6.06 The microbiota-derived metabolite butyrate modulates the inflammatory and bacterial responses of lung macrophages and monocytes against *Streptococcus pneumoniae*.

Kate Roche[1], Craig P. McEntee[1], Ross W. Ward[1], Ed C. Lavelle[1] and Natalia Muñoz-Wolf[1]

[1]Trinity College Dublin, Ireland.

Background: *Streptococcus pneumoniae* is the leading cause of community acquired pneumonia and can cause invasive disease in susceptible cohorts. The gastrointestinal microbiota is the most diverse microbial niche in the body and has emerged as a potential regulator of respiratory infection through the gut-lung axis of immune regulation. Alterations in the intestinal microbiota can influence susceptibility to pneumococcal pneumonia by modulating circulating innate immune cells. Short chain fatty acids (SCFA) are microbiota-derived metabolites with immunomodulatory properties that can reach the lung via the circulation. The SCFA butyrate, may modulate the phenotype and response of respiratory macrophages and monocytes during infection.

Methods: An *in vivo* model of invasive pneumococcal pneumonia was used. *Ex vivo* alveolar macrophages (MexAMs), bone marrow derived macrophages and the human monocytic cell line THP-1 were stimulated with TLR2 and TLR4 agonists or pneumococcal antigens from three clinical isolates in the presence or absence of butyrate.

Results: Butyrate enhanced monocyte recruitment during *S. pneumoniae* infection and increased survival while limiting disease severity *in vivo*. Butyrate moderately increased IL-1β production and demonstrated a potential role in priming NLRP3 inflammasome activation.

Conclusions: Butyrate modulates macrophage phenotype and function in the context of *S. pneumoniae* infection.

Keywords: Gut-lung axis, short chain fatty acids, *S. pneumoniae*

Disclosures: This project is funded by Health Research Board (HRB). The authors declare that they have no conflict of interest.