Master's degree in Biology – Chemistry-Biology Department

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Master 2 internship project
Year 2024-2025

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Laboratory/Institute: Grenoble Institut Neurosciences (GIN)   **Director:** Dr. E. Barbier
Team: Functional neuroimaging and brain perfusion   **Head of the team:** Dr. B. Lemasson

Name and status of the scientist in charge of the project: Dr F. Fauvelle & Dr M. Le Maréchal
                                                                HDR: yes X   no ☐

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Program of the Master's degree in Biology:

x Microbiology, Infectious Diseases and Immunology   ☐ Structural Biology of Pathogens
☐ Physiology, Epigenetics, Differentiation, Cancer   x Neurosciences and Neurobiology

<u>**Title of the project**</u>:

Metabolomics study by NMR of the metabolome of patients with central nervous system infection

<u>Objectives (up to 3 lines)</u>:

To evaluate whether it is possible to discriminate, using untargeted metabolomics of CSF: 1) viral meningitis from healthy; 2) viral meningitis from viral encephalitis; 3) to study the metabolomic profile of the pediatric subpopulation.

<u>Abstract (up to 10 lines)</u>:

Encephalitis is a serious brain condition defined as the presence of acute or subacute cerebral inflammatory processes clinically manifesting with neurological symptoms (Tunkel, 2008). Encephalitis can be infectious, autoimmune or paraneoplastic origin. Meningitis is distinguished from encephalitis by the absence of central neurological symptoms. The clinical differentiation between meningitis and encephalitis can be challenging especially in case of cofounding factors (such as hyponatremia, acute urinary retention). Lumbar puncture biological analysis alone do not distinguish between meningitis and encephalitis. Only MRI can reveal brain parenchymal involvement but is rarely available urgently within the first hours of management. The first-line treatment for encephalitis is intravenous acyclovir. However, high-dose acyclovir must be administered to ensure adequate penetration into the central nervous system. A major side effect of acyclovir is nephrotoxicity, caused by tubular crystal precipitation (Perazella, 1999). Recent studies estimate the incidence of acute kidney injury during acyclovir treatment between 13 and 17.8% (Ryan et al., 2018; Lee et al., 2018). Thus, the therapeutic consequences can be significant for patients initially presenting with meningitis accompanied by neurological symptoms of non-cerebral etiology. Metabolomics is a powerful method to identify cellular damage through metabolic products, directly linked to pathophysiology. It can improve diagnostic accuracy and provide insights into the dysregulated mechanisms underlying studied pathologies.

<u>Methods (up to 3 lines)</u>:

CSF samples of patients will be analysed using very high-field NMR (950MHz). Data will be processed using dedicated software, and advanced multivariate statistical analysis (PCA, PLS-DA) will be performed to extract the most discriminant metabolites from the metabolome, and to investigate whether a diagnostic biomarker can be built.

Up to 3 relevant publications of the team:

MALLET D., DUFOURD T., DECOURT M., CARCENAC C., BOSSÙ P., VERLIN L., FERNAGUT PO., BENOIT-MARAND M., SPALLETTA G., BARBIER EL., CARNICELLA S., SGAMBATO V., **FAUVELLE F.*** BOULET S.* (* Co-senior authors). A metabolic biomarker predict Parkinson's disease at early stages in patients and in animal models, Journal of Clinical Investigations DOI: 10.1172/JCI146400, **2022**

LO PRESTI C., **FAUVELLE F**., JACOB MC., MONDET J., MOSSUZ P. The metabolic reprogramming in acute myeloid leukemia patients depends on their genotype and is a prognostic marker, Blood Advances doi.org/10.1182/bloodadvances.2020002981, **2021**

HAMELIN S., STUPAR V., MAZIERE L., GUO J., LABRIJI W., LIU C., BRETAGNOLLE L., PARROT S., BARBIER EL., DEPAULIS A., **FAUVELLE F**. In vivo GABA increase as a biomarker of the epileptogenic zone : an unbiased metabolomics approach, Epilepsia doi.org/10.1111/epi.16768, **2020**

Requested domains of expertise (up to 5 keywords):

Comfortable with analytical methods, statistics and with software handling. Some knowledge in R software.