“*Segatella copri* outer membrane vesicles compromise epithelial barrier integrity and trigger innate immune activation.”

Poster

Mucosal Immunology

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Background. The intestinal Gram-negative bacterium *Segatella*(*S.*) *copri* is increasingly associated with systemic inflammatory conditions, including rheumatoid arthritis (RA). It is enriched in the gut microbiota of early and pre-clinical RA patients, elicits specific T cell responses characteristic to RA patients and aggravates arthritis in mouse models. We have recently demonstrated that *S. copri* releases outer membrane vesicles (OMVs). OMVs from other intestinal pathobionts have been shown to transport virulence factors or bioactive molecules to distant tissues, promoting systemic inflammation. The epithelial-immune interface is critical in mediating host-microbiota interactions, however, the impact of *S. copri*-derived OMVs on epithelial and immune cells at this interface remains unclear. **Objective.** We investigated the internalization of *S. copri* OMVs and their effects on intestinal barrier integrity and pro-inflammatory responses in intestinal epithelial cells (IECs) and macrophages. **Methods.** OMVs were isolated from *S. copri* DSM18205 and characterized by TEM, NTA and proteomics. OMVs were used to stimulate C2BBe1 cells and THP1-derived

macrophages. Internalization of DiO-labelled OMVs was assessed by confocal microscopy and flow cytometry. Proinflammatory cytokine and tight junction expression was determined by RT-qPCR and confocal microscopy, respectively. **Results.** *S. copri* OMVs were internalized by IEC and macrophages, albeit with distinct kinetics. Furthermore, exposure to OMVs altered tight junction expression in IECs and promoted pro-inflammatory cytokine responses in both, IECs and human macrophages. **Conclusions.** *S. copri*-derived OMVs compromise the intestinal barrier integrity and activate innate immune responses. This highlights their potential role in promoting pro-inflammatory crosstalk at the epithelial-immune interface which might drive systemic inflammation.

Palabras Clave

(1) Epithelial-immune interface, (2) Outer Membrane Vesicles, (3) Pro-inflammation, (4) innate immune responses.

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