

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

Quarterly newsletter

INSIDE THIS ISSUE:

- Second industry placement returns
- Workshops and rotations
- Our newest ICHDR

Image credit - Dr Joshua Hardy



Australian Government Australian Research Council





bio21 institute

MOLECULAR HORIZONS





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 Deputy Director

Assoc. Prof. Isabelle Rouiller Deputy Director, UoM/Bio21 Node Leader

Welcome to the 13th instalment of the ARC CCeMMP quarterly newsletter. With Director, Prof. Patrick Sexton currently on long service leave, this message comes from our Deputy Director.



It is with great pleasure and honour to lead our Centre during Patrick's sabbatical. This newsletter presents a wonderful opportunity to reflect on the outstanding work accomplished by our Director, node leaders, and all members of the Centre. I am also consistently impressed by how much our students and postdocs achieve when they are given the opportunity and confidence to push beyond their comfort zones. Their exceptional work is a testament to the potential that is unleashed when they are empowered.

This month, we welcome back our first students returning from their placements, eager to share their unique experiences. They pave the way for our GRs who have recently begun their industrial journeys. What a long and rewarding path it has been!

The Centre has now paired all our ICHDR members with a mentor from industry or academia. The mentorship program not only promotes engagement but also provides valuable networking opportunities, fosters knowledge exchange, and supports the personal and professional development of our members.

Assoc. Prof. Isabelle Rouiller Deputy Director

Did you know?....

Scientists, combining CryoEM and CryoET, achieved outstanding resolution in imaging respiratory supercomplexes within their native membrane environment, setting new standards in structural biology. The authors utilized a novel *in situ* CryoEM approach to image porcine mitochondria, reaching an average resolution of approximately 2.5 Å, with local resolution as high as 1.8 Å. This exceptional clarity, combined with the preservation of the native membrane environment, represents a significant advancement, overcoming the limitations and potential artifacts of traditional *in vivo* purification methods. This approach not only highlights the precision achieved but also paves the way for its application to other membrane complexes, such as those found in cilia, Golgi, and lysosomes.

Interested in how they did it ...? Read the whole manuscript Zheng et al., High-resolution in situ structures of mammalian respiratory supercomplexes. Nature, 631: 232–239 (2024). <u>https://doi.org/10.1038/s41586-024-07488-9</u>

On the cover: From our WEHI Node, Cryo-EM structure of murine thrombopoietin receptor ectodomain in complex with thrombopoietin, PDB 8U18. Sarson-Lawrence et al., Nat Commun, 15: 1135 (2024). https://doi.org/10.1038/s41467-024-45356-2 Image credit: Dr. Joshua Hardy

Centre Updates



Jack Tovey, Astex, Cambridge UK

ICHDR Update

Industry Placements

Our second student has returned from a 3-month immersive industry placement. Monash ICHDR Jack Tovey was at industry partner Astex Pharmaceuticals (Cambridge UK), returning early July. Jack was kind enough to share the real-world industry experience with us.



I've been fortunate to spend the last 3 months of my life in Cambridge, working with Astex Pharmaceuticals.

Moving to the UK was a new experience for me, and yet without conscious effort, I find myself having built new friendships and lasting connections that have filled my time here with happiness.

From the first day of my placement, I was welcomed as a new member of the Molecular Sciences Team, embedded in a project completely unknown to me. I had a pre-formed idea that industry was modular, and that I would likely be responsible for generating structures and little else. Yet, Astex is a relatively small company by pharmaceutical standards, and project members here are flexible and capable at a different range of techniques, making each project team a new combination of overlapping skills and perspectives. During that first week alone, I found myself working on an entire project pipeline, from reviewing expression efficiency, to optimizing target purifications, testing different grid making conditions, to screening cryo-EM grids in a 200kV Glacios, to setting up full data collections on a 300kV Titan.

The approach by industry to a particular problem, relative to academia, was perhaps the biggest shock. The same scientific rigour, the same techniques, the same outcome all planned and executed with a vastly different perspective and set of priorities. This adjustment for me was made easier by some of the fantastic people I had the opportunity to work with, in particular: Dr. Amir Apelbaum, Dr. Scott Jackson, Dr. Alex Berndt, Dr. Pamela Williams, and Dr. Joanna Brown.

The Astex desire for well-rounded employees extended beyond the Molecular Sciences Team, as I found myself in meetings with medicinal chemists, translational biologists, clinical trial administrators, and on a smaller second secondment to the pharmacokinetics team. A testament to their willingness to ensure I had a diverse and excellent experience during my time with them.

Over the course of these months, I observed the ins and outs of the drug discovery and development pipeline, while watching our main project advance from new construct designs to grids and preliminary datasets. A development in one phase, being echoed in the larger development pipeline, in a sort of satisfying philosophical symmetry that few people find in their careers.

All in all, I understand the role of industry far better than I would have if my only exposure had been through seminars and networking events. And I will look back on my life in Cambridge with fondness for the rest of my life.



Current placements include: Alok Pradhan (Dimerix, Fitzroy, 12 months, one day per week). Alok continues to spend a day a week with local industry partner, Dimerix, in Fitzroy; Dongju Lee and Qinghao Ou started at Boehringer Ingelheim, Biberach, Germany, May 1st, they will return in August). We hope that each will have their own version of the invaluable hands-on experience described by Isabella in the last Newsletter and Jack.

New ICHDR

We have had another new ICHDR commence their PhD at the Centre. Emily Park will be at WEHI with supervisors Prof. Isabelle Lucet, Dr. Joshua Hardy and Dr. Andrew Thompson. Read more about Emily in the WEHI Node update. We currently have 19 ICHDR students enrolled through the Centre.

Peer Review Training Workshop, May 16, 2024

Peer review is critical to the advancement of science, and through application of their expertise, reviewers help maintain the quality of the published literature and advance the field. Reviewers also get a preview of the latest research and gain insight into best practices when it comes to



Peer Review Training, May 2024

preparing their own manuscripts. Our CCeMMP Director, Prof. Patrick Sexton, a past and current member of many editorial advisory boards, presented a workshop on Peer Review Training, May 16, 2024. The workshop was designed to educate the audience on good peer review practices, including ethics in peer review and how to become a more thorough and objective reviewer. This workshop was open to all Centre members and affiliates. Ten ICHDRs attended (either in person or via zoom), they were joined by 14 other members and affiliates.

Mentoring Best Practices Session, 12 June, 2024

Director, Prof. Patrick Sexton and Centre Manager, Dr. Jackie How held a mentoring session, 'How to be a good Mentee' (via zoom) for all ICHDRs, 12 June, 2024. They covered the basics of how to be a proactive and engaged mentee and also what to look for in a good mentor. This session has prepared students for their first meeting with a mentor and given them tips on how to drive a mentoring session and to get the most out of the relationship. Since the session, most of our ICHDRs have been teamed with an industry mentor and most have opted into the optional CCeMMP Academic Mentoring Program.

CCeMMP Academic Mentoring Program

As part of the feedback received from the CCeMMP Strategic Annual Retreat in December 2023, an area for development was establishing an in-house mentoring program to support the career development of ECRs and students. Earlier this year, CCeMMP targeted researchers within the Centre to volunteer to be mentors for Centre ECRs and students. We had an overwhelming response from 32 researchers across the Centre agreeing to support the program as mentors. CCeMMP called out for Centre students and ECRs to be part of the program as mentees and had 16

people sign up. The mentees and mentors have been paired and mentoring has commenced in July, with mentees driving the meetings and conversations.

We look forward to hearing the experiences from both mentees and mentors, and will continue to build on this program with the feedback we receive, for the 2025 intake.

Process of Drug Discovery, 10-28 June 2024

Centre students in Year 2 of their PhDs take part in what is called "Unit 3 - The Process of Drug Discovery", at MIPS. This is a 3-week intensive in-person program within the Drug Discovery Biology (DDB) Theme that is run for DDB PhD students. We are very fortunate that we are able to include all the Centre students in this training program. The program is made up of 12 modules and covers: the process of drug discovery, structural biology in drug discovery, biopharmaceuticals, formulation and delivery, preclinical development, hit discovery, clinical development, pharmacoepidemiology, practical applications of HTS, hit assessment, hit-to-lead and lead optimisation. This year David and MK (UoW Node), Marialena (UoM Node), Xiaomin (WEHI Node) and Ania (Monash Node) took part. This marks the end of formal training for these students.

Rotation 2 – Cryo-EM Practical Training, 1-12 July

Rotation 2' is a series of Cryo-EM lectures and interactive tutorials, covering the theoretical and practical aspects of cryo-EM delivered by Centre members and experts in the field. For the CCeMMP ICHDRs, lectures were interspersed with hands-on practical training with ICPDs Dr. Aidan Grosas (UoW Node) and Dr. Sepideh Valimehr (UoM/Bio21 Node). Following the success of 2023, we also gave Centre members and affiliates the opportunity to join in these lectures online; 7 members and affiliates registered to join in person and 12 to join online.

The lectures covered: Introduction to Transmission Electron Microscopy (Hari Venugopal, Ramaciotti Centre for Cryo electron microscopy), Negative stain and its application (Dr. Manasi Kumar, Bio21), Sample preparation & vitrification for SPA of membrane proteins (Dr. Alisa Glukhova, WEHI), Introduction to image formation - TEM (Dr. James Bouwer, UoW), Electron detector technology (Dr. Matt Belousoff, Monash Node), Practical considerations for microscope set up- SPA (Dr. Matt Belousoff, Monash Node).

Rotation 3 – Data Processing and Analysis

The final training rotation for our first year ICHDRs started 29 July. Three ICHDRs will take part in this two-week intensive course. They will be joined by 11 other affiliates from two foundation Nodes, our external affiliates and a visiting postdoctoral fellow (1) : Monash Node (7); WEHI (2); UQ (1) and Florey (1) who applied for a place in the rotation. This rotation will continue until 9 Aug.

In the Spotlight.....

This quarter we are showcasing two of our ICPDs, Dr. Sepideh Valimehr from the UoM/Bio21 Node and Dr. Aidan Grosas, from the UoW Node.

If you would like to be featured "In the Spotlight" please contact the chair of the Outreach and Public Engagement Committee, Dr. Sarah Piper (sarah.piper@monash.edu). Otherwise someone may tap you on the shoulder....

In the spotlight

Sepideh Valimehr

Store Land

CCeMMP Postdoc at Bio21 node Twitter/X: @SValimehr

Background

I earned a bachelor's and master's in cell and molecular biology in Iran and a PhD in biochemistry at Melbourne University, Bio21 institute.

Current research

CryoEM sample preparation optimisation, data collection and processing. Organising teaching and instructing the cryoEM workshops. I'm happy to collaborate on cryoEM projects.

Looking forward

Advice for students: Always ask questions. Don't postpone tasks to the future and learn things more in depth.

About me

I enjoy hiking, cycling, playing board games, and spending time with friends. I am also an ice cream lover.

If you're a CCeMMP member and would like to be featured, please reach out to the CCeMMP Outreach and Public Engagement Committee (sarah.piper@monash.edu).

In the spotlight

Aidan Grosas

CCeMMP Postdoc at **UoW node** witter/X: @AidanGrosas

ALT MAK

Background

I completed my PhD at the ANU where I used biophysical and structural techniques to study protein folding and aggregation problems.

Current research

I'm working on membrane transport proteins using cryo-EM. I am also elucidating the structure of amyloid fibrils by cryo-EM using helical processing – please feel free to chat to me about it!

Looking forward

The advances in cryo-electron tomography are exciting, in situ structural biology is going to be a game changer!

About me

What inspired me to pursue a career in research: An innate desire to know how the world around me works and the ability to satisfy my scientific curiosity.

If you're a CCeMMP member and would like to be featured, please reach out to the CCeMMP Outreach and Public Engagement Committee (sarah.piper@monash.edu).

Node Updates Monash Node

Prof. Denise Wootten Node Leader, Monash University

Dr. Celine Valant and Dr David Thal Promoted to Level D

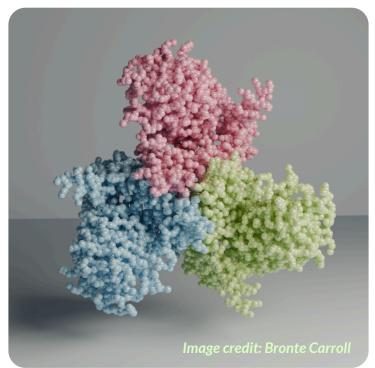


Assoc. Profs. Celine Valant and David Thal

Celine and David are both co-leads of the Analytical and Structural Neuropharmacology (ASNP) laboratory within the Drug Discovery Biology (DDB) Theme at MIPS. Celine has an international profile in the study of orthosteric, allosteric and bitopic ligands at G protein coupled receptors. Her current research interests encompass allosteric modulation, biased signalling, and bitopic ligands. With a PhD in Medicinal Chemistry, her research combines medicinal chemistry, analytical pharmacology and translational biology. David's research focuses on understanding how different types of chemical ligands interact with therapeutically relevant proteins to facilitate drug discovery research; he is particularly interested in using biophysical techniques, molecular pharmacology, and chemical biology approaches to understand protein allostery. Congratulations to both on their welldeserved promotion to Associate Professors.

Blender Workshops

Just in time for the CCeMMP Bench to Art Competition, Dr. Sarah Piper (Monash Node) facilitated two Blender3D workshops over this guarter. The first was held online on the 4th of June with the able assistance of Dr. Joshua Hardy (WEHI Node) and Dr. Sepideh Valimehr (Bio21/UoM Node). The second, to accommodate the high local interest generated by the first workshop, was held on the 11th of July. These were interactive workshops where the attendees were taken step-by-step through the creation of an image, learning little tips and tricks along the way.Sarah provided extensive notes to work from, that will also help later to create images. On June 4th, there were 11 attendees for the online workshop for the beginners and advanced sessions across all and external affiliates; The our nodes University of Sydney was well represented



PDB:6GCT--Top down view of the Alanine Serine Cysteine Transporter 2 (ASCT2); the three identical protomers are highlighted in pink, green, and blue.

with 7 affiliates (including students of affiliates). Other members/affiliates were from University of Queensland, University of Canterbury (NZ), UoW Node and UoM Node. On July 11th, there were 10 attendees registered from the Monash (8) and UoM (2) Nodes, including new affiliates.

Bronte Carroll (The University of Sydney) was kind enough to share the image created from the June 4th workshop–Alanine Serine Cysteine Transporter 2 (ASCT2), PDB code 6GCT.

Blender3D workshops are a regular feature of the Centre and are well attended and highly valued by the participants. Here's some of the feedback received from the latest workshops:

"Sarah was great at talking us through the steps, and made it easy to follow along with. The handout was also detailed and helpful."

"Sarah was a great teacher, especially useful as I am not a structural biologist"

"I really enjoyed the course! Thanks so much for running it! I would be interested in attending future workshops to really hone my skills more but will keep playing around with the software. Thanks again!!"

CCeMMP members awarded at DDB Scientific Symposium



Profs Denise Wootten & Rebecca Ritchie

Monash Node Leader Prof. Denise Wootten and member Dr. Jesse Mobbs were awarded for their presentations at the recent DDB Scientific Symposium held on the 18th of July 2024, Monash University, Parkville, VIC.

Denise won the People's Choice Award for her talk: "Biased GLP-1 agonism at the GLP-1 receptor, from structure to animal models of disease"; and Jesse the ECR award for "Structural investigation of allosteric modulation of the delta opioid receptor".



Dr. Jesse Mobbs & Prof. Rebecca Ritchie

Dr. Jason Cao awarded Mollie Hollman Medal



Dr. Jason Cao

Dr. Jason Cao was awarded the prestigious Mollie Holman Medal for best Doctoral Thesis (2023), Faculty of Pharmacy and Pharmaceutical Sciences, Monash University. The presentation was made at the DDB Scientific Symposium. The Mollie Holman Award was established at Monash University in 1998 in honour of Emeritus Professor Mollie Holman AO. This is one of the highest academic honours Monash University bestows on doctoral students, with a maximum of 10 awarded per year (one per faculty). The medal recognises the awardee as a researcher of the highest order. This is the third year in a row that a CCeMMP member has won this important award; previous awardees have been Dr. Xin (Cindy) Zhang (2021) and Dr. Wessel Burger (2022).

New members/affiliates

Nadeesha Athukorala, student affiliate

University of Melbourne (Bio21) Node

Assoc. Prof. Isabelle Rouiller Node Leader and Deputy Director, University of Melbourne

Single Particle Analysis Workshop, 12-14th June, 2024

Dr. Sepideh Valimehr (ICPD, UoM/Bio21) organised another single particle cryo-EM workshop at the Ian Holmes Imaging Centre at Bio21, 12-14th June, 2024. The workshop covered training in sample preparation (room temperature and cryo), use of TEMs and data collection. Dr. Alisa Glukhova (WEHI Node) delivered some of the lectures, along with Dr. Nicholas Kirk (WEHI) while all of the practical training was presented by Dr. Sepideh Valimehr (UoM/Bio21 Node), Dr Matthew Belousoff (Monash Node), Dr Hamish Brown (UoM/Bio21 Node) and Dr. Joshua Hardy (WEHI Node).



June SPA Workshop, Bio21



There were 10 attendees from Monash University, The University of Melbourne, WEHI and from New Zealand (The University of Canterbury and University of Otago).

The workshop was supported by Thermo Fisher Scientific.

Marialena Georgopoulou Wins Departmental 3MT Competition



ICHDR Marialena Georgopoulou

On May 8th, CCeMMP ICHDR Marialena Georgopoulou won the Department of Biochemistry and Pharmacology, University of Melbourne 3MT competition. This competition helps students sharpen their communication skills by explaining their research in just three minutes to a general audience. It's not about oversimplifying—it's about making the science and its impact on health easy to understand and engaging! In the Department of Biochemistry and Pharmacology competition, the only rule is the time limit: three minutes. This allows students to not only present their research but also showcase their additional skills and passion. Marialena excelled in this format, demonstrating her exceptional ability to create an engaging and entertaining video that effectively communicated the essence of her PhD project in just three minutes.

New members/affiliates

Shubha Udupa, student affiliate; Milad Reyhani, student affiliate

University of Wollongong Node

Assoc. Prof. Gökhan Tolun Node Leader, University of Wollongong

Assoc. Prof. Gökhan Tolun Returns from Sabbaticcal



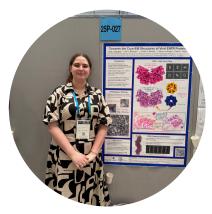
We welcomed back Assoc. Prof. Gökhan Tolun from sabbatical July 15 and thank Prof. Lezanne Ooi for stepping in as diligent Acting Node Leader during his absence. We really appreciate all the effort and work that was put in by Lezanne during this time.

Prof. Lezanne Ooi

Assoc. Prof. Gökhan Tolun

Lucy Fitschen Awarded Poster Prize

At the recent joint congress of the 21st International Union of Pure and Applied Biophysics (IUPAB2024) and the 62nd Biophysics Society of Japan, held in Kyoto, Japan, student affiliate Lucy Fitschen was awarded the Student and Early Career Researcher Poster Award. Lucy was also awarded a congress bursary for travel and registration to attend the meeting (1200 Euros).



Lucy Fitschen, IUPAB2024 Japan

Grants Awarded

Haibo Yu, Aidan Grosas, Nicholas Dixon, "A high-throughput computational pipeline for the development of experimentally testable inhibitors of efflux pumps relevant to antimicrobial resistance", 2024 Molecular Horizons Collaborative Grant, 9 July 2024.

This project aims to computationally discover and experimentally validate inhibitory peptides targeting the RND transporter family efflux pump MexB, which is an essential component of the antimicrobial resistance mechanisms of multi-drug resistant Pseudomonas aeruginosa. Using a high-throughput pipeline that leverages the predictive power and speed of AlphaFold2 with a computational inhibitory scoring method and molecular dynamics simulations to uncover potent and specific peptide inhibitors derived from both the target protein's own sequence and its known protein binding partners. Binding and interaction sites of the predicted peptide inhibitors will then be experimentally verified through fluorescence polarisation assays and cryo-EM. The project expects to generate new knowledge related to efflux inhibitors and antimicrobials, deploying a modern software pipeline to generate experimentally testable outcomes.

WEHI Node

Professor Isabelle Lucet Node Leader, WEHI



Emily Park

Meet ICHDR Emily Park

Welcome to our newest ICHDR, Emily Park. Emily is a PhD candidate supervised by Prof. Isabelle Lucet at the Walter and Eliza Hall Institute of Medical Research Node. Her project aims to understand the structure and function of Ephrin receptor pseudokinases EphA10 and EphB6 by integrating structural biology with advanced imaging technologies, chemical biology, and proteomics approaches. Emily completed her BSc Hons in Biochemistry at the University of Otago, New Zealand, and outside of research enjoys hiking, swimming, and spending time at the beach with a book.

Dr Winnie Tan Promoted to Level B

Congratulations to Dr. Winnie Tan who was promoted to Level B, Senior Research Officer. Using biochemistry, structural biology, molecular biology, epigenetics and cancer biology, Winnie's mission is to understand how protein machinery works at the molecular level to unlock new ways to treat cancer. Her research collaborations extend to TU Berlin, Seoul National University and University of Melbourne tackling the challenging questions of epigenetic proteins.

Winnie is currently a Senior Venture Research Officer where she is involved in a small molecule program targeting a rare genetic disorder at WEHI Ventures.



Dr. Winnie Tan

External Affiliates Update

New Affiliates

The Centre continues to reach out to scientists, both within our existing Nodes 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. If you are interested in becoming a member or affiliate, please reach out to us at ccemmp@monash.edu.

New Affiliate Members

Dr. James Davies, PostDoc (Victor Chang Cardiac Research Institute)

Upcoming Events



Our seminar series continues on the second Tuesday of the month, 10:00 AM - 11:00 AM (AEST); this quarter will see the first of our special seminars with Dr. Basil Greber (Institute of Cancer Research, UK) on October 1st. Over the next quarter, we will hear from Dr. Elizabeth Kellogg (St Jude Children's Research Hospital, Memphis, Tennessee), August 13th; affiliate Prof. Megan O'Mara (The University of Queensland), September 17th, WEHI Node Leader Prof. Isabelle Lucet (Node Leader, WEHI), October 8th.

Missed a seminar? Most are recorded and accessible from our website (<u>https://ccemmp.org/events/ccemmp-seminar-series/</u>) or our you tube channel.

We would also like to thank all members of the seminar committee for the diverse and interesting program they have put together for 2024. With the program for 2024 complete, we farewell ICHDR Alok Pradhan and student affiliate Bindusmita Paul and thank them both for their time on the committee. We welcome ICHDR Marialena Georgopoulou and student affiliate Shubha Udupa as our 2024-2025 representatives. Drs Aidan Grosas and Fabian Bumbak will continue on the committee along with the Chair Dr Sepidah Valimehr and Dr Jackie How/Dr Tracie Pierce. Planning for the 2025 program has already commenced.

CCeMMP Art Exhibition, 13-27 August, 2024



The inaugural ARC CCeMMP Bench to Art Exhibition will soon be on display! CCeMMP will open the virtual art gallery to align with National Science Week 2024 (10-18 August). Creations submitted to the Bench to Art Competition will be exhibited virtually for two weeks, 13th to 27th August, 2024. The link to the virtual gallery will open at 9:00 AM AEST on 13th of August, 2024 and voting for the People's Choice Award will commence (voting closes 27th August). There will be prizes (First prize and People's Choice) and plenty of glory up for grabs! Scan the QR code in the flyer for details.

FB Rice - IP Seminar, 27 August 2024

CCeMMP are pleased to invite members and affiliates to an IP seminar to be presented by our educational partner and IP lawyers, FB Rice. The seminar will be via zoom only 27 August, 10:00 - 11:00 AM (AEST).



Presented by Dr. Brittany Ashton (Senior Associate) and Dr. Declan

McKeveney (Partner) from FB Rice, this seminar will arm researchers with a comprehensive understanding of the various forms of IP protection, particularly as they relate to research and development in the life sciences. With a focus on patents, this seminar will delve into:

- the requirements to obtain a granted patent,
- the patenting process,
- timing academic publications with a patent application filing,
- preparing experimental data to support a patent application,
- a consideration of trade secrets, and
- who is an inventor and who is an owner.

The seminar will conclude with a discussion on the value of patents, and how they can be used to facilitate commercialisation of research and development in the life sciences.

This opportunity is for **CCeMMP members and affiliates only.** Please <u>register</u> (<u>https://ccemmp.org/events/arc-ccemmp-fb-rice-ip-seminar/</u>) by COB Monday 26th August to receive the Zoom link.



FB Rice is a top tier leading Australian Intellectual Property firm. The firm works with a diverse range of domestic and international clients including manufacturers, software companies, universities, hospitals, co-operative research centres and research institutes. FB Rice is the recipient of 15 Australian Client Choice Awards, including being named Best Specialist IP Firm 7 years running, Best Client Experience Firm for Specialist IP since 2021, and Most Innovative Specialist IP & Related Services Firm since 2022.

EduWeek, 9-13 Sept 2024

EduWeek is back for 2024! EduWeek is a series of professional development activities organised by CCeMMP annually for students and CCeMMP members/affiliates.

This year, workshops include:

- How and when to use Bibliometrics Mario Sos & Penny Prasta (Monash Librarians)
- BASH Scripting (Basic to intermediate) Workshop Dr. Matthew Belousoff (Monash Node) & Dr. Joshua Hardy (WEHI Node)
- IP Protection and Commercialisation in the Life Sciences Workshop - Dr. Brittany Ashton (Senior Associate, FB Rice)
- Equity, Diversity and Inclusion in Action: Enhancing Collaboration through Inclusive Teamwork - Dr. Betty Exintaris & Dr. Nil Karunaratne (MOSIAC, MIPS)



- Resume/CV Writing and Interview Training Dr. Matthew Belousoff (Monash Node)
- **Tips and Tricks for Grants and Fellowships Workshop** Monash Research Development Team led by Dr. Amanda Walmsley (Senior Manager, Major Initiatives)
- Essential Elements of a Research Grant Proposal: Hands-on Grant Writing Workshop Dr. Benedicta Rousseau (The GrantED Group)

Important things to note:

- All workshops are hands-on and in-person only.
- Places are limited, please register your attendance as soon as possible (see below). If you can no longer attend, please deregister so that the place may go to someone else.
- Workshops are *only* available to Centre members and affiliates.

Please see the details for each workshop and register your attendance <u>here</u> (https://ccemmp.org/events/arc-ccemmp-eduweek-2024/). Details will be updated as they come. If you have any questions or issues, please contact Dr. Jackie How (jackie.how@monash.edu).

SPA Workshop, Oct 7-8, 2024

Dr. Sepideh Valimehr will be running a two-day introductory workshop on single particle cryoEM data processing using cryoSPARC at the Ian Holmes Imaging Centre, Bio21. The workshop is designed for beginners with no prior experience in cryo-EM. This workshop free but is strictly limited to 10 participants and registration is essential.

For registration and more details, please go to <u>https://rduevents.unimelb.edu.au/event/single-particle-cryoem-data-processing-oct24</u>

CCeMMP Scientific Symposium, 11-12 November, 2024



The committee is in place and planning is underway. Thanks to all on the organising committee for putting your hands up. The committee consists of Dr. Sepideh Valimehr, Dr. Wessel Burger, Dr. Winnie Tan, and ICHDRs Riya Joseph, Xiaomin Wang and Emily Park with support from Dr. Jackie How.

CCeMMP is excited to invite our members and affiliates and the scientific community to an in-person CCeMMP Symposium 11-12th November 2024. This event will be held in Melbourne at Bio21 Molecular Science & Biotechnology Institute, Parkville. Our exciting keynote speakers are **Prof. Renae Ryan** (The University of Sydney, Sydney, Australia) and **Assistant Prof. Oliver Clarke** (Columbia University, New York, USA). Their biosketches and research can be found on our website.

Our generous sponsors include Thermo Fisher Scientific, BioCurate and MiTegen.

Registration and abstract submission details can be found via the QR code on the attached flyer - please follow the link and save the date to your calendars!

Please note, due to the Symposium our November seminar has been rescheduled to Tuesday 19th Nov, Prof Renwick Dobson, The University of Canterbury (NZ).



ARC Centre for Cryo-electron Microscopy of Membrane Proteins Research Symposium 2024

Showcasing research in cryo-EM and membrane proteins International and national keynote speakers Poster and oral prizes Opportunities to build networks and collaborations

11 & 12 NOVEMBER 2024

IN-PERSON ONLY, BIO21 INSTITUTE, PARKVILLE





BioCurate Calls for Applications to Proof-of-Concept Fund 2024

BioCurate Proof-of-Concept (POC) Fund is expanded in 2024 to allow eligible companies as well as academic researchers to apply.

BioCurate is delighted to announce the opening of the POC Fund for 2024. This commercial funding scheme is designed to support early stage therapeutic projects that need further experimental validation to address key scientific gaps, generate additional compelling data to support the opportunity, de-risk projects and propel them to the next value inflection point.

The POC fund is expanded for this year to welcome applications from eligible companies alongside academic researchers. Successful applicants can receive up to \$500K in funding over a period of 12-24 months to expedite therapeutic discoveries. In addition to financial support, recipients will benefit from BioCurate's industry expertise and mentoring, which includes assistance in developing commercialisation and IP strategies, as well as crafting experimental plans to advance the opportunity and mitigate project risks. BioCurate staff will provide support throughout the project to maximise the chances of a successful outcome.

Dr. Kathy Nielsen, CEO of BioCurate Pty Ltd, states, "BioCurate is pleased to announce our new, flexible model for POC project funding. By expanding the scheme to include spin-outs from our shareholder universities and eligible medical research institutes (MRIs), we are adapting to include a greater range of commercialization pathways. We look forward to continuing to fund early-stage therapeutic projects with promising commercial potential, from academic and now, eligible spin-out companies. This provides further support for researchers and founders, leveraging third-party funding, and helping to maximise the chance of a tangible commercial outcome. "

Eligibility for this funding scheme includes researchers from the University of Melbourne, Monash University, or their affiliated Medical Research Institutes as well as companies which are either spinouts from these research organisations, or where the IP underpinning the project originated from them.

Unlike traditional granting schemes, the POC scheme is a source of both funding and drug development support in a flexible arrangement that can lead to a number of commercialisation pathways. Following successful completion of a POC, the project may receive further BioCurate support, through in-licensing or extended POC funding, or alternatively through investment into a spin out.

The application consists of an online component with links to a downloadable Expression of Interest form (separate templates for academic and company applicants).

Submissions are due by 5:00 pm on Friday, 6th September 2024.

Click here to view the online application form and access the EOI templates.

Click here to download the slide deck from 2024 POC info sessions and here for a list of FAQs.

We encourage all qualified researchers and eligible companies to apply and seize this unique opportunity to advance their therapeutic discoveries with BioCurate's support and funding. For more information, please contact the BioCurate POC team at poc@biocurate.com.

Outreach

In the Media

Prof. Chris Langmead - Faculty of Pharmacy and Pharmaceutical Sciences website: May 24, 2024; The Aussies still hoping for better treatments after 75 years <u>https://www.monash.edu/news/articles/the-aussies-still-hoping-for-better-treatments-after-75-years</u>. Write up of an opinion piece published in the Canberra Times.

Social Media

Dr. Winnie Tan - Twitter X on bioRxiv preprint @winn5tan

Prof. Patrick Sexton - 17 July 2024. @NHMRC Twitter/X and instagram pages. Congratulations to the recipient of Peter Doherty Investigator Grant Award in Leadership, @PatrickMSexton1 of @MIPS_Australia, @CCeMMP and @MIPS_DDB for his research on improving our understanding of G protein-coupled receptors. Read more on our website: <u>https://ow.ly/JwK750Sswpj</u>

Dr. Manasi Arcot Anil Kumar, Assoc. Prof. Gokhan Tolun, Dr. Sepideh Valimehr - 24 July 2024. Twitter/X and Linked In: Workshop 4 Cryo electron microscopy, Biomolecular Horizons conference https://twitter.com/bmh2024Melb/status/1815913650433188199 ; https://www.linkedin.com/feed/update/urn:li:activity:7221680818648236036/

Prof. Denise Wootten - 24 July 2024. @NHMRC Twitter/X and instagram pages. Professor Denise Wootten from @MIPS_Australia, @CCeMMP and @MIPS_DDB received the 2023 NHMRC Elizabeth Blackburn Investigator Grant Award for leadership in basic science research. Her research focuses on protein receptors and how they can translate to drug discoveries.

Social Media



Outreach - Training

Centre members continue to present training to Centre members/affiliates and externally, on more than just Cryo-EM.

Peer Review Training Workshop, May 16, 2024: Prof Patrick Sexton.

Mentoring Best Practices Session, 12 June, 2024: Prof Patrick Sexton, Dr. Jackie How.

CCeMMP Rotation 2, 1-12 July, 2024: Dr. Alisa Glukhova (WEHI Node), Dr. James Bouwer (UoW Node), Dr. Matthew Belousoff (Monash Node), Dr. Aidan Grosas (UoW Node), Dr. Sepideh Valimehr (UoM/Bio21 Node).

Single Particle Analysis Workshop, 12-14th June, 2024: Dr. Alisa Glukhova



Sepideh Valimehr (WEHI Node), Dr (UoM/Bio21 Node), Dr Matthew Belousoff (Monash Node), Dr Hamish Brown (UoM/Bio21 Node) and Dr. Joshua Hardy (WEHI Node).

Blender Workshops, June 4 and July 11, 2024: Dr. Sarah Piper (Monash Node) Dr. Joshua Hardy (WEHI Node) and Dr. Sepideh Valimehr (Bio21/UoM Node).



Training

Attendees

- Brooke Hayes CCeMMP 3 Day SPA workshop June 2024 Ian Holmes Centre
- Marialena Georgopoulou Refeyn TwoMP Mass Fluidics system hands-on training
- Dr. Sepideh Valimehr CryoET workshop at Ramaciotti Centre, 27-31 May, 2024

Industry Engagement

Members and student members continue to have their regular meetings with their respective industry partners (Boerhinger Ingelheim, Astex, Servier, AstraZeneca, Dimerix and Pfizer). ICHDRs and their supervisors are also talking with industry partners regarding their 3 month embedded placements.

- Jack Tovey spent 3 months (April-July) with industry partner Astex, Cambridge, UK.
- · Qinghao Ou and Dongju Lee are spending 3 months (May-August) with industry partner Boehringer Ingelheim, Germany.
- Alok Pradhan, 12 months placement (1 day/week) Dimerix, Fiztroy.













Recent Centre Activities and Achievements

Structural Biology Symposium, 5, July 2024

ICPD Dr. Matthew Belousoff and affiliate James Lingford were two of the organisers of the recent Structural Biology Symposium held at Monash University (Clayton). The Monash Structural Biology Symposium is designed to share the current structural biology techniques (including Protein design and Crystallography) available at Monash University, establish new "in-house" collaborations, share



exciting science and discuss future developments.

CCeMMP members and affiliates were in attendance presenting posters and talks.



Prof. Denise Wootten

Prof. Denise Wootten delivered the keynote address, Prof. Trevor Lithgow delivered an invited talk on surveying membrane landscapes for a new look at the bacterial cell surface and Dr. Sarah Piper presented her work on application of data visualization to her structural biology research.

Dr. Sarah Piper

CeMMP was also one of the sponsors of this event.

Conference Presentations

International Meetings

Prof. Arthur Christopoulos: Keynote. Hallmarks of GPCR allostery:structure, function and beyond. 9th European Congress of Pharmacology, EPhar 2024, Athens, Greece 23-26 June, 2024.

Prof. Patrick Sexton: Keynote. Efficacy and biased agonism at the Class B1 glucagon-like peptide-1 (GLP-1) GPCR.n 9th European Congress of Pharmacology, EPhar 2024, Athens, Greece 23-26 June, 2024.

Dr. Alastair Stewart: Invited talk. E. coli ATP synthase after the addition of ATP or ADP. 21st International Union of Pure and Applied Biophysics (IUPAB 2024), 24-28 June 2024, Kyoto, Japan.

Lucy Fitschen: Poster presentation. Towards the Cryo-EM Structures of Viral Annealase Proteins. 21st International Union of Pure and Applied Biophysics (IUPAB 2024 satellite) Eve Fest., 23 June 2024, Kyoto, Japan.

Lucy Fitschen*: Poster presentation. Towards the Cryo-EM Structures of Viral Annealase Proteins" 21st International Union of Pure and Applied Biophysics (IUPAB 2024), 24-28 June 2024, Kyoto, Japan. **IUPAB 2024 Student & Early Career Researcher Poster Award*

Assoc. Prof. Gökhan Tolun: Poster presentation. Cryo-EM structure of Salmonella Bacteriophage P22 annealase ERF reveals mechanistic details of SSA DNA recombination. Viruses of Microbes 2024, 15-19 July 2024, Cairns, Australia.



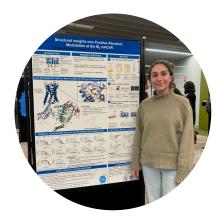
Lucy Fitschen, IUPAB 2024, Kyoto, Japan

National Meetings

Dr. Aidan Grosas: Selected talk. Exploring the polymorphic structural landscape of alpha-synuclein amyloid fibrils using cryo-EM. East Coast Protein Meeting, 17-19 July, 2024, Poal Cove Resort, Coffs Harbour, NSW.

Local Meetings

Prof. Denise Wootten: Keynote speaker. Harnessing CryoEM to probe the structure and function of Class B1 G protein coupled receptors. Structural Biology Symposium, 5 July 2024, Monash University, Clayton, VIC.



Michaela Kaoullas*, Structural Biology Symposium

Dr. Natalie Diepenhorst: Invited talk. CXCR3 antagonists to treat autoimmune disorders. DDB Scientific Symposium, 18 July 2024, Monash University, Parkville, VIC.

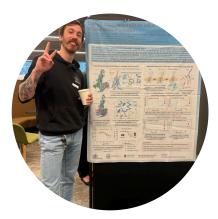
Dr. Aidan Grosas: Invited talk. The structural elucidation of amyloid fibrils in health and disease using cryo-EM. 27 June 2024, Molecular Horizons Symposium, Wollongong, NSW.

Prof. Trevor Lithgow: Invited talk. Surveying membrane landscapes for a new look at the bacterial cell surface. Structural Biology Symposium, 5 July 2024, Monash University, Clayton, VIC.

Dr. Jesse Mobbs*: Invited talk. Structural investigation of allosteric modulation of the delta opioid receptor. DDB Scientific Symposium, 18 July 2024, Monash University, Parkville, VIC. *Best ECR presentation.

Prof. Denise Wootten*: Invited talk. Biased GLP-1 agonism at the GLP-1 receptor, from structure to animal models of disease. DDB Scientific Symposium, 18 July 2024, Monash University, Parkville, VIC. *People's choice award

Dr. Xin (Cindy) Zhang: Invited talk. Structural insights into allosteric modulation of a class B GPCR. DDB Scientific Symposium, 18 July 2024, Monash University, Parkville, VIC.



Theo Nettleton, Structural Biology Symposium

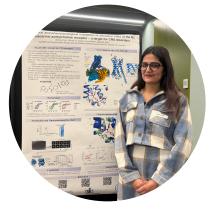
Dr. Sarah Piper: Oral presentation. Seeing is believing: using structural biology data to visualise Class B1 GPCR motions in 3D animations. Structural Biology Symposium, 5 July 2024, Monash University, Clayton, VIC.

Marialena Georgopoulou^{*}: 3MT. Department of Biochemistry and Pharmacology (DBP), University of Melbourne, 08/05/2024, Bio21 Institute, Parkville, VIC. * *winner of 3MT competition*

Riya Joseph: 3MT. Department of Biochemistry and Pharmacology (DBP), University of Melbourne, 08/05/2024, Bio21 Institute, Parkville, VIC.

Michaela Kaoullas*: Poster presentation. Structural insights into positive allosteric modulation at the M4 mAChR. Structural Biology Symposium, 5 July 2024, Monash University, Clayton VIC. * *winner poster prize*

Michaela Kaoullas: Poster presentation. Structural insights into positive allosteric modulation at the M4 mAChR. Melbourne Protein Group Student Symposium, 11 July 2024, WEHI, Parkville, VIC.



ICHDR Bkavika Rana, Structural Biology Symposium

Theo Nettleton: Poster presentation. Cryo-EM structures and HDX-MS data of PAC1R splice isoforms in different states of activation. Structural Biology Symposium, 5 July 2024, Monash University, Clayton, VIC.

Bhavika Rana: Poster presentation. Structural and pharmacological validation of allosteric sites at the M5 Muscarinic acetylcholine receptor – a target for CNS disorders. Structural Biology Symposium, 5 July 2024, Monash University, Clayton, VIC.

Bhavika Rana: Poster presentation. Structural and pharmacological validation of allosteric sites at the M5 Muscarinic acetylcholine receptor – a target for CNS disorders. Melbourne Protein Group Student Symposium, 11 July 2024, WEHI, Parkville, VIC.

Academic Seminars

Dr. Tracy Putoczki: "Untangling the complex conversations in the tumour microenvironment." Monash BDI Seminar, 18 June 2024.

Ada Quinn: "The regulatory handshake between membrane lipids and neurotransmitter transporters: Computational studies towards novel analgesics". UQ QBI Early Career Research Seminar Series, 17 May 2024.

Ada Quinn: "The regulatory handshake between membrane lipids and neurotransmitter transporters: Computational studies towards novel analgesics." UQ Centre for Theoretical and Computational Molecular Science Seminar Series, 21 June 2024.

Dr. Winnie Tan: "MORC2 phosphorylation fine tunes its DNA compaction activity". Department of Biochemistry and Pharmacology Research Fellows Seminar, bio21, 23 June 2024.

Academic Presentations

International

Assoc. Prof. Karen Gregory: "Enhancing translatability of preclinical drug discovery models for dementia and associated neuropsychiatric symptoms". PharmAlliance Week (June 16-20, 2024) presentation at UNC Chapel Hill, North Carolina, USA - Progress report from PARCDT team (Gregory & Ali, UCL)

Prof. Peter Czabotar: Identifying molecular targets to manipulate apoptosis through BAK and VDAC2. International Cell Death Seminar (online), 5 June 2024.

Publications New Publications

Abrahamsen HL, Sanford TC, Collamore CE, **Johnstone BA**, Coyne MJ, García-Bayona L, **Christie MP**, Evans JC, Farrand AJ, Flores K, Morton CJ, **Parker MW**, Comstock LE, Tweten RK. Distant relatives of a eukaryotic cell-specific toxin family evolved a complement-like mechanism to kill bacteria. Nat Commun, 15: 5028 (2024). https://doi.org/10.1038/s41467-024-49103-5

Harikumar KG, **Piper SJ, Christopoulos A, Wootten D, Sexton PM**, Miller LJ. Impact of secretin receptor homo-dimerization on natural ligand binding. Nat Commun, 15: 4390 (2024). https://doi.org/10.1038/s41467-024-48853-6

Harikumar KG, **Zhao P, Cary BP**, Xu X, Desai AJ, Dong M, **Mobbs JI**, Toufaily C, Furness SGB, **Christopoulos A, Belousoff MJ, Wootten D, Sexton PM**, Miller LJ. Cholesterol-dependent dynamic changes in the conformation of the type 1 cholecystokinin receptor affect ligand binding and G protein coupling. PLoS Biol, 22(7): e3002673 (2024). doi: 10.1371/journal.pbio.3002673

Hills FR, Eruera A-R, Hodgkinson-Bean J, Jorge F, Easingwood R, **Brown SHJ, Bouwer JC**, Li Y-P, Burga LN, Bostina M. Variation in structural motifs within SARS-related coronavirus spike proteins. PLoS Pathogens Published May 28, 2024. https://doi.org/10.1371/journal.ppat.1012158

Keov P, Christopoulos G, Hick CA, Glendorf T, Ballarín-González B, **Wootten D**, **Sexton PM**. Development of a novel assay for direct assessment of selective amylin receptor activation reveals novel differences in behaviour of selective and non-selective peptide agonists. Mol Pharmacol, 105(5): 359-373 (2024), *with industry partner Novo Nordisk*. DOI: https://doi.org/10.1124/molpharm.123.000865

Liu B, Thompson G, Manuela J Barnes N, **Thal D, Christopoulos A**, Capuano B, **Valant C**, Scammells P. Discovery of 2-methyl-5-(1H-pyrazol-4-yl)pyridines and related heterocycles as promising M4 mAChR positive allosteric modulators for the treatment of neurocognitive disorders. J Med Chem (accepted).

Miller MS, Cowan AD, Brouwer JM, Smyth ST, Peng L, Wardak AZ, Uren RT, Luo C, Roy MJ, Shah S, Tan Z, Reid GE, Colman PM, **Czabotar PE**. Sequence differences between BAX and BAK core domains manifest as differences in their interactions with lipids. FEBS Journal, 291(11): 2335–2353 (2024). doi: 10.1111/febs.17031. *Editor's Choice; Research Highlights* <u>https://doi.org/10.1111/febs.17162</u>; Cover illustration.

Payne CM, Baltos J-A, Langiu M, Lu CS, Tyndall JDA, **Gregory KJ**, May LT, Vernall AJ. Development of putative bivalent dicovalent ligands for the adenosine A1 receptor. ChemBioChem, 28 May 2024. <u>https://doi.org/10.1002/cbic.202400242</u>



Shajan B, Marri S, Bastiampillai T, **Gregory KJ**, Hellyer SD, Nair PC. Trace amine associated receptor 1: predicted effects of single nucleotide variants on structure-function in geographically diverse populations. Human Genomics, 18(1): 61 (2024). doi: 10.1186/s40246-024-00620-w **Tan W**, Park JV, Venugopal H, Lou JQ, Dias PS, Baldoni PL, Dite T, Moon K-W, Keenan CR, Gurzau AD, Leis A, Yousef J, Vaibhav V, Dagley LF, Ang C-S, Corso L, Davidovich C, Vervoort SJ, Smyth GS, Blewitt ME, Allan RS, Hinde H, D'Arcy S, Ryu J-K, **Shakeel S.** MORC2 phosphorylation fine tunes its DNA compaction activity. bioRxiv 28 June 2024. doi: https://doi.org/10.1101/2024.06.27.600912

Tomašević N, Emser FS, Muratspahić E, Gattringer J, Hasinger S, Hellinger R, **Keov P**, Felkl M, Gertsch J, Becker CFW, Gruber CW. Discovery and development of macrocyclic peptide modulators of the cannabinoid 2 receptor. J Biol Chem, 300(6):107330 (2024). DOI: https://doi.org/10.1016/j.jbc.2024.107330

Yuliante E, Trinh PNH, Hick C, Ebenhoch R, Nar H, Weichert D, **Christopoulos, A, Sexton PM**, **Wootten D**. Isoquinoline small molecule ligands are agonists and probe-dependent allosteric modulators of the glucagon subfamily of GPCRs. Biochem Pharmacol (in press) [Preprint SSRN Elsevier (22 May 2024)] with industry partner Boehringer Ingelheim. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4831303.

Updated Publications

Baltos J-A, Casillas-Espinosa PM, Rollo B, **Gregory KJ**, White, PJ, **Christopoulos A**, Kwan P, O'Brien TJ, May LT. The role of the adenosine system in epilepsy and its comorbidities. Br J Pharmacol, 181(14): 2143-2157 (2024). doi: 10.1111/bph.16094

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

Jiang Y, Yeasmin M, Gondin AB, **Christopoulos A, Valant C, Burger WAC, Thal DM**. Importance of receptor expression in the classification of novel ligands at the M2 muscarinic acetylcholine receptor. Br J Pharmacol, 181(14): 2338-2350 (2024). https://doi.org/10.1111/bph.16021

Lu Y, Hatzipantelis CJ, Langmead CJ, Stewart GD. Molecular insights into orphan G protein-coupled receptors relevant to schizophrenia. Br J Pharmacol, 181(14): 2095-2113 (2024). doi: 10.1111/bph.16221

McNeill SM, Lu J, Marion C Carino C, Inoue A, Zhao P, Sexton PM, Wootten D. The role of G protein-coupled receptor kinases in GLP-1R β -arrestin recruitment and internalisation. Biochem Pharmacol, 222:116119 (2024). doi: 10.1016/j.bcp.2024.11611

McNeill SM, **Zhao P.** The roles of RGS proteins in cardiometabolic disease. Br J Pharmacol, 181(14): 2319-2337 (2024). doi: 10.1111/bph.16076.

Nguyen HTM, Valant C, van der Westhuizen ET, Langmead CJ, Tobin AB, Sexton PM, Christopoulos A. Opportunities and challenges for the development of M1 muscarinic receptor positive allosteric modulators in the treatment for neurocognitive deficits. Br J Pharmacol, 181(14): 2114-2142 (2024). https://doi.org/10.1111/bph.15982

Released Structures

Matthew Belousoff, Brian Cary, Arthur Christopoulos, Jesse Mobbs, Sebastian Furness, Patrick Sexton, Denise Wootten, Elva Zhao; PLoS Biol, 22(7):e3002673 (2024). doi: 10.1371/journal.pbio.3002673.

- PDB:9BKJ, EMD-44642 (CCK1R (Y140A mutant)-Gq chimera complex)
- PDB:9BKK, EMD-44643 (CCK1R (sterol 7M mutant)-Gq chimera complex)

Bronte Johnstone, Michelle Christie, Michael Parker; Nat Commun 15: 5028 (2024). https://doi.org/10.1038/s41467-024-49103-5

• PDB: 8G32, Pro-form of a CDCL short from E. anophelis (X-ray crystallography)

CCeMMP Cryo-EM Structure Image Gallery

