

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

Quarterly newsletter

INSIDE THIS ISSUE: Visiting scientists to CCeMMP Rotation 2 & 3 complete Welcome back Jackie



Australian Government Australian Research Council



Tee credit. Or Sarah Piper (@Sarah J_Piper, @Pipe









CCeMMP acknowledges the peoples of the Kulin, Dharawal, Yuin and Wadi Wadi Nations on whose land the Centre and its Nodes operate. We pay our respects to their Elders, past, present and emerging.

From the Director

Professor Patrick Sexton Centre Director

Welcome to the 10th instalment of the ARC CCeMMP quarterly newsletter where we welcomed back Dr. Jackie How from maternity leave, resuming her key role as Centre Manager. We are very grateful for the excellent work of Dr. Tracie Pierce who fulfilled the role in Jackie's absence and who is continuing to support the Centre as Jackie transitions back to full time.

The last 3 months has seen the execution of a new Centre managed project agreement with one of our industry partners and visits from leading international cryo-EM researchers from both academia and industry. Our latest cohort of ICHDRs have just completed rotations 2 and 3 of their cryo-EM training, while many of our students and student affiliates have been presenting their research at local and international meetings. We have also seen a broad array of new research papers from across the Centre, including papers in leading journals such as Nat Chem Biol, Nat Commun, Nat Genetics and Blood.

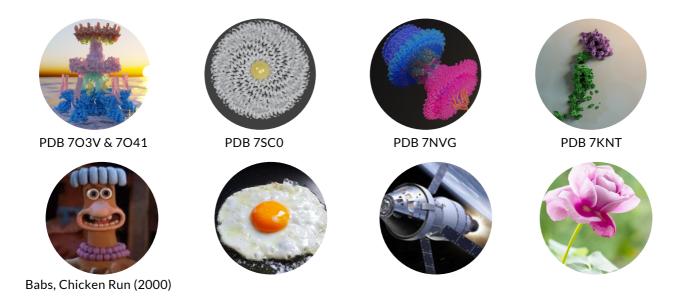
We congratulate all of our members and affiliates on their recent achievements.

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Professor Patrick Sexton Centre Director

Did you know?....

The Oxford English Dictionary defines pareidolia (parr-uh-DOH-lee-uh) as "the perception of recognizable patterns or images, in random or vague arrangements of shapes, lines, colours, etc." It's the human ability to see shapes or make pictures out of randomness; it's that potato that looks like a face, the cloud that looks like a dragon, that membrane protein that looks like 'Babs' from Chicken Run! What does your brain (or your Blender render) create out of your membrane protein?



On the cover: 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 membrane component of the tripartite RND-efflux pump which spans the membrane bilayer to shuttle compounds from the cytoplasmic and periplasmic space into the extracellular environment. The protein assembles into an asymmetric trimer arrangement with each subunit adopting a different conformation, purported to be a particular stage within the solute transport cycle. MexB, and RND transporters like it, are one of the major reasons for the development of antibiotic resistance.



Centre updates

ICHDR Update

"Rotation 2": Theoretical and Practical Aspects of Cryo-Electron Microscopy; Lecture Series, August 14-28, 2023

Five CCeMMP ICHDRs participated in this Cryo-EM training rotation. With lectures co-ordinated by Dr. Matt Belousoff and presented by Centre members (Associate Prof. Isabelle Roullier, Dr. Debnath Ghosal, Dr. Alisa Glukhova, Dr. James Bouwer, Dr. Matthew Belousoff) and our partner organisation (Dr. Lingbo Yu, Thermo Fisher Scientific), they covered the topics: Introduction to transmission electron microscopy (TEM); Negative stain and its application; Sample preparation & vitrification for SPA of membrane proteins; Introduction to image formation (TEM); General considerations for microscope set up (SPA); Electron detector technology.

This year, an additional 30 zoom attendees registered for the lectures from our nodes: Monash, UoM/Bio21, UoW; external affiliates: ANU, University of Sydney; and partner organisations: Dimerix, Pfizer and Boehringer Ingelheim. 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, Dr. Aidan Grosas and Dr. Matthew Belousoff.

"Rotation 3": Data Processing and Analysis, September 11-22, 2023

This was a two week intensive hands-on training in data processing of cryo-EM data, co-ordinated by Dr. Matthew Belousoff. Five CCeMMP ICHDRs came to the Monash node to partake in the training. They were joined by an additional 5 student affiliates from each of our nodes who applied to attend (one even securing a travel grant to come to Melbourne); Monash (1), UoM/Bio21 (2), WEHI (1), UoW (1). Dr. Matthew Belousoff and Dr. Sepideh Valimehr delivered most of the components of this rotation. Dr. Joshua Hardy (WEHI) and Dr. Andrew Thompson (WEHI) presented on point group symmetry and protein construct design choices for structural biology analysis. Dr. Sarah Piper and Dr. Cindy Zhang presented PDB validation and final steps for ensuring your data is ready for publication.



The final day, Rotation 3: Structure Validation & Visualisation with Dr. Sarah Piper & Dr. Cindy Zhang

We will continue to provide access to this training opportunity to affiliate student members. In subsequent years, more places will be available to Centre members/affiliates who would like to attend.

With the completion of rotations 2 and 3, our current ICHDRs have now finished all the training rotations. In year two these students will complete "The Drug Discovery Process" unit. For the most part, they can now concentrate on their projects and put all their training to good use, once they have submitted their post analysis for Rotation 3, that is!

Students have completed their 12 month confirmation: Mayada Mazher, Minakshi Baruah , Alok Pradhan, Ania Beyger; 24 month confirmation: Dongju Lee, Qinghao Ou

Welcome back Jackie!

In September we happily welcomed back our Centre Manager, Jackie How, from maternity leave. Jackie will be back three days a week (Monday, Tuesday and Thursday) until the end of the year. Her hours will increase in 2024. Welcome back Jackie, it's great to have you back on deck!

Visiting Scientists

Claudio Ciferri, Genentech, visits the Monash Node

With the IUCr meeting being held in Parkville during this year, we were fortunate to have one of our industry partners, Dr. Claudio Ciferri from Genentech, take some time to meet with Centre students and Postdocs. Claudio is the Executive Director of Structural Biology and a Biomolecular Resources Senior Principal Scientist (Structural Biology). He is a very experienced industry scientist who was responsible for setting up one of the first worldwide industry CryoEM groups. 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.



Visit by Dr. Claudio Ciferri, Aug 2023. Mentoring session, with centre PhD's and PostDocs (in person and zoom).

Jose-Maria Carazo visits the Bio21 Node



Prof. José-Maria Carazo seminar (in person and zoom), Aug 2023, Bio21.

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. Another welcome addition from the IUCr conference was Prof. Jose-Maria Carazo. Prof. Carazo is Head of the Biocomputing Unit at the National Center of Biotechnology. 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. José-Maria Carazo met with a group of centre PhD students at Bio21, Aug 2023.

Expanding CCeMMP Membership

As part of its strategic plan, the Centre has been reaching out to scientists, 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. Of course, we continue to actively seek inclusion of new staff and students from within our existing Nodes, as part of the Centre.

New affiliate members from around the country joining this quarter:

Dr. Ben Gully, Monash BDI; Amy Chen, University of Sydney; Yi Zeng, Victor Chang Cardiac Research Institute

Node Updates Monash Node

Professor Denise Wootten Node Leader, Monash University

HRM Workshop for EMCRs



Karen Gregory was a key organiser and contributor to a workshop on "How to perfect your bio" organised by the outreach group Her Research Matters, targeted to MIPS EMCRs at the Monash Node.

Patrick Sexton and Denise Wootten were also expert contributors to this workshop.

Associate Prof. Karen Gregory

CCeMMP 3-day workshop on single particle analysis, Jan 31st - Feb 2nd, 2024.

Immediately prior to the Lorne Proteins Meeting (Feb 4-8, 2024), CCeMMP will be running a 3-day workshop on single particle analysis (SPA). The workshop will cover the fundamental theoretical and practical aspects of SPA cryo-EM. Over the three days the entire image processing workflow will be covered from micrographs to 3D map calculation. This will be done in the context of cryoSPARC. Attendees will receive hands-on training and the course will cover everything from motion-correction, particle picking, 2D and 3D classification, ab initio map generation and high resolution 3D refinement. On top of this, more advanced topics will be covered to include 3D-variability analysis and how to perform focused 3D refinements. By the end of the course the attendees will have a firm theoretical foundation for SPA and be able to use cryoSPARC to process their own research data. Places are limited, so please submit a 200 word summary of your project and how SPA will play a role in your research. Send your application to Dr. Jackie How (jackie.how@monash.edu) by December 11, 2023. Successful applicants will be notified by December 20, 2023. Priority will be given to Centre members and affiliates.

University of Melbourne (Bio21) Node

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

Single Particle Cryo-EM Workshop - October 23-25 - sponsored by Thermo fisher Scientific

October 23-25, Dr. Sepideh Valimehr ran a SPA cryoEM data processing workshop at Ian Holmes Imaging Centre (IHIC) at Bio21 Institute, with the help of Dr. Hamish Brown (IHIC) and Dr. Matthew Belousoff (MIPS). This was a hands-on Cryo EM data processing workshop with 8 attendees from various regions across Australia: University of Sydney, Griffith University, WEHI, Monash and University of Melbourne.

This workshop was sponsored by our industry partner ThermoFisher Scientific.



SPA workshop at Bio21, October 23-25, 2023



The world leader in serving science

Travel Award



CCeMMP ICHDRs, Riya Joseph and Marialena Georgopoulou, were each awarded a Graduate Researcher Travel Award, Department of Biochemistry and Pharmacology, The University of Melbourne, \$400. This award enabled Riya and Marialena to register for the recent international crystallography meeting in Melbourne, IUCr2023 Aug 22-29, 2023.



Riya Joseph

Marialena Georgopoulou

University of Wollongong Node

Associate Professor Gökhan Tolun Node Leader, University of Wollongong

Gökhan Tolun Taking Sabbatical



Associate Professor Gökhan Tolun will be taking sabbatical leave first semester 2024. Professor Lezanne Ooi will be acting node leader during his absence



Prof. Lezanne Ooi

Associate Prof. Gökhan Tolun

Simon Brown Received Continuing Appointment

Dr. Simon Brown received a continuing appointment at the University of Wollongong; level 8/9 professional staff.

Bhanu Mantri Awarded PhD

Student affiliate, Bhanu Mantri, was awarded a PhD from the University of Wollongong in the School of Chemistry and Molecular Biosciences, Thesis title "Understanding the Molecular Mechanism of Single-Strand Annealing Homologous DNA Recombination in Viruses by Cryo-Electron Microscopy." Bhanu is no longer at the UoW node; he is now at the University of Sydney running their biological CryoEM facility and continues to be an affiliate of the Centre.

Grants Awarded



Dr. Lisanne Spenkelink

Dr. Lisanne Spenkelink was co-CI on a small equipment grant and an ARC Discovery Grant.

Lisanne Spenkelink: Small Research Equipment Grant, co-CI, \$25,000.

ARC Discovery Project (DP240101399): High-throughput singlemolecule directed evolution. Dr. Lisanne Spenkelink; Professor Antoine van Oijen; Professor Andrew Griffiths, \$598, 737.

This project aims to develop a new single-molecule directed-evolution system to evolve better polymerases in order to identify DNA polymerases with improved performance that benefit biotechnological applications.

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

Jhonnatan Reales-Gonzalez was awarded a travel grant for costs associated with attending the ARC CryoEM Data Processing Rotation, September 11th - 22th, Monash University, Parkville. Jhonnatan applied to attend this rotation alongside the CCeMMP ICHDRs and spent two weeks in Parkville at MIPS to participate in 'Rotation 3'.

WEHI Node

Associate Professor Isabelle Lucet Node Leader, WEHI

Chacot-Marie-Tooth Australia visits WEHI

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 cryoEM research conducted at WEHI.



Dr. Winnie Tan hosts members of CMT Australia on their visit to WEHI

External Affiliates Update

Professor Renae Ryan AM awarded the Eureka Prize for Outstanding Mentor of Young Researchers



Prof. Renae Ryan

The Australian Museum Eureka Prizes were announced at the end of August at an award ceremony at the Australian Museum. These awards celebrate outstanding scientific achievement both within and outside of the lab: Research and Innovation, Leadership, Science Engagement, and School Science.

Professor Renae Ryan AM, was awarded the University of Technology Sydney Eureka Prize for Outstanding Mentor of Young Researchers-"Ryan has advanced the careers of many young researchers through mentorship, networking and advocacy. Driving university-wide gender equity initiatives and founding the Sydney Medical School Early Career Researcher Network, she helped increase representation of women at professor level in her faculty, fostering a more inclusive and supportive academic environment."

Prof. Ryan also became a Fellow of the Royal Society of NSW.

Prof. Ryan (AM, FRNS) will be giving a seminar in person at MIPS, Parkville November 8, 2023. CCeMMP students have the opportunity to meet with Renae prior to her seminar.

Dr. Alice Shin was awarded a \$600 bursary to attend CryoOz 2023, the 4th CryOz Symposium, November 23 and 24, at the University of Queensland, Brisbane.

Upcoming Events



Seminar Series

Our seminar series continues on the second Tuesday of the month, 10:00 AM - 11:00 AM. In our final quarter for 2023 we will hear from the lab of Dr. Susan Bucahanan, NIH (Nov 14) and Distinguished Professor Scott Prosser, University of Toronto (Dec 12). We will also have our final special seminar for 2023, Prof. Ariane Briegel, Leiden University, 4:00 PM Nov 28, note the later start time. Mark your calendars!

With the conclusion of our seminar series for the year, we would like to extend our thanks to the seminar committee for putting on such a diverse and interesting program for us. We thank the committee members for their time (Chair: Dr. Sepideh Valimehr; Dr. Tracie Pierce and members Dr. Aidan Grosas, Dr. Fabian Bumbak, Dongju Lee and Doulin Shepherd). We also bid farewell to Dongju and Doulin and welcome both Alok Pradhan (ICHDR, Monash node) and Bindusmita Paul (PhD student affiliate, UoM/Bio21) onto the committee. The new committee has already been busy to secure speakers for February, March, April and May 2024 with Dr. Cindy Zhang (Monash University), Associate Professor Isabelle Lucet (WEHI node leader), Professor Brett Collins (UQ) and Dr. Alastair Stewart (Victor Chang Cardiac Research Institute), respectively.

CCeMMP Retreat

The date is set – December 4th and 5th – for the Centre retreat. There will be various scientific presentations from ICHDRs and members and affiliates from the founding nodes and new external affiliates. There will also be time spent on strategic planning for the future. The retreat will take place in Parkville; separate from but centrally located for the Monash, WEHI and UoM/ Bio21 nodes. The schedule is currently being planned. We look forward to hearing about the current research from Centre ICHDRs greater than twelve months into their PhD's and from scientists around the Centre. We will also be planning for the future of CCeMMP with current members and affiliates.

Outreach

In the Media

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

September 14, 2023; Monash University Faculty of Pharmacy and Pharmaceutical Sciences web page; write up on the Nature Communications paper [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. Nature Communications 14(1): 5440, 2023. doi: 10.1038/s41467-023-41199-5.]

"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."

<u>https://www.monash.edu/pharm/about/news/news-listing/latest/scientists-uncover-new-and-unexpected-information-about-schizophrenia-drug</u>

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

September 27, 2023, WEHI Facebook page CMT Australia visit to meet Dr Winnie Tan at WEHI. <u>https://www.facebook.com/photo/?</u>

fbid=630936099189774&set=a.562623272687724&paipv=0&eav=AfaqeqIjusiC0vjEA1yR1A8uoaPeGri OntoX9Eo0COKWHrN7NBzpx8DfLwGfMJvfCAo& rdr

October 6, 2023: Nature Reviews Drug Discovery, News in Brief. 'Novel schizophrenia therapy filed for FDA approval' [Article refers to **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) et al, Nature Communications 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

October 5, 2023. <u>https://ashpublications.org/blood/article/142/14/1180/498142/Pass-the-12-LOX</u> Blood, commentary on Mobbs JI, Black KA, Tran M, Burger WAC, Venugopal H, Holman TR, Holinstat M, Thal DM, Glukhova A (2023). Cryo-EM structures of human arachidonate 12S-Lipoxygenase (12-LOX) bound to endogenous and exogenous inhibitors. Blood Oct 5;142(14):1233-1242. doi: 10.1182/blood.2023020441

Outreach - Training

Eric Hanssen: CryoEM lectures in the Graduate coursework: Biomolecular Structure Determination (SCIE90026 at University of Melbourne)

Isabelle Roullier: Workshop. Virology and Structure Biology, Bio21, September 17 2023. Hokkaido University/UoM - a delegation from Hokkaido University visited thanks to funding secured through an UoM-Japan initiative.

Isabelle Roullier: Cryo-EM: historical perspectives and concepts; CCeMMP Electron Microscopy Tutorial/Lecture- CCeMMP rotation

Isabelle Roullier: Protein Structure and Function, 3x 2h lecture videos, 3x 2x2h workshop, subject coordinator (BCMB30001 at University of Melbourne)

Winnie Tan: regular training sessions on the mass photometer at WEHI training 1-4 new users per week.

Winnie Tan: facilitator for the Women in Science Parkville Precinct (WISPP), hosting 5 x 2 hours workshops on grant writing to 7 female postdoctoral researchers.

Recent Centre Activities and Achievements

Industry Engagement

Monash University and Novo Nordisk entered into a new 15-month Project Agreement through the Centre to study structure and function of peptide hormone GPCRs commencing October 2023.

Dr. Claudio Ciferri (Genentech) visit CCeMMP in August 2023, meeting with Centre ICHDRs and members.

Denise Wootten: Septerna Learn seminar Series 2023, Targeting GLP-1R and GIPR; from cryo-EM structures to animal models of disease, Sept 22, 2023

Members and student members continue to have their regular meetings with their respective industry partners (Boerhinger Ingelheim, Astex, Servier, Astra Zeneca, Dimerix and Pfizer).

Training

Marialena Georgopoulou and Riya Joseph from the University of Melbourne Node were participants in the "Biocore training for beginners" workshop run by Cytiva.

Amy Chen: Attended SP cryoEM data processing workshop at Bio21

Conference Presentations

International

Debnath Ghossal: Invited talk. Understanding the structural basis of T-DNA translocation through the Agrobacterium tumefaciens Type IV Secretion System. International Microscopy Congress, Sept 11-15, 2023, Busan, Korea.

Patrick Sexton. Invited talk. Application of cryo-EM to understanding peptide and small molecule binding to G protein-coupled receptors. August 26th. International Union of Crystallography, IUCr2023 Aug 22-29, 2023, Parkville, Australia.

Alastair Stewart: Invited talk. Structures of the F1-ATPase Rotary Catalytic Cycle; Aug 16. International Conference on Biological Physics Aug 14-18, 2023, Seoul, Korea.

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

Fabian Bumbak: Selected talk. The neurotensin peptide agonist retains conformational flexibility upon binding to neurotensin receptor 1, International Society of Magnetic Resonance, ISMAR23, August 20-25, 2023, Brisbane.

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

Isabelle Roullier: Contributed talk. Understanding the conformational landscape p97 from cryo-EM and massspectrometry data; Aug 25. International Union of Crystallography, IUCr2023 Aug 22-29, 2023, Parkville, Australia.

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

Riya Joseph: Poster presentation. Structural studies of recently identified *B. fragilis* cholesterol-dependent cytolysin like proteins. International Union of Crystallography, IUCr2023 Aug 22-29, 2023, Parkville, Australia.

Winnie Tan: Poster presentation. Human MORC2 is an ATP-dependent DNA compaction machine. International Union of Crystallography, IUCr2023 Aug 22-29, 2023, Parkville, Australia.

National

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

Academic Seminar Presentations

Natalie Diepenhorst: Lab to Market: Pitch Workshop. The importance of keeping the end user in mind for research commercialisation, October 10, 2023, Victorian Comprehensive Cancer Centre (VCCC) Alliance.

Jessica Lu: PhD exit seminar. Structural and Pharmacological Characterisation of Splice Isoforms of the Pituitary Adenylate Cyclase- Activating Polypeptide Type 1 (PAC1) Receptor, August 29, 2023, Monash University, Parkville.

Isabelle Roullier: Understanding the conformational landscape p97 from cryo-EM and mass-spectrometry data, October 3, 2023, Sorbonne University, Paris, France.

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

Academic Presentations

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

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



Minakshi Baruah: 3MT

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

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

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



Dongju Lee: 3MT

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

Mayada Mazher: Poster presentation. Studying the role of TACAN membrane protein in Pain sensing . University of Melbourne Department of Biochemistry & Pharmacology Graduate Research Conference Sept 25-26, 2023.

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

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

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

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

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

Jack Tovey: Oral presentation. Small Molecule Agonism of CCK-1R, Different Angles for the Treatment of Obesity, DDB Student Symposium Oct 26, 2023, Monash University, Parkville.





Jack Tovey



Publications

New Publications

Brown HG, Smith D, Wardle BC, **Hanssen E** (2023). Fitting a square beam in a square camera: novel condenser apertures for low-dose transmission electron microscopy. BioRxiv posted Aug 16, 2023. https://www.biorxiv.org/content/10.1101/2023.08.13.553155v2.abstract

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8F0K/EMD-28759; 8F2A/EMD-28810; 8F0J/EMD-28758; 8F2B/EMD-28812

Cao J, Belousoff MJ, Gerrard E, Danev R, Fletcher MM, Dal Maso E, Schreuder H, Lorenz K, Evers A, Tiwari G, Besenius M, Li Z, Johnson RM, Wootten D, Sexton PM (2023). Structural insight into selectivity <u>o</u>f amylin and calcitonin receptor agonists. Nature Chemical Biology, Aug 3, online ahead of print,

doi: 10.1038/s41589-023-01393-4. *With industry partner Sanofi.* 8F0K/EMD-28759; 8F2A/EMD-28810; 8F0J/EMD-28758; 8F2B/EMD-28812

Fernando CD, Jayasekara WSN, Inampudi C, Kohonen-Corish MJR, Cooper WA, Beilharz TH, **Josephs TM**, Garama DFJ, Gough DJ (2023). A STAT3 protein complex required for mitochondrial mRNA stability and cancer. Cell Reports 42(9):113033. Epub Sept 12, 2023. doi: 10.1016/j.celrep.2023.113033

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Lagou V, Jiang L, Ulrich A, Zudina L, González KSG, Balkhiyarova Z, ... **SextonPM...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. Nature Genetics 55 (9): 1448-1461. doi: 10.1038/s41588-023-01462-3.

Mobbs JI, Black KA, Tran M, **Burger WAC**, Venugopal H, Holman TR, Holinstat M, **Thal DM, Glukhova A** (2023). Cryo-EM structures of human arachidonate 12S-Lipoxygenase (12-LOX) bound to endogenous and exogenous inhibitors. Blood 142(14):1233-1242. doi: 10.1182/blood.2023020441. Commentary in Blood, October 5, 2023.

8GHB/EMDB-40039; 8GHC/EMDB-40040, EMDB-40299, EMDB-40301, EMDB-40300; 8GHE/EMDB-40042; 8GHD/EMDB-40041, EMDB- 40302, EMDB-40304 .

Quah PS, Tran BM, Corbin VDA, Chang JJ-Y, Wong CY, Diaz-Méndez A, Hartley CA, Zeng W, **Hanssen E**, Trifunovic Z, Reading PC, Jackson DC, Vinca E, Coin LJM, Deliyannis G (2023). Development of matrixembedded bovine tracheal organoids to study the innate immune response against bovine respiratory disease. Organoids, 2(2): 82-101. https://doi.org/10.3390/organoids2020007

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Wu Q, Ong L, Chen GQ, Varshney S, **Hanssen E**, Kentish SE, Gras SL (2023). The effect of calcium removal from skim milk by ion exchange on the properties of the ultrafiltration retentate. Food Research International 173 (1): 113305. https://www.sciencedirect.com/science/article/pii/S0963996923008505

Zeng YC, Sobti M, Quinn A, Smith NJ, Brown SHJ, Vandenberg JI, Ryan RM, O'Mara ML, Stewart AG. (2023). Structural Basis of Promiscuous Substrate Transport in Organic Cation Transporter 1. Nature Communications, 14:6374. doi: 10.1038/s41467-023-42086-9. 8SC1/EMD-40334, 8SC6/EMD-40339, 8SC4/EMD-40337, 8SC3/ EMD-40336, 8SC2/EMD-40335

Updated Publications

Pham V, Jansen MCCH, Thompson G, Heitman LH, **Christopoulos A**, **Thal DM**, Valant C. (2023). Role of conserved tyrosine lid residues in the activation of the M2 Muscarinic Acetylcholine Receptor. Molecular Pharmacology, 104 (3): 92-104. DOI: 10.1124/molpharm.122.000661.

Released Structures

Black KA, Mobbs JI, Venugopal H, Thal DM, Glukhova A.

Mobbs et al., Blood, 2023, https://doi.org/10.1182/blood.2023020441

- 8GHB/EMDB-40039 (12-LOX monomers)
- 8GHC/EMDB-40040, EMDB-40299, EMDB-40301, EMDB-40300 (12-LOX dimers)
- 8GHE/EMDB-40042 (12-LOX tetramers)
- 8GHD/EMDB-40041, EMDB- 40302, EMDB-40304 (12-LOX hexamers)

Cao J, Sexton PM, Wootten DL.

Cao et al., Nat Chem Biol, 2023, https://doi.org/10.1038/s41589-023-01393-4

- 8F0K/EMDB-28759 (San385-AMY3R-DNGs complex)
- 8F2A/EMDB-28810 (San385-AMY3R-DNGs complex, cluster 5 conformation)
- 8F0J/EMDB-28758 (San45-CTR-DNGs complex)
- 8F2B/EMDB-28812 (San45-AMY3R-DNGs complex)

Mobbs JI, Glukhova A, Sexton PM, Thal DM.

Burger et al., Nature Comm, 2023, https://doi.org/10.1038/s41467-023-41199-5

• 8FX5/EMDB-29524 (xanomeline-M4 muscarinic acetylcholine receptor-Gi1 complex)

Zeng YC, Sobti M, Stewart AG.

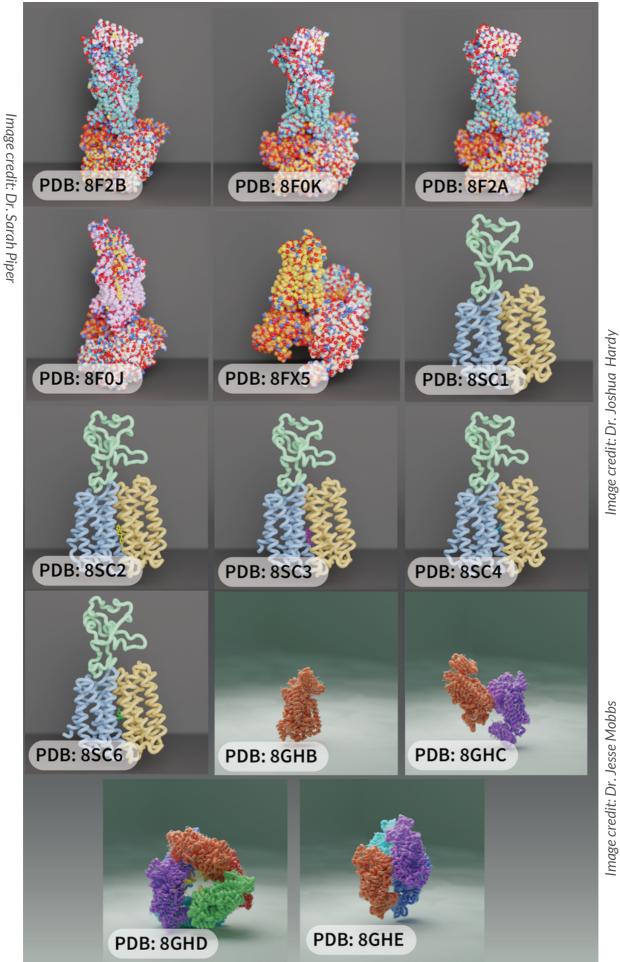
Zeng et al., Nat Comm, 2023, doi: 10.1038/s41467-023-42086-9

- 8SC1/EMDB-40334 (organic ion transporter 1 (OCT1), apo)
- 8SC6/EMDB-40339 (thiamine-OCT1)
- 8SC4/EMDB-40337 (metformin-OCT1)
- 8SC3/ EMDB-40336 (fenoterol-OCT1)
- 8SC2/EMDB-40335 (diltiazem-OCT1)





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