Interactions between bacterial liposaccharides and an “X” shaped peptide oligomer at interfaces: The X-factor in antimicrobial strategy?

To design new antimicrobial drugs, it is crucial to understand intimately the structure of, and the interactions at, the bacterial cell envelope. Gram-negative bacteria are a particularly difficult target as they possess an additional, highly asymmetric outer membrane, composed of bacteria-specific glycolipids called lipopolysaccharides (**LPS**). LPS is a component consisting of three parts: *Lipid A*, core oligosaccharide, and O-antigen, which differ in chemical structure and biological activity. The main objective of the project is to study interactions between LPS and surfaces with different chemistry – **especially the oligoglycine (an X-shaped peptide)**. The adsorption behaviour of LPS on surfaces of different physicochemical properties as a function of temperature, cation valency and concentration will be studied by Quartz Crystal Microbalance with Dissipation (QCM-D), Atomic Force Microscopy (AFM), Synchrotron X-Ray Reflectivity (XRR) and Neutron Reflectivity (NR). Furthermore, to shed light on the role of polysaccharide segments in LPS, we will compare it with its analogue LA without the saccharides. The layers will be formed by the adsorption and rupturing of LPS liposomes at the surfaces with different chemistry. Different types of surfaces will be used, including hydrophobic polystyrene (**PS**)-coated, and polyelectrolyte branched polyethyleneimine (**PEI**) or α-poly-L-lysine (**PLL**)/ hyaluronic acid (**HA**) coated surfaces, as well as the **X-peptide**-coated surfaces. Concurrently, self-assembly of the LPS molecules of different architectures in the solution will be investigated. The measurements will be made using Dynamic Light Scattering (DLS) and Small-angle Neutron Scattering (SANS) as a function of the solution conditions. Such knowledge will provide mechanistic understanding of the interactions between LPS/LA and other surfaces, and the correlations with different relevant physical parameters that characterise LPS and the medium.

There are two motivations for this study. **First**, successful surface arrest of LPS would point to a strategy for immobilising bacteria, particularly if it could be correlated with the molecular architecture of the X-peptide. This is important for designing related bacteria capturing and killing mechanisms. **Secondly**, such surface LPS layers will provide an ideal model system for studying the interactions mediated by LPS. The research proposed in this project will have **a positive and important impact on the development of our knowledge concerning the design and development of a new antimicrobial strategies.** The collected results will inform us on the feasibility of the strategy of using the X-shaped peptide for capturing (and then killing) Gram-negative bacteria at surfaces, which will be also a new scientific issue of practical significance and will lead to innovative approaches for novel biomedical applications.