

Nutrition Society Live 2020, 14-15th July 2020

## Microbiota-independent immunological effects of Bimuno<sup>®</sup> galactooligosaccharide in the context of inflammatory bowel diseases

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Inflammatory bowel diseases (IBD) are chronic conditions affecting the gastrointestinal tract. Individuals with IBD display an aberrant immune response to commensal microbiota, resulting in extensive mucosal inflammation and increased gut permeability<sup>(1)</sup>. Galactooligosaccharides (GOS) are prebiotics with a positive role in supporting gut health. They reach the colon and are fermented by commensal bacteria, resulting in the production of short chain fatty acids with immunomodulatory properties<sup>(2)</sup>. Since the gut of IBD patients is leaky, prebiotics may also bypass the intestinal barrier and directly interact with immune cells<sup>(3,4)</sup>. The aim of this study was to assess the microbiota-independent immunological effects of Bimuno® galactooligosaccharide on peripheral blood mononuclear cells (PBMCs) challenged with lipopolysaccharide (LPS).

PBMCs (n = 5) were cultured with Bimuno® galactooligosaccharide (GOS 12 mg/mL) and LPS (1 µg/mL) for 24 h. Cell viability and immune cell phenotypes were evaluated by flow cytometry. Ten secretory cytokines and granzyme B were assessed by Luminex assay. One-way ANOVA followed by Bonferroni *post hoc* test or Kruskal-Wallis followed by Dunn's post hoc tests were performed dependent upon distribution of data.

PBMCs tolerated treatment with Bimuno® galactooligosaccharide, with mean viability >80% and no significant differences compared to unstimulated control or LPS-challenge only. Bimuno® galactooligosaccharide did not alter the proportions of immune cell phenotypes. PBMCs cultured with Bimuno® galactooligosaccharide and challenged with LPS demonstrated lower secretion of several mediators involved in the TLR response, such as IL-1 $\alpha$  (0.08  $\pm$  0.09 vs 0.36  $\pm$  0.22 ng/mL), IL-1 $\beta$  (0.67  $\pm$  0.26 vs 14.3  $\pm$  2.1 ng/mL) and IL-1 $\alpha$  (5.6  $\pm$  2.7 vs 45.2  $\pm$  5.1 ng/mL) compared to LPS-challenge alone (all P < 0.05). These results suggest that Bimuno® galactooligosaccharide may directly act on monocytes and T cells, with a proposed mechanism of action through toll-like receptors.

Available literature and our findings support a role for Bimuno® galactooligosaccharide in directly interacting with immune cells and modulating the secretion of cytokines. Future research will be required to explore how observed changes in both pro-inflammatory and anti-inflammatory cytokine secretion of PBMC relate to the anti-inflammatory *in vivo* effects of prebiotic supplements observed in both animal models and human studies.

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