M2 internship position (by January 2019 to June 2019)

Opening of a Blood Brain Barrier on-a-chip

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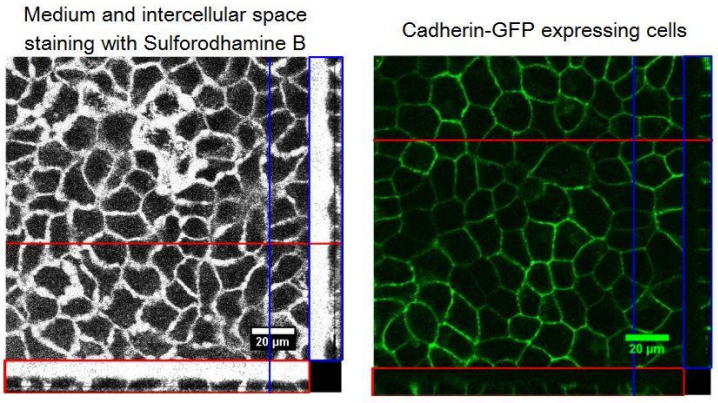
Brain is a notoriously difficult organ for therapeutic agents to reach due to the presence of the blood brain barrier (BBB), a specialized structure in the blood vessels and capillaries of central nervous system (CNS). The CNS-blood permeability can be significantly enhanced using ultrasound techniques, through the temporal opening of the BBB, providing a promising strategy to increase delivery of therapeutic agent into the brain.

The CARIBBBOU project associates the Laboratory of Therapeutic Applications of Ultrasound (LabTAU, Lyon, http://labtau.univ-lyon1.fr/ coordinator Claude INSERRA) and the Biophysics team of iLM (Jean-Paul RIEU). It aims to design and implement a real-time signal feedback for cavitation control to facilitate ulrasound-based gene therapy or drug delivery, with a particular focus on the BBB opening both in vitro (organ-on-chip models in Lyon) and in vivo (mouse, collaboration with two Taiwanese medical laboratories under an international ANR program). Control of cavitation is already implemented as well as the in vivo proof of concept. We concentrate now on the mechanisms of BBB opening in vitro.

For that, we focus on the BBB opening using MDCK cell monolayers standing on a porous membrane separating two channels. Stabilized air bubbles are inserted on one side together with soluble fluorescent agents (fluo-dextrans) mimicking therapeutic genes or drugs and we observe by fluorescence microscopy the BBB opening after insonification.



Before working with a homemade or commercial organ-on-a-chip, we need to establish the permeability properties MDCK cell monolayers in presence or absence of ultrasounds on more robust and easy to handle devices: we use transwells membranes with cell culture porous inserts. **The intern will perform cell culture on these inserts and microscopy experiments using epifluo and confocal single and two-photon microscopy. He will be in charge of the image analysis part using ImageJ and Matlab routines already existing but to be adapted**.

Please send by Email your CV with cover letter, and the names of referees familiar with your work to Jean-Paul, RIEU (jean-paul.rieu@univ-lyon1.fr)