

**Title:** Nuclear protein quality control in neurodegeneration (NCN/SONATA)

**Supervisor:** Lidia Wrobel, PhD, **Promotor:** Jacek Jaworski, Professor

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

**Laboratory:** Laboratory of Cellular Proteostasis

**www:** <https://shorturl.at/Fkl31>

**Project description:**

Maintenance of cellular protein homeostasis (proteostasis) requires temporally and spatially controlled protein quality control and degradation of regulatory proteins, as well as the continuous removal of erroneous proteins. Clearance of damaged or misfolded proteins is critical for cell health and survival, as accumulation of toxic protein species is associated with many neurodegenerative diseases, including Huntington's, Alzheimer's, and Parkinson's diseases. The removal of proteins is mainly mediated by the ubiquitin-proteasome system (UPS) which is active both in the cytosol and the nucleus. Recent studies demonstrated that misfolded cytosolic proteins are actively translocated into the nucleus for deposition and proteasomal degradation. However, it is not understood how these proteins are recognized, targeted and transported from cytosol into the nucleus and how insufficient targeting of these toxic proteins impacts cellular proteostasis. Moreover, it is not clear how this process is regulated in response to internal and external stressors and how it is altered in neurodegeneration.

**Aim:**

The project aims to understand the mechanisms governing mammalian protein quality control (PQC), focusing on the ubiquitin-proteasome system (UPS) in the nucleus. With the use of cutting-edge protein trafficking assays combined with quantitative mass spectrometry, state-of-the-art microscopy and biochemical methods, we aim to identify, characterise and define novel factors and pathways key for protein trafficking and degradation in the nucleus. By using a variety of cellular models, from established cell lines to human induced pluripotent stem cell (iPSC)-derived neurons, we aim to broaden our understanding of the nuclear UPS and how it is affected in neurodegeneration.

**Requirements:**

- MSc degree in biology, biochemistry or related field
- Solid knowledge in at least one of the following disciplines: molecular biology, biochemistry, cell biology, neuroscience
- Understanding of mechanisms important for cellular proteostasis
- Basic hands-on experience in one of the fields: molecular biology, cell biology, fluorescent microscopy
- Prior experience in working with human induced pluripotent stem cell (iPSC)-derived neurons would be an advantage but not essential
- Interest in cellular proteostasis and neurodegeneration
- Written and spoken fluency in English
- Willingness to learn and take new challenges, ability to work independently, analytical thinking
- Good interpersonal skills and a collaborative attitude

**Number of positions available:** 1

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