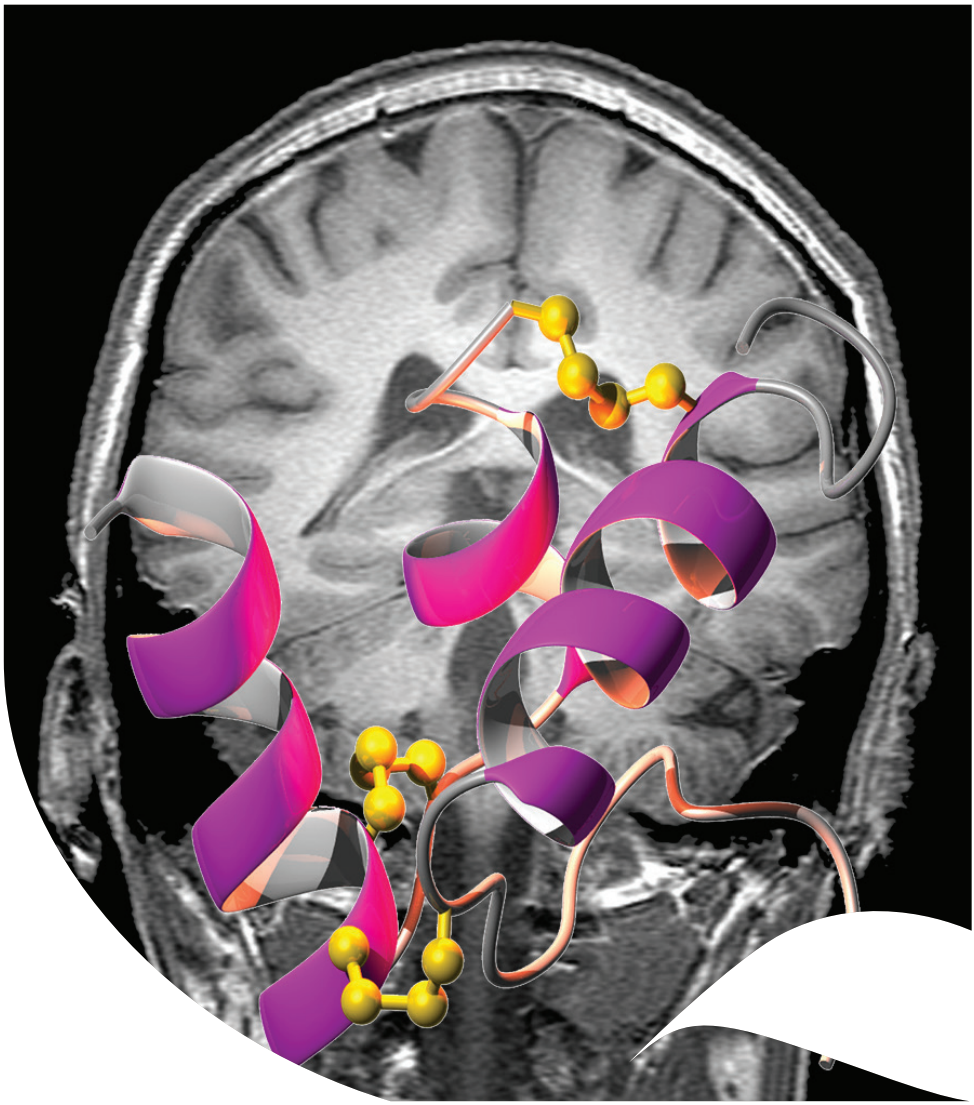
The University Of Queensland
AUSTRALIA

CREATE CHANGE

Biomedical Sciences

Peptide and protein chemistry and structural biology

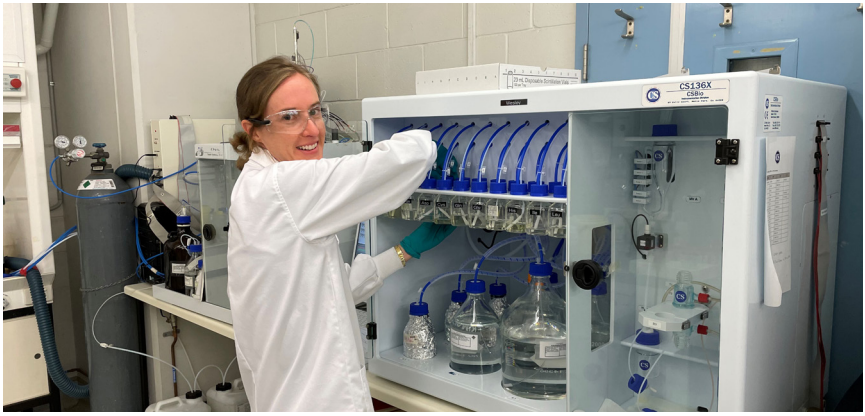


Goals/Overview

We study the chemical biology, structure and bioactivity of peptides and proteins with a view to understand their pharmacology and biological function and to develop novel peptide therapeutics.

Expertise/Capabilities

- Design and synthesis of custom peptides using solid phase peptide synthesis. Manual and automated peptide synthesis, purification (HPLC) and characterisation (mass spectrometry). Peptide stapling, orthogonal disulfide bond formation, peptide conjugates.
- Peptide drug development. Improving drug-like properties of bioactive peptides – membrane permeability, blood-brain barrier penetration, serum stability.
- Receptor activity. Mammalian cell culture and GPCR expression for activity assays.
- Electrophysiology for ion-channel characterisation. Structure-activity relationships of venom peptides. Bioactive peptides for elucidation of ion channel interactions.
- Protein modification and semi-synthesis. Protein expression in bacterial systems, purification (affinity, HPLC) and characterisation. Protein conjugation, incorporation of site-specific post-translational modifications, labels and tags, segmental isotope labelling for structural biology.
- Peptide and protein three-dimensional structures and dynamics from NMR spectroscopy data. Structure-activity relationships of peptide-receptor interactions for structure-based drug design. Structural characterisation of cyclic peptide natural products.



Dr. Anne Conibear working at the solid phase peptide synthesis platform.

Projects

- Relaxin – structure-function studies of relaxin analogues and receptor mimics.
- Venom peptides – cone snails, spider, scorpion etc.
- Acid-sensing ion channels
- Complement system receptor ligands
- Cyclic peptides – cell-penetrating cyclic peptides, seed storage peptides.
- Protein posttranslational modifications – phosphorylation, methylation, acetylation, sulfation, ubiquitination

Recent key publications

- *A chameleonic macrocyclic peptide with drug delivery applications*. Payne CD, Franke B, Fisher MF, Hajiaghaalipour F, McAleese CE, Song A, Eliasson C, Zhang J, Jayasena AS, Vadlamani G, **Clark RJ**, Minchin RF, Mylne JS, **Rosengren KJ**. Chem Sci. 2021 Apr 11;12(19):6670-6683. doi: 10.1039/d1sc00692d.

- *Synthetic hookworm-derived peptides are potent modulators of primary human immune cell function that protect against experimental colitis in vivo.* Smallwood TB, Navarro S, Cristofori-Armstrong B, Watkins TS, Tungatt K, Ryan RYM, Haigh OL, Lutzky VP, Mulvenna JP, **Rosengren KJ**, Loukas A, Miles JJ, **Clark RJ**. J Biol Chem. 2021 Jul;297(1):100834. doi: 10.1016/j.jbc.2021.100834. Epub 2021 May 27.

- *Mambalgin-3 potentiates human acid-sensing ion channel 1b under mild to moderate acidosis: Implications as an analgesic lead.* Cristofori-Armstrong B, Budusan E, **Rash LD**. Proc Natl Acad Sci U S A. 2021 Feb 23;118(8):e2021581118. doi: 10.1073/pnas.2021581118.

- *Development of relaxin-3 agonists and antagonists based on grafted disulfide-stabilized scaffolds*. Lee, Han Siean, Postan, Michael, Song, Angela, **Clark, Richard J.**, Bathgate, Ross A. D., Haugaard-Kedström, Linda M. and **Rosengren, K. Johan** (2020). Frontiers in Chemistry, 8 87, 87. doi: 10.3389/fchem.2020.00087.

- *Pharmacological characterisation of small molecule C5aR1 inhibitors in human cells reveals biased activities for signalling and function*. Li, Xaria X., Lee, John D., Massey, Nicholas L., Guan, Carolyn, Robertson, Avril A. B., **Clark, Richard J.** and Woodruff, Trent M. (2020). Biochemical Pharmacology, 180 114156, 114156. doi: 10.1016/j.bcp.2020.114156.

UQ's School of Biomedical Sciences – mission statement:

By harnessing our diversity across the breadth of biomedical science, we will generate, disseminate and apply foundational biology underpinning health and disease to inspire and empower the next generation of leading researchers, educators, and healthcare professionals to innovate together for better health outcomes globally. Our innovative research encompasses basic discovery through translational pathways to medical solutions:

Cell architecture: We use sophisticated molecular and imaging techniques to explain how various cellular components and pathways contribute to building healthy bodies.

Receptors and signalling: We decipher the passage of external messages from the cell surface, through cytoplasmic signalling pathways, and ultimately to genetic regulatory circuits in the nucleus.

Chronic disease: We characterise the genetic, molecular and cellular microenvironments associated with diseases, such as Alzheimer's disease, cancer, MND and others.

Drug design and development: We identify critical biological targets and design drugs based on structural analyses to develop novel therapies.

Functional and comparative anatomy: Our interdisciplinary studies of structure and function across phylogenetically disparate species advance our understanding of the human body in healthy, aging and diseased states.

Injury and repair: We study fundamental mechanisms of cells in response to stress, consequences of repair processes and how these may be influenced for optimal outcomes.

Musculoskeletal and motor control: We develop and apply novel tools, to investigate muscle function and neural control of muscles in humans.

Neurobiology and brain function: We search for and discover genetic and environmental factors that lead to and maintain healthy nervous systems.

Reproduction: We investigate the genetic and molecular environment during early fetal development to advance reproductive technologies and facilitate healthy pregnancies.

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