

P18 & FP – Gut microbiota lipopolysaccharides: reverting the concept from bad to good

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The Gut Microbiota (GM) is an essential actor in the modern concept of human health driving many host physiological and pathological processes, including immune system modulation. Initial sensing of microbes by the host immunity is mediated by the recognition of microbial-associated molecular patterns, such as lipopolysaccharides (LPS), which are highly conserved among bacteria, thus shared by both commensals and pathogens. The LPS structure strongly influences the biological effects on the host immune system. Defined LPS structures can act as potent agonists on the immune receptors whereas others can operate as antagonists reducing or inhibiting the cytokine production otherwise induced by toxic LPSs.^[1,2] Thus, a crucial question to address is how the immune system distinguishes between permanently established commensal LPS and pathogen LPS.

The elucidation of the structure and the immunological activity of LPS isolated from gut microbes will bear new advances in the medicinal chemistry and in the field of search of new molecules able to antagonize pathogens LPS effect, as well as of GM LPS-inspired molecules able to prevent uncontrolled host immune response against our microbiota. This will also shed light on the structure-activity relationship of LPS itself, which is an open question in immunology field. In particular, this will improve the knowledge of the still poorly investigated GM world, giving insights in the host-microbe interaction mechanisms both at intestinal and systemic level furnishing, in parallel, information about the elicitation/modulation of immune response triggered by pathogens and commensals LPS, thus improving the overall knowledge of the immune system.

In this communication, I will show some very recently elucidated GM LPS structures and their immunological properties that revealed to express unique and interesting features. Among others, I will discuss about the structure and activity of LPS from *Bacteroides vulgatus* mpk, a commensal bacterium whose beneficial effects on health were clearly demonstrated.^[3,4] The full structure of such an LPS and of all the LPSs that will be presented, was defined by employment of a multi-technique approach comprising wet chemistry, NMR spectroscopy and mass spectrometry. The evaluation of the immunological properties of the above GM LPS has been investigated and will be also presented.

Insights gained from the structural and molecular analysis of GM LPSs might also help to chemically design novel inflammation-silencing drugs as a potential alternative therapeutic approach for the treatment of inflammatory disorders.

References

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- ^[3] Waidmann M et al *Gastroenterol.* 2003, 125, 162-177
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