PHD STUDENT POSITION OFFER	
Title	Development of a therapeutic screening platform for intestinal pathologies thanks to a controlled environment colon-on-chip
Acronym	GutScreen
Funding	CDD (funded by Défi Clé Biothérapie & ANR) *Emploiement:* INSERM
Contract lenght	36 months
Position starts on	1/10/ 2022
Teams	Equipe 'Interaction entre l'environnement et l'épithélium intestinal' Institut de Recherche en Santé Digestive (IRSD) INSERM U.1220, INRA UMR1416, ENVT, UT3 Bât B, CHU Purpan CS 60039 31024 Toulouse EliA Group (Engineering in Life sciences and Applications) LAAS CNRS 7 avenue du Colonel Roche 31031 Toulouse Cedex 4 – BP 54200 France
PhD Project	The intestinal epithelium is one of the main interfaces between the outside world and our internal organism. It establishes a dynamic barrier allowing the absorption of food nutrients and the exclusion of harmful compounds from light, while allowing the collection of antigens within the digestive tract. This ability to control absorption and protect against damage from harmful substances is defined as gut barrier function (IBF). IBF is altered in inflammatory bowel disease (IBD), but also cancer. IBD is characterized by chronic inflammation and impaired intestinal regeneration leading to an abnormal and incomplete healing process. Inflammation can be treated with anti-inflammatories, but no treatment allows the regeneration of the epithelium with all its functional characteristics. The intestinal stem cells (ISC) present in the intestinal crypts ensure the renewal of the entire intestinal mucosa within a week. In IBD, the regenerative capacities of ISCs are impaired. Despite research efforts, the understanding of the mechanisms involved in the regenerative capacities of human ISCs remains partial. 3D intestinal organoids allow the re-creation of intestinal epithelial mini-organs to study the ability of the ISC to reconstitute a fully functional epithelium. However, being cultured in 3D within a matrigel™, they do not correctly reproduce the intestine/colon topology and make access to the luminal compartment difficult. Thus, synthetic in vitro models such as organs-on-chip allowing the control of specific parameters (tissue topology, stiffness and distribution of nutrient fluxes) are necessary to study the light/epithelium interface and the impacts of tissue architecture on the behavior and fate of cells. Indeed, the human colon-on-chip is an innovative technology that has the potential to replace in vivo animal studies with in vitro models that mimic human physiology at basic levels. Organs-on-a-chip are designed to overcome the limitations of two-dimensional (2D) cell culture systems by mimicking 3D tissue organization and microenvironmental signals that are physiologically and clinically relevant. Unlike animal studies, these models can be configured for high-content or high-throughput screening in preclinical drug development. We have recently patented a colon-on-chip designed to provide dynamic luminal and basal control by injection into the system (culture medium, drugs, dyes, antibodies, microbiota, ...) as well as the creation of gradients and the possibility collect and analyze the outgoing flow in real time (metabolic parameters-pH, oxygen, lactate, etc.; analysis by mass spectrometry (MS)). This device, seeded with patient-derived colon organoids and fibroblast cultures

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	(healthy and IBD), will be an innovative and powerful tool to study human intestinal regeneration, as well as the events that affect or may affect the colon epithelium in IBDs such as IBF, interaction with microbiota, and impacts of nutrients/food contaminants/pollutants on the epithelium, as well as drug screening.
Contacts et Lieu d'activité	**Dr Audrey FERRAND** Equipe 'Interactions entre l'environnement et l'épithélium intestinal' Institut de Recherche en Santé Digestive (IRSD) INSERM U.1220, INRA UMR1416, ENVT, UT3 Bât B, CHU Purpan CS 60039 31024 Toulouse Tel : +33562744522 E-Mail : audrey.ferrand@inserm.fr **Dr Laurent MALAQUIN** ELiA Group LAAS CNRS 7 avenue du Colonel Roche 31031 Toulouse Cedex 4 – BP 54200 tel : +33 (0) 5 61 33 63 84 E-mail : laurent.malaquin@laas.fr *The thesis will be under the co-direction of Drs Audrey Ferrand (IRSD) and Laurent Malaquin (LAAS), the student will work within the IRSD but also on the LAAS site.*
Candidate	The candidate must have validated a Master 2 (or equivalent) with Honors in the fields of cell biology, biochemistry, oncology, physiopathology or biophysics. Ideally, he/she would also have knowledge of primary culture of human cells, transcriptional analyses, biomaterials, image analysis. He/she is motivated, organized, rigorous, autonomous and has an excellent team spirit. Two contacts (former internship supervisors, teachers, etc.) for the student's recommendation are necessary to validate the application. Please include their contact details in your letter of recommendation..
Contacts and Deadline for submitting your application	Please send your CV and a cover letter no later than **Wednesday July 20, 2022** to audrey.ferrand@inserm.fr and laurent.malaquin@laas.fr **Recruitment interview period** **If your application is accepted, an e-mail will be sent to you to invite you to an interview which will take place during the last week of July.**