| Who | Activity | 2022 Dates | Requirements | |
|----------------|-----------------------------------------|----------------------------------|-------------------------------------------------------------------------------------------------------------------|--|
| Cohort 1 | Node inductions | First 1-2 weeks of commencing | veeks Complete all required Node-specific inductions and relate activities. | |
| Cohort 1 | Centre induction | May 2022 | Attendance | |
| Cohort 1 | Rotation 1: Biochemistry | From 2nd May (6-8 weeks) | Student are required to complete all pre- and post-tasks, read activities provided at the Node for this rotation. | |
| 2021 Cohorts | Unit 3: The process of drug discovery | 23rd May - 10th June | This workshop runs for 3 weeks. Attendance is mandatory 2nd year PhD students. | |
| All students | Annual professional development retreat | 20th - 24th June | All students are requires to particpate in the professional de opment activities and masterclass workshops. | |
| Cohort 2 | Node inductions | First 1-2 weeks of commencing | Complete all required Node-specific inductions and related activities. | |
| Cohort 1 and 2 | Rotation 2: Cryo-EM Training | 8th August - 2nd September | Complete this rotation and all required assessments, pre-apost-tasks and activities. | |
| Cohort 1 and 2 | Rotation 3: Process- ing & analysis | 5th September - 7th October | Complete this rotation and all required assessments, pre- post-tasks and activities. | |
| All students | Research symposium | ТВА | Complete this rotation and all required assessments, pre- | |
| Cohort 2 | Rotation 1: Biochemistry | From 17th October (6-8 weeks) | Student are required to complete all pre- and post-tasks, read activities provided at the Node for this rotation. | |

Please note that due to unforeseen circumstances (i.e. Covid restrictions), these dates are subject to change.

Cohort 1 refers to students who commenced in before June 2022 Cohort 2 refers to students who commenced from June 2022









Drug Discovery

Doctoral Program Handbook April 2022

Cemp ARC Training Centre for Cryo-Electron Microscopy of Membrane Proteins for

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Welcome to the Centre!

Welcome to the Australian Research Council Centre for Industrial Transformative Training Centre for Cryo-Electron Microscopy of Membrane Proteins in Drug Discovery (CCeMMP)! The CCEMMP aims to train industry-ready, world class graduates in cryo-electron microscopy of membrane proteins. The Centre's graduates and research results will enable tomorrow's industrial expansion in structure-enhanced drug design. Expected outcomes are world-first structural biology knowledge and techniques, and the entrepreneurial and technical skills desired by industry. The Centre aims to provide significant benefits including advancing Australian biotechnological capacity and improved linkages with major pharmaceutical partners. It also aims to provide a substantive competitive advantage to nascent Australian biotechnology companies that also links into new National investment into drug discovery and development infrastructure. The world leaders in this field will be providing students with skills and training that will ensure that they are industry ready.

The CCeMMP Doctoral Handbook will provide students with information and requirements specific to the CCeMMP Doctoral Program. Students will receive Node booklets and handbooks from their respective Nodes, and these should be read as a general resource in conjunction with the Centre Handbook. The CCeMMP Doctoral Handbook will take precedence.



Centre vision

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



Centre team

This Centre is a joint collaboration between Monash University, The University of Melbourne (UoM), University of Wollongong (UoW) and the Walter and Eliza Hall Institute (WEHI). The investigators are Australia's academic leaders in the biochemistry and structure of pharmaceutically important membrane proteins. The team will work together with our industry and educational partners to train the next cohort of industry-ready, world-class graduates with tailored skills for the pharmaceutical sector.

Senior leadership team

Centre Director Centre Deputy Director Monash Node Leader WEHI Node Leader UoM Node Leader UoW Node Leader Centre Manager Professor Patrick Sexton Associate Professor Isabelle Rouiller Associate Professor Denise Wootten Associate Professor Isabelle Lucet Associate Professor Isabelle Rouiller Professor Antoine van Oijen Dr Jackie How









MOLECULAR HORIZONS



UNIVERSITY OF WOLLONGONG AUSTRALIA

Partners

Industry partners

- Astex Pharmaceuticals
- AstraZeneca
- Boehringer Ingelheim
- Catalyst Therapeutics
- Dimerix Bioscience
- Genentech
- Novo Nordisk
- Pfizer
- Sanofi Aventis
- Servier
- Thermo Fisher Scientific

Educational partners

- BioCurate
- Clarivate Analytics
- FB Rice
- MASSIVE
- LabArchives



Professor Patrick Sexton, Director, patrick.sexton@monash.edu Associate Professor Isabelle Rouiller, Deputy Director and UoM Node Leader, isabelle.rouiller@unimelb.edu.au Associate Professor Isabelle Lucet, WEHI Node Leader, lucet.i@wehi.edu.au Associate Professor Denise Wootten, Monash Node Leader, denise.wootten@monash.edu Professor Antoine van Oijen, UoW Node Leader, vanoijen@uow.edu.au Professor David Adams, Member (UoW), djadams@uow.edu.au Professor Peter Czabotar, Member (WEHI), czabotar@wehi.edu.au Professor Michael Parker, Member (UoM), mwp@unimelb.edu.au Dr Michael Griffin, Member (UoM), mgriffin@unimelb.edu.au Professor Michael Parker, Member (UoM), mwp@unimelb.edu.au

Centre ICPDs (postdocs)

Dr Matthew Belousoff, Member (Monash), matthew.belousoff@monash.edu Dr Sepideh Valimehr, Member (UoM), s.valimehr@unimelb.edu.au Dr Aidan Grosas, Member (UoW), agrosas@uow.edu.au

Facility managers Dr James Bouwer, Member (UoM), jbouwer@uow.edu.au Professor Eric Hanssen, Member (UoM), ehanssen@unimelb.edu.au



Monash University Node

The Monash Parkville Node is located at the Monash Institute of Pharmaceutical Sciences (MIPS), which is also the administrative headquarters for the Centre. MIPS is the research arm of the Faculty of Pharmacy and Pharmaceutical Sciences, Australia's leading Pharmacy and Pharmaceutical Sciences Program and among the top 3 Institutions in the world for Pharmacy and Pharmacology. MIPS uniquely integrates all aspects of the preclinical drug discovery research pipeline, from target discovery and validation, to medicinal chemistry, drug candidate optimisation and the formulation of drugs for delivery. MIPS houses international leaders in the application of cryo-EM to membrane proteins, with a particular focus on understanding the structure and dynamics of G protein-coupled receptors (GPCRs), the largest family of cell surface receptors and a major target class for therapeutic drug development. There are over 800 GPCRs in the human genome including hundreds of receptors of potential therapeutic interest. MIPS researchers have extensive links to both cryo-EM technology leaders and the pharmaceutical industry.





The University of Melbourne Node

The University of Melbourne Node of the CCeMMP is located in the Bio21 Molecular Science and Biotechnology Institute (Bio21). Bio21 is one of Australia's largest biotechnology research centres, housing state-ofthe-art equipment, scientists, students, university departments and industry groups. Bio21 has international leaders in the characterization of membrane proteins including their structure determination by the complimentary methods of X-ray crystallography and electron microscopy. Members of Bio21, and their collaborators, have world-class facilities to express, purify and optimise samples for cryo-EM including a diverse range of membrane protein targets such as ion channels, bacterial transporters, viral glycoproteins, pore forming toxins and cell signaling receptors.

Bio21 researchers are able to discover and develop small molecules and biologic (eg. antibodies) drugs and study their interaction with key membrane proteins including determination of protein-drug complex structures using cryo-EM.







University of Wollongong Node

Molecular Horizons is a new molecular life sciences institute at the University of Wollongong. As a home to the Wollongong Node of the CCeMMP, it houses world-class research in structural biology, molecular biophysics, and cell biology. The facility support team consists of researchers with experience in the entire cryo-EM workflow, from sample preparation to computational analysis.

The CCeMMP research at Molecular Horizons, in collaboration with the adjacent Illawarra Health and Medical Research Institute (IHMRI), focuses on the structural study of a number of channels involved in pain regulation and understanding the relationship between structural information to functional behaviour.







The Walter & Eliza Hall Institute Node

The Walter and Eliza Hall Institute (WEHI) Node of the CCeMMP houses international leaders in the application of Structural Biology to understand the structure and dynamic of key membrane-bound signalling receptors that control essential signalling transduction pathways involved in cell development, fate determination, and polarity. Their dysregulation underlies the cause of many human cancers, classifying them as a major target class for therapeutic drug development.

This program of research at WEHI focuses on using cryo-EM to explore the druggability of target receptor membrane proteins.







Centre Organisational Chart





Executive Committee

The Executive Committee (ExeC) is a senior advisory body that supports the Centre Director and the Centre to achieve its purpose. The ExeC is comprised of the Centre Director, Centre Deputy Director, Centre Manager, and all the Node Leaders from Monash, University of Melbourne, University of Wollongong and WEHI. The purpose of the ExeC is to provide support and strategic advice to the Centre Director to support the day-to-day operations of the Centre through policy development, risk management, and the review, and monitoring of progress and performance of the CCEMMP.

Graduate Research Committee

The Graduate Research Committee is responsible for creating and delivering coursework, monitoring student progress and assisting in graduate research related matters. The committee comprises of the Centre Deputy Director, Centre Manager, Node Leaders and Expert Members in the key training areas. This committee reports to the ExeC.



Partner Engagement Committee

The Partner Engagement Committee provides support to the Centre through the identification and management of partnerships with stakeholders, in particular with Industry and Biotechnology companies. The committee comprises of the Centre Director, Centre Manager, a Centre Member and business development managers from each Node.

Science and Industry Advisory Committee

The Science and Industry Advisory committee (SIAC) reviews and provides advice on the strategic direction and performance of the CCEMMP and provides support to the Centre to achieve its purpose. The SIAC is comprised of experts that support the function of the Centre across all of its activities including engagement with and advancement of the biotechnology and pharmaceutical industry, innovation in membrane protein cryo-EM, graduate education, and drug discovery and development. The SIAC reports to the Centre Director and ExeC.



Inductions

During the first 1-2 weeks of the Centre Doctoral Program, all students in the cohort will be expected to complete the necessary Node and Centre induction activities. These inductions are designed to ensure that students have completed the general and laboratory specific training for work within their Nodes, including Institutional Occupational Health and Safety and specific laboratory operation and safety requirements to undertake their graduate studies within the Node and Centre.

Important notes

- Please be sure to check with your supervisor in the first instance, to ensure you undertake the necessary Node induction required of you.
- Please note there will be some Node-specific inductions that will not run during this period. You will need to consult your Node-specific information booklet for timing of these inductions.





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Doctoral program coursework

The Centre provides advanced training in all aspects of membrane protein cryo-EM, including sample biochemistry, vitrification, 3D image reconstruction, extraction of protein dynamics, and independent operation of 120kV, 200kV and 300kV instruments that are used for high-resolution structure determination. Training will run across 3 modules.

Upon successful completion of the rotations, the student will be given a document that certifies that they have successfully completed all rotations and achieved the learning objectives of coursework. Students should attach this document to their 6-month milestone report (see below).



Centre coursework

Rotation I: Biochemistry 6-8 weeks

Coordinators: Isabelle Rouiller (Bio21), Isabelle Lucet (WEHI), Aidan Grosas (UoW), Denise Wootten (Monash).

This module will focus on the protein biochemistry of membrane proteins, including expression, solubilisation and purification of stabile protein complexes and their reconstitution in detergent micelles or nanodiscs.

Students will:

- Be taught the theoretical basis of expression construct design and basic practical skills for protein characterisation, and;
- Characterise particle behaviour in negative stain TEM, and cryo-EM in vitrified ice using the 200kV instruments.

Students will focus primarily on samples within their expertise group (supervisors and laboratory), however samples of different classes of membrane proteins will be prepared by Centre staff so that students are exposed to different particle behaviours.



Rotation 2: Cryo-EM training and imaging 4 weeks

Coordinators: Matthew Belousoff, Sepideh Valimehr, Eric Hanssen and James Bouwer

The students will focus on cryo-EM imaging of exemplar membrane proteins using the 200 kV and 300 kV instruments.

Students will:

- Evaluate particle behaviour in vitreous ice, including tomographic imaging to understand particle distribution;
- Learn to identify optimal areas of ice for data collection and how to image, including beam alignment, and correction, and;
- Be introduced to collection of tilt data for 3D reconstruction of particles with limited angular distribution. Students will be trained in the latest acquisition software and imaging methods.



Rotation 3: Data processing and analysis 4 weeks

Coordinators: Matthew Belousoff and James Bouwer

This module will focus on the principles and practice of cryo-EM data processing, modelling and analysis.

Students will:

- Cover different software packages for motion and contrast transfer function correction, 2D and 3D classification and the use of filters and masks to enhance particle alignment, selection and calculation of maps, as well as different methods for post processing sharpening of maps, and;
- Progress from idealised data sets of proteins with high symmetry to data sets of high complexity.



Centre coursework

The process of drug discovery Unit

Coordinators: TBA

Drug discovery scientists in academia and industry must appreciate how different facets of discovery science are integrated into the discovery pipeline. Unit 3 will provide an in-depth understanding of the different stages of the drug discovery process, including target validation, drug screening methods, computational modelling, drug design and physicochemical optimisation, preclinical development, clinical development, and pharmacoepidemiology. The unit will conclude with candidates designing their own drug discovery program.

This unit is Unit 3 from Drug Discovery Biology Theme at the Monash Node.



Professional development and transferrable skills

In addition to the training in the theory and practice of cryo-EM, graduate research students will also complete training sessions on the Drug Discovery and Development process, and in entrepreneurship, innovation and commercialisation to provide the requisite understanding to engage with industry partners on drug discovery. Students will be provided with more information regarding these training sessions throughout their candidature. During years 2 – 4, CCEMMP trainees will undertake target specific research projects aligned to the research interests of the host institutions and the commercial interests of industry partners.

The Centre will also run annual retreats, where students will be provided professional development and training. More information regarding the retreat and other training sessions will be provided to the student during candidature.



| Cohort 1 start - April 2022 | | Cohort 2 | Cohort 2 start - August 2022 | | | | |
|-----------------------------|-----------------------------------------------|----------------------|-------------------------------------------------------------|-----------------------------------------------------|-----------------------------------------------|--|--|
| 1.5 weeks | 6-8 weeks | 1 we | eek 4 weeks | 5 weeks | 6-8 weeks | | |
| Cohort 1 Inductions | Cohort 1 Rotation 1 Biochemistry | Coho Induc | ort 2 Cohort 1 & 2 ctions Rotation 2 Cryo-EM training | Cohort 1 & 2 Rotation 3 Processing & Analysis | Cohort 2 Rotation 1 Biochemistry | | |



Milestones

The students will complete the 3 rotations and commence their PhD project within the first 6 months.

Students should consult with their supervisory team to ensure that they have a clear understanding of what is required of them ahead of time (recommended 6 weeks prior to submitting documentation for the milestone meeting).



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6 month panel/pre-confirmation meeting

Prior to the meeting

Students are required to submit:

- A written report (approx. 3000-4000 words) that outlines the background to the project and a detailed research proposal for the PhD project. A detailed timeline should also be included. This should include any progress on the project (if any); skills acquired during rotations should also be outlined.
- Documentation that demonstrates satisfactory completion of all coursework and rotations.

At the meeting

- Present a 20-30 minute oral presentation that summarises the research project background, hypothesis and aims together with key data generated.
- Participate in the panel discussion/questions regarding the research project and the student's background knowledge of the project area.



12 month confirmation meeting

Prior to the meeting

Students are required to submit:

- A thesis standard literature review that should be a minimum of 40 pages (double spaced, Times New Roman, font pt 12) on their research area. This should form the basis of their thesis introduction that can be updated each year.
- A written report (approx. 4000 words) on the progress of their project (and any updates/changes to the project proposal) and timelines.

At the meeting

- Present a 20-30 minute oral presentation that summarises the research project background, hypothesis and aims together with key data generated.
- Participate in the panel discussion/questions regarding the research project and the student's background knowledge of the project area.



24 month panel meeting

Prior to the meeting

Students are required to submit (Monash Node requirement):

- One of the following:
 - A published paper
 - A submitted manuscript
 - A draft thesis chapter containing students results
- A progress report (approx. 4000 words) that details the progress since last panel meeting and updated timelines. Students must request that the supervisor(s) certify that the thesis introduction (literature review completed and submitted as part of the 12 month milestone) has been updated with the most recent literature and has accommodated any new background information as required for any changes to project direction. A line confirming this should be included at the beginning of this report.

At the meeting

- Present a 20-30 minute oral presentation that summarises the research project background, and progress
- Participate in the panel discussion/questions.



36 month panel meeting

Prior to the meeting

Students are required to submit:

• A progress report approx. 4000 words detailing the progress since last panel meeting.

At the meeting

- Present a 20-30 minute oral presentation that summarises the research project background, and key data/progress to date.
- Participate in the panel discussion/questions.



42 month panel meeting (as required)

The purpose of this milestone is to ensure students are on track for submission at 48 months. If the student, supervisor and panel do not think that this meeting is required, it may be skipped.

At the meeting

- Present a short oral presentation with progress update.
- Participate in the panel discussion/questions.



Pre-submission seminar

Monash and UoW Nodes: 1 to 2 months prior to planned submission UoM and WEHI Nodes: No earlier than 6 months prior to thesis submission

Students are required to:

- Present a 45 min Oral presentation to Node/Centre (and any relevant departments) followed by questions from the audience.
- Participate in a short panel meeting to assure everything is in place for timely thesis submission.

Important notes

- Interim meetings with the full student advisory panel can be held in between the formal milestone meetings if deemed necessary by the panel.
- Monash Node students all panel oral presentations need to be open to the Drug Discovery Biology Theme to attend (but the remainder of the meeting is a closed panel).



Industry placement

Students are required to complete a 12 month placement with one of our industry partners. This placement will normally take place in either Year 2 or 3. The timing of the placement may be delayed to Year 4 under certain circumstances. More information will be provided after the coursework component has been completed.





CCeMMP seminar series

The CCeMMP Seminar Series Subcommittee organise and run a monthly research seminar series for interested researchers, research staff, students and enthusiasts. The seminars are based mainly around cryo-electron microscopy of/and membrane proteins with a mixture of domestic and international speakers in this field. Speakers will be announced monthly with a calendar invitation with speaker and virtual conferencing details.

The seminar will be held at 10:00-11:00am AEDT/AEST on every second Tuesday of each month. At least twice a year, there will be special seminars organised outside of the normal timeslot.

Mandatory attendance for students

It is a mandatory requirement for Centre students to attend all the seminars. If students are unable to attend due to personal reasons, unforeseen circumstances or annual leave, please let the Centre Manager know. Experiments should be planned around the seminar series and should not overlap with the seminar.



Data management

LabArchives

Electronic Laboratory Notebook

Students are required to document all research and coursework using the electronic laboratory notebook, LabArchives. Access to LabArchives and training will be provided to students during induction. Students will access, complete and submit all coursework assessments, pre- and post tasks and activities using their coursework LabArchives Notebook.

For Centre and general questions related to LabArchives, please contact Jackie How (jackie.how@monash.edu). For technical difficulties, please contact LabArchives Support (support@labarchives.com).



MASSIVE

Multi-modal Australian ScienceS Imaging and Visualisation Environment The Multi-modal Australian ScienceS Imaging and Visualisation Environment (MASSIVE) is Australia's specialised high performance computing facility for imaging and visualisation. MASSIVE provides hardware, software and expertise to drive research in biomedical sciences, materials research, engineering and geosciences. Students will have access to computing resources and tools through MASSIVE to capture and analyse large data sets.

