2023: Prof. Renae Ryan featured in **Cosmos Magazine**; Unlocking the brain's building blocks https://cosmosmagazine.com/science/biology/unlocking-the-brains-building-blocks/

Prof. Arthur Christopoulos, March 10, 2024: Prof. Arthur Christopoulos featured in **Neos Kosmos**; "Professor Arthur Christopoulos receives ASPET Goodman and Gilman Award in Receptor Pharmacology."

https://neoskosmos.com/en/2024/03/10/news/australia/professor-arthur-christopoulos-receives-aspet-goodman-and-gilman-award-in-receptor-pharmacology/

Digital and Social Media

Dr. Jason Cao, November 21, 2023 - Faculty of Pharmacy and Pharmaceutical Sciences post on Early Career Research Publication Award - **Monash University Faculty of Pharmacy and Pharmaceutical Sciences web page:** (https://www.monash.edu/pharm/research/facultyawards/early-career-research-publication-award

Prof. Arthur Christopoulos, Dr. Celine Valant, Dr. David Thal, September 14, 2023 – **Monash University Faculty of Pharmacy and Pharmaceutical Sciences web page:** "Drug discovery researchers from Monash University have uncovered new, and unexpected, information about 'xanomeline', a potential-first-in class drug currently progressing through Phase III clinical trials for the treatment of patients with schizophrenia." https://www.monash.edu/pharm/about/news/ news-listing/latest/scientists-uncover-new-and-unexpected-information-about-schizophrenia-drug. **Burger** et al., Nat Commun 14(1): 5440, 2023. doi: 10.1038/s41467-023-41199-5.





Dr. Alastair Stewart, November 29, 2023 - NHMRC post on the Commonwealth Health Minister's Award for Excellence in Health and Medical Research - **NHMRC web page (and twitter/X)** https://www.nhmrc.gov.au/about-us/news-centre/dr-alastair-stewart-recognised-outstanding-achievement-health-and-medical-research

Dr. Winnie Tan, December 15, 2023 - **WEHI LinkedIn post** congratulating their Investigator grant awardees https://www.linkedin.com/feed/update/urn:li:activity:7141267467661623298/

Dr. Winnie Tan, December 15, 2023 - **WEHI Twitter post** congratulating their Investigator grant awardees https://twitter.com/WEHI_research/status/1735499277957476645

Dr. Winnie Tan, September 27, 2023, **WEHI Facebook page** CMT Australia visit to meet Dr. Winnie Tan at WEHI. https://www.facebook.com/photo/?fbid=630936099189774&set=a.562623272687724 &paipv=0&eav=AfaqeqIjusiC0vjEA1yR1A8uoaPeGriOntoX9Eo0C0KWHrN7NBzpx8DfLwGfMJvfCAo&_rdr

Dr. David Thal, May 30, 2023 (images prepared by Dr. Sarah Piper) **Monash University Faculty of Pharmacy and Pharmaceutical Sciences web page** https://www.monash.edu/pharm/ about/news/news-listing/latest/world-first-monash-led-study-unlocks-key-new-information-onmajor-drug-target-for-psychiatric-and-cognitive-disorders,-including-schizophrenia

Assoc. Prof. Gökhan Tolun - **The Cryo-Talk podcast (June 14, episode 10)** from Thermo Fisher Scientific and Bitesize Bio interviewed Assoc. Prof. Gökhan Tolun. The interview is available as an audio podcast (https://cryo-talk.bitesizebio.com/) and YouTube video (https://bit.ly/cryotalk10-gt)

IWD 2024 - CCeMMP posted 12 member/affiliate profiles on social media (@CCeMMP twitter/X and LinkedIn) during the week of International Women's Day: Marialena Georgopoulou, Riya Joseph, Mayada Mazher, Xiaomin Wang, Bhavika Rana, Dr. Natalie Diepenhorst, Dr. Shadi Maghool, Dr. Isabella Lambert-Smith, Dr. Winnie Tan, Assoc. Prof. Isabelle Rouiller, Prof. Isabelle Lucet, Prof. Lezanne Ooi.

Profs. Patrick Sexton and Denise Wootten - March 27, 2024 - **NHMRC Twitter/X -** Research Excellence Awards

Profs. Patrick Sexton and Denise Wootten - March 28, 2024 - Faculty post on NHMRC Research Excellence Awards - **Faculty of Pharmacy and Pharmaceutical Sciences web page** https://www.monash.edu/pharm/about/news/news-listing/latest/monash-universitypharmaceutical-scientists-honoured-in-nhmrc-research-excellence-awards

Profs. Patrick Sexton and Denise Wootten - March 28, 2024 - **Monash Twitter/X** - Research Excellence Awards; **CCeMMP Twitter/X** - Research Excellence Awards

Profs. Patrick Sexton and Denise Wootten - NHMRC webpage - Research Excellence Awards https://www.nhmrc.gov.au/about-us/nhmrc-awards/2023-research-excellence-awards





Governance













Changes to Governance

Centre Manager

The Centre Manager Dr. Jackie How returned from maternity leave September 2023.

Executive Committee

Assoc. Prof. Gökhan Tolun is currently on sabbatical until July 2024. Prof. Lezanne Ooi is acting Node Leader in his absence. Mr. Qinghao Ou (Monash Node) completed his twelve month term as ICHDR representative at the end of January 2023. Ms. Minakshi Baruah (Monash Node) was elected by a ballot of the current ICHDR cohort, as the new ICHDR representative for 2024.



Performance

PDB:8DPT









RELEASED

EMD STRUCTURES



51



Key Performance Measures



ndustry Related Performance Measures

investigators





Structures Published in Publicly Accessible Databases (PDB & EMD)

Structures have been published from all of our Nodes and also our external affiliates. Some structures were published through collaborations between nodes (Monash-WEHI); or between external affiliates (from multiple institutions) and UoW (VCCRI-UQ-USyd-UoW). Following is a list of all structures published and released in PDB and/or EMD. Visual images of these structures are found later in this report ("Structures Published Year 3"; note * are not in this gallery).

PUBLISHED IN	NATURE METHODS	BLOOD	NATURE COMMUNICATIONS	NATURE CHEM BIOLOGY
13	1	1	4	1
MANUSCRIPTS	IMPACT FACTOR 48	IMPACT FACTOR 20.3	IMPACT FACTOR 16.6	IMPACT FACTOR 14.8

- PDB:7TRK, EMD-26099 [Human M4 muscarinic acetylcholine receptor (mAChR) in complex with iperoxo]
- PDB:7TRP, EMD-26100 [Human M4 mAChR in complex with iperoxo and a PAM (LY)]
- PDB:7TRQ, EMD-26101 [Human M4 mAChR in complex with iperoxo and a PAM (VU)]
- PDB:7TRS, EMD-26102 [Human M4 mAChR in complex with acetylcholine]
- PDB:8CHB, EMD-16659 [Inward facing ABC Transporter, cross linked mutant]
- PDB:8DPS, EMD-27641[Human Interleukin 11 signalling complex with truncated gp130]
- PDB:8DPT, EMD-27642 [Human interleukin 11 signalling complex with full length extracellular gp130]
- PDB:8F0J, EMD-28758 [Human calcitonin receptor in complex with Gs and San45]
- PDB:8F0K, EMD-28759 [Human amylin 3 receptor in complex with Gs and San385]
- PDB:8F2A, EMD-28810 [Human amylin 3 receptor in complex with Gs and San385, cluster 5 conformation]
- PDB:8F2B, EMD-28812 [Human amylin 3 receptor in complex with Gs and San385]
- PDB 8FX5, EMD-29524 [Human M4 mAChR in complex with Gi1 and xanomeline]
- PDB:8GHB, EMD-40039 [Human arachidonate 12S-Lipoxygenase (12-LOX) monomer]
- PDB:8GHC, EMD-40040, EMD-40299, EMD-40300, EMD-40301[Human 12-LOX dimer]
- PDB:8GHD, EMD-40041, EMD- 40302, EMD-40304 [Human 12-LOX hexamer]
- PDB:8GHE, EMD-40042 [Human 12-LOX tetramer]
- PDB:8GIY, EMD-40079 [E. coli clamp loader with closed clamp]
- PDB:8GIZ, EMD-40080 [E. coli clamp loader with open clamp]
- PDB:8GJ0, EMD-40081[E. coli clamp loader with open clamp on primed template DNA (form 1)]
- PDB:8GJ1*, EMD-40082 [E. coli clamp loader with open clamp on primed template DNA (form 2)]
- PDB:8GJ2, EMD-40083 [E. coli clamp loader with closed clamp on primed template DNA]
- PDB:8GJ3, EMD-40084 [E. coli clamp loader on primed template DNA]
- PDB:800E, EMD-18535 [Inward facing ABC transporter]
- PDB:8SC1, EMD-40334 [Human organic ion transporter 1(0CT1), inward conformation]
- PDB:8SC2, EMD-40335 [Human OCT1-diltiazem, inward conformation]
- PDB:8SC3, EMD-40336 [Human OCT1-fenoterol, inward conformation]
- PDB:8SC4, EMD-40337 [Human OCT1-metformin, inward conformation]
- PDB:8SC6, EMD-40339 [Human OCT1-thiamine, inward conformation]



- PDB:8SPV, EMD-40687 [Rotorless F1 ATPase, no ATP]
- PDB:8SPW, EMD-40688 [Rotorless F1 ATPase, low ATP]
- PDB:8SPX, EMD- 40689 [Rotorless F1 ATPase, high ATP]
- PDB:8U18, EMD-41805 [Murine thrombopoietin receptor ectodomain in complex with Tpo]
- PDB:8U8F, EMD- 42023 [Human orphan receptor GPR3 with dominant negative Gs] **ICHDR student** project with industry partner AstraZeneca
- PDB:9AUC, EMD-43877 [Human amylin 1 receptor in complex with Gs and CGRP]
- EMD-42882 [Amylin 1 receptor bound to salmon calcitonin reconstructed from cryo-EM datasets recorded using a rectangular aperture]
- EMD-41938* [apoferritin determined for benchmarking square and rectangular apertures for cryo-EM(Gatan K3 rectangular beam)]
- EMD-41937* [apoferritin determined for benchmarking square and rectangular apertures for cryo-EM(Falcon IV square beam)]
- EMD-41936* [apoferritin determined as a reference for benchmarking square and rectangular apertures for cryo-EM (Falcon IV round beam)]
- EMD-41933 [apoferritin determined as a reference for benchmarking square and rectangular apertures for cryo-EM]

*not illustrated in "Structures Solved Year 3"

Leveraged Research Funding

Industry







Funding

Major Funding

2023 University of Wollongong Major Equipment Grant, Assoc. Prof. Gökhan Tolun, \$250,000.

ARC Discovery Project, DP240101399: "High-throughput single-molecule directed evolution". **Dr. Lisanne Spenkelink; Prof. Antoine van Oijen**; Prof. Andrew Griffiths, \$598,737.

ARC Linkage Infrastructure, Equipment and Facilities grant, LE240100054 (administered through The University of Sydney) Prof. Chris Ling; Dr. William Lewis; **Prof. Renae Ryan**; Prof. Rongkun Zheng; Prof. Antonio Tricoli; Dr. Lauren Macreadie; Assoc. Prof. Neeraj Sharma; Prof. Philip Gale; Dr. Fei Liu; Dr. Feng Li; Prof. Valeska Ting; Prof. Bostjan Kobe; Prof. Jack Clegg; Prof. Jennifer Pringle; Prof. Christopher Sumby. Funding is over 1 year in order to establish a dedicated high-throughput 3D-electron diffractometer, the first in the Southern Hemisphere, \$1,341,398.

Cumming Global Centre for Pandemic Therapeutics (CGPT) (round 1 Foundation grants): "A comprehensive structural (-cell) biology platform for rapid characterisation of any pathogen of pandemic potential". Cl's, **Dr. Debnath Ghosal, Prof. Michael Parker, Prof. Eric Hanssen, Dr. Matthew Johnson** and Dr. Roxanne Smith, \$1.5M.

NHMRC Investigator EL1 Grant (2026635): "Capturing atomic snapshots to visualise chromatin remodelling machinery for disease insights and drug discovery", **Dr. Winnie Tan**, \$662,000.

NHMRC L2 Leadership Investigator grant (2026300): "Mechanistic understanding of biased agonism and dimerisation for co-targeting incretin receptors for metabolic diseases".(2024-2028), **Prof. Denise Wootten**, \$2,897,165.

NHMRC L3 Leadership Investigator grant (2025694): "Structure, function and modulation of peptide hormone G protein-coupled receptors (GPCRs)". (2024-2028), Prof. Patrick Sexton, \$2,953,040.

US Department of Defense, (Congressionally Directed Medical Research Programs), Rare Cancers Research Program Concept Award: "Unleashing the Power of Silence: Investigating the epigenetic regulator HUSH as a new target for treating acute myeloid leukaemia.", Dr. Shabih Shakeel (PI) and Dr. Winnie Tan (co-CI), \$100,000 USD (2024-2025).

Small Grants (<\$100,000)

University of Wollongong, EMCR Enabling Grant 2023, Dr. Aidan Grosas (\$2,893).

University of Wollongong, Advancement and Equity Grant Scheme (AEGiS) Research Grant 2023 (ADVANCE Stream), **Dr. Aidan Grosas** "Structural studies of the post-translational modification phosphorylation on alpha-synuclein amyloid fibrils associated with Parkinson's Disease" (\$16,051).

Small Research Equipment Grant, **Dr. Lisanne Spenkelink** (co-CI; \$25,000).

WEHI's New Medicines and Advanced Technologies, Dr. Shabih Shakeel (\$24,000).



Travel Grants

- Marialena Georgopoulou: Graduate Researcher Travel Award, Department of Biochemistry and Pharmacology, The University of Melbourne; used for registration to IUCr 2023.
- Riya Joseph: Graduate Researcher Travel Award, Department of Biochemistry and Pharmacology, The University of Melbourne; used for registration to IUCr 2023.
- Riya Joseph: 4th Small Angle Scattering (SAS) Workshop, Australian Synchrotron, Clayton. Riya secured free registration to the workshop being selected as one of the top three submissions applying to attend; the workshop was limited to 20 participants only.
- Dr. Sarah Piper: Monash Early Career Network Travel Grant to visit collaborators.
- Jhonnatan Reales-Gonzalez: SMAH HDR Travel Grant: awarded for costs associated with attending the ARC CryoEM Data Processing Rotation, September 11th 22th, Monash University, Parkville.
- Dr. Alice Shin: Vice-Chancellor's HDR Travel Grants to attend international conference.
- Dr. Alice Shin: Bursary awarded to attend the CryOz 2023.
- Dr. Winnie Tan: CASS Foundation, CASS Travel Award to attend the EMBL Chromatin and Transcription Conference 24-27 August 2024, Heidelberg, Germany.

Society Fellowships



- Assoc. Prof. Karen Gregory Fellowship of the Higher Education Academy.
- Prof. Renae Ryan Fellow of the Royal Society of NSW.



Prof. Renae Ryan

Assoc. Prof. Karen Gregory

Awards

- Dr. Wessel Burger Mollie Hollman Medal, Best Doctoral Thesis, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University.
- Dr. Jason Cao Faculty of Pharmacy and Pharmaceutical Sciences (Monash University) Early Career Research Publication Award.
- Prof. Arthur Christopoulos American Society for Pharmacology and Experimental Therapeutics (ASPET) Louis S. Goodman and Alfred Gilman Award in Receptor Pharmacology.



Dr. Wessel Burger



Dr. Jason Cao



Prof. Arthur Christopoulos





- Prof. Megan O'Mara McAuley-Hope Prize for Original Biophysics.
- Prof. Renae Ryan the International Award from the Biochemical Society (April 5, 2024; to be presented in 2025).
- Prof. Renae Ryan Eureka award for Outstanding Mentor of Young Researchers.
- Prof. Patrick Sexton 2023 NHMRC Peter Doherty Investigator Grant Award (Leadership).



Prof. Megan O'Mara



Prof. Renae Ryan



Prof. Patrick Sexton

- Dr. Alastair Stewart Commonwealth Health Minister's Award for Excellence in Health and Medical Research.
- Dr. Sepideh Valimehr AU-NZ Knowledge Exchange award (Microscopy Australia).
- Prof. Denise Wootten 2023 NHMRC Elizabeth Blackburn Investigator Grant Award (Leadership, Basic Science).



Dr. Alastair Stewart



Dr. Sepideh Valimehr



Prof. Denise Wootten

Conference Awards

- Felix Bennetts Early Career Research Prize (WCP2023) Oral presentation. Using Cryo-EM to solve the P2X1 receptor structure a target for male contraception. World Congress of Pharmacology (WCP2023), 2-7 July, 2023 Glasgow, UK.
- Dr. Jason Cao Anders Early Career award Decoding AMYR and CTR activation: structural insights for obesity therapeutics. Lorne Proteins 2024, 4 8th February, 2024, Lorne, VIC.
- Dr. Jason Cao Best Postdoctoral Poster Presentation Prize (CCeMMP sponsored) Structural understanding of amylin receptors targeted therapeutics for obesity. MPGPCR 2023, 15th - 17th November, 2023, Melbourne.



Felix Bennetts



Dr. Jason Cao





- Marialena Georgopoulou Poster prize Structural studies of cell signalling adaptor protein Stimulator of Interferon Genes (STING) in complex with small molecule inhibitors. Lorne Proteins 2024, 4 - 8th February, 2024, Lorne, VIC.
- Michaela Kaoullas Poster Prize, ASCEPT Special Interest Group (SIG) prizes (Neuropharmacology section) Structural insights into positive allosteric modulation at the M4 mAChR. ASCEPT 2023, 20-23 November, 2023, Sydney.
- Jordan Nicholls Best student poster Unravelling Herpesvirus DNA Annealing: Cryo-EM structure of BALF2. CryOz 2023, 23-24 November,2023, The University of Queensland, Brisbane.
- Jordan Nicholls Best student talk Unravelling Herpesvirus DNA Annealing: Cryo-EM structure of BALF2. ASB 2023, 3-6 December, 2023, The University of Wollongong, Wollongong.
- Bindusmita Paul Best student talk Characterisation of the structure and dynamics of oral polymicrobial biofilms at molecular resolution. CryOz 2023, 23-24 November 2023, The University of Queensland, Brisbane.



Marialena Georgopoulou



Michaela Kaoullas



Jordan Nicholls



Bindusmita Paul

- Isabella Russell Student oral presentation prize Lipid-dependent activation of the orphan G protein-coupled receptor, GPR3. MPGPCR 2023, 15th 17th November, 2023, Melbourne.
- Dr. Alice Shin Poster prize Structural investigation of multi-drug resistance ABC transporter CDR1 of Candida albicans. ASBMB, 15-17th November, 2023, ANU, Canberra.
- Dr. Alice Shin Oral presentation prize (runner up) Structurally investigating multidrug resistance ABC transporter of pathogenic Candida yeast using cryo-EM. RSB HDR conference, 9 April, 2024, ANU, Canberra, ACT.
- Dr. Xin (Cindy) Zhang Anders Early Career award Structural insights into the activation and modulation of a class B1 GPCR by small-molecule ligands. Lorne Proteins 2024, 4 8th February, 2024, Lorne, VIC.



Isabella Russell



Dr. Alice Shin



Dr. Xin (Cindy) Zhang



Other Achievements

- Prof. Patrick Sexton and Prof. Arthur Christopoulos have been included in the list of the world's most influential researchers as 2023 Clarivate analytics Highly Cited Researchers in the category 'Pharmacology & Toxicology'.
- Jessica Lu PhD awarded, Thesis title: "Structural and Pharmacological Characterisation of Splice Isoforms of the Pituitary Adenylate Cyclase- Activating Polypeptide Type 1 (PAC1) Receptor."



Prof. Arthur Christopoulos



Prof. Patrick Sexton



Jessica Lu

- Bhanu Mantri PhD awarded. Thesis title is, "Understanding the Molecular Mechanism of Single-Strand Annealing Homologous DNA Recombination in Viruses by Cryo-Electron Microscopy."
- Prof. Megan O'Mara elected President of the Association of Molecular Modellers of Australasia (AMMA).
- Prof. Renae Ryan awarded an Order of Australia.



Prof. Megan O'Mara



Prof. Renae Ryan

Academic Promotions

- Dr. Simon Brown, continuing appointment level 8/9, Professional Staff.
- Prof. Isabelle Lucet promoted to Level E.
- Dr. Lisanne Spenkelink promoted to Level C.



Dr. Simon Brown



Prof. Isabelle Lucet



Dr. Lisanne Spenkelink



Conference Presentations

International Conference Presentation (invited)

Prof. Arthur Christopoulos - World Congress of Pharmacology (WCP2023), 2-7 Jul 2023 Glasgow, UK. Allosteric drug discovery: from theory to practice.

Dr. Debnath Ghosal - International Microscopy Congress, 11-15 Sep 2023, Busan, Korea. Understanding the structural basis of T-DNA translocation through the Agrobacterium tumefaciens Type IV Secretion System.

Assoc. Prof. Karen Gregory - 11th International Molecular Pharmacology of GPCRs meeting (MPGPCR 2023), 15-17 Nov 2023, Parkville, Australia. Fine tuning glutamate receptor activity in space and time.

Assoc. Prof. Isabelle Rouiller - International Union of Crystallography (IUCr2023), 22-29 Aug 2023, Melbourne, Australia. Understanding the conformational landscape p97 from cryo-EM and mass-spectrometry data.

Prof. Renae Ryan - Gordon Research Conference, Ligand Recognition & Molecular Gating: Structure, Mechanism, & Drug Interactions of GPCRs, Ion Channels, & Transport Proteins, 24-29 Mar 2024, Ventura USA. Unique transport mechanism of a Drosophila melanogaster glutamate transporter informs ion-coupling mechanisms in the SLC1A family.

Prof. Patrick Sexton - 26th Swedish Conference on Macromolecular Structure & Function (SWEPROT), 16-22 Jun 2023, Tällberg, Sweden. Advancing GPCR drug discovery using cryo-EM.



Prof. Patrick Sexton, MPGPCR

Prof. Patrick Sexton - World Congress of Pharmacology (WCP2023), 2-7 Jul 2023 Glasgow, UK. Understanding structure and activation of amylin and calcitonin receptors.

Prof. Patrick Sexton - International Union of Crystallography (IUCr2023), 22-29 Aug 2023, Melbourne, Australia. Application of cryo-EM to understanding peptide and small molecule binding to G protein-coupled receptors.

Prof. Patrick Sexton - Great Lakes GPCR Retreat, 2-4 Nov 2023, Montebello, Canada. Biased agonism at the GLP-1 receptor: from structure to animal models of disease.

Prof. Patrick Sexton - 11th International Molecular Pharmacology of

GPCRs meeting (MPGPCR 2023), 15-17 Nov 2023, Melbourne, Australia. Towards a Structural Understanding of Class B1 GPCRs.

Prof. Patrick Sexton - 68th Annual meeting of the Biophysical Society, 10-14 Feb 2024, Philadelphia, USA. Structural mechanisms of class B GPCR activation and signaling.

Dr. Alastair Stewart (presented by PhD student Yi Zeng) - Gordon Research Conference: Mechanisms of Membrane Transport, 18-23 Jun 2023, Les Diablerets, Switzerland. Insights into Substrate Translocation of Organic Cation Transporter 1.

Dr. Alastair Stewart - International Conference on Biological Physics, 14-18 Aug 2023, Seoul, Korea. Structures





of the F1-ATPase Rotary Catalytic Cycle.

Dr. Alastair Stewart (Discussion Leader) - Gordon Research Conference, Bioenergetics, 25-30 Jun 2023, New Hampshire, USA. ATP Synthase in Health and Disease.

Dr. David Thal - 11th Adrenoceptor Symposium, 30 Jun-1 Jul 2023, Glasgow, UK. Where the allosteric modulators are.

Prof. Denise Wootten - Gordon Research Conference, Molecular Pharmacology: Progressive Technologies & Approaches Revealing Novel GPCR Biology & Drug Development Potential, 11-16 Jun 2023, Les Diablerets, Switzerland. Structural approaches to deciphering the nature of Class B receptor biology.

Prof. Denise Wootten - World Congress of Pharmacology (WCP2023), 2-7 Jul 2023 Glasgow, UK. Mechanisms of signalling and biased agonism in G protein-coupled receptors.

Prof. Denise Wootten - 13th International Peptide Symposium; 15th Australian Peptide Conference (IPS 2023), 15-20 Oct 2023, Brisbane, Australia. GLP-1 receptor biased agonism: from structure to animal models of disease.

Prof. Denise Wootten - Gordon Research Conference, Ligand Recognition & Molecular Gating: Structure, Mechanism, & Drug Interactions of GPCRs, Ion Channels, & Transport Proteins, 24-29 Mar 2024, Ventura, USA. Biased agonism at the GLP-1 receptor: from structure to animal models of disease.

Prof. Denise Wootten - Endocrine Metabolic GPCRs - from molecules and mechanisms to medicine, 22-23 Apr 2024, Birmingham, UK. Biased agonism at the GLP-1 receptor: from structure to animal models of disease.

Dr. Xin (Cindy) Zhang (Discussion Leader) - Gordon Research Conference, Ligand Recognition & Molecular Gating (GRS): Structure, Mechanism, & Drug Interactions of GPCRs, Ion Channels, & Transport Proteins, 23-24 Feb 2024, Ventura, USA.

International Conference Presentation (selected oral presentation)

Felix Bennetts* - World Congress of Pharmacology (WCP2023), 2-7 Jul 2023, Glasgow, UK. Using cryo-EM to solve the P2X1 receptor structure - a target for male contraception. ***Early Career Research Prize**

Dr. Fabian Bumbak - International Society of Magnetic Resonance (ISMAR23), 20-25 Aug 2023, Brisbane, Australia. The neurotensin peptide agonist retains conformational flexibility upon binding to neurotensin receptor 1.

Dr. Wessel Burger - 11th International Molecular Pharmacology of GPCRs meeting (MPGPCR 2023), 15-17 Nov 2023, Melbourne, Australia. Positive allosteric modulation at a GPCR ternary complex.

Dr. Brian Cary - 13th International Peptide Symposium; 15th Australian Peptide Conference (IPS 2023), 15-20 Oct 2023, Brisbane, Australia. Structure and activity of backbone-modified class B1 GPCR agonists.

Prof. Chris Langmead - World Congress of Pharmacology (WCP2023), 2-7 Jul 2023, Glasgow, UK. Academic drug discovery: misnomer or master-stroke?

Dr. Jesse Mobbs - Gordon Research Conference, Ligand Recognition & Molecular Gating: Structure, Mechanism, & Drug Interactions of GPCRs, Ion Channels, & Transport Proteins. 24-29 Mar 2024, Ventura USA. Structural investigation of allosteric modulation of the delta opioid receptor.



Isabella Russell* - 11th International Molecular Pharmacology of GPCRs meeting (MPGPCR 2023), 15-17 Nov 2023, Melbourne, Australia. Lipid-dependent activation of the orphan G protein-coupled receptor, GPR3. ***Best student oral presentation award**

Dr. David Thal - World Congress of Pharmacology (WCP2023), 2-7 Jul 2023 Glasgow, UK. Discovery of novel allosteric binding sites for selective allosteric modulators at the M5 mAChR.

International Conference Presentation (posters)

Dr. Wessel Burger - 11th International Molecular Pharmacology of GPCRs meeting (MPGPCR 2023), 15-17 Nov 2023, Melbourne, Australia. 1.96 Å cryo-EM structure of the M5 mAChR with a selective allosteric modulator reveals novel binding site.

Dr. Jason Cao^{*} - 11th International Molecular Pharmacology of GPCRs meeting (MPGPCR 2023), 15-17 Nov 2023, Melbourne, Australia. Structural understanding of amylin receptors targeted therapeutics for obesity. ***Best postdoctoral trainee poster presentation**

Susovan Das - 11th International Molecular Pharmacology of GPCRs meeting (MPGPCR 2023), 15-17 Nov 2023, Melbourne, Australia. Structural insight into G protein coupling and activation of human FZD5 receptor.

Marialena Georgopoulou - International Union of Crystallography (IUCr2023), 22-29 Aug 2023, Melbourne, Australia. Structural studies of cell signalling adaptor protein STimulator of INterferon Genes (STING) in complex with small molecule inhibitors.

Riya Joseph - International Union of Crystallography (IUCr2023), 22-29 Aug 2023, Melbourne, Australia. Structural studies of recently identified B. fragilis cholesterol-dependent cytolysin like proteins.

Michaela Kaoullas - 11th International Molecular Pharmacology of GPCRs meeting (MPGPCR 2023), 15-17 Nov 2023, Melbourne, Australia. Structural Insights into Positive Allosteric Modulation at the M4 mAChR.

Dr. Peter Keov - 11th International Molecular Pharmacology of GPCRs meeting (MPGPCR 2023), 15-17 Nov 2023, Melbourne, Australia. Novel profiles of selective and non-selective peptide agonists of calcitonin and amylin receptors revealed by a selective amylin receptor activation system.

Dr. Jesse Mobbs - Gordon Research Conference, Ligand Recognition & Molecular Gating (GRS): Structure, Mechanism, & Drug Interactions of GPCRs, Ion Channels, & Transport Proteins, 23-24 Mar 2024, Ventura, USA. Structural investigation of ligand recognition of the P2X1 receptor.

Dr. Nazanin Mohebali - 11th International Molecular Pharmacology of GPCRs meeting (MPGPCR 2023), 15-17 Nov 2023, Melbourne, Australia. Development of biochemical methods for purification of dimeric secretin receptors for structure determination using cryo-EM.

Assoc. Prof. Isabelle Rouiller - 2024 VCP International Conference: Cure VCP Disease. 22-25 Feb 2024, Pasadena , USA. Unveiling the impact of IMPFD mutations on VCP dynamics: a biophysical multimodal investigation.

Isabella Russell - 11th International Molecular Pharmacology of GPCRs meeting (MPGPCR 2023), 15-17 Nov 2023, Melbourne, Australia. Lipid-dependent activation of the orphan G protein-coupled receptor, GPR3.

Dr. Alice Shin - Gordon Research Conference, Mechanisms of Membrane Transport: Structure, Dynamics & Allosteric Regulation. 18 - 23 Jun 2023, Les Diablerets, Switzerland. Structural investigation of multi-drug





resistance ABC transporter CalbCDR1 of Candida albicans.

Dr. Winnie Tan - International Union of Crystallography (IUCr2023), 22-29 Aug 2023, Melbourne, Australia. Human MORC2 is an ATP-dependent DNA compaction machine.

Jack Tovey - 11th International Molecular Pharmacology of GPCRs meeting (MPGPCR 2023), 15-17 Nov 2023, Melbourne, Australia. A structural investigation into the agonism and allosteric modulation of the cholecystokinin type 1 receptor.

Dr. Xin (Cindy) Zhang - Gordon Research Conference, Ligand Recognition & Molecular Gating; Structure, Mechanism, and Drug Interactions of GPCRs, Ion Channels, and Transport Proteins, 24-29 Mar 2024, Ventura USA. Structural insights into GLP-1R activation and allosteric modulation by non-peptidic ligands.

Dr. Elva Zhao - Gordon Research Conference, Molecular Pharmacology: Progressive Technologies & Approaches Revealing Novel GPCR Biology & Drug Development Potential, 11-16 Jun 2023, Les Diablerets, Switzerland. RGS proteins, new player in the class B game?

National Conference Presentation (invited)

Dr. Joe Brock - 4th CryOz symposium (CryOz 2023), 23-24 Nov 2023, The University of Queensland, Brisbane, QLD. The structural basis of multidrug transport.

Dr. Matthew Johnson - 4th CryOz symposium (CryOz 2023), 23-24 Nov 2023, The University of Queensland, Brisbane, QLD. Exploring microbial dark matter using CryoET and in situ structural biology.

Assoc. Prof. Michael Landsberg - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. New insights into mechanism of activation and cell recognition by bacterial



Dr. Xin (Cindy) Zhang, Lorne Proteins 2024

ABC toxins.

Dr. Jesse Mobbs - 4th CryOz symposium (CryOz 2023), 23-24 Nov 2023, The University of Queensland, Brisbane, QLD. Cryo-EM structures of human arachidonate 12S-Lipoxygenase (12-LOX) bound to endogenous and exogenous inhibitors.

Bindusmita Paul* - 4th CryOz symposium (CryOz 2023), 23-24 Nov 2023, The University of Queensland, Brisbane, QLD. Characterisation of the structure and dynamics of oral polymicrobial biofilms at molecular resolution.* *Best student talk*

Dr. Shabih Shakeel - 18th Australian Cell Cycle, DNA Repair & Telomere Meeting, 23-25 Oct 2023, Melbourne, VIC. Structure and mechanism of FANCD2-FANCI clamping onto DNA.

Dr. Winnie Tan - CMT Australia National Conference, Sept 9 2023, Online. Understanding how MORC2 mutations contribute to the Charcot-Marie-Tooth (CMT) disease.

Dr. Xin (Cindy) Zhang - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4 - 8 Feb 2024, Lorne, VIC. Structural insights into the activation and modulation of a class B1 GPCR by small-molecule ligands.



National Conference Presentation (selected oral presentation)

Joydeep Baral - Melbourne India Postgraduate Academy Conference (MIPAC 2023), 15-17 Nov 2023, Carlton, VIC. Structure-function insight into the two component DNA repair system of Mycobacterium tuberculosis.

Dr. Hamish Brown - 4th CryOz symposium (CryOz 2023), 23-24 Nov 2023, The University of Queensland, Brisbane, QLD. Square beams for dreams: Development of CryoEM novel condenser aperture plates four square and rectangular illumination.



Dr. Wessel Burger - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4 - 8 Feb 2024, Lorne, VIC. Cryo-EM reveals novel drug binding modes at GPCRs.

Dr. Jason Cao - (Moving & Shaking session) 49th Lorne Conference on Protein Structure & Function (Lorne



Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Decoding AMYR and CTR activation: structural insights for obesity therapeutics.

Dr. Emily Furlong - 4th CryOz symposium (CryOz 2023), 23-24 Nov 2023, The University of Queensland, Brisbane, QLD. Molecular structure of an axle-less F1-ATPase.

Dr. Joshua Hardy - 4th CryOz symposium (CryOz 2023), 23-24 Nov 2023, The University of Queensland, Brisbane, QLD. TEMPO: Training in Electron

Microscopy Processing and Optics.

Dr. Matthew Johnson - (Cool Techniques) 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. In Situ structural determination of cell-cell interactions in Archaea by cryotomography.

Jordan Nicholls* - Australian Society of Biophysics (ASB 2023), 3-6 Dec 2023, University of Wollongong, Wollongong, NSW. Unravelling Herpes virus DNA annealing: cryo-EM structure of BALF2. *Best student talk

National Conference Presentation (posters)



Joydeep Baral - 49th Lorne Conference on

Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Structure-function insight into the two component DNA repair system of Mycobacterium tuberculosis.





Performance



Proteins 2024

Felix Bennetts - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Cryo-EM reveals the molecular basis of P2X1 receptor activation and inactivation.

Dr. Jason Cao - 4th CryOz symposium (CryOz 2023), 23-24 Nov 2023, The University of Queensland, Brisbane, QLD. Structural understanding of amylin receptors targeted therapeutics for obesity.

Dr Jason Cao - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Decoding AMYR and CTR activation: structural insights for obesity therapeutics.

Prof. Brett Collins - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Molecular basis for the assembly of yeast SNX-BAR proteins with retromer trafficking coat.

Somavally Dalvi - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Unravelling the structural complexity of enveloped bacteriophages and exploring the role of phage proteins in the infection cycle.

Susovan Das - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4 - 8 Feb 2024, Lorne, VIC. Structural insight into G protein coupling and activation of human Frizzled 5 receptor.

Lucy Fitschen - EMBL Australia Postgraduate Symposium (EAPS) 2023, 1-3 Nov 2023, Garvan Institute of Medical Research, Sydney, NSW. Towards the cryo-EM structures of viral annealase proteins.



Proteins 2024

Lucy Fitschen - 67th Annual Meeting of the Australian Society for Biochemistry & Molecular Biology (ASBMB 2023), 15-17 Nov ANU, Canberra, ACT. Towards the cryo-EM structures of viral annealase proteins.

Lucy Fitschen - 4th CryOz Symposium (CryOz 2023), 23-24 Nov 2023, The University of Queensland, Brisbane, QLD. Towards the cryo-EM structures of viral annealase proteins.



Lucy Fitschen - Australian Society for Biophysics (ASB 2023), 3-6 Dec 2023, The University of Wollongong, Wollongong, NSW. Towards the cryo-EM structures of viral annealase proteins.

Lucy Fitschen - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Towards the cryo-EM structures of viral annealase proteins.

Dr. Emily Furlong - 67th Annual meeting of the Australian Society for Biochemistry & Molecular Biology (ASBMB 2023), 15-17 Nov 2023, ANU, Canberra, ACT. Molecular structure of an axle-less F1-ATPase.



Dr. Emily Furlong - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Molecular structure of an axle-less F1-ATPase.

Marialena Georgopoulou^{*} - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Structural studies of cell signalling adaptor protein Stimulator of Interferon Genes (STING) in complex with small molecule inhibitors. ***Poster Award**

Dr. Aidan Grosas - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Investigating the mechanisms of substrate polyspecificity of the RND transporter MexB using cryo-EM.



Riya Joseph - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Structural studies of recently identified Bacteroides fragilis cholesterol-dependent cytolysin-like (CDCL) proteins.



Marialena Georgopoulou, Lorne Proteins 2024

Michaela Kaoullas^{*} - Australasian Society of Clinical and Experimental Pharmacologists & Toxicologists annual scientific meeting (ASCEPT 2023), 20-23 Nov 2023, Sydney, NSW. Structural insights into positive allosteric modulation at the M4 mAChR. **Neuropharmacology Special Interest Group Prize Winner.*

Michaela Kaoullas - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Structural insights into positive allosteric modulation at the M4 mAChR.

Jacob Lewis - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Fast and efficient purification of cross-linked stabilised samples for structural biology.

Mayada Mazher - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Structural insights into

how the membrane protein TMEM120A interacts with mechanosensitive ion channel inhibitors.

Dr. Jesse Mobbs - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Structural investigation of allosteric modulation of the delta opioid receptor

Dr. Sarah Mueller - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. The orphan G protein-coupled receptor GPR55.

Jordan Nicholls* - 4th CryOz symposium (CryOz 2023), 23-24 Nov 2023, The University of Queensland, Brisbane, QLD. Unravelling herpes virus DNA annealing: cryo-EM structure of BALF2. **Best student poster*

Jordan Nicholls - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Unravelling Herpesvirus DNA annealing: Cryo-EM structure of BALF2.



Michaela Kaoullas, Lorne Proteins 2024





Bhavika Rana - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, VIC. Structural and pharmacological validation of allosteric sites at the M5 Muscarinic acetylcholine receptor –



Mayada Mazher, Lorne Proteins 2024

a target for CNS disorders.

Jhonnatan Reales-Gonzalez - 4th CryOz symposium (CryOz 2023), 23-24 Nov 2023, The University of Queensland, Brisbane, QLD. Structural characterization of full- length human RAD52 using cryo-EM: towards its mechanism of action.

Jhonnantan Reales-Gonzalez - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Structural characterization of full-length human RAD52 using cryo-EM: towards its mechanism of action.

Bindusmita Paul - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Characterization of the structure and dynamics of oral polymicrobial biofilms.

Solace Roche - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb, 2024 Lorne, VIC. The elusive pore-forming mechanism of the Yersinia entomophaga toxin complex.

Doulin Shepherd - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Investigating the molecular basis of effector delivery through the bacterial type IV secretion system.

Dr. Alice Shin* - 67th Annual Meeting of the Australian Society for Biochemistry & Molecular Biology (ASBMB 2023), 15-17 Nov 2023, ANU, Canberra, ACT. Structural investigation of multi-drug resistance ABC transporter CDR1 of Candida albicans. *Poster prize.



Dr. Jesse Mobbs, Lorne Proteins 2024

Dr. Alice Shin - 49th Lorne Conference on Protein Structure & Function

(Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Unveiling Candida albicans' multi-drug resistance: a biophysical and structural analysis of its ABC transporter.



Bhavika Rana, Jhonnatan Reales-Gonzalez and Susovan Das, Lorne Proteins 2024

Muhammad Zahir Siddiqui - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Structural characterization of the Escherichia coli primosome.

Dr. Lisanne Spenkelink - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Directed evolution - one molecule at a time.

Dr. Sepideh Valimehr - 4th CryOz Symposium (CryOz 2023), 23-24 Nov 2023, The University of Queensland, Brisbane, QLD. The effect of the blot force and blot time of the Vitrobot on the ice thickness of the CryoEM grid.



Dr. Liudi Zhang - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4 - 8 Feb 2024, Lorne, VIC. Cryo-EM structures of the human adenosine A3 receptor in various states.

Dr. Xin (Cindy) Zhang - 49th Lorne Conference on Protein Structure & Function (Lorne Proteins 2024), 4-8 Feb 2024, Lorne, VIC. Structural insights into the activation and modulation of a class B1 GPCR by small-molecule ligands.



2024

Academic Presentations

Dr. Joe Brock - CCeMMP Seminar Series 2023, online, 9 May 2023. The structural basis of multi-drug transport: A story of a SynBio curious structural biologist.

Prof. Brett Collins - CCeMMP Seminar Series 2024, online 9 Apr 2024. Structure of the endosomal commander complex mutated in Ritscher-Schinzel syndrome: combining crystallography, cryoEM and AlphaFold2.

Jessica Lu - PhD exit seminar, Monash University, Parkville, 29 Aug 2023. Structural and pharmacological characterisation of splice isoforms of the pituitary adenylate cyclase-activating polypeptide type 1 (PAC1) receptor.

Dr. Sarah Piper - Chemistry Society, University of Sydney, Sydney, NSW 16 Jun 2023. Seeing is believing: Visualising dynamics of membrane receptors using structural biology data in 3D animations.

Dr. Sarah Piper - Division of Biomedical Science and Biochemistry, ANU, Canberra, ACT, 22 Jun 2023. Membranes under the lens: Using structural biology data to visualise receptor dynamics.

Assoc. Prof. Isabelle Rouiller - Sorbonne University, Paris, France, 3 Oct 2023. Understanding the conformational landscape p97 from cryo-EM and mass-spectrometry data.

Prof. Renae Ryan - CCeMMP Seminar Series 2023, on line, 13 Jun 2023. The split personality of glutamate transporter: a chloride channel and a transporter.

Prof. Renae Ryan - Children's Medical Research Institute (CMRI), Westmead, 1 Mar 2024. The twisted link between a dual function glutamate transporter and episodic ataxia.

Dr. Lisanne Spenkelink - CCeMMP Seminar Series 2024, on line 12 Mar 2024. Revealing biological stochasticity: insights from single-molecule visualisation.

Prof. Denise Wootten - Imperial College London, UK, 24 Apr 2024. Class B GPCR biased agonism and allosteric modulation.

Dr. Xin (Cindy) Zhang - CCeMMP Seminar Series 2024, on line 13 Feb 2024. Structural insights into the activation and modulation of a class B1 GPCR by small-molecule ligands.





Academic Presentations (oral presentation at local meetings)



Minakshi Baruah, DDB Student Symposium, Oct 2023

Minakshi Baruah - DDB Student Symposium (3MT), Monash University, Parkville, 26 Oct 2023. Revealing the hidden face of GPCRs - mapping inactive states.

Minakshi Baruah - CCeMMP Retreat, 4 Dec 2023, Treacy Conference Centre, Parkville. Development of approaches for inactive state GPCR structure determination using cryoEM.

Ania Beyger - CCeMMP Retreat, 4 Dec 2023, Treacy Conference Centre, Parkville. Pharmacological characterisation of CXCR3 splice variants to aid drug design.

Dr. Brian Cary - CCeMMP Retreat, Treacy Conference Centre, Parkville, 4 Dec 2023. Structure and activity of backbone-modified class B1 GPCR agonists.

Susovan Das - CCeMMP Retreat, Treacy Conference Centre, Parkville, 4 Dec 2023. Structural insight into G protein coupling and activation of human Frizzled 5 receptor.

Lucy Fistchen - SCMB HDR Student Conference, University of Wollongong, 30-31 Oct 2023. Towards the cryo-EM Structures of Viral Annealase Proteins.

Marialena Georgopoulou - CCeMMP Retreat, Treacy Conference Centre, Parkville, 4 Dec 2023. Structural studies of cell signalling adaptor protein STimulator of INterferon Genes (STING) in complex with small molecule inhibitors.

Dr. Debnath Ghosal - CCeMMP Retreat, Treacy Conference Centre, Parkville, 5 Dec 2023. Exploring microbial dark matter using cryoelectron tomography.

Dr. Alisa Glukhova - CCeMMP Retreat, Treacy Conference Centre, Parkville, 4 Dec 2023. Role of lipids in G protein coupling of FZD receptors.

Dr. Aidan Grosas - CCeMMP Retreat, Treacy Conference Centre, Parkville, 4 Dec 2023. Investigating the mechanisms of substrate polyspecificity of the RND transporter MexB using cryo-EM.

Dr. Joshua Hardy - CCeMMP Retreat, Treacy Conference Centre, Parkville, 5 Dec 2023. Cryo-EM structure of the extracellular domain of murine thrombopoietin receptor in complex with thrombopoietin.

Riya Joseph - CCeMMP Retreat, Treacy Conference Centre, Parkville, 4 Dec 2023. Structural studies of recently identified cholesterol dependent cytolysin like protein from B fragilis.

Assoc. Prof. Michael Landsberg - CCeMMP Retreat, Treacy Conference Centre, Parkville, 5 Dec 2023. Insights into mechanisms of ABC toxin activation and cell recognition from cryoEM.



Dongju Lee, DDB Student Symposium, Oct 2023

Dongju Lee - DDB Student Symposium (3MT), Monash University, Parkville, 26 Oct 2023. An orphan GPCR with potential to treat neuropathic pain.



Dongju Lee - CCeMMP Retreat, Treacy Conference Centre, Parkville, 4 Dec 2023. Structural & pharmacological insights into orphan GPCR, GPR151 with G protein couplings.

Dr. Jesse Mobbs - CCeMMP Retreat, Treacy Conference Centre, Parkville, 4 Dec 2023. Structural investigation of the delta opioid receptor (DOR).

Jordan Nicholls - Sydney Protein Group Thompson Prize, The University of Sydney, 24 Nov 2023. Unravelling Herpesvirus DNA Annealing: Cryo-EM structure of BALF2.

Alok Pradhan - DDB Student Symposium (3MT), Monash University, Parkville, 26 Oct 2023. Structure determination of GPCR heteromers.

Alok Pradhan - CCeMMP Retreat, Treacy Conference Centre, Parkville, 4 Dec 2023. Structure determination of GPCR heteromers.

Isabella Russell - CCeMMP Retreat, Treacy Conference Centre, Parkville, 4 Dec 2023. Impacts of constitutive activity on structural determination of GPCRs.

Isabella Russell - DDB Student Symposium, Monash University, Parkville, 26 Oct 2023. Lipid dependent activation of the orphan GPCR, GPR3.

Dr. Alice Shin - Canberra Protein Group EMCR showcase (Flash Talk), Canberra, 28 Jul 2023. Structurally investigating promiscuous Cdr1 protein of Candida albicans.

Dr. Alice Shin^{*} - RSB HDR conference, ANU, Canberra, 9 Apr 2024. Structurally investigating multidrug resistance ABC transporter of pathogenic Candida yeast using cryo-EM. **Runner up; talk presentation runner up prize*



ack Tovey, DDB Student Symposium, Oct 2023

Dr. Winnie Tan - CCeMMP Retreat, Treacy Conference Centre, Parkville, 5 Dec 2023. Human MORC2 is an ATP-dependent DNA compaction machine.

Dr. David Thal - DDB 2023 Scientific Symposium, Monash University, Parkville, 9 Aug 2023. Mechanism of arachidonate 12S-Lipoxygenase (12-LOX) inhibition by endogenous and exogenous inhibitors.

Jack Tovey - DDB Student Symposium, Monash University, Parkville, 26 Oct 2023. Small molecule

agonism of CCK-1R, different angles for the treatment of obesity.

Jack Tovey - 18th Annual Graduate Research Symposium, Monash University, Parkville, 22 Nov 2023. Structural insights into the activation of the Cholecystokinin Type 1 Receptor.

Jack Tovey - CCeMMP Retreat, Treacy Conference Centre, Parkville, 4 Dec 2023. Structural Insights into the Activation of the Cholecystokinin Type 1 Receptor.

Xiaomin Wang - CCeMMP Retreat, Treacy Conference Centre, Parkville, 4 Dec 2023. Interaction studies between SARS-CoV2 & it's co-receptors.

Yi (Jack) Zeng - CCeMMP Retreat, Treacy Conference Centre, Parkville, 5 Dec 2023. Structural basis of





promiscuous drug binding & transport by organic cation transporter 1.

Academic Presentations (poster presentation at local meetings)

Ania Beyger - DDB Student symposium, 26 Oct 2023, Monash University, Parkville. Pharmacological characterisation of CXCR3 splice variants to aid drug discovery.

Marialena Georgopoulou - University of Melbourne, Dept of Biochemistry & Pharmacology Graduate Research Conference 25-26 Sep 2023. Structural studies of cell signalling adaptor protein STimulator of INterferon Genes (STING) in complex with small molecule inhibitors.

Riya Joseph - University of Melbourne Dept of Biochemistry & Pharmacology Graduate Research Conference, 25-26 Sep 2023. Structural studies of recently identified B. fragilis cholesterol-dependent cytolysin like proteins.

Mayada Mazher - University of Melbourne Dept of Biochemistry & Pharmacology Graduate Research Conference 25-26 Sep 2023. Studying the role of TACAN membrane protein in pain sensing.

Dr. Sarah Piper - Melbourne Emerging Leaders in Biomedical Research Symposium 2023, 1 Sep 2023. Seeing is believing: Visualising dynamics of GPCRs, important drug targets, using structural biology data in 3D animation.

Bhavika Rana - DDB Student symposium, Monash University, Parkville, 26 Oct 2023. Structural and pharmacological validation of allosteric sites at M5 muscarinic receptors.

Monica Suehiro - DDB Student symposium, Monash University, Parkville, 26 Oct 2023. Understanding TDP-43 driven mitochondrial dysregulation in neurodegenerative disorders.

Publications

1. Alexander SPH, **Christopoulos A... Gregory KJ... Leach K... Thal D... Valant C...**Ye RD (2023). The Concise Guide to Pharmacology 2023/24: G protein-coupled receptors. Br J Pharmacol, 180 (Suppl 2): S23-S144. https://doi.org/10.1111/bph.16177.

2. Ameen SS, Griem-Krey N...**Lucet IS**...Ang C-S, Cheng H-C (2023). N-terminomic changes in neurons during excitotoxicity reveal proteolytic events associated with synaptic dysfunctions and potential targets for neuroprotection. Mol Cell Proteomics, 22 (5): 100543. doi: 10.1016/j.mcpro.2023.100543.

3. Baltos J-A, Casillas-Espinosa PM, Rollo B, **Gregory KJ**, White, PJ, **Christopoulos A**, Kwan P, O'Brien TJ, May,LT (2023). The role of the adenosine system in epilepsy and its comorbidities. Br J Pharmacol, Epub May 8 2023, online ahead of print. doi: 10.1111/bph.16094.

4. **Brown HG,** Smith D, Wardle BC, **Hanssen E** (2024). Square condenser apertures for square cameras in low-dose transmission electron microscopy. Nat Methods, 21: 566–568. https://doi.org/10.1038/s41592-024-02206-9. [EMD-41933, EMD-41936, EMD-41937, EMD-41938, EMD-42882].

5. **Bumbak F**, Bower JB, Zemmer SC, Inoue A, Pons, M, Paniagua JC, Yan F, Ford J, Wu H, Robson SA, Barthgate RAD, Scott DJ, Google PR, Ziarek JJ (2023). Stabilization of pre-existing neurotensin receptor conformational states by β -arrestin-1 and the biased allosteric modulator ML314. Nat Commun, 14: 3328. https://doi.org/10.1038/s41467-023-38894-8.











6. Burger WAC, Pham V, Vuckovic ZA, Powers AS, Mobbs JI, Laloudakis Y, Glukhova A, Wootten D, Tobin AB, Sexton PM, Paul SM, Felder CC, Danev R, Dror RO, Christopoulos A, Valant C, Thal DM (2023). Xanomeline displays concomitant orthosteric and allosteric binding modes at the M4 mAChR. Nat Commun, 14 (1): 5440. doi: 10.1038/s41467-023-41199-5. [PDB:8FX5, EMD-29524] With industry collaborators, Karuna.



7. Bye LJ, **Finol-Urdaneta RK, Adams DJ** (2023). Calcium imaging of non-adherent cells. Methods Mol Biol (Springer Protocols), 2644: 361-369. doi: 10.1007/978-1-0716-3052-5_23.

8. Cao J, Belousoff MJ, Danev R, Christopoulos A, Wootten D, Sexton PM (2024). Cryo-EM structure of the human amylin 1 receptor in complex with CGRP and Gs protein. Biochemistry, 63 (9): 1089–1096. https://doi.org/10.1021/acs.biochem.4c00114 [PDB:9AUC, EMD-43877].



9. Chandrashekar C, Lin F, Nishiuchi Y, Mohammed SF, White BF, Arsenakis Y, **Yuliantie E**, **Zhao P**, van Dun S, Koijen A, Kajihara Y, **Wootten D**, Dodd GT, van den Bos LJ, Wade JD, Hossain MA (2024). Engineering of a biologically active glycosylated glucagon-like peptide-1 analogue. J Med Chem, 67 (9): 7276–7282. https://doi.org/10.1021/acs.jmedchem.4c00093.

10. Chandrashekar C, Nishiuchi Y, White BF, Arsenakis Y, Lin F, McNeill SM, **Zhao P**, van Dun S, Koijen A, Kajihara Y, **Wootten D**, van den Bos LJ, Wade JD, Hossain MA (2023). Glycosylation improves the proteolytic stability of exenatide. Bioconjugate Chem, 34 (6): 1014-1018. https://doi.org/10.1021/acs.bioconjchem.3c00120.



GHC

11. Di Cesare M, Kaplan E, Rendon J, Gerbaud G, **Valimehr S**, Gobet A, Ngo T-A T, Chaptal V, Falson P, Falson M, Dorlet P, Hanssen E, Jault J-M, Orelle C (2024). The transport activity of the multidrug ABC transporter BmrA does not require a wide separation of the nucleotide-binding domains. J Biol Chem, 300 (1): 105546. doi: 10.1016/j.jbc.2023.105546 [PDB:800E, EMD-16659; PDB:8CHB, EMD-18535].

12. Diao J, Lam M, **Gregory KJ, Leach K**, Bourke JE (2023). Calcium-sensing receptor negative allosteric modulators oppose contraction of mouse airways. Am J Respir Cell Mol Biol, 69 (2): 182-196. doi: 10.1165/rcmb.2021-05440C.



14. **Finol-Urdaneta RK**, Zhorov BS, Baden DG, **Adams DJ** (2023). Brevetoxin versus brevenal modulation of human Nav1 channels. Mar Drugs, 21(7): 396. doi: 10.3390/md21070396.



15. **Fitschen LJ**, Newing TP, Johnston NP, Bell CE, **Tolun G** (2024). Half a century after their discovery: structural insights into exonuclease and annealase proteins. Engineer Microbiol, 4 (1): 100120. https://doi.org/10.1016/j.engmic.2023.100120.

16. Gibadullin R, **Cary BP**, Gellman SH (2023). Differential responses of the GLP-1 and GLP-2 receptors to N-terminal modification of a dual agonist. J Am Chem Soc, 145 (7): 12105-12114. https://doi.org/10.1021/jacs.3c01628.



17. Jörg M, van der Westhuizen ET, Choy KHC, Shackleford DM, Khajehali E, Tobin AB, **Thal DM**, Capuano B, **Christopoulos A**, **Valant C**, Scammells PJ (2023). Design, synthesis and evaluation of novel 2-phenyl-3-(1H-pyrazol-4-yl)pyridine positive allosteric modulators for the M4 mAChR. Eur J Med Chem, 258: 115588. DOI: 10.1016/j.ejmech.2023.115588.




18. Kusi-Appauh N, Ralph SF, **van Oijen AM, Spenkelink LM** (2023). Understanding G-quadruplex biology and stability using single-molecule techniques. J Phys Chem B, 127 (25): 5521-5540. https://doi.org/10.1021/acs.jpcb.3c01708.

19. Lagou V, Jiang L, Ulrich A... Sexton PM...Wootten D...Kaakinen MA, Jones B, Prokopenko I (2023). GWAS of random glucose in 476,326 individuals provide insights into diabetes pathophysiology, complications and treatment stratification. Nat Genet, 55 (9): 1448-1461. doi: 10.1038/s41588-023-01462-3.

20. Liang L-Y, Geoghegan ND, Mlodzianoski M, Leis A, Whitehead LW, Surudoi MG, Young SN, Janes P, **Shepherd D, Ghosal D**, Rogers KL, Murphy JM, **Lucet IS** (2024). Co-clustering of EphB6 and ephrinB1 in trans restrains cancer cell invasion. Commun Biol, 7: 461. https://doi.org/10.1038/s42003-024-06118-4.

21. Lu Y, Hatzipantelis CJ, Langmead CJ, Stewart GD (2023). Molecular insights into orphan G proteincoupled receptors relevant to schizophrenia. Br J Pharmacol, Epub Sept 2023, online ahead of print. doi: 10.1111/bph.16221.

22. **Maksour S, Ooi L**. (2023). Innovations advancing our understanding of microglia in Alzheimer's disease: From in vitro to in vivo models. J Neurochem, 166 (6): 497-516. doi: 10.1111/jnc.15885.

23. Manolios N, Papaemmanouil J, **Adams DJ** (2023). The role of ion channels in T cell function and disease. Front Immunol, 14: 1238171. doi: 10.3389/fimmu.2023.1238171.

24. McNeill SM, Lu J, Carino CMC , Inoue A, Zhao P, Sexton PM, Wootten D (2024). The role of G protein-coupled receptor kinases in GLP-1R β -arrestin recruitment and internalisation. Biochem Pharmacol, 222:116119. doi: 10.1016/j.bcp.2024.116119.

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conformation, purported to be a particul space into the extracellular environment membrane component of the tripartite RND-efflux From UoW Node: a top view of the structure of the multi-drug efflux transporter, MexB, from Pseudomonas aeruginosa at 2.16 Å. MexB is the inner the development of antibiotic resistance. th spans the me into d bilayer to shuttle compounds from the cytoplasmic and periplasmic ric trimer arrangement with each subunit adopting a different and RND transporters like it, are one of the major reasons for

Image credit: Dr. Sarah Piper



Image credit: Dr. Jesse Mobbs

From our External Affiliates: Organic Cation Transporter 1 (OCT1). PDB:8SC1; EMD-40334. Nat Commun, 14: 6374, 2023. doi: 10.1038/s41467-023-42086-9.

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