Towards the in-situ characterization of LipoPolySaccharides recognition by immunity C-type lectin receptors

Résumé

The outer membrane of Gram-negative bacteria is compositionally asymmetric with LipoPolySaccharides (LPS) covering most of the outer membrane surface, while phospholipids compose the inner leaflet. LPSs form a highly impermeable barrier and are critical in bacterial virulence; their structural variability and tight assembly protect bacteria against uptake of antimicrobials and in evasion from host defenses. C-type lectin receptors (CLRs) recognize exposed sugar residues present on self/non-self-structures and modulate immune responses. The recognition of specific glycans occurs through their carbohydrate recognition domains (CRDs) in a Ca2+-dependent manner. Macrophage Galactose-type C-type lectin (MGL) is a trimeric CLR expressed on the cell surface of macrophages and dendritic cells from skin and lymphoid organs. We show here that MGL is capable to bind *E. coli* cells that present a specific glycan motif. This high affinity interaction furthermore occurs in an independent manner with respect to the calcium binding site. Nuclear Magnetic Resonance, Small-angle X-ray scattering and Molecular Dynamics were used to characterize the novel MGL glycan binding mode that allows, through avidity high affinity interaction of MGL with the bacterial surface. Nevertheless, the accurate description of recognition events occurring at the bacterial cell-surface require experimental setups that mimic the outer membrane. We have developed the production of LPS nanodiscs from purified LPS and directly extracted from the outer membranes of pathogenic/non-pathogenic bacteria. The characterisation of those nano-objects by a combination of biophysical methods shows they provide an excellent model for the bacterial outer membrane and open perspectives for its study at high resolution in complex with proteins or antimicrobials.

Mots-Clés: LipoPolySaccharides, E. coli, lectins