



Centre for Cryo-electron  
Microscopy of Membrane Proteins

## SEMINAR SERIES 2022

### **Dr. David Thal**

*Drug Discovery Biology*

*Monash Institute of Pharmaceutical Sciences*

*Monash University*

David Thal is an NHMRC EL2 Investigator Fellow and co-leader of the Analytical & Structural Neuropharmacology group in the Drug Discovery Biology Theme at the Monash Institute of Pharmaceutical Sciences (MIPS). Dr Thal received a PhD in Chemical Biology (2010) from the University of Michigan, where he received training in structural biology from the lab of John Tesmer. In 2011, he moved to Australia to begin his post-doctoral research under Arthur Christopoulos and Patrick Sexton at MIPS, which included a year-long training sabbatical in the lab of Brian Kobilka at Stanford University. After completing an ARC DECRA fellowship in 2019, he established a research group within MIPS that focuses on determining the molecular structure and function of proteins with a particular emphasis on understanding novel paradigms of drug action and drug design on targets that are of therapeutic relevance.



### **The Ups and Downs of Structure-Based Drug Discovery**

Cryo-EM has revolutionised the determination of protein structures and holds great promise for structure-based drug discovery. I will present recent structural studies from our group utilising cryo-EM to determine the structures of therapeutically relevant protein targets in complex with novel chemical ligands. This will include examples from different types of proteins, including G protein-coupled receptors (GPCRs), ion channels, and soluble enzymes. Specific examples will include cases where the cryo-EM structures revealed ligands in expected binding sites, ligands in unexpected binding sites, unexpected ligands in expected binding sites, no ligand at any site, and examples in between. I will also discuss validating these ligand binding sites and current limitations.