



SEMINAR SERIES 2025

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Dr. Brian Cary

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Brian Cary is an ARC DECRA fellow in the Drug Discovery Biology theme of the Monash Institute of Pharmaceutical Sciences. He obtained a Bachelor of Science from the University of Michigan (2015) working with Peter J.H. Scott to generate radiolabeled small molecules for molecular imaging. He earned a PhD from the University of Wisconsin-Madison (2021), with research under Samuel H. Gellman focusing on polypeptides. In 2021, he joined the group of Patrick M. Sexton and Denise Wootten at Monash University. As a member of the ARC Centre for Cryo-Electron Microscopy of Membrane Proteins, Dr. Cary's research focuses on the structure and function of G protein-coupled receptors.



Prolonged signaling of backbone-modified glucagon-like peptide-1 analogues with diverse receptor trafficking

The glucagon-like peptide-1 (GLP-1) receptor (GLP-1R) is the target of blockbuster anti-obesity drugs, including peptides such as semaglutide and tirzepatide. GLP-1R has a complex signaling profile, and the effects of modulating this profile are not completely understood. Therefore, tools to dissect the receptor's activities are desirable. Here, we report a pair of synthetic peptide agonists, both with sustained signaling capacities compared to GLP-1. Surprisingly, these two close analogues showed markedly distinct abilities to induce intracellular receptor trafficking. Structure-activity relationship studies, cryo-EM analysis, and molecular dynamics simulations shed light on the behavior of GLP-1R in response to the new analogues. Collectively, our results support the hypothesis that peptide dynamics play a key role in signal transduction outcomes.