

Project 9.6 Adaptation of Proteins to Avoid Premature Degradation by the Ubiquitin-Proteasome System (NCN/SONATA BIS)

Supervisor: Wojciech Pokrzywa, PhD, DSc

Institute: International Institute of Molecular and Cell Biology in Warsaw

Unit: Laboratory of Protein Metabolism

www: pokrzywalab.com

Background:

Our recent discovery revealed a fascinating correlation between organismal complexity in eukaryotes and the appearance of lysine deserts. Furthermore, we found that the most evolutionarily conserved lysine deserts are rich in ubiquitin-proteasome system (UPS) proteins. Through studies on E3 ubiquitin ligases such as VHL and SOCS1, we identified a unique evolutionary elongation of their lysine deserts, resulting in ubiquitination independent of lysines. Remarkably, this unusual ubiquitination does not impact protein stability. This project is designed to delve into the evolutionary significance of lysine-desert sequence elongation in selected proteins, including E3 ubiquitin ligases. The aim is to understand how this process might enhance their specificity, non-canonical regulation, and function.

Aim:

The main objective of this project is to construct specific tools in *C. elegans* that will use proximity labeling and NanoBRET to pinpoint tissue-specific substrates for selected E3 ubiquitin ligases and probe their physiological roles. The PhD candidate will have the opportunity to acquire practical experience in advanced techniques such as molecular biology methods, *C. elegans* genetics, mass spectrometry, and imaging techniques. Additionally, part of the research will be conducted using cell culture methods in collaboration with a PostDoc hired in this project, providing a comprehensive research experience. If desired, the candidate can also participate in bioinformatics-related side projects ongoing in our laboratory. The literature relevant to the project, which candidates are strongly advised to get familiar with:

- <https://www.biorxiv.org/content/10.1101/2023.01.18.524605v1>
- <https://pubmed.ncbi.nlm.nih.gov/36336956/>
- <https://www.biorxiv.org/content/10.1101/2022.05.19.492622v1>
- <https://pubmed.ncbi.nlm.nih.gov/35762422/>

Requirements:

- holds a master's degree in biology, biochemistry, genetics or related field,
- solid knowledge and hands-on laboratory experience in molecular biology methods,
- keen interest in regulation of proteostasis network,
- prior experience with *C. elegans*, cell culture, CRISPR/Cas9 technology, mass spectrometry, and imaging techniques will be an advantage,
- excellent written and verbal communication skills in English,
- proven ability to work independently,
- a proactive approach to achieving objectives, collaborative attitude, willingness to learn and take new challenges

Key Responsibilities:

- plan and conduct laboratory experiments pertaining to the project goals,

- analyze data,
- intellectually contribute to the development and progress of the project

Number of positions available: 1

Contact: wpokrzywa@iimcb.gov.pl