

LIPOPOLYSACCHARIDES FROM MICROBIOTA: A JOURNEY FROM THE STRUCTURE TO THE FUNCTION

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The gut microbiota plays a fundamental role in modern health concepts, influencing various physiological and pathological processes in the human body, including immune system regulation. A key aspect of host immune surveillance involves the recognition of microbial-associated molecular patterns, such as lipopolysaccharides (LPS), which are characteristic of Gram-negative bacteria. These molecules are present not only in pathogenic species but also in commensal and mutualistic bacteria residing in the intestines [1,2].

Due to its chemical composition, LPS is widely recognized as a powerful inducer of inflammatory responses in mammals and is often linked to harmful bacteria and adverse health effects. However, LPS is also a structural component of the outer membrane of beneficial Gram-negative bacteria within the gut microbiota. The mechanisms that allow LPS from these commensal bacteria to be tolerated without triggering overt immune activation remain largely unexplored, representing a key frontier in our understanding of innate immunity [3]. Unraveling the chemical structure and immunological properties of LPS from gut microbes, particularly those maintaining a neutral or beneficial relationship with the human host, is of critical importance for both fundamental biology and clinical research. A thorough investigation of LPS from the gut microbiota will shed light on host-microbe interactions at both intestinal and systemic levels. This, in turn, will enhance our understanding of how gut bacteria influence immune responses through their LPS structures, ultimately expanding our knowledge of immune system dynamics. By analyzing microbiota-derived LPS, it will be possible to generate novel structural and functional insights that may drive innovation in biomedical research. These findings have the potential to contribute to the development of new immunotherapies and facilitate the identification of biomarkers for diagnosing, prognosticating, and predicting immune-mediated diseases.

In this communication, I will share recent and unprecedented findings on the structure and distinctive immunological characteristics of LPS from specific commensals of the human gut. Additionally, I will show some important advancements in structure-to-function studies on gut microbiota LPS, building on our previously published work.

References:

1. F. Di Lorenzo, C. De Castro, A. Silipo, A. Molinaro. *FEMS Microbiol. Rev.* **2019**, 43, 257
2. S. De Chiara, L. De Simone Carone, R. Cirella, E. Andretta, A. Silipo, A. Molinaro, M. Mercogliano, F. Di Lorenzo. *ChemMedChem* **2025**, e202400780.
3. F. Di Lorenzo, K.A. Duda, R. Lanzetta, A. Silipo, C. De Castro, A. Molinaro *Chem. Rev.* **2022**, 122, 15767-15821