MASTERBIOSCIENCES
ECOLE NORMALE SUPERIEURE DE LYON

Offre de stage de Master / Master Internship offer

Tuteur du stage et Laboratoire d'accueil / Internship supervisor and Host laboratory:

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Host team :
BIORAN – Radiopharmaceutical and Neurochemical Biomarkers
https://crnl.univ-lyon1.fr/index.php/en/Research/CRNL-teams-2016-2020/14
located at CERMEP – Imagerie du Vivant (https://www.cermep.fr/)

Titre du projet de recherche / Research project title:

Brain PET imaging after ultrasound-mediated BBB opening

Description du projet / Project description:

Blood-brain barrier (**BBB**) is a specialized structure that regulates molecular passage from the circulatory system into the brain. Focused ultrasound (**FUS**) combined with intravenously circulating microbubbles can transiently and selectively increase BBB permeability to enable targeted drug delivery to the brain (reviewed in **[1]**). An overlooked additional application consists in facilitating the entry of brain radiotracers for Positron Emission Tomography (**PET**), a nuclear imaging technique. In the process of radiotracer development, it is common to reject candidate molecules with high affinity and selectivity because they show poor brain uptake **[2]**. In the BIORAN team, we have developed a promising radiotracer targeting the serotonin receptor type 6 (5-HT6) **[3]**, which might have crucial implication in obesity and neurodegenerative diseases. However the use of [18F]2FNQ1P in rodent models is hampered by a strong P-gp efflux evidenced by cyclosporine treatment (**Fig.1**). In collaboration with the Laboratory of Therapeutic Applications of Ultrasound (LabTAU), we aim at testing the ability of focused ultrasound to promote an efficient and reproducible entry of the radiotracer, thus allowing quantitative and longitudinal PET imaging. Practical work will include combined FUS and PET experiments, high-resolution autoradiography, and image analysis.

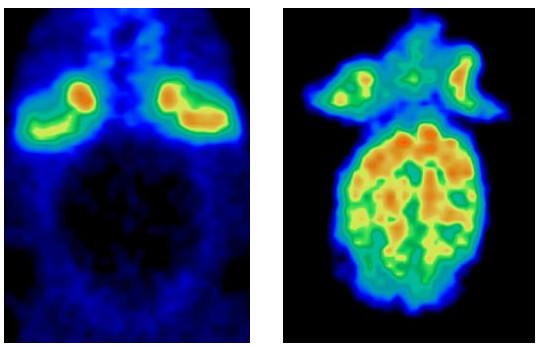

Figure 1. In vivo microPET summed images of rat brain after [18F]2FNQ1P injection (axial view; images summed for 0 – 90 min). Pseudo-colour scale is from low (blue) to high binding level (red).
(right) Lack of brain penetration in a control animal.
(left) Increased brain penetration after pre-treatment with cyclosporin (50 mg/kg, i.v.).

Publications du laboratoire (5 max) / Lab publications (5 max):

Publications related to project description:

1. TIMBIE KF, MEAD BP, PRICE RJ. 2015. Drug and gene delivery across the blood–brain barrier with focused ultrasound. Journal of Controlled Release 219:61-75.

2. LANCELOT S, ZIMMER L. 2010. Small-animal positron emission tomography as a tool for neuropharmacology. Trends in Pharmacological Sciences 31(9):411-417.

3. BECKER G, COLOMB J, SGAMBATO-FAURE V, TREMBLAY L, BILLARD T, ZIMMER L. 2015. Preclinical evaluation of [18F]2FNQ1P as the first fluorinated serotonin 5-HT6 radioligand for PET imaging. Eur J Nucl Med Mol Imaging 42(3):495-502.

Other lab publications:

VERDURAND M, LEVIGOUREUX E, LANCELOT S, ZEINYEH W, BILLARD T, QUADRIO I, PERRET-LIAUDET A, ZIMMER L, CHAUVEAU F. 2018. Amyloid-Beta Radiotracer [18F]BF-227 Does Not Bind to Cytoplasmic Glial Inclusions of Postmortem Multiple System Atrophy Brain Tissue. Contrast Media Mol Imaging 2018:9165458.

VERDURAND M, LEVIGOUREUX E, ZEINYEH W, BERTHIER L, MENDJEL-HERDA M, CADAROSSANESAIB F, BOUILLOT C, IECKER T, TERREUX R, LANCELOT S, CHAUVEAU F, BILLARD T, ZIMMER L. 2018. In Silico, in Vitro, and in Vivo Evaluation of New Candidates for α-Synuclein PET Imaging. Mol Pharmaceutics 15(8):3153-3166.