Postdoctoral/PhD position

Impact of mechanical confinement on bacterial physiology and antibiotic sensitivity

Research Project

Microbes frequently proliferate within complex space-limited environments, where they experience and adapt to mechanical forces to survive and proliferate. This occurs to many bacterial species during biofilm formation and inside specific niches during infection, however the mechanisms involved remain poorly understood. In the case of **meningococcal infection**, bacterial proliferation within the limited luminal space of blood vessels leads to the formation of dense colonies, blood flow drop and severe pathologies such as septic shock. We hypothesize that in these conditions, mechanical constraints sensed by bacteria might explain the pathophysiological features of the disease, in particular vascular damage and the emergence of antibiotic resistance.

We are looking for a talented researcher willing to investigate **how bacteria sense and adapt to mechanical cues and their physiological impact on bacterial communities.** To address this, we have designed the bacterial confiner in tight collaboration with the lab headed by Morgan Delarue (Cells under pressure, LAAS, Toulouse), a microfluidic chamber to monitor bacterial growth in a controlled mechano-chemical environment. This device has been validated on numerous bacterial species with varying shapes and envelopes, including pathogens. Thanks to the combination of last generation Spinning-Disk microscopy and advanced image analysis tools (Ershov et al, *Nat Methods*, 2022), we are now able to dynamically observe the impact of confinement on the morphology of different bacterial components and gene transcription using GFP-fusion reporters. Recent work on the biofilm-forming model organism *Escherichia coli*, allowed us to identify novel molecular pathways triggered upon confinement to allow adaptation under mechanical constraints, with potential implications in antibiotic response and infection outcome (Le Blanc et al, *in preparation*). Extension of this interdisciplinary approach to other bacteria including pathogens will provide **novel insights on the key parameters dictating mechanical resilience, bacterial physiology and stress adaptation from the single cell to the multicellular scale.**

Host Lab

This project will be hosted and funded by the Pathogenesis of Vascular infections Unit (Head: Guillaume Duménil) at Institut Pasteur, Paris and tightly supervised by a young investigator with an expertise in the biophysics of infection, Daria Bonazzi. Design and fabrication of adapted microfluidic chips will be performed at the LAAS. The candidate will be integrated in an interdisciplinary team that combines biochemistry, microbiology, cell biology, biophysics and animal models of infection, including a large expertise in the genetics of *Neisseria meningitidis*.

Activities

The candidate will apply innovative and ambitious approaches to reveal the impact of mechanical signals on bacterial physiology (*e.g.* growth and division, morphology of subcellular components, transcriptional response). This includes microfluidics, high-resolution live microscopy, image analysis and bacterial genetics. All these expertises are present in the host lab and reinforced by well-established collaborations inside and outside Institut Pasteur. Ideally, the candidate will start by the end of the year 2023 in order to be trained by Laure Le Blanc, a current PhD student who developed all the tools required for this project and will defend her thesis in the fall.

Knowledge & Skills

Expertise in the field of microbiology is strongly recommended. Prior experience with microfluidics, microscopy and image analysis will be a strong plus. The ability to interact with scientists across multiple labs specialized in quantitative imaging, biophysics and infectious diseases will be key to succeed in this project.

Please send a CV, a cover letter, a research statement summarizing previous work experience and research interests, and contact information of two references to Daria Bonazzi (daria.bonazzi@pasteur.fr) and Guillaume Duménil (Guillaume.dumenil@pasteur.fr)