OC04 & P02 - **The Role of Exopolysaccharide in Modulating Host Immune Responses towards *Bifidobacterium breve***

Ana C. Hickey[1,2,3], Valerio Rossini[1], Panagiota Stamou[1], Sreeram Udayan[1,2,3], Francesca Bottacini[1,3], Silvia Melgar[1], Douwe Van Sinderen[1,3], Ken Nally[1,2]

[1]*APC Microbiome Ireland, University College Cork, Ireland.*

[2]*School of Biochemistry and Cell Biology, University College Cork, Ireland.*

[3]*School of Microbiology, University College Cork, Ireland.*

ana.hickey@umail.ucc.ie

Bifidobacteria are one of the earliest colonisers of the human infant intestine. Their presence in the gastrointestinal tract has been linked to improved epithelial barrier function and reduced inflammation through the induction of Treg cells and interleukin-10 production[1]. While different surface features of Bifidobacteria have been linked to these immunomodulatory effects, exopolysaccharide (EPS) has shown interesting effects in different mouse and human systems[2]. EPS is a high molecular weight polysaccharide which can be surface associated or secreted. In *B. breve* and other commensal bacteria EPS has been linked to T cell homeostasis and protection from infectious models of murine colitis[3].

Our work focused on characterising the role of EPS in modulating host responses towards different *B. breve* strains. To do this we used a panel of wild-type *B. breve* strains and EPS negative mutants of two of these strains – *B. breve* UCC2003 and JCM7017. We firstly assessed the ability of these strains to produce EPS. Following this, we used parental and MyD88 deficient THP-1 monocyte reporter cell lines to assess if EPS status correlated with NF-κB responses. We subsequently concentrated on defining the role of EPS in *B. breve* UCC2003 and JCM7017 using their EPSneg mutants. We screened these bacteria for their ability to induce cytokine production from fluorescence activated cell sorting (FACS) sorted bone marrow derived macrophages and dendritic cells and examined their ability to persistence within these cells. We have also compared the role of EPS in the colonisation of *B. breve* JCM7017 in vivo.

Our results show that there is a heterogeneity of EPS expression between different *B. breve* strains and that the NF-κB response to these cells, although being MyD88 dependent for all, did not correlate with EPS status of the bacteria. While it appeared that *B. breve* UCC2003 utilises EPS to dampen macrophage cytokine responses, the opposite was observed for *B. breve* JCM7017. Likewise, EPS played a different role in the persistence of these bacteria intracellularly and impacted *B. breve* JCM7017 colonisation in vivo differently to what has been observed previously for *B. breve* UCC2003.

These results suggest that EPS from *B. breve* UCC2003 and *B. breve* JCM7017 and perhaps other Bifidobacteria has divergent effects on host immune responses and on the behaviour of the bacteria in vivo.

References

1. *Bifidobacteria and Their Molecular Communication with the Immune System*. Ruiz, L., Delgado, S., Ruas-Madiedo, P., Sánchez, B., Margolles, A. Frontiers Microbiology 2017;8(2345).

2. *Bifidobacterial surface-exopolysaccharide facilitates commensal-host interaction through immune modulation and pathogen protection*. Fanning S, Hall LJ, Cronin M, Zomer A, MacSharry J, Goulding D, et al. Proc Nat Acad Sci. 2012;109(6):2108-13.

3. *Protection from Intestinal Inflammation by Bacterial Exopolysaccharides*. Jones, SE, Paynich, ML, Kearns, DB, Knight, KL. J Immunology. 192 (10) 4813-4820