

ARC Industrial Transformation Training Centre for Cryo-electron Microscopy of Membrane Proteins

Quarterly newsletter

58.2

Image credit - Dr Sarah Piper

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ARC CCeMMP Symposium ARC CCeMMP Interactive workshop Advanced Technical Training













Welcome

Professor Patrick Sexton Centre Director

Welcome to the 6th instalment of the ARC CCeMMP quarterly newsletter.

In this newsletter we welcome new staff and students joining the Centre, including Dr. Tracie Pierce who will be filling in as Centre Manager while Jackie is on maternity leave, provide an update on activities over the last quarter and present recent highlights from our member nodes.

This last quarter also saw a passing of the guard at our University of Wollongong Node, with Prof. Antoine van Oijen stepping down as Node Leader. Antoine was an inaugural member of the Centre and CI on our successful ARC funding application. He has played an important role in the establishment of the Centre and expansion of our membership and activities within the UoW Node. We are very grateful for Antoine's leadership and commitment to the Centre in its formative years, and we are pleased that he will continue as a member of the Centre. However, the change is also an opportunity and we welcome Dr Gökhan Tolun as the new Node Leader and we look forward to working with Gökhan as part of the senior leadership group.

Key activity highlights include our first in-person ARC CCeMMP Research Symposium on "Cryo-EM of Membrane Proteins", an in-person workshop with one of our industry partners, and the review of Centre operations, strategy and achievements by our Science and Industry Advisory Committee.

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Professor Patrick Sexton Centre Director

Did you know?

The 2017 Nobel Prize in Chemistry was awarded for advances in cryo-EM that enabled it to become one of the most powerful tools for understanding protein structure and dynamics? Jacques Dubochet, Joachim Frank and Richard Henderson made key breakthroughs that provided methods for preservation of biological materials while being imaged with high energy electrons, that advanced the stability of microscopes and sensitivity of detection for low contrast images and provided the foundation for mathematical reconstruction of high-resolution 3D maps of proteins. Continual advances to cryo-EM technology have led to new generations of detectors capable of collecting orders of magnitude greater amounts of data, and new approaches to data analysis that enable visualisation of protein motions captured during sample preparation.

On the cover: a recent structure from UoW node (PDB 7UJL). Newing TP, Brewster JL, Fitschen LJ, Bouwer JC, Johnston NP, Yu H, Tolun G. Red β 177 annealase structure reveals details of oligomerization and λ Red-mediated homologous DNA recombination. Nat Commun. 2022 Sep 26;13(1):5649. https://doi.org/10.1038/s41467-022-33090-6

Centre updates

Introducing Dr. Tracie Pierce and Jordan Hyndman



Tracie will be replacing Jackie as Centre Manager while she is on maternity leave. Jordan will be joining the Centre for 12 months as an Administrative Officer. For those at the Symposium, you would have met both of them at the registration desk.



Introducing baby Mia

Welcome baby Mia! Many of you would have seen a very pregnant Jackie at the Symposium - just over a month later, baby Mia was born, October 7th, weighing 3.91 kg and measuring 53 cm. Mum and bubs are doing well.

Centre Operational Review by the Science & Industry Advisory Committee (SIAC)

The Centre is fortunate to have an expert team of academic and industry advisors who assist in ensuring that the Centre fulfills its key objectives. In-line with our goals of continued improvement, we asked members of the SIAC to review the operation, performance and strategic planning of the Centre on August 30th. This marked ~2 years since award of the ITTC grant from the ARC and 18 months of establishment and operation of the Centre. The committee provided expert advice on ways to prioritise our strategic planning and improvements to the operational structures of the Centre. The committee also acknowledged the many achievements of the Centre's Executive committee and general members in development and operation of the Centre to date, much of which was achieved despite the complications arising from a global pandemic during the crucial establishment phase. We are very grateful to all members of our SIAC for making time in their busy schedules to support the Centre.

(left to right): Jackie How, Anne-Laure Puaux (WEHI), Raymond Schrijver (Thermo Fisher Scientific, The Netherlands), Leigh Farrell, Denise Wootten, Isabelle Lucet, Isabelle Rouiller, Tracie Pierce, Cathy Drinkwater (Biocurate), Antoine van Oijen, Patrick Sexton, Mike Ryan (Monash Univ.) Lisa Dubé (MTP Connect) and Alastair Stewart (Chair Univ Melbourne)[absent Rado Danev Univ Tokyo, Japan, who attended via zoom]



ARC CCeMMP Symposium, "Cryo-electron microscopy of membrane proteins"



The team behind it all! LR: Dr Cindy Zhang, Dr Fabian Bumbak, Dr. Aidan Grosas, Dongju Lee, Haitian Chen

The Centre held its second, first in-person, research symposium on September 1st. The meeting was organised entirely by a committee comprising Centre HDR students and Postdoctoral fellows from different Nodes; Dr. Cindy Zhang, Dongju Lee, Dr. Fabian Bumbak, Dr. Aidan Grosas and Haitian Chen, who did an amazing job across all facets of organisation, from venue, catering, posterboards, and prize committees to program design and execution. Indeed, they have set a very high benchmark for all future symposiums.

The symposium included 8 invited speakers, 20 posters and was attended by 129 registrants from across the country.

We began the day with our opening keynote speaker Dr. Raymond Schrijver from ThermoFisher (The Netherlands) who spoke on Impact of Advances in Cryo-EM for Drug Discovery. Raymond also facilitated a workshop the following day (see below).

We also heard from Dr Gökhan Tolun, Dr Sarah Piper, Dr Debnath Ghosal, Dr Hamish Brown, Dr Rachel Johnson, and Dr Rhys Grinter presenting on a wide variety of topics.

Our closing keynote speaker (and our only zoom session for the day!) was Prof Rado Danev who spoke on Optimising cryo-EM for GPCRs and first steps in cryo-tomography.



The prize winning talk, presented by Dr Gökhan Tolun



Session Chairs: Dr. Emily Furlong, Dr Katrina Black and Dr Cindy Zhang

A special thank you to our morning and afternoon session chairs Dr Katrina Black and Dr Emily Furlong and our opening and closing keynote Chairs Prof Patrick Sexton and Dr Cindy Zhang. It was a pleasure to *finally* see people in the auditorium, discussions around posters during tea breaks and lunch, as well as people enjoying the VR setup - although maybe this wasn't ALL science...



An interactive Poster session



Centre members at the VR display

Finally, Dr Aidan Grosas closed the symposium and presented the Oral and Poster prizes. The audience voted Dr. Gökhan Tolun from the University of Wollongong as the most popular oral presentation. Gökhan received a certificate of recognition, a 3D printed model of choice and 2D print of choice.

We are also grateful to Thermo Fisher Scientific who sponsored the Poster Prizes; The winner was Yi Zeng, a PhD student from the Victor Chang Cardiac Research Institute. Yi received a certificate of recognition, \$250 AUD and a 3D printed model of choice. ICHDR student MariaKatarina Lambourne from the University of Wollongong was Runner Up and received a 2D print of choice.



Prize winners LR: Dr Gökhan Tolun (UoW), for most popular oral presentation; PhD student Yi Zeng (Victor Chang), for ThermoFisher Best Poster Prize; and MariaKatarina Lambourne (UoW), for ThermoFisher Runner Up Poster Prize

ARC CCeMMP Interactive Workshop



Dr Raymond Schrijver presented a workshop after the symposium. Centre members, Post Docs and students participated



Dr. Raymond Shrijver facilitated an interactive discussion workshop: **Optimization of the Single Particle Analysis pipeline, from vitrification to the microscope to a structure** on September 2nd. Raymond has vast experience in the application of Single Particle Analysis (SPA) within the pharmaceutical industry and has been instrumental in the progress that Thermo Fisher Scientific is making to accelerate the time from sample to structure. Assisted by Dr. Matt Belousoff (Monash University ICPD), Raymond chaired an interactive forum on behalf of the ARC CCeMMP. The discussions were aided by local experts from the Monash Institute of Pharmaceutical Sciences (MIPS), the Walter and Eliza Hall Institute of Medical Research (WEHI), the Monash Biomedical Discovery Institute (BDI) and the Bio21 Institute to workshop both practical considerations and technological improvements to relieve some of the major bottlenecks experienced in the application of SPA. This was an intimate, in-person, session with a focus on collaborative discussion with local colleagues who have years of experience in various aspects of this technique

Advanced technical training in cryo-EM



Centre ICPD Dr. Sepideh Valimehr with ICHDR students from various Nodes

The last quarter also saw the second (and largest to date) cohort of ICHDRs undertake their intensive, advanced, hands on, technical rotations in the Theory and Operation of Cryo-EM instruments and in Data Processing and Analysis. As with raising of children - it takes a village - so many thanks to all of our trainers from within the Centre, Dr. Matthew Belousoff, Dr. Sarah Piper, Dr. Rachel Johnson, Dr. Cindy Zhang (Monash Univ. Node), A/Prof. Isabelle Rouiller, Dr. Debnath Ghosal, Dr. Sepideh Valimehr (Univ. Melbourne Node), Dr. Isabelle Lucet, Dr. Josh Harding (WEHI Node) and Dr. James Bouwer (Univ. Wollongong Node). Thanks also to our external instructors, Dr. Lingbo Yu (Thermo Fisher Scientific), Jay van Schyndel (Monash MASSIVE facility) and Prof. Rado Danev (Univ. Tokyo). The "Cryo-EM" training was a hybrid of local practical training and Zoom (Univ. Wollongong) and in-person (Monash, Melbourne and WEHI) lectures and workshops.

Excitingly, all ICHDRs were able to gather in Melbourne for the first 2 weeks of the Data Processing and Analysis rotation before returning to their respective Nodes for application of their newly acquired knowledge to increasingly complex data analysis tasks, supported by weekly feedback.

By all accounts, much learning was had, while also being a great opportunity for the students to network with each other.

Upcoming events



ARC CCeMMP Seminar series

The seminar series concludes for the year with our December seminar, Dr Kliment Verba, December 13, 10 AM (AEDT), title TBA. We will resume Feb 14, 2023 with Prof. Eva Nogales (University of California, Berkeley). Thank you to the committee for the amazing program this year and to our student chairs, you've done a great job! The committee farewells Dr. Jodi Brewster, Jack Tovey and Dr. Josh Harding and thanks them for all their efforts and welcomes Dr Fabian Bumbak, Dr. Aidan Grosas, Dongju Lee and Doulin Shepherd, who will join Dr Sepideh Valimehr and Dr Tracie Pierce on the committee to help develop and deliver the 2023 program.

Outreach activities

Dr Winnie Tan hosted a donor lab tour at WEHI on October 7th for 6 people with lived experience of Charcot-Marie-Tooth in conjunction with a philanthropic partner, Charcot-Marie-Tooth Australia.

Dr. Shabih Shakeel hosted year 10 students through the 2022 WEHI Secondary School Work Experience Program September 12th-16th and also held a visit of CMT (Charcot-Marie-Tooth disease) Australia members on October 7th.



Lab tour (WEHI) with CMT Australia. Dr Winnie Tan (3rd from left) and Dr Shabih Shakeel (3rd from right)

In the Media

Dr Jodi Brewster and Dr Gökhan Tolun

- Media Release: https://www.uow.edu.au/media/2022/researchers-at-uows-molecular-horizons-unlockstructure-of-a-protein-from-bacteria-killing-virus.php
- NEWS: https://www.miragenews.com/researchers-at-uows-molecular-horizons-unlock-867272/

Dr Gökhan Tolun

• RADIO: https://www.abc.net.au/illawarra/programs/drive/drive/14068276 (38:40 mins)

Monash Node

Professor Denise Wootten Node Leader, Monash University

Introducing ICHDR student Ania Beyger!

A big CCeMMP welcome to Ania Beyger! Ania is investigating the structure and pharmacology of CXCR3 - a GPCR implicated in a number of diseases, including cancer and auto-immunity. Her project will also examine the mode of activation of the receptor, by its chemokines, as well as their agonist-bound active states using Cryo-EM, and the structural and pharmacological basis of its inhibition by monoclonal antibodies. Her project is in collaboration with Servier – a pharmaceutical company based in Paris. She has completed her Master's degree in Medicinal Chemistry at the University of Glasgow where she utilised computational methods for docking and SAR studies which is when she became fascinated by the structure-directed drug discovery process. Outside of the lab, she can be found exploring the great outdoors, with her favourite activities being hiking, camping and surfing.



Supervisors: Dr Natalie Diepenhorst, Dr Greg Stewart, Prof Chris Langmead

Denise Wootten promoted to Professor



Denise is an NHMRC senior research fellow and an international leader in the study of G protein-coupled receptors (GPCRs). Her research program employs a multidisciplinary approach (structural biology, molecular pharmacology, analytical pharmacology, computational biology and in vivo studies of disease) to investigate the molecular mechanisms and the functional consequences of GPCR signalling and biased agonism with a particular emphasis on the therapeutically important class B1 GPCR subfamily. She has published 101 peer reviewed research articles and reviews, many in the highest-ranking multidisciplinary journals, including Cell, Science and Nature, and is a current Clarivate Analytics Highly Cited Researcher in the Cross-field discipline.

As well as being the Monash node leader, Denise is the DDB HDR coordinator and an executive and founding member of Her Research Matters. She is also a scientific advisor for Septerna, Inc; a US-based start-up company focused on GPCR drug discovery, Chair of the Special Interest Group on Drug Discovery for the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT), an associate member of the Faculty of 1000 and a member of the editorial board of the British journal of Pharmacology. Over her career she has supervised 30 PhD students (15 completed, 15 current) and 9 honours students. She has been instrumental in the development and implementation and delivery of two four-year doctoral training programs; a laboratory rotation model with an advanced coursework program in drug discovery and development in the DDB theme, and our bespoke training program in cryo-EM of membrane proteins, delivered across four research institutes. Congratulations Denise!

Prof Patrick Sexton awarded the 2022 Gordon Hammes Lectureship Award.

The Gordon Hammes Lectureship Award of the American Chemical Society honours an individual whose scientific contributions have had a major impact on research across all of biological chemistry. Professor Sexton's contribution is to significantly influence the progress of our understanding of ligand-GPCR interactions, how these interactions induce receptor activation, and how receptor dynamics contribute to the sophisticated and multi-layered chemistry that characterises GPCRs. He is the first non-US based researcher to win the Award.



Poster Prize awarded to Dr Sarah Piper, 4GPCRnet conference, 26th - 29th Sept, Leipzig, Germany



A group of Centre members and students recently presented at 4GPCRnet conference, with our very own Dr Sarah Piper winning a Poster Prize.

Prize: 100 euro

New Funding

Dr Cindy Zhang awarded ARC DECRA

Dr Cindy (Xin) Zhang was a recipient of an ARC Discovery Early Career Researcher Award (DECRA). The DECRA scheme provides research support for early career researchers, giving them the opportunity to develop and apply their research skills in a supportive environment in projects important to Australia.

Cindy's project: *Cryo-electron microscopy determination of G protein-coupled receptor states*, Cindy's project aims to address fundamental knowledge gaps in our understanding of the molecular mechanisms of peptide hormone GPCR activation, using cryo-electron microscopy determination of the structure and dynamics of key intermediate states in activation. Using the glucagon receptor as an exemplar, novel biochemical approaches will be applied to capture these distinct functional states. The knowledge gained from these studies will advance the fundamental understanding of physiologically important receptor activation and efficacy, while the approaches developed will enable similar investigation of other receptor classes.



Profs Denise Wootten and Patrick Sexton

Last quarter saw new funding into the Node with completion of our project agreement with Novo Nordisk to support structural and pharmacological evaluation of amylin and calcitonin receptors.

Dr Darren Riddy, Prof Denise Wootten, Prof Patrick Sexton and Dr Paul Stupple

Monash Commercialisation Incubator Program grant to support in vivo assessment of novel small compound series with potential future utility for treatment of obesity.

New members

CCeMMP welcomes student affiliate Maleesha Ubhayarathna.

University of Melbourne (Bio21) Node

A/Professor Isabelle Rouiller Node Leader and Deputy Director, University of Melbourne

Introducing ICHDR student Mayada Mazhar!

Welcome to Mayada! Mayada is a PhD candidate in Isabelle Rouiller's laboratory based at the University of Melbourne/Bio21 node. Her PhD will investigate the role of TACAN membrane protein as a mechanosensitive ion channel in chronic pain using cryo EM, electrophysiology and NMR. Mayada grew up in Cairo, Egypt and completed her MSc at The American University in Cairo. Mayada is enchanted by structural biology and protein biochemistry. In her free time, she loves acrylic painting and listening to music.



Superviser: A/Prof Isabelle Rouiller

New Funding

A/Professor Michael Griffin awarded CUREator grant



CUREator is a national incubator run by Brandon BioCatalyst that is funded by the Medical Research Future Fund to support the development of Australian biomedical innovations, getting them to a point where they will be investment- or partneringready. The \$500,000 grant awarded to A/Prof Griffin and A/Prof. Tracy Putoczki (WEHI), will enable their teams to advance a new target identified for inflammatory bowel disease. Congratulations Michael!

University of Wollongong Node

Dr. Gökhan Tolun Node Leader, University of Wollongong

New Node Leader appointed, Dr Gökhan Tolun

We welcome new node leader Dr. Gökhan Tolun and thank outgoing Node Leader Professor Antoine van Oijen for his time and commitment in the critical establishment phase of the Centre

Dr Tolun's main area of research is the investigation of bio-nanomachines that carry out processes involving nucleic acids such as DNA recombination, replication and repair and RNA transcription. Many of you would have enjoyed his talk, '*Cryo-EM structure of phage* λ annealase *Red* β provides insights into its molecular mechanism and evolution, half a century after its discovery', at our recent Research Symposium on September 1st.



New Funding

Prof. David Adams awarded MRFF 2021 Genomics Health Futures Mission grant



The 4-year grant, awarded to a cross-institutional team comprising J Vandenberg, CA Ng, C Cox, K Wu, S Waters, DJ Adams, and E Palmer will enable 'High throughput functional genomics assays for ion channelopathies'. This award will complement David's structural and functional work on ion channels.

New members

CCeMMP UoW welcomes Bhanu Mantri, Lucy Fitschen and Jordan Nicholls as Student Affiliates.

WEHI Node

A/Professor Isabelle Lucet Node Leader, WEHI

New Funding

Shabih Shakeel awarded Investigator Grant (EL2)

Dr. Shabih Shakeel was awarded a NHMRC Investigator grant for the project *Capturing atomic snapshots to visualise epigenetic silencing machinery for identification of novel therapeutic targets*

Heterochromatin, a tightly packed form of DNA prevents genes from being turned on. We know very little about heterochromatin biology at the molecular level, despite its critical role in gene silencing. Through cryoEM, Shabih will study the protein complexes that lead to heterochromatin formation and maintenance. This information will enable the rational design of a targeted drug discovery program to treat diseases caused by epigenetic dysregulation.



Prof. Peter Czabotar awarded MRFF funding



Prof. Peter Czabotar was a member of a multi-laboratory, WEHI-led team, awarded \$1M of MRFF funding for the development of COVID-19 antivirals.

Read the full story here: https://www.wehi.edu.au/news/funding-boosthome-grown-treatment-covid-19. Congratulations Peter!

Dr. Winnie Tan awarded Charcot-Marie-Tooth Australia Research Grant

Dr. Winnie Tan was awarded \$20,000 for the grant "Understanding how MORC2 mutations contribute to Charcot-Marie-Tooth disease".

"Charcot-Marie-Tooth (CMT) is a genetic condition associated with profound muscular weakness, typically becoming noticeable in children and young adults. More than 80 genes have been identified in CMT, with each gene linked to one or more types of the disease. The level of disability varies from mild to severe.

This project focuses on CMT caused by the MORC2 gene, where there is severe muscle weakness. These patients have an early onset, sometimes as young as two or three, with loss of sensation in the hands and feet, causing major difficulties in patients' daily lives. Recent developments at WEHI has opened up exciting opportunities to make significant advances in this area.



The grant will fund the first high resolution structural modelling of MORC2 protein and contribute to significant knowledge gain in the CMT field. By mapping MORC2 patient mutation variants on a protein structure model, we can predict and determine the effect of MORC2 patient variant in causing CMT. The structural model of MORC2 will also be used to design structure-guided drugs that has the potential to treat CMT associated with MORC2 mutations."

Centre Activities and Achievements

Industry Workshops

• Raymond Schrijver (Thermo Fisher Scientific), Matthew Belousoff (Monash): Optimization of the Single Particle Analysis pipeline, from vitrification to the microscope to a structure.

Presentations

Presentations to Industry

- Patrick Sexton "Application of cryo-EM to understanding of ligand binding and activation of class B peptide hormone GPCRs" AstraZeneca, Cambridge, UK, August 2022.
- Dr. David Thal briefing with Karuna Therapeutics
- Dr. David Thal briefing with Boehringer-Ingelheim
- Dr. Nazanin Mohebali poster to Scientific Advisory Board meeting, Astex Pharmaceuticals UK, 'Membrane mimetic systems and their effect on the structure resolution, conformation and dynamics of G protein-coupled receptors', 6 October 2022.

International Conference Presentations

- Patrick Sexton (invited) "Structural insight into ligand binding and activation of class B peptide hormone GPCRs" RegPep24, 24th International Symposium on Regulatory Peptides (International Regulatory Peptide Society), Stirling, Scotland, August 1st-5th 2022.(including collaboration with Sanofi and Thermo Fisher Scientific)
- Denise Wootten (invited) "Mechanistic insights into class B1 GPCR signalling and allostery" 4GPCRnet conference, Leipzig, Germany, 26th 29th September 2022.
- Brian Cary (selected oral) "Structural and functional diversity among agonist-bound states of the GLP-1 receptor" 4GPCRnet conference, Leipzig, Germany, 26th 29th September 2022.
- Sarah Piper (poster) "Dynamic drug targets: Using Cryo-EM data and MD simulations to create realistic 3D animations of Class B1 GPCR activation" 4GPCRnet conference, Leipzig, Germany, 26th 29th September 2022.
- Jessica Lu (poster) "Characterisation of the transducer coupling profiles of PAC1 receptor splice isoforms" 4GPCRnet conference, Leipzig, Germany, 26th 29th September 2022.
- Cindy (Xin) Zhang (poster) "Structural insights into GLP-1R activation and allosteric modulation by non-peptidic ligands" 4GPCRnet conference, Leipzig, Germany, 26th 29th September 2022.
- Peter Czabotar (invited) "Species deceases: Understanding phylogenetic differences in the RIPK3-MLKL necroptotic switch" European Cell Death Organisation EDCO 2022, Bonn, Germany, September 26th- 29th 2022.
- Jessica Lu (poster) "Characterisation of the transducer coupling profiles of PAC1 receptor splice isoforms" 2nd IRN i-GPCRnet meeting, Wurzburg, Germany, September 30th – October 1st 2022.
- Eric Hanssen (invited) "Cryo-electron microscopy at the Bio21 Ian Holmes Imaging Centre" Queenstown Research Week, Queenstown, NZ, August/September 2022.
- Lezanne Ooi (invited) "Disparate phenotypes of microglia in Alzheimer's Disease in vitro" International Society of Neurochemistry, Kyoto, Japan, August 28th September 1st, 2022.
- Lezanne Ooi (invited) "Reversing early phenotypes of neurodegeneration in Alzheimer's disease iPSC-derived neurons" Asia-Pacific Association for Neural Transplantation and Repair, Hobart, Australia, October 2022.
- Karen Gregory (invited) "Fine-tuning glutamate receptor activity with allosteric modulators for neurodegenerative and psychiatric disorders" Dr. GPCR Summit (virtual meeting), October 10th 16th 2022.

National Conference Presentations

- Michael Griffin (invited) "Structures of the interleukin 11 signalling complex reveal dynamics of gp130 extracellular domains and a surprising inhibitory mechanism of a cytokine variant" ComBio2022, Melbourne, September 27th – 30th 2022.
- David Thal (invited) "Two for one: the clinical candidate xanomeline displays a dual orthosteric and allosteric binding profile at the M4 muscarinic acetylcholine receptor" ComBio2022, Melbourne, September 27th 30th 2022.
- Lisanne Spenkelink (invited) "Single-molecule studies of DNA replication: The plasticity of the replisome" ComBio2022, Melbourne, September 27th – 30th 2022.
- Mohsen Kazemi (poster) "ENRICH; a fast method to improve the quality of flexible macromolecular reconstructions" ComBio2022, Melbourne, September 27th 30th 2022.
- Yao (Jackie) Lu (poster) "Agonist-mediated GPR52 trafficking and their binding pocket revealed by cryo-EM" ComBio2022, Melbourne, September 27th 30th 2022.
- Mehdi Youseffi Matak (poster) "Structural and functional characterisation of AAA+ ATPase p97 protein homologs from malaria parasite "ComBio2022, Melbourne, September 27th 30th 2022.
- Antoine van Oijen (invited) "Half a century after their discovery, cryo-EM structures of Redβ and Erf annealases provide insights into their evolution and molecular mechanisms" Australian Society for Microbiology Conference, Sydney, July 11th – 14th 2022.
- Yao Lu (invited) "Using cryo-EM to enable novel CNS drug discovery" Neurotherapeutics Symposium, Melbourne, 26th October 2022.
- Gökhan Tolun (invited) "Cryo-EM structure of phage λ annealase Redβ provides insights into its molecular mechanisms and evolution, half a century after its discovery" ARC CCEMMP symposium on Cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022.
- Sarah Piper (invited) "Dynamic drug targets: Using Cryo-EM data and MD simulations to create realistic 3D animations of Class B1 GPCR activation" ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022.
- Rachel Johnson (invited), "Applications of cryo-EM for drug discovery programs: from conformational dynamics to inactive state structures", ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022.
- Mohsen Kazemi (poster) "Understanding the structural basis of manganese transport by streptococcus pneumoniae" ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022.
- Bhanu Mantri (poster) "A preliminary cryo-EM map of human herpes virus 8 ORF6 illustrates the overall structural similarity with Herpes Simplex Virus 1 ICP8 single-stranded annealing homologous recombination protein" ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022.
- MariaKatarina Lambourne (poster) "The cryo-EM structure of the Erf annealase provides insights into its molecular mechanisms and evolution" ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022.
- Isabella Russell (poster), "Stabilisation Methods for the parathyroid receptor 1 and its constitutively active mutants", ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022.
- Joydeep Baral (poster), "Structure-function insight into the two-component DNA repair system of mycobacterium tuberculosis", ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022.
- Wessel Burger (poster), "Structure of xanomeline bound M4 muscarinic acetylcholine reveals an unexpected dual orthosteric and allosteric binding profile", ARC CCEMMP symposium on Ccyo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022.

- Jianjun Cao (poster), "Toward a structural understanding of amylin receptor phenotype: implications for therapeutic development for obesity", ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022
- Brian Cary (poster), "Prolonged signaling of backbone-modified glucagon-like peptide-1 analogues with diverse receptor trafficking", ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022
- Hai-Tian Chen (poster), "Application of cryo-EM to understand the molecular structure and signal transduction of the Ephrin Receptor Pseudokinase EphA10", ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022
- Lucy Fitschen (poster), "Towards the cryo-EM structure of bacteriophage λ EATR complex", ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022
- Jessica Lu (poster), "Characterisation of the transducer coupling profiles of PAC1 receptor splice isoforms", ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022
- Nazanin Mohebali, (poster), "Membrane mimetic systems and their effect on structure resolution, conformation and dynamics of GPCRs", ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022
- Theodore Nettleton (poster), "Structure of the pituitary adenylate cyclase activating polypeptide 1 receptor in the apo-state and bound to non-canonical signal transducers", ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022
- Jordan Nicholls (poster), "Characterisation of the essential epstein-barr virus annealase BALF2", ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022
- Qinghao Ou (poster), "Investigating the structure of GIPR/GLP-1R co-agonists in complex with GIPR-Gαs and GLP-1R-Gαs", ARC CCEMMP symposium on cryo-electron microscopy of membrane proteins, Bio21 Institute, Melbourne, September 1st 2022

Academic Seminar Presentations

- Patrick Sexton, "Structural insight into ligand binding and activation of class B peptide hormone GPCRs" University of Glasgow, Glasgow, Scotland, August 1st, 2022
- Jessica Lu, "Optimisation of the protein purification of the PAC1 receptor splice isoforms in complex with Gs" and visit to School of Biomedical Sciences, University of Leeds, UK, October 2022
- Cindy Zhang, "Structural insights into GLP-1R activation and allosteric modulation by non-peptidic ligands", Coventry University, UK, October 2022.
- Cindy Zhang, "Structural insights into GLP-1R activation and allosteric modulation by non-peptidic ligands," MRC Laboratory of Molecular Biology LMB, Cambridge, UK, October 2022.
- Sarah Piper, "Dynamic drug targets: Using cryoEM and MD simulations to understand peptide binding and selectivity of VPAC receptors" Coventry University, UK. 4th October 2022.
- Sarah Piper, "Using CryoEM, MD simulations and 3D animations to understand GPCR activation" Osnabrueck University, Germany. 10th October 2022.

Publications

1) Newing TP, **Brewster JL**, **Fitschen LJ**, **Bouwer JC**, Johnston NP, Yu H, & **Tolun G**. Red β 177 annealase structure reveals details of oligomerization and λ Red-mediated homologous DNA recombination. *Nature Communications*. 2022 Sep 26;13(1):5649. https://doi.org/10.1038/s41467-022-33090-6. PMID: 36163171; PMCID: PMC9512822.

2) Cary, BP, Gerrard, EJ, Belousoff, MJ, Fletcher, MM, Jiang, Y, Russell, IC, Piper, SJ, Wootten, D, & Sexton, PM. Molecular insights into peptide agonist engagement with the PTH1 receptor. *bioRxiv*, preprint, 2022.

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Patents granted

WO/2022/184849 A1; Olivier Mirguet, Guillaume Poissonnet, Nicolas Faucher, Bjorn Tyrberg, **Christopher Langmead**, **Patrick Sexton**, **Denise Wootten**, Yu Huang, Yin Yin. "GLP1R agonists, uses and pharmaceutical compositions thereof" (status: Granted). (collaboration with Servier)

CCeMMP cryo-EM structure image gallery

UoW

Cover image PDB 7UJL https://www.rcsb.org/structure/7UJL; EMD-26566 https://www.ebi.ac.uk/emdb/EMD-26566

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• Eric Hanssen: EMD-25619, https://www.ebi.ac.uk/emdb/EMD-25619



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