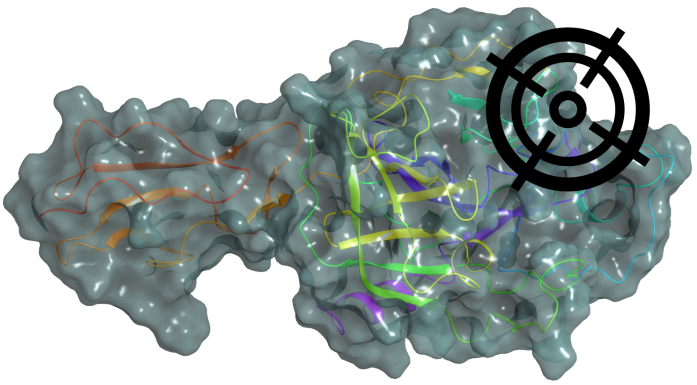
Establishment and Automation of Enzymatic Screening Assays for Drug Discovery

Project Background

The complement system is a central component of innate immunity and plays a key role in host defense, inflammation, and immune homeostasis. Dysregulated complement activation is implicated in a wide range of diseases, including rare genetic disorders, autoimmune and inflammatory diseases, thromboinflammatory conditions, and complications of infection. Targeted drug development within the complement system offers the opportunity to modulate disease-driving pathways with high specificity, addressing significant unmet medical needs.

The **Molecular Pharmacy** group at the University of Basel is part of an international Innosuisse-funded research project aimed at accelerating early drug discovery through systematic experimental screening of designed small molecules. A key contribution of the group is the **development, validation, and application of robust biochemical assays** to experimentally evaluate enzyme inhibition and selectivity for drug candidates.

This Master's thesis focuses **exclusively on the experimental (wet-lab) component** of the project and is embedded in a research environment that closely mirrors industrial drug discovery workflows.



Project aim: Targeting Serine Proteases

Project Aim

The primary goal of this thesis is to **establish, optimize, and automate screening assays for multiple enzymatic targets**, with a particular emphasis on serine proteases involved in biologically and clinically relevant pathways like the **complement and coagulation system**. These assays will serve as the experimental backbone for high-throughput compound profiling and selectivity assessment.

Objectives

During the project, the student will:

- **Establish and optimize enzymatic inhibition assays**
  - Set up chromogenic and/or fluorogenic assays for different enzymes
  - Optimize assay conditions (enzyme concentration, substrate, buffer, incubation time)
  - Assess assay robustness, reproducibility, and dynamic range
  - Perform dose–response experiments to determine IC_{50} values
  - Establish data quality controls and evaluation criteria

- **Learn and apply laboratory automation**
  - Transfer assays to an **in-house liquid handling robot**
  - Optimize automated liquid handling protocols
  - Increase throughput, reproducibility, and data consistency

- **Optional exposure to data analysis and computational tools**
  - Basic analysis and visualization of screening data
  - Optional interaction with computational workflows that use experimental data as input (depending on interest and time)

Methods and Techniques

- Enzymatic activity and inhibition assays
- Chromogenic and fluorogenic readouts
- Automated liquid handling (pipetting robot)
- Data analysis and quality control
- Protein handling and basic biochemical techniques

Learning Outcomes

By the end of the thesis, the student will have:

- Hands-on experience in **drug discovery–relevant assay development**
- Practical training in **laboratory automation and high-throughput screening**
- A solid understanding of **enzyme kinetics and inhibitor profiling**
- Insight into how experimental data feeds into larger discovery pipelines
- Experience working in a **collaborative, industry-aligned research environment**

Requirements

- Open to UniBas students
- Willingness to establish methods
- Interest in proteins and chemistry
- Interest in biochemical enzymatic assays.
- Optional: Willingness to develop or extend skills in Python scripting for data analysis
- Comfort with scientific reading, data analysis, and documentation

Target Audience
This project is well suited for Master's students in **Pharmacy, Pharmaceutical Sciences, Drug Sciences, or related life science programs** who are interested in experimental drug discovery, assay development, and automation. No prior experience with automation or bioassays is required.

Duration

Possible durations:

- 2 months (research project)
- 6 months (Master thesis)

Possible start date: Mai. 2026 – Aug. 2026

Supervisors

Dr. Peter Rüthemann
PostDoc
Molecular & Computational Pharmacy
peter.ruethemann@unibas.ch

Application

Please apply with a *curriculum vitae* and a motivation letter to Dr. Peter Rüthemann