Université de technologie de Compiègne – Thesis proposal

Part 1: Scientific sheet	
Thesis proposal title	Development of fat-on-chip model to study liver/fat tissue interactions during NAFLD progression.
PhD grant	Thesis funded by CNRS in the framework of the" Joint PH D Programme call University of Tokyo and CNRS.
Research laboratory	Lab of Biomechanics and Bioengineering BMBI UMR CNRS 7338, UTC. Website: https://bmbi.utc.fr/
Thesis supervisor(s)	Rachid Jellali, IR UTC/BMBI (directeur de thèse), Cécile Legallais, DR1 CNRS/BMBI (HDR, co-directeur de thèse), Eric Leclerc, DR1 CNRS/LIMMS (HDR, co-encadrent).
Scientific domain(s)	Biology, biomedical and health sciences Science and technology
Research work	Among metabolic diseases, non-alcoholic fatty liver disorder (NAFLD) is becoming the most frequent liver disease. Nowadays, it is estimated that around 24% of European adults develop NAFLD, 10-30% of them will evolve to NASH, among which 10-15% will develop fibrosis/cirrhosis and liver hepatocarcinoma. NAFLD prevalence increases to 57% in obese subjects, 70% in diabetic subjects and 90% in morbidly obese people. Although the food was identified as one source, the origin and the sequence of the development of the NAFLD is still controversial. Because NAFLD is systemic disease, the challenges are to consider the interactions between the different organs involved in the disease progression. In fact, the fat accumulation (adipocytes expansion) associated to NAFLD constitutes a serious threat in the disease development. Adipose tissue secretes free fatty acids (FFAs) and hormones, known as adipokines, and thus seems to play a major role in the development of NAFLD. To our knowledge, there is no relevant in vitro human "classical" 2D culture recapitulating the liver/adipose tissue interactions. Furthermore, animal studies fail to produce data that can be extrapolated to human. To address these issues, we propose an organ-on-chip strategy allowing to reproduce the fat and liver crosstalks. BMBI has developed a large panel of liver-on-chip models using cell line and primary hepatocytes. BMBI collaborates also with LIMMS (U Tokyo), which developing healthy and NAFLD multicellular liver-on-chip using hiPSCs. The present PhD project will focus on the development of fat-on-chip model. The first part of the PhD will request to optimize the fat cell culture conditions as well as the microfluidic system, to ensure the biological functionality of the model. For that purpose, adipocyte cell line will be cultured in spheroids in microfluidic biochip. To optimize the model, we will study the influence of several parameters: spheroids size, spheroids inoculation density, biochip design and flow rate. Then, human primary adipocyte will be used to propose relevant human fat-on-chip model. In the framework of the "Joint PHD Programme call University of Tokyo and CNRS", a second PhD student will develop healthy and NAFLD liver-on-chip model in Tokyo (LIMMS). The connection/crosstalks between the two developed organ-on-chip will be performed/studied during exchange visits between BMBI and LIMMS.
Key words	Adipocytes, 3D cell culture, microfluidics, organoid, organ-on-chip, NAFLD
Requirements	Candidate's experience: MS degree or engineering diploma with skills in cell culture, biotechnology, bioengineering and microfluidic devices. Autonomy

	and capacity to work within a group. B1/B2 Level in English (B2 level mandatory at the end of the PhD).
Starting time	October 1st, 2023
Location	The experiments will be located in Compiègne, France at BMBI (UTC). Visits to Tokyo University (LIMMS, Sakai-Nishikawa Lab) are planned as part of the "Joint PHD Programme call University of Tokyo and CNRS" program.

Part 2: Job description	
Duration	36 months
Additional missions available	Teaching (hands-on, internship follow-up) in the engineering school (UTC) will be possible during the second and third year of the PhD.
Research laboratory	**The laboratory of Biomechanics and Bioengineering** (a joint CNRS-UTC research Lab) covers a broad scope in the field of biomechanics and bioengineering. The multidisciplinary nature of the unit brings international expertise in biomedical engineering and tissue engineering for the design of bioartificial organs, fluid mechanics and microfluidics, transport phenomena, and the interactions between cells and tissues with the biomaterials.
Material resources	The lab is fully equipped for cell culture (L1 & L2 levels), microscopy, biological assays and mechanical characterization of the biohybrid tissues. It has also its own microfabrication platform.
Human resources	BMBI: 35 permanent staff, 28 PhD, 7 postdocs, distributed in 3 teams.
Financial resources	Financial support will be provided in the framework of the PhD program. Other resources will come for the labs' funds and from responses to calls (pending).
Working conditions	Office shared with other PhD students, computer, lab and UTC facilities. The candidate should be able to interact with the supervisors located in France and Japan. A degree of autonomy is therefore expected. Interactions with other PhDs, post-doc students and technical staff are also to be considered.
Research project	Joint PHD Programme call University of Tokyo and CNRS.
National collaborations	
International collaborations	**LIMMS** (a joint CNRS research laboratory with U. Tokyo) is internationally known for its strong expertise in bioengineering and microtechnology. Researchers are leaders in the differentiation of hiPSCs into hepatocytes and other hepatic cell phenotypes.
International cosupervision (cotutelle)	
Contact	***JELLALI Rachid (IR – UTC)*** rachid.jellali@utc.fr ***LEGALLAIS Cécile (DR1 CNRS)*** cecile.legallais@utc.fr ***LECLERC Eric (DR1 CNRS)*** *eleclerc@iis.u-tokyo.ac.jp*

Please contact first the thesis supervisor before applying online on https://webapplis.utc.fr/admissions/doctorants/accueil.jsf