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BIFIDOBACTERIUM SPECIES REDUCE LIPOPOLYSACCHARIDE-INDUCED SMALL INTESTINAL EPITHELIAL CELL SHEDDING IN VIVO IN A MYD88-DEPENDENT MANNER AND PROTECT AGAINST DSS-INDUCED COLITIS

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Introduction Cell shedding, the process by which intestinal epithelial cells (IECs) are extruded from the small intestinal (SI) villus is known to be elevated in patients with inflammatory bowel disease (IBD) and is correlated with disease relapse. Importantly, there is evidence that the gut bacterial communities (microbiota) influence intestinal epithelial function including gene expression, cell division and energy balance. We thus sought to determine whether specific members of the microbiota, ‘probiotic’ bifidobacterial species, modulate rates of cell shedding and progression of Dextran sodium sulphate (DSS)-mediated colitis.

Methods C57BL/6 mice (WT) or mice deficient in echinulin Melody (Vil-Cre +; Melody KO) were orally gavaged with 1 × 10^8 bifidobacterium breve UC2003, B. longum NCIMB8809 or PBS (control) in 3x daily doses. To induce SI cell shedding, mice were injected with 1.25 mg kg^-1 Lipopolysaccharide (LPS) intraperitoneally. Animals were euthanized and post-LPS and SI tissue sections analysed for cell shedding along the first 50 cell positions from the villus tip. For colitis studies, control mice or mice colonised with B. breve were administered 2% DSS in drinking water for 6 days and euthanized 8 days post-DSS. Disease activity index (DAI) was recorded daily and histology performed on formalin-fixed tissue sections including periodic acid/Schiff (PAS) stain (goblet cell stain).

Results Mice receiving B. breve and B. longum showed less CC3 +ve shedding cells (3.6% +/-0.6, p < 0.001 and 7.6% +/-2.9, ns, respectively) compared to WT mice (10.6% +/-1.3). Interestingly, the protective effect of B. breve was lost in Melody KO mice receiving LPS as numbers of CC3 +ve IECs were the same in mice receiving B. breve or vehicle control (13.3% +/-1.7 vs 10.4% +/-1.3; ns), indicating that the protective effect may be mediated by Toll-like receptors. In our colitis model, mice colonised with B. breve had reduced DAI compared to control mice, coupled with a significant increase in numbers of PAS +ve goblet cells per crypt (8.2% +/-1.6 vs 16.0% +/-2.6; p = 0.03).

Conclusion Bifidobacterial species modulate a reduction in rates of cell shedding from the SI villus, potentially via the Melody signalling pathway. B. breve is also able to partially ameliorate the adverse effects of DSS-induced colitis through induction of goblet cells. In summary, bifidobacteria, particularly B. breve, may be beneficial as a therapeutic agent for IBD.

Disclosure of Interest None Declared.