

**Title:** Compartment-specific ups dysfunction in neurodegenerative disease mutations (NCN/SONATA BIS)

**Supervisor:** Lidia Wrobel, PhD

**Institute:** International Institute of Molecular and Cell Biology in Warsaw

**Laboratory:** Laboratory of Cellular Proteostasis

**www:** <https://shorturl.at/octlf>

**Project description:**

Protein degradation is a key mechanism for adapting protein levels to cellular and environmental changes. Maintenance of cellular proteostasis requires temporally and spatially controlled degradation of regulatory and aberrant proteins. In several neurodegenerative diseases, mutations in disease-associated proteins can directly or indirectly impair proteasome function. However, the mechanistic link between these mutations and proteasome dysfunction remains poorly understood, and the compartment-specific nature of these alterations is largely unknown.

As a PhD student, you will develop human neuronal reporter lines to investigate the compartment-specific function of the ubiquitin–proteasome system upon disruption of genes linked to neurodegenerative diseases. Using CRISPR/Cas9-based gene editing, state-of-the-art confocal microscopy, and FACS-based assays, you will uncover molecular mechanisms underlying observed phenotypes and evaluate their role in early neuronal degeneration in models of Parkinson’s and Huntington’s disease. You will also conduct literature reviews, participate actively in lab meetings, present your work at national and international conferences, and contribute to scientific publications.

**Aim:**

The aim of this project is to determine how neurodegenerative disease–associated mutations disrupt compartment-specific function of the ubiquitin–proteasome system in human neurons. Using neuronal models and functional assays, the project will define how these mutations impair proteasome activity and contribute to early neuronal degeneration in Parkinson’s and Huntington’s disease.

**Requirements:**

- Master's degree in biology, biotechnology, biochemistry or related field
- Hands-on experience with mammalian cell culture is required. Experience with stem cell culture (e.g., iPSCs) or primary cells would be an advantage but is not essential
- Experience with biochemical and molecular biology techniques
- Strong organizational skills and the ability to maintain accurate experimental records.
- Ability to work both independently and collaboratively in a multidisciplinary research team.
- Good communication skills and proficiency in written and spoken English.

**Number of positions available:** 1

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