

# Protein Engineering of a Leech-Derived Protein

30.04.2024

Is it not ironic that parasites we dodge whenever possible are the very creatures that might unlock new doors in medicine?

Our research group has recently uncovered the function of a novel, previously uncharacterized protein derived from a leech. This protein simultaneously modulates the host's defense mechanisms and the coagulation system in humans. Its ability to regulate immune responses renders it a promising candidate for treating diseases linked to an overactive immune system, such as acute respiratory distress syndrome—a condition that gained increased focus during the COVID-19 pandemic.

In this project, we aim to delve deeper into the properties of this leech-derived protein using advanced biophysical and molecular biology techniques. Through rational design and computational tools, we plan to modify this leech-derived inhibitor and explore its interactions with targets in the complement cascade and coagulation system. We will utilize cutting-edge protein engineering methods, including mutagenesis, to further clarify the protein's binding modes and elucidate its structure-activity relationships (SAR).

As a student researcher, you will develop essential skills in molecular biology, bioinformatics, and computational chemistry.

## Methods

The students gets the possibility to learn the following skills:

- Empirical methods:
  - Protein expression in E.coli
  - Protein purification: His-tag affinity purification
  - Site-directed mutagenesis / PCR
  - Biophysical assays
  - Enzymatic assays: Direct competitive inhibition assays,  $K_i$ ,  $IC_{50}$
  - Complement cascade activation assay: Enzyme-linked immunosorbent assay (ELISA)
  - SDS-PAGE / Western blot

- Computational methods
  - Scripting: R / Python
  - Alphafold and other AI tools
  - Structural Biology: PyMol, Schrödinger Maestro
  - Multiple sequence alignment, sequence similarities
  - Molecular Dynamics

### **Availability**

The master thesis is available for all motivated students of the University of Basel as well as external students with interest in protein engineering, biology and biochemistry. The student will be working within an interdisciplinary team. No practical nor computational skills are required.

The project can be started between August 2024 and January 2025.

### **Contact**

Please send your application to Peter Rüthemann ([peter.ruethemann@unibas.ch](mailto:peter.ruethemann@unibas.ch)) or ask me for further infos.