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## Cytokine production by peripheral blood mononuclear cells (PBMCs) stimulated by *Bifidobacteria* spp. or galactooligosaccharide

M. Baran<sup>1</sup>, S. Kolida<sup>1</sup>, C. Childs<sup>1</sup>, P. Yaqoob<sup>1</sup>, G. Tzortzis<sup>2</sup> and R. Rastall<sup>1</sup><sup>1</sup>University of Reading, Food Biosciences, PO Box 226, Whiteknights, Reading RG6 6AP and <sup>2</sup>Clasado Ltd, 5 Canon Harnett Court, Milton Keynes MK12 5NF, UK

The relationship between gut microbiota and intestinal immune response has been intensively studied. Several studies showed that bifidobacteria enhance many aspects of immune function<sup>(1–3)</sup>. It is suggested that probiotic strains can be screened *in vitro* for their immunomodulatory potential using peripheral blood mononuclear cells (PBMCs), before clinical (*in vivo*) investigations<sup>(1)</sup>. Galactooligosaccharides (GOS) are one of the best established prebiotic compounds; however, immunomodulatory properties of prebiotics are not yet fully understood.

*In vitro* studies to date have employed either live<sup>(1,3)</sup> or heat-killed bacterial cells<sup>(4)</sup>, but rarely both. This study compares cytokine production in response to live and heat-killed bifidobacteria by human PBMC. Furthermore, it investigates different concentrations of GOS, which will induce TNF- $\alpha$  production by PBMCs.

In this study live and heat-killed *Bifidobacterium lactis* HOWARU and *Bifidobacterium bifidum* NCIMB 41171 were co-cultured with human PBMC isolated from the blood of healthy donors ( $n = 4$ ). Their effects on pro- and anti-inflammatory cytokine production were investigated.

In order to determine the effect of GOS, PBMCs were incubated in the presence of different concentrations of GOS with or without LPS (0.001  $\mu\text{g/l}$ ).

Regardless of whether bacteria were live or heat-killed, both *B. lactis* and *B. bifidum* stimulated cytokine production by PBMC. *B. lactis* induced a significant increase in the production of IL-1 $\beta$  ( $P \leq 0.01$ ) and TNF- $\alpha$  ( $P < 0.05$ ) compared to the unstimulated control, and *B. bifidum* NCIMB41171 showed a similar trend. No significant change in IL-10 production was observed. There was no effect of heat killing on cytokine production, or on the ratio between pro-inflammatory and anti-inflammatory cytokines for either bacterial strain.

7 and 5.5 g/l of GOS stimulate significantly PBMCs to produce TNF- $\alpha$ . In the presence of LPS, GOS stimulate the TNF- $\alpha$  level significantly higher than in the absence of LPS thus LPS have additive effect.

In conclusion, both species of bifidobacteria induced production of IL-1 $\beta$  and TNF- $\alpha$  but not on IL-10, regardless of whether the cells were live or heat-killed. High concentration of GOS is also able to induce PBMCs to produce cytokines.

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