Biomimetic LPS nanoparticles for interaction studies at the surface of Gram-negative bacteria

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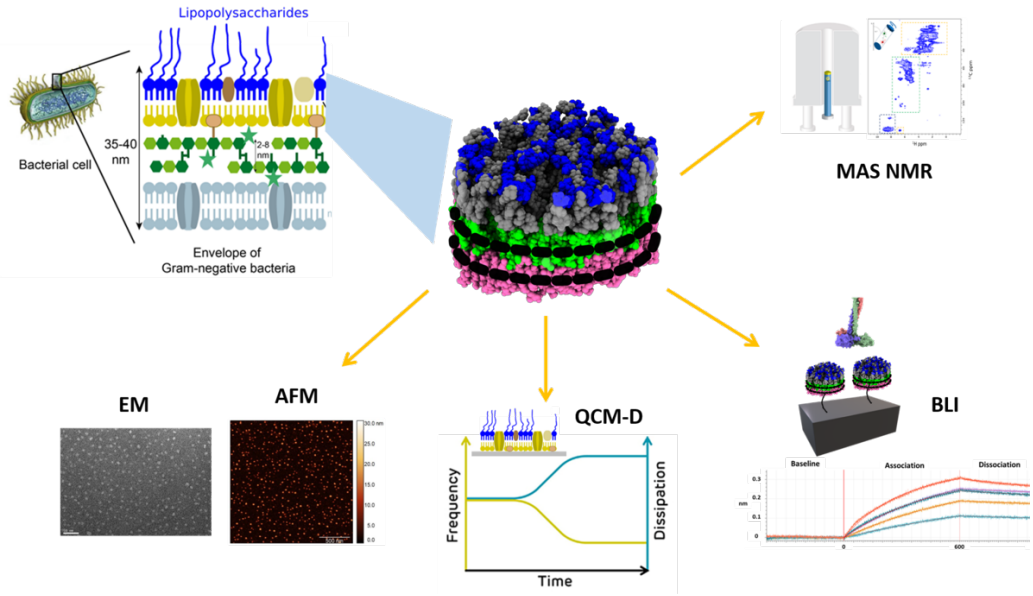
The envelope of Gram-negative bacteria is decorated with Lipopolysaccharides (LPSs) representing the main lipid component of its surface. They form an impermeable barrier and are key in antimicrobial resistance and virulence[1]. Ample studies have been conducted on LPSs' chemistry and biology, however, their interactions ruling the immune response modulation and antimicrobial resistance are not fully understood. In this context, there is a clear need for new methodologies to study intact LPS in a membrane-like environment. We have exploited the amphipathic copolymer nanodiscs technology[2] to form nanodiscs from purified LPSs or directly from bacterial outer membranes of pathogenic and non-pathogenic strains. This cell surface mimetic model was studied and validated by several biophysical methods; LPS nanodiscs can be obtained from a wide range of *E. coli* strains and form stable objects. Their size distribution and thickness were assessed by Dynamic Light Scattering and Atomic Force Microscopy. The different components of bacterial outer membranes can be observed at atomic scale, including phospholipids and the different LPS moieties, by solid-state NMR. LPS nanodiscs were also successfully used to monitor interactions with immunity C-type lectins and antibiotics by Quartz Crystal Microbalance and BioLayer Interferometry. LPS nanodiscs constitute a promising approach for the study of structure and interactions of LPSs. They could serve as an important tool in biomedical applications[3] and be used for high-throughput screening of gram-negative outer membrane binding profiles.



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