

DC3: Synthesis, processing and degradation of mitochondrial RNA

Host institution: Radboud Center for Mitochondrial Medicine, Department of Paediatrics, Radboud University Medical Center, Nijmegen, The Netherlands.

Supervisor: Dr. Hans Spelbrink

Co-Supervisors: Dr. Roman Szczesny, Institute of Biochemistry and Biophysics, Polish Academy of Science, Warsaw, Poland (Academic); Dr. Thomas Frischmuth, baseclick GmbH, Neuried, Germany (Industrial).

Project description: Both strands of the small circular mtDNA molecule are almost fully transcribed to give two large polycistronic transcripts. While one of these transcripts yields most functional RNA species, namely 10 mRNAs, two ribosomal RNAs (rRNAs) and 14 transfer RNAs, the other strand yields 1 small mRNA and the remaining 8 tRNAs. This means that most RNA from this second strand is non-coding and indeed so-called long non-coding RNAs from this second strand have been identified. Although it is common practice to analyse steady-state mitochondrial RNA (mtRNA) nascent mtRNA analysis is largely unexplored. With the technological advances offered by Click chemistry and RNAseq, it is becoming a more easily accessible method allowing us to systematically analyse synthesis, processing and degradation of mtRNA. We can further combine Click chemistry labelled nascent RNA with a mitochondrial targeted RNA-binding proteome isolation method and mass spectrometry developed by this group to identify and establish roles for early and late protein partners in mtRNA homeostasis. The doctoral candidate for this project will work on the optimization of the analysis of nascent mtRNA synthesis, processing and degradation and the identification and characterization of the proteins involved during the various steps of mtRNA metabolism.

Host laboratory: Dr. Hans Spelbrink, who for many years has worked mostly on mtDNA maintenance, has in recent years expanded his interests towards studying mitochondrial gene expression in a broader sense, also in light of the ever-increasing number of disease genes identified in this process and the many levels of interplay between mtDNA and mtRNA metabolism. The Spelbrink laboratory is affiliated with the department of paediatrics and embedded in the Nijmegen Center for Mitochondrial Medicine, which is a national expertise center for the study, diagnosis and treatment of mitochondrial disorders. The Radboudumc and Radboud University has many state-of-the-art facilities, including a large variety of cell imaging microscopy instruments, modern mass spectrometry facilities, cell and tissue culture, genome analysis facilities for WES and WGS as well as RNAseq, etc etc.

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. Thomas Frischmuth, baseclick GmbH, Neuried, Germany;
- Dr. Roman Szczesny, Institute of Biochemistry and Biophysics, Polish Academy of Science, Warsaw, Poland.



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Eligibility conditions

- Master's degree in Biology, Medical Biology, Biochemistry, 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 RNA biology and/or mitochondrial 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. Former supervisors 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) or send an email to (info@mitgest.eu).
- For additional information on this project please contact Dr. Hans Spelbrink (Hans.Spelbrink@radboudumc.nl).

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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