



INSERM : the French National Institute of Health and Medical Research

INSERM U1205 - BrainTech Lab Medicine and Pharmacy University Grenoble Alpes

Bât Jean Roget - Domaine de la Merci

Place du Commandant Nal | 38700 La Tronche – Grenoble- France

Secretary: Andrea Randrianarisoa andrea.randrianarisoa@inserm.fr

+33 4 76 63 75 80 and/or +33 4 56 52 03 73

Fast-Field Cycling NMR relaxometry: towards physics driven precision medicine exploring glioblastoma water biology

This call of projects is launched by French Medical Research Foundation « Fondation de Recherche Médicale FRM » to promote the mobility of high level researchers in order to create their own team inside the host institution which should offer the required facilities. The application to this project proposal is considered as a required step to obtain a permanent researcher position in France.

Project: Oncogenic processes are complex and involve a huge number of molecular and physiological mechanisms. In recent decades, the identification and understanding of many causes of carcinogenesis at the cellular and molecular levels paved the way for the precision medicine breakthrough. However, many cancer types remain resistant to therapies. Among them, glioblastoma (GBM) is a typical example, which still resists to radio-chemotherapies as well as to the last generation targeted therapies with a median survival of 15 months. Tumor heterogeneity, molecular adaptation, as well as brain invasive and hypoxic/acidosic deregulated metabolic territories are key drivers of tumor aggressiveness. Therefore, new research approaches, in synergy with biomolecular information, are needed for deciphering the physical chemistry of cancer tumors and of their microenvironments. This requires a strong interdisciplinary effort integrating engineering sciences, biology, clinical investigation and modelling that is paradigmatic of BrainTech Lab INSERM U1205.

At the European level, we initiated extensive studies of GBM tissues, human glioma cells and glioma mouse models, using Fast-Field-Cycling NMR (FFC-NMR). This technology consists on using low and variable magnetic fields (<1T). We obtain T_1 -dispersion curves (T_1 vs magnetic field) which introduce field strength as new NMR dimension giving valuable information on the molecular dynamics of water from nano- to micrometer scale. As the part of H2020 IDentIFY project, we have recently shown that FFC-NMR signals are correlated with glioma invasion.

Based on this result, the objective of this collaborative project is to explore the major role of water dynamics in cancer processes by studying the role of the extra / intracellular water exchange by using aquaporin inhibitors and/or by acting on K^+ / Na^+ ion pump and the role of Warburg effect by modulating hypoxia, glycolysis, acidosis and invasion using inhibitors or pharmacological drugs.

This research axis should benefit from the Grenoble instrumentation developed by the H2020 IDentIFY project as well as on models available in the lab including different cell lines, organoids, preclinical models and human tissues from Grenoble biobank.

Laboratory of host institution: BrainTech Lab is a translational group aiming to develop innovative technologies to enhance the understanding, diagnosis and therapies of brain diseases. It is a research INSERM Unit (U1205) dedicated to the development of innovative technologies and methods for brain micro-environment theranostic, from basic to clinical research. The lab is organized around INSERM and hospital-university researchers involved in 3 themes : (i) Brain micro-structure micro-function imaging, (ii) Theragnostic micro-nano-implants for micro-environment deciphering and modulation, and (iii) Neurotechnologies for next generation precision medicine. Activities are supported by using different platforms including: Grenoble IRMaGe, FFC-NMR relaxometers of CEA, Grenoble neurosurgery biobank... This collaborative project is multidisciplinary, at the interface of physics, imaging, biology and medicine.

Applicant: Ph.D in sciences with a strong interdisciplinary experience in biophysics and/or biotechnology or equivalent. The applicant should be the head of a new team around the proposed project. The key responsibility will be to develop and conduct own line of research in cellular biology by designing biological research in line with the project. An experience in NMR/MRI will be appreciated. The applicant will also perform and follow FFC-NMR/MRI experiments and will use dedicated software and statistical analyses for data modelling and exploitation.

At least 3 years postdoctoral experience is desirable.

Procedure of selection: The date of application is between September the 10th and October the 31th. The project, if selected will be funded by the French Medical Research Foundation « Fondation de Recherche Médicale FRM».

The maximum allowed funding is 300K€ for 2 years. It is dedicated to the realisation of the research project, to the purchase of small equipments and should include salary of the candidate as well as the salary of postdoctorant, engineer or technician.

The candidate selection will be performed on 3 steps:

- (1) The interested candidate will be auditioned and ranked by a jury at host institution.
- (2) If selected by the jury, the candidate should provide to FRM : CV, list of its publications in which he is first and last author as well as a scientific project in line to the proposed one by the host Lab.
The number of auditionned candidates, the list of jury members, candidate ranking and the organigramm of the host institution should also be submitted to FRM.
- (3) The final decision comes from FRM institution and should depend on the candidates proposed by the other French labs.

Contact: If interested, please submit a CV, a cover letter as well as a recommended letter from the previous research institutions before October the 15th, to Hana Lahrech and François Berger and don't hesitate to contact them for more information on the job role.

Dr. Hana Lahrech (Physicist) and Prof François Berger (Neurooncologist)

hana.lahrech@univ-grenoble-alpes.fr and fberger@me.com

HL : +33 6 76 99 12 73 and FB : +33 7 82 46 20 26