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SEMINAR SERIES 2025

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Dr. Sarah Piper

ARC DECRA Fellow
Monash Institute of Pharmaceutical Sciences, Monash University , Parkville.

Sarah obtained her PhD at the University of Queensland, Australia, focusing on protein biochemistry and cryo-electron microscopy of pore-forming, bacterial toxin complexes.

Since 2019, Sarah has been working on GPCR structures and dynamics at the Monash Institute of Pharmaceutical Sciences (MIPS) in the lab of Prof. Patrick Sexton and Prof. Denise Wootten.

In 2024, she received an early-career ARC DECRA fellowship to pursue her research on understanding the structure, dynamics and function of the PAC1 receptor. Sarah is also passionate about science visualisations to communicate biological processes to broad audiences.

Structures, dynamics and function of PAC1 receptor variants: staying 'in the loop'.

Class B1 peptide hormone G protein-coupled receptors (GPCRs) have a broad range of regulatory metabolic effects and are therefore important drug targets. The PAC1R, a Class B1 GPCR, is a potential drug target for the treatment of migraine and other central nervous system (CNS) disorders yet remains underutilized as a target.

More interestingly, PAC1R exists as multiple splice variants, including PAC1nR ('null' variant) and PAC1sR ('short' variant, missing 21 amino acids), which can be activated by endogenous peptide agonists VIP and PACAP. VIP signaling and regulatory functions are globally enhanced at PAC1sR relative to PAC1nR, yet the pharmacology of other PAC1R agonists is similar between these two splice variants. Using cryo-EM structures, MD simulations and mutagenesis, we propose mechanisms for the altered VIP-mediated signaling by distinct interactions in these receptor variants.

Furthermore, we load our structural data into Blender, an open-source 3D computer graphics software, to develop 3D animations based on our experimental data, and tell visual stories about how these receptor variants work.