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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 PhD students for projects centred around (i) the oxytocin and vasopressin signalling system in health and disease, (ii) the trefoil factor peptides and gastrointestinal disorders, (iii) molecular probe development to study memory formation, and (iv) venom peptide drug discovery. Please see the project descriptions below for further details.

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

Requirements

Strong chemistry background and synthetic lab skills (organic chemistry, peptide/protein chemistry)
Strong ambition and good work ethics

Techniques likely to learn (project dependent)

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

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 – From 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.