CBH Graduate School
Université Grenoble Alpes

"Sub-cellular NMR metabolomics"

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Host laboratories:

- Institute for Advanced Biosciences (IAB) INSERM U1209/CNRS UMR 5309/UGA (Team Hainaut, group Metabolic trajectories of Cancer) https://iab.univ-grenoble-alpes.fr
- Laboratory of Fundamental and applied bioenergetics (LBFA), INSERM U1055/UGA - https://lbfa.univ-grenoble-alpes.fr

Doctoral School: ED Chemistry and Life Sciences (ED CSV – n°218)

Employer : University Grenoble Alpes
Starting date: Between Oct 1st and 31st Dec 2022 (3-years PhD contract)

Keywords

Nuclear Magnetic Resonance (NMR), Metabolomics, organelles, cell fractionation.

Project Summary

Our current inability to observe and quantify in a reliable manner the subcellular compartmentalization of metabolites in eukaryotic cells poses severe limitations to our understanding of the role played by small molecules in the regulation of many cellular processes. As metabolites typically have different functions in different cell compartments, metabolic profiling conducted at the global cellular level provides a blurred representation of organelle specific alterations of metabolic pathways associated with pathogenesis.

This project will provide a new analytical and spectroscopic framework to decipher the subcellular compartmentalization of the metabolome in eukaryotic cells. On the one hand, fast biochemical cell fractionation strategies will be optimized for metabolites extraction from subcellular fractions, such as the mitochondrial matrix and nucleosol, and their subsequent profiling by Nuclear Magnetic Resonance (NMR) spectroscopy. On the other hand, new NMR methods for in-organelle metabolite detection based on diffusion-ordered spectroscopy (DOSY) will be developed, to provide an innovative platform for investigation of the subcellular compartments at the metabolite level. Proof-of-concept studies will assess in model biological systems the specific subcellular metabolome relevant to post-translational modifications of proteins and histones.

Profile and skills required

Applicants should hold a Master of Sciences in Physical chemistry, Biology, or Biochemistry.
The candidates should have a strong interest in NMR spectroscopy (methods developments), cell biology, metabolism and omics analytical strategies. Either practical experience and/or theoretical knowledge on NMR spectroscopy OR a significant experience of bench work in molecular and cellular biology is expected. Applicants should have a strong interest in working in a cross-disciplinary environment at the chemistry-biology interface.

Good English level is required.

Application

Candidates should send a cover letter and a CV with references and grade transcripts by email to benedicte.elena@univ-grenoble-alpes.fr.

Applications should be received as early as possible, by **Sept 15th 2022**.

Relevant publications from the teams :

1. Lacombe, M.L., Lamarche, F., De Wever, O., Padilla-Benavides, T., Carlson, A., Khan, I., Huna, A., Vacher, S., Calmel, C., Desbourdes, C., Cottet, C., Hininger-Favier, I., Attia, S., Nawrocki-Raby, B., Raingeaud, J., Machon, V., Guitton, J., Le Gall, M., Clary, G., Broussard, C., Chafey, P., Thérond, P., Bernard, D., Fontaine, E., Tokarska-Schlattner, M., Steeg, P., Bièche, I., **Schlattner, U.***, and Boissan, M.* The mitochondrially-localized nucleoside diphosphate kinase D (NME4) is a novel metastasis suppressor *BMC Biology* **19**, 228 (2021).
2. Mili M., Panthu B., Madec A.-M., Berger M.-A., Rautureau G. J. P. & **Elena-Herrmann B.** Fast and ergonomic extraction of adherent mammalian cells for NMR-based metabolomics studies. *Anal. Bioanal. Chem.* **412**, 5453-5463 (2020); doi:10.1007/s00216-020-02764-9.
3. **Elena-Herrmann B.*,** Montellier E., Fages A., Bruck-Haimson R. & Moussaieff A. Multi-platform NMR Study of Pluripotent Stem Cells Unveils Complementary Metabolic Signatures towards Differentiation. *Scientific Reports* **10**, 1622 (2020); doi:10.1038/s41598-020-58377-w.
4. Pelosse, M., Cottet-Rousselle, C., Bidan, C., Dupont, A., Gupta, K., Berger, I., and **Schlattner, U.** Synthetic energy sensor AMPfret deciphers adenylate-dependent AMPK activation mechanism. *Nat. Commun.* **10**, 1-13 (2019).
5. Panthu, B., Ohlmann, T., Perrier, J., **Schlattner, U**., Jalinot, P., **Elena-Herrmann, B.***, and Rautureau, G. Cell-free protein synthesis enhancement from real-time NMR metabolite kinetics: redirecting energy fluxes in hybrid RRL systems. *ACS Synth. Biol.* 19, 218-226 (2018).
6. **Schlattner, U.**, Klaus, A., Ramirez-Rios, S., Guzun, R., Kay, L., Tokarska-Schlattner, M. Cellular compartmentation of energy metabolism: creatine kinase micro-compartments and recruitment of B-type creatine kinase to specific subcellular sites. *Amino Acids* **48**, 1751-74 (2016).
7. Moussaieff A., Rouleau M., Kitsberg D., Cohen M., Levy G., Barasch D., Nemirovski A., Shen-Orr S., Laevsky I., Amit M., Bomze D., **Elena-Herrmann B.**, Scherf T., Nissim-Rafinia M., Kempa S., Itskovitz-Eldor J., Meshorer E., Aberdam D. & Nahmias Y. Glycolysis-Mediated Changes in Acetyl-CoA and Histone Acetylation Control the Early Differentiation of Embryonic Stem Cells. *Cell Metabolism* **21**, 392-402 (2015); doi:10.1016/j.cmet.2015.02.002.