PhD program 2020 call for proposals: LabEx fellowships

Title of the subject: Role of mRNA binding by organellar echoforms of multi-localized aminoacyl-tRNA synthetases

LabEx MitoCross

Research Unit

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Research team and team leaders

Team:Dynamique et Plasticité des Synthétases

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3 relevant publications:

1. Frechin, M., Enkler, L., Tetaud, E., Laporte, D., Senger, B. Blancard, C., Hamman, P., Bader, G., Clauder-Münster, S., Steinmetz, M. L., Martin, R. P., di Rago, J-P. & Becker, H.D. (2014). Expression of nuclear and mitochondrial genes encoding ATP synthase is synchronized by disassembly of a multisynthetase complex. *Mol. Cell* **56,** 763-776.

2. Debard, S., Bader, G., De Craene, O. J., Enkler, L., Bär, S., Laporte, D., Myslinski-Carbon, E., Senger, B., Friant, S. & **Becker, H.D.** (2017) Nonconventional localizations of cytosolic aminoacyl-tRNA synthetases in yeast and human cells. *Methods* **113,** 91-104.

3. Frechin, M., Senger, B. Brayé, M., Kern, D., Martin, R. & **Becker, H. D.** (2009) Yeast mitochondrial Gln-tRNA^{Gln} is generated by a GatFAB-mediated transamidation pathway involving Arc1p-controlled subcellular sorting of cytosolic GluRS. *Genes Dev.* **23,** 1119-1130.

Number of PhDs in progress: (starting date) 4 (2015, 2016, 2017, 2018)

PhD supervisors

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http://labex-ibmc.u-strasbg.fr/NetRNA/team.php?id=2

PhD subject

Title: Role of mRNA binding by organellar echoforms of multi-localized aminoacyl-tRNA synthetases

Description:

Besides producing aminoacylated tRNAs, aminoacyl-tRNA synthetases (aaRSs) exert numerous noncanonical functions that are equally crucial for the cell physiology. In human, malfunctioning of these nontranslational roles through mutations in specific aaRS genes have been causally linked to major physiological disorders and diseases such as cancer, autoimmunity and neuronal pathologies. Among these additional functions, it was recently shown that all fungal cytoplasmic aaRSs are binding to mRNAs, including their own mRNA, and that by doing so, they regulate their own translation but also that of other genes. The selectivity in mRNA binding of each aaRS and the physiological consequences of this mRNA capture by aaRSs are not well understood. Another intriguing feature of some of these cytoplasmic fungal aaRSs is their capacity to be dual-localized both in the cytoplasm and in mitochondria. **Our objective is to establish the mRNA binding repertoires of the mitochondrial echoforms (the mitochondrial isoform of a cytoplasmic protein) of these dual-localized aaRSs, to study how binding selectivity is mediated and the role this mRNA sequestration plays in the organelle's physiology**. We intend to establish, the mRNA (RIP-Seq) and protein-binding repertoires (TAP, BioID, IP) of these mitochondrial echoforms, to study their modes of mRNA and protein recognition and the consequences of disrupting specific mRNA and/or protein interactions on the organelle's physiology.

Key words: mitochondrial echoform, mRNA binding, fungi, aminoacyl-tRNA synthetases, noncanonical functions, interactomics, next generation sequencing