DC1: Molecular mechanisms involved in the degradation processes of damaged mitochondrial messenger RNAs

Host institution: Institute of Hematology and Transfusion Medicine, Department of Experimental Hematology, Warsaw, Poland.

Supervisor: Dr. Carlo Vascotto

Co-Supervisors: Dr. Roman Szczesny, Institute of Biochemistry and Biophysics, Polish Academy of Science, Warsaw, Poland (Academic); Dr. Angel Picher, 4basebio, (Industrial).

Project description: Oxidative stress refers to increased intracellular levels of reactive oxygen species (ROS): highly reactive molecules that can alter and damage lipids, proteins, and nucleic acids. Aerobic organisms have biochemical defense mechanisms to neutralize the oxidative effects of ROS, but when the imbalance increases toward ROS, oxidative stress results. This condition is associated with various pathologies, including cardiovascular and metabolic diseases, cancer, neurodegenerative disorders, and ageing. Mitochondria are the major endogenous source of ROS and, as for DNA, also RNA is subject to oxidative damage that can alter RNA structure and function and affect the interaction between RNA and other cellular molecules. In addition, oxidation of mRNA leads to decreased translation efficiency and abnormal protein production and causes ribosome dysfunction. Despite many efforts, information on the mitochondrial RNA degradation process is still scanty. With this project, we will elucidate the molecular mechanisms, protein partners, and kinetics of mt-mRNAs degradation processes that are currently unknown. We will use proteomics-based approaches based on mass spectrometry to identify proteins associated with mitochondrial APE1 and damaged mt-mRNAs. By using biochemical approaches, we will then investigate their roles and functions and which downstream effects are determined by impaired degradation of damaged mt-mRNAs.

Host laboratory: Research activities in the group of Dr. Vascotto are focused on the study of DNA repair mechanisms, mitochondrial RNA degradation processes, and the role of mitochondria in tumour progression and resistance. The laboratory has full access to laboratories for handling mammalian cell cultures and primary human cells; flow cytometry facility; instruments for monitoring cell parameters (e.g. viability, apoptosis, mitochondrial respiration, and more).

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. Roman Szczesny, Institute of Biochemistry and Biophysics, Polish Academy of Science, Warsaw, Poland;
- Dr. Antonella Spinazzola, University College London, London, UK;
- Dr. Angel Picher, 4basebio, Cambridge, UK.

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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 and/or RNA 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 visit the project website (www.mitgest.eu) or send an email to (info@mitgest.eu).

For additional information on this project please contact Dr. Carlo Vascotto (carlo.vascotto@uniud.it).

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 15th 2022**.

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