PhD program 2020 call for proposals: LabEx fellowships

Study of mitochondrial ribosome assembly factors involved in neurodegenerative diseases

LabEx : MitoCross

Research Unit

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Research team and team leader

Team: "Intracellular RNA transport and mitochondrial diseases"

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3 relevant publications:

Summer S, Smirnova A, Gabriele A, Toth U, Mandela F, Förstner KU, Kuhn L, Chicher J, Hammann P, Mitulovic G, Entelis N, Tarassov I, Rossmanith W, Smirnov A (in review) YBEY is an essential biogenesis factor for mitochondrial ribosomes. bioRxiv 2019.12.13.874362

Jeandard D, Smirnova A, Tarassov I, Barrey E, Smirnov A, Entelis N (2019) Import of non-coding RNAs into human mitochondria: a critical review and emerging approaches. *Cells* 8: 286

Smirnov A, Schneider C, Hor J, Vogel J (2017) Discovery of new classes and global RNA-binding proteins. *Curr Opin Microbiol* 39: 152-160

Number of PhDs in progress: 2 (2017, 2019)

PhD supervisors

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PhD subject

Title: **Study of mitochondrial ribosome assembly factors involved in neurodegenerative diseases**

Description:

Ribosome assembly is a complex process, involving specialised biogenesis factors that ensure rRNA processing, modification and an orderly recruitment of ribosomal proteins. Some of them are remarkably conserved, including YBEY and ERAL1, which are required for the small subunit biogenesis in bacteria and bacteria-derived organelles (such as mitochondria), and their partner protein p32, critically required for mitochondrial gene expression and involved in cancer progression. They present a key interest as potential targets of new broad-spectrum antimicrobials and as disease hotspots, associated with a number of severe, and often fatal, mitochondrial disorders (e.g. Perrault syndrome and cardiomyopathy).

In our group, we study the molecular mechanism used by human YBEY, ERAL1 and p32 to complete the assembly of the mitochondrial ribosome. The working model suggests that YBEY, in complex with p32 and assisted by ERAL1, recruits an essential ribosomal protein, uS11m, to the nascent small subunit to ensure final stages of maturation of initiation-competent mitoribosomes. However, molecular details of the YBEY mechanism and the role of its auxiliary proteins remain elusive.

In the present study, we will address the enzymatic and structural aspects of the YBEY pathway and attempt to rationalise the effects of known mutations in these factors, resulting in mitochondrial diseases in human.

Key words: YBEY; p32; uS11; mitochondria; ribosome assembly; OXPHOS; neurodegenerative disease; structure-function relationship