Internship proposal (6 months, LAAS-CNRS + IRSD + IMFT, Toulouse, France)

Study of bacteria behaviour under an oxygen gradient in a 3D printed microfluidic chip

Subject:

In the gut, an oxygen gradient takes place from the epithelium lining (5% oxygen) toward the lumen (0% oxygen, anoxic condition). The microbiota therefore experiences different oxygen concentration, having a large impact on the bacteria's motility, metabolism and toxin secretion. In particular, the production of a mutagenic toxin called colibactin by some *Escherichia coli* strains is increased at low oxygen concentrations, a situation that arises in the anoxic lumen and in pathological context like inflammatory bowel disorders or cancers.



In the team "Pathogenesis and commensalism of enterobacteria" at the Institut de Recherche en Santé Digestive (IRSD), colibactin production in these situations has been studied for >3 years. For this proposed internship subject, a collaboration with the team "Porous & Biological media" in the Institut de Mécanique des Fluides de Toulouse (IMFT), specialist in the in-vitro study of bacteria and biofilms, and the team ELiA in the LAAS-CNRS, specialist in fabrication of microfluidic systems, has been set up to create a microfluidic chip containing an oxygen gradient and allowing the imaging of mobile and growing *E. coli* colonies and the production of colibactin with a fluorescent reporter. In this internship, we propose to explore the possibilities offered by stereolithography 3D-printing, associated with the integration of glass coverslip, in order to build a gradient generator from two medium inlets (one at 10%, the second at 0% oxygen) and a shallow imaging chamber. After the design, fabrication, characterization and validation of this microfluidic system and the generated oxygen gradient, the intern will culture genetically modified reporter *E. coli* strains inside the system and study optically the colibactin production depending on the oxygen gradient. This last part of the work will be performed in close collaboration with a PhD student already working between IMFT and IRSD as part of an ongoing collaboration.

Tasks and techniques:

During this internship, training on several techniques will be offered, including:

- Stereolithography 3D printing (design, fabrication)
- X-ray tomography
- Optical fluorescence microscopy
- Oxygen tension measurement
- Bacteria culture
- Molecular microbiology

Profiles with skills and knowledge in engineering, microfabrication, microfluidics, biophysics and/or microbiology are welcome.

Location and duration:

The internship will primarily take place in the LAAS-CNRS (3D printing microfabrication) among the ELiA team, specialized in the development of organ-on-chip and microphysiological systems, using clean room, 3D printing and bioprinting techniques. The intern will also visit regularly and perform experiments at IRSD and IMFT, both located on the same campus of the University Hospital (CHU Purpan).

The lab in the "Institut de Recherche en Santé Digestive" (IRSD) has a long-standing experience in the microbiology of genotoxic *E. coli* and developed reporters tools to follow toxin production under a fluorescence microscope.

The lab in IMFT uses microfluidic tools to study the biophysics of bacteria in controlled microenvironments. Microscopy experiments will be performed in the lab at IMFT in Purpan.

The internship is planned for a 6 months duration, starting on around February 2023 with a monthly allowance around $600 \in$.

Continuation as a PhD is planned.

<u>Contacts</u>

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