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Conotoxin Discovery using Artificial Intelligence (AI)

Neuropeptides are key mediators in many biological functions, and understanding 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 regarding *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.

The Project: Conotoxins are venom peptides produced by the predatory marine cone snail for predation and defence. Cone snail venom is a rich source of pharmacological probes and therapeutic leads. This project will utilise recent advances in AI, specifically AlphaFold2, to predict novel venom peptide target receptor (GPCRs and ion channels) interactions to accelerate the discovery pipeline. The project objectives are (i) computational method development for *in silico* conotoxin discovery using AlphaFold2, (ii) conotoxin synthesis, folding and purification, and (iii) pharmacological characterisation of identified leads and validation of the new screening methodology.

Requirements

Strong chemistry background and synthetic lab skills (organic chemistry, peptide 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, Proteomics
Nuclear magnetic resonance spectroscopy
Cell culture and pharmacological assays

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