

## **Paid student Internship opportunity in protein crystallization and drug design**

The Jinek lab at UZH offers a 4 months internship with a stipend of 5000 CHF in the field of protein crystallization and drug design. This project is a collaboration with the Caffisch Group, aimed at designing a molecular probe to disrupt the function of the tRNA ligase complex (tRNA-LC).

Across all domains of life, a small subset of tRNAs is encoded with a short intragenic sequence which is removed during the maturation process. In humans this process is catalyzed in a two-step reaction. Intron removal is mediated by the tRNA splicing endonuclease (TSEN) whereas tRNA ligation is catalyzed by the tRNA-LC. The ligase subunit HSPC117 of the tRNA-LC is a unique enzyme in the human biochemistry and thus interesting as a potential drug target. We aim to rationally design a small molecule inhibitor based on the atomic structure of HSPC117. With the help of a student employee, we will establish conditions which will allow for rapid screening of binding modes of computationally designed inhibitors to HSPC117 by X-ray crystallography.

### About the Project

In order to assess the atomic binding mode of the computationally designed inhibitors, the project is split into multiple objectives. Firstly, we want to establish protein crystallization conditions for HSPC117 which can be used for soaking or co-crystallization with small molecules. Therefore, we will try to reproduce already established and published conditions and screen for novel crystallization conditions. In parallel we will work with different expression constructs of HSPC117 to increase the chances of successful protein crystallization experiments. Secondly, we will try to improve crystallization conditions in regards of reproducibility and diffraction by established methods such as seeding or additive screening. Finally, we aim to obtain co-crystals of HSPC117 with computationally designed inhibitors.

### About the role

You will be involved in protein expression, purification and crystallization. This will include the generation of expression constructs, generation of baculoviruses and preparation of large scale expression cultures in insect cells. Furthermore, you will be purifying the target protein with the help of affinity purification methods (mainly IMAC) and use FPLC systems (ÄKTA). Finally, you will be submitting the purified protein to the Protein Crystallization Center, monitor the progress of the crystallization experiments and optimize initial crystallization conditions. You will be documenting your work during all experimental stages. With progression of the internship you will gradually become independent and plan and execute the research based on your schedule.

### Requirements

We are looking for motivated students with a strong interest in molecular biology and structural biology.

- Basic knowledge of:
  - o recombinant protein expression
  - o protein purification workflows (FPLC, purification methods, etc.)
  - o molecular techniques (PCR, cloning technologies, etc.)
  - o protein crystallization and structural biology principles
- Familiarity with laboratory work in molecular biology
- Curiosity and enthusiasm for tackling scientific challenges

While this research project has a specific intended goal, this internship is also a training opportunity. Hands-on experience on the above mentioned topics is a plus but not required.

### How to apply

Interested candidates are invited to submit their CV to Moritz Pfeleiderer ([m.pfleiderer@bioc.uzh.ch](mailto:m.pfleiderer@bioc.uzh.ch)).

We look forward to your application!