University of Basel

Non-viral gene therapy and genetic engineering via CRISPR/Cas9

Genetic disorders give rise to severe diseases that often cause significant suffering and offer only limited treatment options. Despite remarkable progress in viral **gene therapy** over the past two decades, its widespread application remains constrained by serious side effects and prohibitively high production costs. This is particularly problematic for **rare genetic diseases**, which have received relatively little research and development attention.

One such condition is **Citrullinemia Type I**, a disorder affecting the urea cycle—a crucial metabolic pathway responsible for removing excess nitrogen from amino acid breakdown. The disease arises from a deficiency of the enzyme argininosuccinate synthetase 1 (ASS1), leading to the accumulation of citrulline and ammonia in the blood. Excess ammonia is highly toxic to the body, causing metabolic alkalosis, a condition in which the blood becomes overly alkaline. If left untreated, this metabolic imbalance can rapidly progress to neurological impairment and coma of the newborn patient.

To simulate this condition, an in-vitro model of Citrullinemia Type I will be developed by manipulating different hepatic cell lines using the **CRISPR/Cas9-system.**

During this project, the MSc student learn the following methods:

- Genetic engineering using CRISPR/Cas9
- DNA-sequencing
- Fluorescence-activated cell sorting
- Cell culture
- mRNA expression analysis (RT-qPCR)
- Western Blotting
- Microfluidics for LNP formation
- Dynamic Light Scattering (DLS)
- Flow cytometry for assessment of successful transfection
- Confocal microscopy
- Biostatistics and experimental design
- Scientific writing

This project is suitable for internal MSc students (Drug sciences or Pharmacy) as well as for external master students with interest in gene therapy, nanoscience and drug delivery.

Applications can be sent to Lorenz Herbster: (Lorenz.herbster@unibas.ch).

Start date: flexible