Master Thesis Project – Clausen lab

Catch me if you can – Addressing the ClpP degradome of mycobacteria and its potential for antibiotic development

There is an opportunity for a Master student in the Clausen lab at the Research Institute of Molecular Pathology (IMP) in Vienna. The Clausen lab studies molecular mechanisms of how cells reduce the amount of aberrant, aggregation-prone proteins. The current project aims to analyze the substrate spectrum of the ClpP protease, an essential protein quality control factor in mycobacteria and established antibiotic target.

Controlled protein degradation is a hallmark of protein quality control in all cells. One of the most prominent members of the quality-control system is the ClpP protease that is essential for survival in all mycobacteria, including Mycobacterium tuberculosis, the number 1 in the WHO list of most threatening pathogens. In mycobacteria, the ClpP system is essential under normal and during stress conditions, most likely due to the identity of the substrates. However, the exact extent of the ClpP substrate spectrum and the nature of the "key", i.e. most troublesome substrates are not known. To analyze the "degradome" of ClpP and its impact for antibiotic development, we plan to express a substrate-trapping ClpP mutant in mycobacteria and identify the in-vivo substrates captured within the ClpP cage. In addition to revealing the ClpP degradome, these results will help to understand how substrates are targeted to and recognized by ClpP proteolytic complexes. For the potential Master student, this project will provide ample opportunities to work with bacterial model systems, in particular Mycobacterium smegmatis, to familiarize with biochemical methods such as protein purification and degradation assays and to learn state-of-the-art mass spectrometric methods to perform proteomic analyses.
An interest in working with proteins and mass-spectrometry is essential for this project, and prior experience in these methods is advantageous.

To apply please send a CV and cover letter to:
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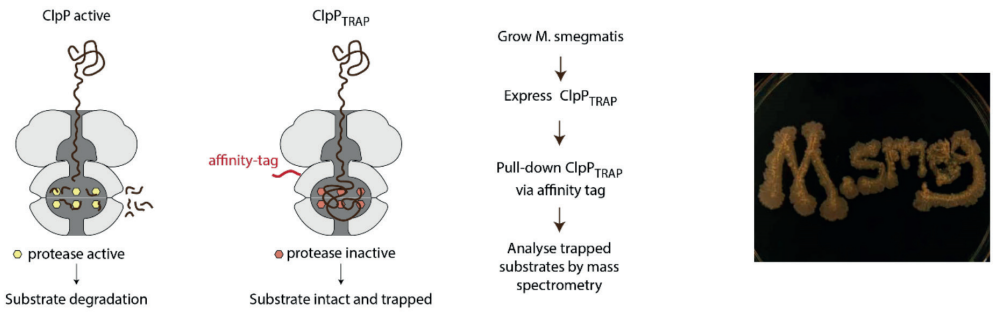

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