

DC4: Functional proteomics of the mitochondrial gene expression system

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

Supervisor: Dr. Hans Spelbrink

Co-Supervisors: Dr. Joanna Rorbach, Karolinska Institute, Department of Medical Biochemistry and Biophysics, Stockholm, Sweden (Academic); Dr. William Leenders, Predica Diagnostics B.V., Nijmegen, The Netherlands (Industrial).

Project description: MtDNA derived RNAs, including 2 ribosomal (r)RNAs, 11 mRNAs coding for 13 proteins, and 22 tRNAs work in concert with a large number of nuclear encoded proteins to synthesize the 13 OXPHOS subunits and ultimately assemble the respective OXPHOS complexes. For example, the 2 mtDNA derived rRNAs and mt-tRNA(Val) make functional mitochondrial ribosomes together with 82 nuclear encoded protein and an unknown number of ancillary, nuclear encoded factors involved in rRNA modification and ribosome assembly. Various steps in mtRNA metabolism, including at least some steps in ribosome biogenesis take place in designated and discrete structures (or protein-RNA complexes) within the mitochondrial network coined mitochondrial RNA granules. Early steps in mitoribosome biogenesis have also been proposed to take place in association with the mtDNA nucleoid. In order to study assembly of mitochondrial protein complexes, complexome analysis via mass spectrometry using various native gel systems (such as Blue Native polyacrylamide gels) has proven very powerful. The DC for this project will test and optimize complexome methodology for the analysis not of protein complexes alone but the anticipated larger protein-RNA, protein-DNA and possibly protein-RNA-mtDNA complexes. Via inhibition-release approaches to temporarily deplete mitochondrial RNA or known nuclear factors involved in RNA biology the DC will use these methods to study the temporal formation of these complexes and identify the (known and novel) protein factors involved at each step.

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. Joanna Rorbach, Karolinska Institute, Department of Medical Biochemistry and Biophysics, Stockholm, Sweden (Academic);
- Dr. William Leenders, Predica Diagnostics B.V., Nijmegen, the Netherlands.

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, protein biochemistry 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**.