VI IBIMED SYMPOSIUM

FROM FUNDAMENTAL RESEARCH TO CLINICAL PRACTICE

The impact of immunomodulation on host response and microbiota evolution

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ABSTRACT

The interplay between gut microbiota and the host is important for immunity development, colonization resistance and host metabolism. Antibiotic use disrupts host-microbiota interactions, potentially decreasing the colonization resistance conferred by the gut microbiota.

Lipopolysaccharide (LPS), an endotoxin present in Gram-negative bacteria, induces potent acute systemic inflammation. Nevertheless, it has also been suggested that treatment with low-dose LPS in a continuous manner, can act as an immunomodulator, conferring protective effects against infection.

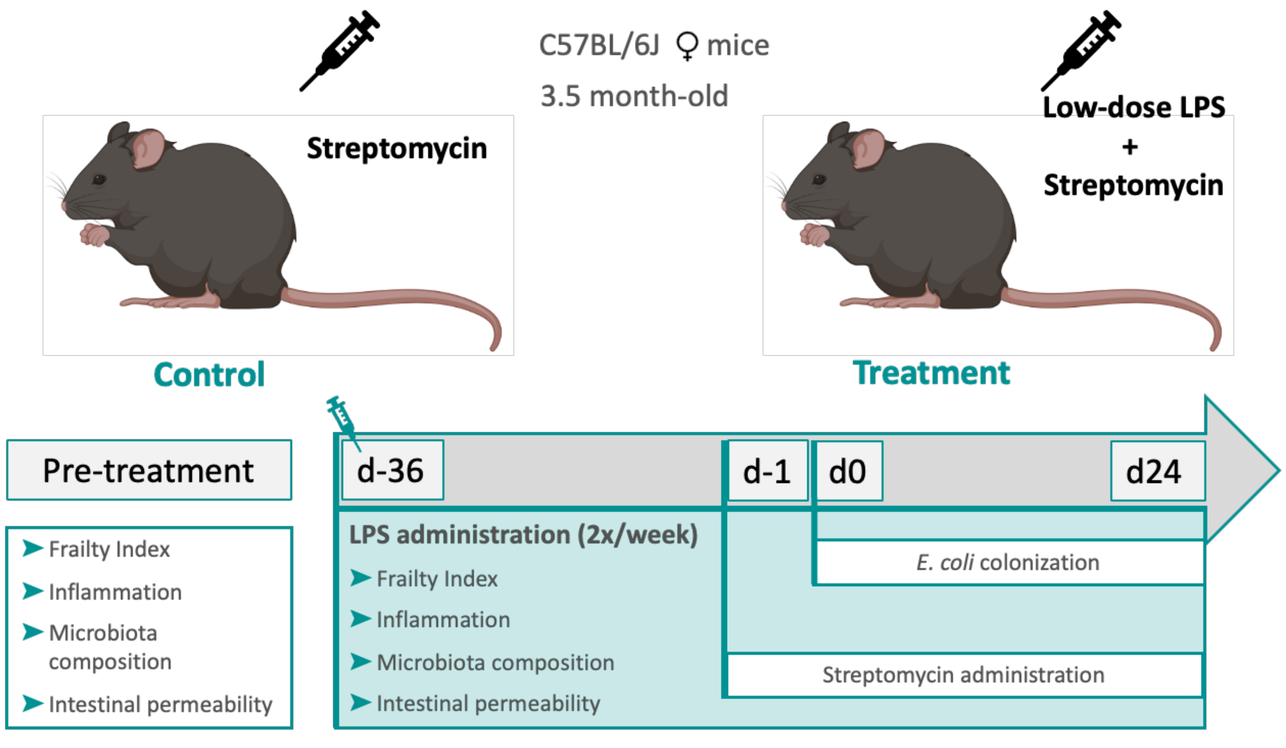
Additionally, the production of antimicrobial peptides (AMPs) impaired by the antibiotic treatment was previously observed to be restored upon LPS administration and therefore thought to be implicated in LPS protective effect. However, little is known about how immunomodulation (with low-dose LPS) impacts colonization resistance to non-pathogenic bacteria or how commensal microbiota evolve in an environment where the innate immune response is strengthened.

To answer these questions, mice were treated with streptomycin, previously reported to induce gut inflammation, and then colonized with a commensal strain of *Escherichia coli* by oral gavage. To test the impact of immunomodulation, LPS was administered to half of the animals prior to antibiotic treatment and gut colonization.

Immunomodulation by LPS led to a decreased production of TNF-α and IFN-γ when comparing with antibiotic treatment alone. Furthermore, LPS animals showed reduced gut damage as observed in the histopathological analysis and permeability assays. Additionally, LPS treatment delayed the colonization by *E. coli* in the gut as shown by the decreased count of CFUs.

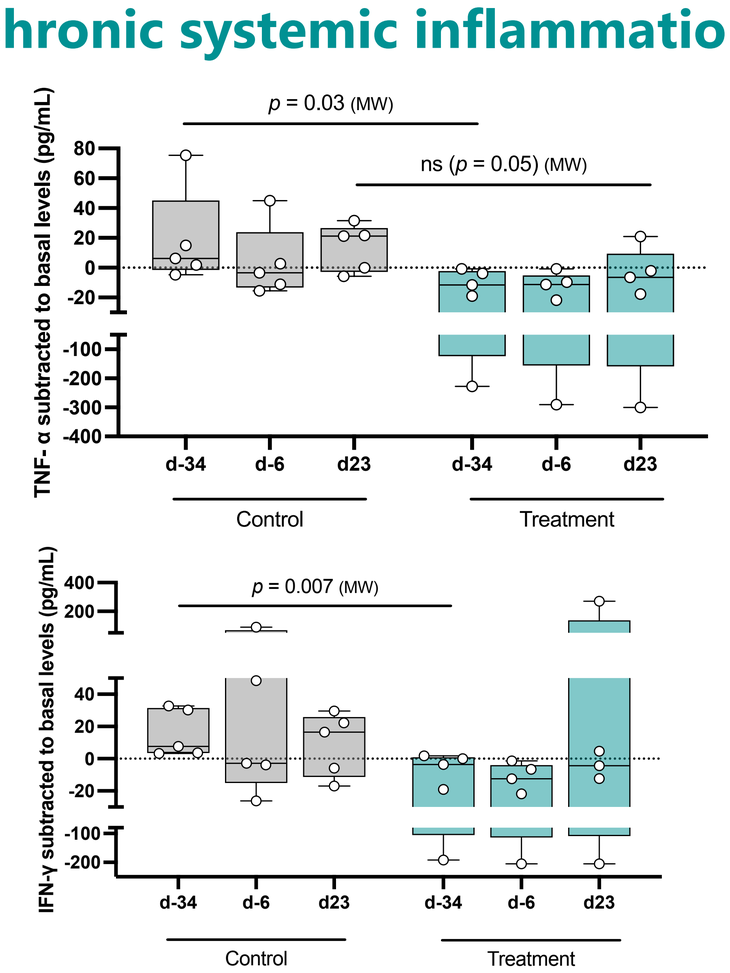
Our on-going project will evaluate how LPS treatment affects AMP expression and microbiota evolution. We expect to uncover distinctive adaptive signatures between LPS-treated and control mice, thus enhancing our understanding of the role of LPS in shaping microbiota and immunity.

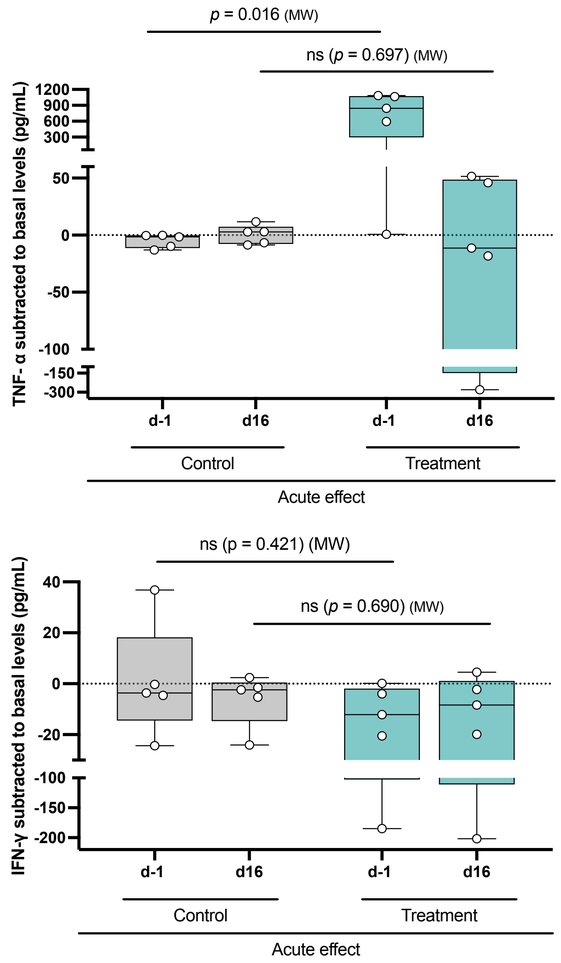
EXPERIMENTAL DESIGN



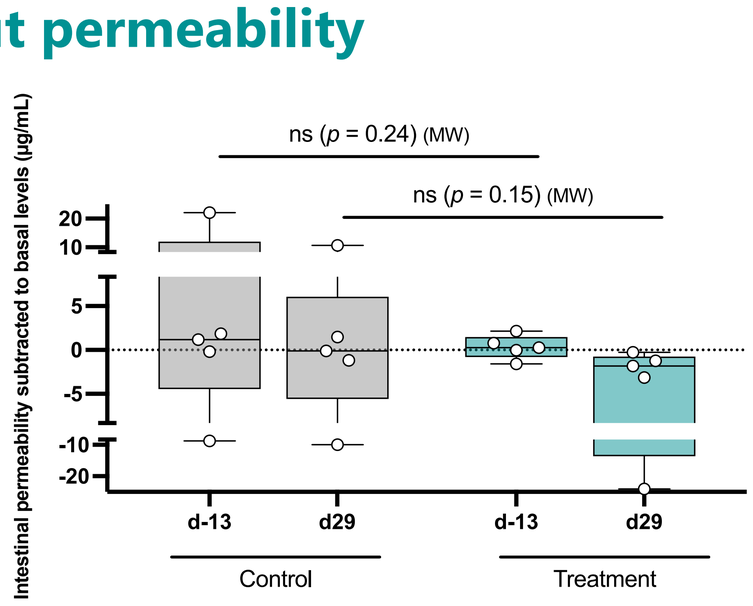
RESULTS

Low dose of LPS administration causes acute, but not chronic systemic inflammation

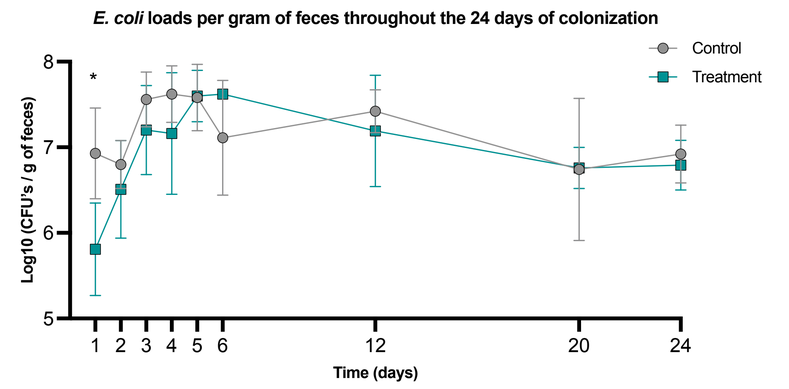


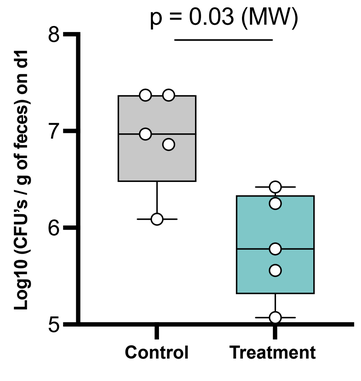


Stimulation with LPS does not affect gut permeability



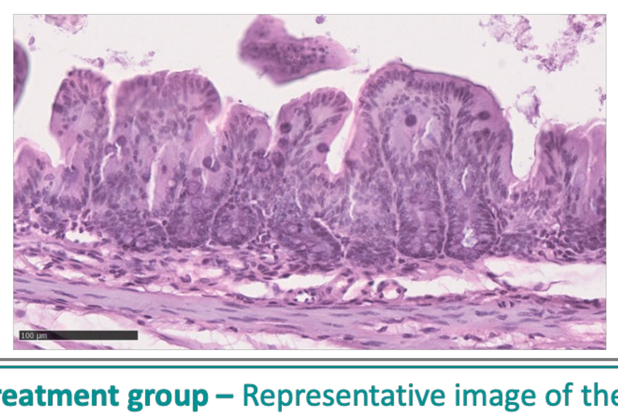
Stimulation with LPS increased gut colonization resistance to *E. coli* invasion after antibiotic treatment



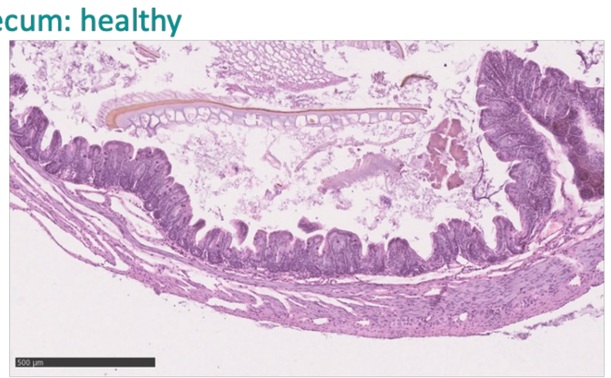


MW – Mann-Whitney test

Control group – Representative image of the cecum: intensive inflammation of the submucosa and muscle layers



Treatment group – Representative image of the cecum: healthy



FUTURE WORK

- **AMP characterization:** AMP levels between LPS-treated and control mice may be distinct and associate with colonization resistance in the gut
- **Microbiota profiling:** microbiota composition between LPS-treated and control mice may be different and associate with immunomodulation
- **Microbiota evolution:** distinct adaptive signatures between LPS-treated and control mice may reveal clues of the LPS interplay in shaping microbiota and immunity

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