

## DC6: Quality control mechanisms involved in mitochondrial translation

**Host institution:** Karolinska Institute, Department of Medical Biochemistry and Biophysics, Stockholm, Sweden.

**Supervisor:** Dr. Joanna Rorbach

**Co-Supervisors:** Dr. Antonella Spinazzola, University College London, Queen Square Institute of Neurology, London, United Kingdom (Academic); Dr. Maurice Hendriks, Lumicks, Amsterdam, The Netherlands (Industrial).

**Project description:** The basic mechanisms of protein synthesis are shared between all kingdoms of life; however, different organisms have evolved distinct structural characteristics of ribosomes and regulatory mechanisms. Interestingly, eukaryotic cells harbor two separate protein synthesis pathways. While the majority of proteins is encoded in the nucleus and translated in the cytoplasm, 13 proteins are encoded by mitochondrial DNA and translated in the mitochondrial matrix. Translation in mitochondria is performed by specialised mitoribosomes that differ significantly from their prokaryotic and cytosolic counterparts. The stalling of ribosomes during protein synthesis results in the production of truncated polypeptides that can have deleterious effects on cells and therefore must be eliminated. This function is carried out by a dedicated surveillance mechanism known as ribosome-associated protein quality control. Over the last decade, intense studies by several research labs allowed to identify surveillance pathways functioning in eukaryotic cytosol and in bacteria, but the corresponding processes in mitochondria remain to be elucidated. In this project, we aim to characterize both biochemically and structurally the components of the mitoribosome rescue pathways. We will apply genetic screening, quantitative proteomics and cryoEM to understand: how is the stalled mitoribosome recognized, how is mitoribosome splitting triggered and what are the physiological consequences of disruption of these processes.

**Host laboratory:** Research activities in the group of Dr. Rorbach are focused on understanding mitochondrial gene expression machinery in health and disease. To identify and characterize different factors and regulatory pathways involved in mitochondrial function, we employ cutting-edge technologies, such as CRISPR-Cas9 screening, next generation sequencing (ribosome profiling), cryo-EM, single-molecule analysis and comprehensive proteomics. The group, which consists of 5 PhD students and 4 postdocs, is embedded in the Division of Molecular Metabolism and is also associated with the Max-Planck Institute for Biology of Ageing (MPI), providing collaborative environment and opportunities to learn novel techniques and to use specialized facilities with state-of-the-art equipment. Importantly, we have also a close collaboration with the Center for Inherited Metabolic diseases (CMMS) at Karolinska Hospital that specializes in the diagnosis of mitochondrial diseases, providing opportunities for translational research.

**Secondments:** This project is carried out in strong collaboration with the following groups, and visits to their laboratories are expected during the project. A willingness to travel and spend time abroad is therefore essential:

- Dr. Antonella Spinazzola, University College London, London, United Kingdom;
- Dr. Noa Sher, Minovia Therapeutics LTD, Haifa, Israel.

### Eligibility conditions

- Master's degree in Biology, Biotechnology or related field.

### Required Skills

- Research experience (e.g. through Master thesis work or research internships) in cellular and molecular biology techniques are required. Experience in mitochondrial biology or structural biology will be a strong advantage.
- Proficiency in the English language is required, as well as good communication skills, both oral and written. Successful candidates will need to provide an English test (e.g. IELTS, TOEFL, Cambridge English). You may be exempt if you are a national of a majority native-English speaking country, or have qualifications / degree that has been taught and assessed in English. The supervisor can also confirm that a candidate has the required level of English.

### Enquiries

For general information about the MITGEST Doctoral Network visit the project website ([www.mitgest.eu](http://www.mitgest.eu)) or send an email to ([info@mitgest.eu](mailto:info@mitgest.eu)).

For additional information on this project please contact Dr. Carlo Vascotto ([ioanna.rorbach@ki.se](mailto:ioanna.rorbach@ki.se)).

### How to apply

To complete your online application, visit the MITGEST recruitment web page (<https://www.mitgest.eu/open-positions/>).

### Application deadline

The closing date for applications is **November 15<sup>th</sup> 2022**.



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