

Deconstructing Proteins for the Development of Non-natural Peptide Analogues with Complement Regulatory Activity

The complement system is essential for innate immunity, yet its dysregulation contributes to a vast variety of diseases. Many natural proteins, including those produced by the host and microbe/parasite evasion mechanisms, are capable of modulating complement activity inspiring new therapeutic strategies. Motivated by the growing success of non-natural peptides in clinical complement modulation (pegcetacoplan, Empaveli/Syfovre, Apellis; Zilucoplan, Zilbrysq, UCB, inc.), this project entails deriving key interaction motifs from natural complement-regulating proteins to generate new, non-natural peptide candidates for complement modulation.

Students will obtain training in state-of-the-art methods, including:

- Automated solid-phase peptide synthesis
- Introduction of non-natural peptide modifications (macrocyclization, backbone modification, conjugations)
- Chromatography and mass spectrometry (HPLC, LCMS)
- In vitro assay of peptide activity (enzyme inhibition assays)
- Biophysical analysis of peptide-protein interactions (SPR, ITC, MST)

This project will be suitable for motivated master's students (University of Basel, or external) with an interest in chemical (peptide) synthesis and medicinal chemistry, while learning state-of-the-art techniques that are invaluable in modern pharmaceutical research.

Interested applicants should contact Alexander Lander (landeraj@unibas.ch).