



## A/Prof. Markus Muttenthaler

Institute for Molecular Bioscience  
The University of Queensland  
Email: [m.muttenthaler@uq.edu.au](mailto:m.muttenthaler@uq.edu.au)  
Web: [www.neuropeptidelab.com](http://www.neuropeptidelab.com)



### The Neuropeptide Research Lab

Neuropeptides are key mediators in many biological functions and understanding of their interaction with target proteins is fundamental to unravel the underlying mechanism of diseases. Over the years, an increasing number of bioactive peptides from animals, plants, and bacteria have been characterised, with the overwhelming realisation that these molecules often show better therapeutic performance than their human counterparts, particularly in terms of *in vivo* stability.

Our main research efforts situated in this area of Chemical Biology focus on the exploration and translation of these vast and untapped natural libraries towards the development of useful research tools and therapeutics. Solid phase peptide synthesis, the main tool to access these compounds, is a powerful technology for the assembly and chemical modification of these highly chiral and structurally complex peptides. We then use these ligands to develop advanced molecular probes and therapeutic leads to address important questions of unmet medical need.

We are currently looking for talented and ambitious Honours, Masters and PhD students for projects centred around (i) the oxytocin and vasopressin signalling system in health and disease, (ii) new therapeutic strategies for gastrointestinal disorders, (iii) probe development to study long-term memory formation, and (iv) venom peptide drug discovery. Please see the project descriptions below for further details. **If interested, then please send your CV, grade transcripts and a brief cover letter to [m.muttenthaler@uq.edu.au](mailto:m.muttenthaler@uq.edu.au)**

#### Requirements

Strong chemistry or pharmacology background  
First Class Honours Degree or Master Degree in related field  
Good hands-on laboratory skills  
Strong ambition and work ethics

#### Techniques likely to learn (project dependent)

Solid phase peptide synthesis  
Organic chemistry  
Medicinal chemistry  
High-performance liquid chromatography  
Mass spectrometry, Proteomics  
Nuclear magnetic resonance spectroscopy  
Recombinant protein expression  
Cell culture and pharmacological assays  
Gastrointestinal stability assays  
Gastrointestinal wound healing assays  
Proliferation and transmigration assays

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### **Project 1 – Oxytocin and Vasopressin Research**

The oxytocin and vasopressin signalling system regulates many fundamental physiological processes such as reproduction, water balance, cardiovascular responses and complex social behaviour. It is also a high-profile target for autism, schizophrenia, stress, depression, anxiety, cancer and pain. Our group is particularly interested in creating a complete molecular toolbox to study this signalling system as well as in discovering novel therapeutic leads for autism, pain, gastrointestinal disorders and breast cancer. This project entails structure-activity-relationship studies and medicinal chemistry approaches to develop novel probes and drug candidates for the oxytocin and vasopressin system.

### **Project 2 – Trefoil factor peptides and their role in gastrointestinal disorders**

The gastrointestinal epithelium is a major physical barrier that protects us from diverse, and potentially immunogenic or toxic content. A damaged epithelium results in increased permeability to such content, thus leading to inflammation, uncontrolled immune response, and diseases, such as irritable bowel syndrome and inflammatory bowel disease that affect 10-15% of the population. Our group is involved in the identification and validation of novel drug targets and therapeutic strategies that can protect or repair this important barrier in order to prevent or treat such disorders. This project is focussed on developing novel trefoil factor peptide probes to understand their mechanisms of action in gastrointestinal protection and wound healing.

### **Project 3 – Neuropeptides and long-term memory formation**

Memory is probably the single most important brain process that defines our personality and gives us the sense of individuality. Emotional events often cause the generation of strong memories that exist for many years, yet the underlying mechanisms are still poorly understood. Neuropeptides are key players in regulating emotions and have been associated with long-term memory formation. This project is focused on the development of advanced molecular probes to understand how neuropeptides can mediate long-term memory formation.

### **Project 4 – Venoms to drugs**

Venoms comprise a highly complex cocktail of bioactive peptides evolved to paralyse prey and defend against predators. Homology of prey/predator receptors to human receptors render these venom peptides also active on human receptors and they have become a rich source for neurological tools and therapeutics. This project comprises discovery, synthesis and structure-activity relationship studies of these venom peptides with the goal to develop novel probes for neuroscientists as well as therapeutic drug leads.

### **Project 5 – Targeting gut biofilms in patients with gastrointestinal disorders**

Gastrointestinal disorders affect 10–15% of the Western population, reduce the quality of life and result in substantial socioeconomic costs. Recently, we have observed bacterial biofilms in the gastrointestinal tract of IBD and IBS patients, but their disease relevance, function and composition are unknown. This project aims to (i) use various analytical techniques to profile these gut biofilms and (ii) to develop biofilm-specific modulators to explore novel therapeutic strategies.

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## Institute for Molecular Bioscience

The University of Queensland's Institute for Molecular Bioscience, located on the main University campus, is Australia's leading biosciences research institute. Established in 2000, the Institute is home to over 420 staff and is located in thriving Brisbane, a city consistently ranked as one of the world's most vibrant and liveable cities.

The Institute, ranked in the Top 20 globally for life sciences research, pursues a multidisciplinary approach to solving some of the world's most serious challenges in the fields of health, disease and sustainable solutions for our cities, fuels and foods. The Institute is housed in a single building and is organised into technological platforms (Divisions) and research themes (Centres). The Divisions support state-of-the art facilities including the Centre for Microscopy and Microanalysis, which houses new cryo-electron microscopes; the NMR facility containing 500, 600 and 900 MHz machines; the Mass Spectrometry Facility accommodating a wide array of instrumentation; suites for work with a variety of model organisms; a plethora of next generation DNA sequencing technologies and the southern hemispheres leading program in complex genetic traits. The Research Centres accommodate 36 groups using a combination of genomics, chemistry and cell biology to take life science discoveries from the genome to drug design and application in the areas of antimicrobial resistance, inflammation, pain, cardiovascular disease and rare and developmental diseases.

Details of the research interests of the Institute may be accessed at: <https://imb.uq.edu.au/>

## The candidate

Both Australian and international applicants are welcome to apply. Candidates should have a First Class Honours Degree or Master Degree (or equivalent) in the fields of chemistry, biochemistry, pharmacology or a related discipline. Strong academic performance, good oral and written communication skills, and published output will be additional assessment criteria. Selected candidates will be provided with assistance to apply for a PhD scholarship. Award of a scholarship will be conditional for entry to the PhD program at UQ.

Applicants must be eligible to enrol in a PhD with the University of Queensland. For a complete list of the University of Queensland's minimum entry requirements please refer to: <https://graduate-school.uq.edu.au/uq-research-degrees>. Please note the English language proficiency requirements <https://graduate-school.uq.edu.au/english-language-proficiency-requirements>.

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