

Master's or specialization project

Location : EPFL AVP-CP CIBM-AIT, Bâtiment CH F.
 Dates: Spring/Autumn semester 2022,
 Spring/Autumn semester 2023

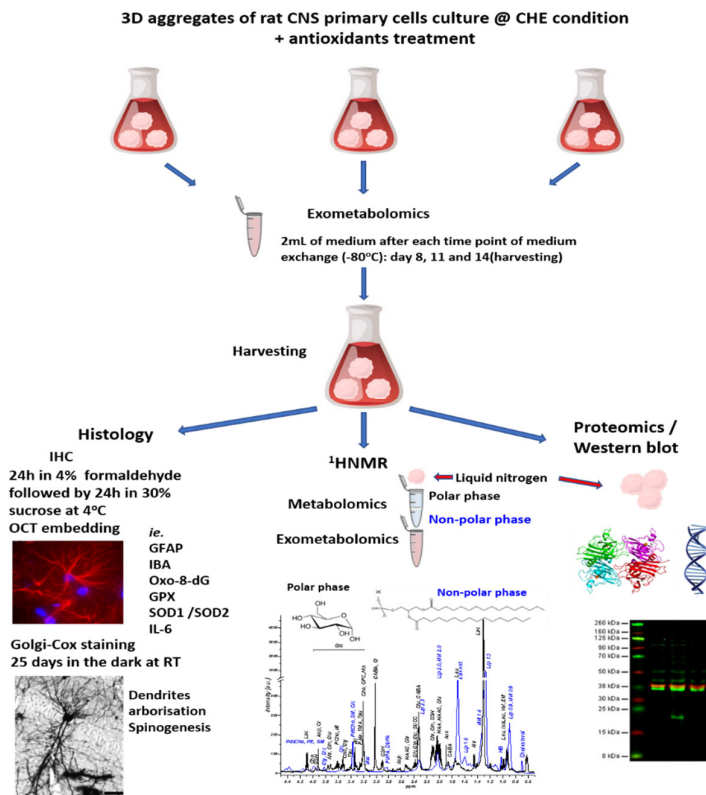
Metabolic Studies of Developing Brain: antioxidants treatment in Chronic Hepatic Encephalopathy

Chronic hepatic encephalopathy (CHE) is accepted to arise in part from brain glutamine (Gln) accumulation secondary to impaired ammonium (NH₄⁺) clearance by the diseased liver. Impaired brain NH₄⁺ detoxification together with Gln increase and glucose deprivation induces reactive oxygen species generation in turn associated with CNS cells morphology changes. In clinical practice several treatments are used, i.e. antibiotics, probiotics and NH₄⁺ scavengers [1-5]. However, the neuroprotective function of antioxidants in CHE have never been studied.

There is a need for developing realistic and reliable in-vitro models of the brain to advance our understanding of CNS during development and disease. Organotypic 3D brain culture is an experimental tool widely used in neuroscience allowing to recapitulate the structural and functional complexity of the brain. We have recently established, in collaboration with Profs O Braissant and V McLin, an Organotypic 3D brain culture model mimicking the developing brain under CHE conditions.

The aim of the study is to assess in-vitro the neuroprotective role of creatine, vit. C and vit. E in 3D organotypic brain cell cultures under CHE. For that we will perform:

- 1) immunohistochemistry (IHC) to reveal the cytoarchitecture and detailed glia and neuronal morphology changes under CHE conditions;
- 2) metabolite extraction from the 3D organotypic brain cell cultures, ¹H-MRS data acquisition and data processing (i.e. determination of metabolite concentrations).



References

[1] Pierzchala K, Simicic D, Rackayova V, Braissant O, Sessa D, Mitrea S, Sienkiewicz A., McLin VA, Gruetter R, and Cudalbu C, Brain regional susceptibility to oxidative Stress in a rat model of Chronic Hepatic Encephalopathy: in-vivo 1H MRS, ex-vivo ESR spectroscopy and histology findings, ISMRM 2019,
 [2] Pierzchala K, Simicic D, Sienkiewicz A, Sessa D, Mitrea S, Braissant O., McLin VA, Gruetter R, and Cudalbu C, Hippocampal and Systemic Oxidative Stress in a rat model of Chronic Hepatic Encephalopathy, a multimodal approach, ISMRM 2020,

[3] Skowronska M. and Albrect J. Oxidative and nitrosative stress in ammonia neurotoxicity, *Neurochemistry International*, 07 Nov 2012, 62(5):731-737

[4] Lachmann V, Görg B, Jürgen Bidmon H, Keitel V, Häussinger D, Precipitants of hepatic encephalopathy induce rapid astrocyte swelling in an oxidative stress dependent manner, *Archives of Biochemistry and Biophysics*, 24 May 2013, 536(2):143-151,

[5] Ariane Sharif and Vincent Prevot, When Size Matters: How Astrocytic Processes Shape Metabolism, *Cell Metabolism*, 01 May 2017, 25(5):995-996.

Supervisor

- **Main Supervisor:** Dr. Katarzyna Pierzchala, CIBM MRI EPFL AIT, LIFMET and CHUV, katarzyna.pierzchala@epfl.ch
- **Co-Supervisor:** Dr. Cristina Cudalbu, CIBM MRI EPFL AIT, <https://cibm.ch/people/cristina.cudalbu@epfl.ch>
- **Collaborators:** Prof. Olivier Braissant, CHUV, Olivier.Braissant@chuv.ch; Prof Valerie McLin, HUG, Valerie.McLin@hcuge.ch

Skills

- **Qualifications, previous experience and background:** This project is suitable for students with a background in physics or biomedical physics or biology/biochemistry who are interested in biomedical applications of proton magnetic resonance spectroscopy (1H-MRS) and microscopy.
- **Desirable:** Course PHYS-438 (Fundamentals of biomedical imaging), Programming experience (Matlab,)

How to apply: Please send your CV and motivation letter to the main supervisor: katarzyna.pierzchala@epfl.ch and co-supervisor cristina.cudalbu@epfl.ch

About CIBM

The CIBM Center for Biomedical Imaging was founded in 2004 and is the result of a major research and teaching initiative of the partners in the Science-Vie-Société (SVS) project between the Ecole Polytechnique Fédérale de Lausanne (EPFL), the Université de Lausanne (UNIL), Université de Genève (UNIGE), the Hôpitaux Universitaires de Genève (HUG) and the Centre Hospitalier Universitaire Vaudois (CHUV), with the generous support from the Fondation Leenaards and Fondation Louis-Jeantet.

CIBM brings together highly qualified, diverse, complementary and multidisciplinary groups of people with common interest in biomedical imaging.

We welcome you in joining the CIBM Community.

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