JOB DESCRIPTION

Job Title: *Search and characterization of molecular partners involved in RNA mitochondrial import in yeast and human*

Job Summary:
(English, max 1000 characters)

Our goals are to identify the proteins beyond enolase that are involved in tRNA mitochondrial import in yeast and human cells. The structure of a stable complex would be solved by combining mass spectrometry, crystallography, XFEL, and SAXS. We also want to investigate the role of preMSK1p. We also plan to evaluate the role of chemical modifications of tRNAs in relation to the import process using a genetic approach conducted in yeast. We will study the impact of stress on changes in the profiles of tRNAs purified from mitochondria by high-throughput sequencing (CLIP-seq) methods. This part of the project will be carried out in the laboratory of Professor Mark Helm (University of Mainz, Germany). We will also improve the methods of affinity purification by using click chemistry to covalently link the molecules destined to interact in order to stabilize the complexes of interest.

Job Description:
(English, detailed information – max 3000 characters)

Many organisms have mitochondrial genomic DNA lacking tRNA genes or only a partial set. The mitochondrial translation necessary for the synthesis of OXPHOS proteins thus requires the import of cytosolic tRNAs. Nonetheless, organisms encoding a complete set of mitochondrial tRNA maintain an active import mechanism, the biological consequences of which are still not understood.

The import of tRNA into yeast mitochondria has been shown experimentally in our laboratory. We study tRK1, tRNALysCUU. TRK1-derived RNAs expressed in human cells are also imported into mitochondria. We use this property for therapeutic purposes. Our strategy consists in inserting into the imported RNA a sequence hybridizing to a region of the mitochondrial mutated "sick" genomic DNA, from which inhibition of mutant DNA replication would have a curative effect.

As part of the LabEx MitoCross, we want to better understand the mechanisms of mitochondrial tRNA import and acquire the knowledge to control the mechanisms of RNA import in mitochondria. In addition to the fundamental aspect of our research, these discoveries would help improve therapeutic approaches.

Only few molecular partners of RNA mitochondrial import are identified. TRK1 is first recognized by the glycolytic enzyme enolase, which masks it from cytosolic pathways. Once in the vicinity of the outer mitochondrial membrane, the tRNA is handed to the mitochondrial lysyl-tRNA synthetase precursor (preMSK1p) which then crosses the membranes up to the matrix, where it is expected to participate in mitochondrial translation.

Our recent data show a more complex picture. Other factors are required to convey tRK1 to the mitochondrial surface. In accordance with our results, the literature describes numerous functions for enolase. Moreover, our affinity assays based on the use of RNA tags allowed the isolation of peptides corresponding to enzymes of tRNA modifications using tRK1 as bait and enolase-enriched yeast extracts as prey. The project is presented in this context.

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Eligibility criteria
The candidate should have graduated with a high level master
degree by the end of June, either from institution outside France or, have completed a
full degree program abroad and have integrated a master's degree from the University of
Strasbourg

Main research field :
WARNING: Please select, trying to be specific, using 'Other' or 'All' will decrease your Job Vacancy visibility

Biological sciences / Chemistry /

JOB DETAIL

Type of contract : Temporary
Status : Full-time
Company / Institute : Université de Strasbourg
Country : France
City : Strasbourg
Postal Code : 67000
Street : 4 rue Blaise Pascal

APPLICATION DETAILS (mandatory)

Provisional start date : 01/10/2017
Application deadline : 30/09/2020
Application e-mail : b.masquida@unistra.fr