Mechanobiology of meningococcal infection

Cells within a tissue experience forces from the surrounding environment and at the same time apply forces. The balance between all these forces is essential for tissue development and homeostasis. Tissue mechanics can also contribute to abnormal cell growth and disease progression, as in the case of cancer. During infection, pathogens enter into physical contact with the host tissue and induce major changes in host cell physiology and behavior, leading for instance to inflammation and tissue damage. Nevertheless, an open question in the host/pathogen interaction field remains: **how does bacterial infection impact host cell mechanics?**

Vascular colonization by *Neisseria meningitidis* is an excellent model in this context, as it depends on a series of mechanical processes, eventually causing severe pathologies such as septic shock and/or meningitis. These processes include bacterial adhesion to the blood vessel wall, proliferation to form aggregates and resistance to blood flow, leading to vascular damage. All these steps rely on type-IV pili, long dynamic fibers at the bacterial surface that can exert high pulling forces.

Interestingly, the study of pili dynamic properties has brought to the **discovery of novel fundamental concepts in the physics of living systems**: for instance, the active viscous fluid behavior of meningococcal aggregates (Bonazzi et al, *Cell*, 2018), and adhesion-mediated plasma membrane deformation through 1D-wetting (Charles-Orszag et al, *Nat Comm*, 2018).

Here, we will focus on **how cytoskeletal remodeling induced by bacteria perturbs host cell mechanics and physiology** at the single cell and tissue scale, potentially leading to force unbalance within the endothelium and vascular damage.

Methods used:

High-resolution live microscopy, biophysical methods such as traction force microscopy and micro-patterning, image analysis and modeling. Last-generation microscopy (FLIM-FRET, SIM, STORM) as well will be available on the Photonic Bioimaging Platform in Pasteur.

Knowledge & Skills

Background knowledge in the fields of cell biology, biophysics and/or microbiology is required. Prior experience with image analysis will be a strong plus.

Lab:

This project will be hosted in the Pathogenesis of Vascular infections Unit (https://research.pasteur.fr/en/team/pathogenesis-of-vascular-infections/, Head: G. Duménil) at Pasteur Institute, and supervised by a young investigator with an expertise in the biophysics of infection, Daria Bonazzi. The candidate will be integrated in an interdisciplinary team that combines biochemistry, microbiology, cell biology, biophysics and animal models of infection.

Contact: Daria Bonazzi (daria.bonazzi@pasteur.fr).