Project 1.19. Ubiquitin as a modulator of the mitochondrial protein import process

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Background:

Cytosolic ribosomes synthesize nearly all of the cellular proteins. Eukaryotic cells are highly compartmentalized with multiple specialized organelles. Thus, more than half of newly synthesized proteins require translocation to their intended localization. Efficient regulation and quality control of the protein translocation process are vital for maintaining protein homeostasis (proteostasis) and cell fitness. Mitochondria are essential cellular organelles defined by two membranes that surround two aqueous compartments. Nearly all mitochondrial proteins originate as precursor proteins in the cytosol and require active import into the organelle. Multiple studies indicate the role of the cytosolic ubiquitin-proteasome system in the regulation of mitochondrial precursor proteins. However, it remains unclear if ubiquitinated precursor proteins can still be imported into mitochondria. Also, the ability of mitochondria to remove ubiquitin from internal proteins is uncertain. Our recent observation indicates that the attachment of ubiquitin can directly interfere with the import of a precursor protein. Thus, we hypothesize a new role for ubiquitination as a direct regulator of mitochondrial precursor proteins import into the organelle.
Recognizing such interplay between precursor protein ubiquitination and transport is of high significance. The activity of the proteostasis network and mitochondria function decline with senescence. Such reduction strongly associates with degenerative disorders that frequently affect humans in aging societies. Addressing possible imbalance between mitochondrial protein import, ubiquitination, and degradation processes will enhance our understanding of molecular mechanisms that underlay such disorders.

Aim:

The project's main objective is to uncover how precursor proteins that utilize different mitochondrial import pathways are affected by ubiquitination. We will also identify the factors that regulate this process at the molecular level. The study will use human cell lines as a model system, supported by the experiments using yeast Saccharomyces cerevisiae.

Requirements:

- MSc degree (or equivalent) in Biology, Biochemistry, Biotechnology or related fields of life sciences
- Solid knowledge and familiarity with laboratory techniques in at least one of the following disciplines: molecular biology, biochemistry, cell biology
- Motivation and passion for experimental work
- Excellent command of English