

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).