Soutenance

THESE

Vendredi 16 Avril 2021 à 14h

Visioconférence

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Deciphering recognition patterns between Lipopolysaccharides and human lectins by Nuclear Magnetic Resonance spectroscopy

Thèse de Doctorat de l'Université de Grenoble

The tolerance of pathogenic strains or their clearance is covered by many immune cell receptors such as Pathogen Recognition Receptors (PRRs) including C-type lectin receptors (CLRs) that specifically interact with carbohydrates moieties. Lipopolysaccharide (LPS), expressed on the surface of bacteria, presents one of the signatures of Gram-negative by being both a structural and recognition motif by the host cell. The molecular diversity of both LPS (i.e. various carbohydrates, lengths and heterogeneity levels) and lectins (variable binding sites architectures) would confer them the particularity of controlling variable situations and targeting specific interactions. Investigating LPS-Lectins interactions is challenging and requires an interdisciplinary approach. On the above basis, we sought to investigate the interaction between a C-type lectin i.e. human Macrophage Galactose-type Lectin MGL and LPSs (from *E. coli* R1, R3 mutants and *E. coli* O157:H7 strain). The difficult experimental handling of such native biomolecules directed the use of a divided set of approaches. Our scientific strategy includes the use of Nuclear Magnetic Resonance NMR spectroscopy, fluorescence microscopy, and molecular binding essays. By combining these methods, we demonstrated that the Extracellular Domain (ECD) of MGL strongly and specifically interacts with *E. coli* R1 glycoconjugates at the surface of bacteria through its terminal di-galactose motif. The contribution of a putative secondary binding site on the Carbohydrate Recognition Domain (CRD) of MGL in *E. coli* glycoconjugates recognition remains to be investigated. This PhD work showed that, despite the difficulties that such large system studies may encounter, many findings are attainable by using our scientific strategy. The possibility of investigating data from atomic to cellular scale on LPS-lectin interactions in either modified or native states, opens prominent horizons for the study of bacterial infections.

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