Prof. Markus Muttenthaler

Institute of Biological Chemistry
Faculty of Chemistry
University of Vienna
Email: markus.muttenthaler@univie.ac.at
Web: www.neuropeptidelab.com

INSTITUT FÜR BIOLOGISCHECHEMIE

universität wien

The Neuropeptide Research Lab

Neuropeptides are key mediators of many biological functions, and understanding their interactions with target proteins is fundamental to unravelling the underlying mechanisms of disease. 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 regarding *in vivo* stability.

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

We are currently looking for talented and ambitious Master's and PhD students for projects centred around (i) the oxytocin and vasopressin signalling system in health and disease, (ii) the trefoil factor peptides and gut protection & repair, (iii) probe development to study memory formation, (iv) venom peptide drug discovery, (v) development of blood-brain barrier shuttles, and (v) targeting gut biofilms for treating gastrointestinal disorders. Please see the project descriptions below for further details.

If interested, please send your CV, grade transcripts and cover letter to markus.muttenthaler@univie.ac.at

Requirements

Chemistry, biochemistry, biotechnology or pharmacology background and strong wet lab skills
(e.g., organic chemistry, peptide/protein chemistry, pharmacology, analytical techniques, bioassays)
Strong ambition and work ethics

Techniques likely to learn (project dependent)

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

Project 1 – Oxytocin and Vasopressin Research

The oxytocin and vasopressin signalling system regulates fundamental physiological processes, including 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 comprehensive molecular toolbox to study this signalling system and 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 systems.

Project 2 – Trefoil factor family peptides and their role in gut protection and repair

The gastrointestinal epithelium is a major physical barrier that protects us from diverse and potentially immunogenic or toxic contents. A damaged epithelium increases permeability to such content, leading to inflammation, an uncontrolled immune response, and diseases such as irritable bowel syndrome (IBS) and inflammatory bowel diseases (IBD), which affect 10-15% of the population. Our group is involved in identifying and validating novel drug targets and therapeutic strategies to protect or repair this important barrier and prevent or treat such disorders. This project focuses on developing novel trefoil factor family peptide probes and drug leads to understand their mechanisms of action in gastrointestinal protection and wound healing.

Project 3 – Neuropeptides and 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 lead to the formation of strong memories that persist for many years, yet the underlying mechanisms remain poorly understood. Neuropeptides are key regulators of emotions and are associated with long-term memory formation. This project focuses on developing advanced molecular probes to understand how neuropeptides 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 renders these venom peptides also active on human receptors, making them a rich source for neurological tools and drug leads. This project comprises discovery, synthesis, and structure-activity relationship studies of these venom peptides, with the goal of developing novel probes for neuroscientists and therapeutic drug leads targeting ion channels and G protein-coupled receptors.

Project 5 – Blood-brain barrier shuttles

The blood-brain barrier (BBB) controls the transfer of substances between the blood and the brain, protecting us from toxic compounds while allowing the transfer of nutrients and other beneficial molecules. The BBB, however, also blocks 98% of drugs reaching the brain. This project focuses on venom peptides capable of crossing the blood-brain barrier to help develop non-toxic peptide-based brain delivery systems. It addresses long-standing challenges and knowledge gaps in the delivery of macromolecules across biological barriers and seeks new ways to efficiently deliver therapeutics across the BBB to improve the treatment of brain diseases.

Project 6 – 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 analytical techniques to profile these gut biofilms and (ii) to develop biofilm-specific modulators to explore novel therapeutic strategies.