STRUCTURAL CHARACTERIZATION AND IMMUNE RECOGNITION OF PAENALCALIGENES HOMINIS LIPOPOLYSACCHARIDES: EXPLORING POTENTIAL HOST-PATHOGEN INTERACTIONS

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The human gut microbiota plays a fundamental role in maintaining immune homeostasis and protecting against pathogenic invasions [1]. However, shifts in microbial composition, particularly in ageing populations, have been linked to inflammatory and neurodegenerative disorders. *Paenalcaligenes hominis*, a Gram-negative bacterium increasingly detected in the gut microbiota of elderly individuals, has been implicated in cognitive decline and gut-brain axis dysfunction. Despite this growing evidence, little is known about its molecular components and their role in host-pathogen interactions [2-3].
In this study, we focus on the structural and immunological characterisation of *P. hominis* lipopolysaccharide (LPS), a key mediator of bacterial-host communication. Using a multidisciplinary approach that combines chemical analyses, spectroscopy, computational modelling, and biophysical assays, we define the structural features of *P. hominis* LPS and its interaction with the immune system. Our findings reveal a distinct O-antigen composition enriched in rhamnose and glucosamine residues, with a non-stoichiometric O-acetylation pattern that could modulate immune recognition. Lipid A analysis identified a penta-acylated structure, correlating with reduced Toll-like receptor 4 (TLR4) activation compared to *Escherichia coli* LPS. Notably, microarray binding assays demonstrated recognition of *P. hominis* LPS by key immune lectins, including Ficolin-3 and Galectin-4, suggesting alternative immune pathways that may compensate for its weak TLR4 stimulation.
These findings provide the first detailed characterisation of *P. hominis* LPS and its immunomodulatory properties, offering insights into its potential role in microbiota-driven inflammation and neurodegeneration. Given its increasing prevalence in ageing individuals, further research is warranted to elucidate its contribution to gut dysbiosis and its broader implications in host immune regulation.

References:
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