Proceedings of the Nutrition Society (2008), **67 (OCE)**, E162 doi:10.1017/S0029665108007945

Joint meeting of the Société Française de Nutrition and The Nutrition Society, 6–7 December 2007

Effect of *Bifidobacterium breve* C50 on intestinal epithelial function in inflammatory condition

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Probiotics and/or commensal bacteria are considered to be beneficial to the host, including at the intestinal level. The mechanisms involved in the cross talk between probiotic bacteria, the intestinal epithelium and the underlying immune system, particularly those allowing the development of anti-inflammatory effects, are not fully understood. Moreover, the effects of probiotics on intestinal hydro–electrolytic balance and the mechanisms involved are poorly studied. Thus, the direct effect of the living probiotic bacteria *Bifidobacterium breve* C50 (*Bb*) or its conditioned media (*Bb*-CM) and of other Gram + bacteria on (1) the release of various epithelial molecules (chemokines, cytokines, growth factors, others) in inflammation and (2) ionic secretion were analysed in order to better understand epithelial–bacteria interactions.

The direct effect of various bacteria (*Bb* or *Bb*-CM, *Lactobacillus rhamnosus ATCC 10863*, *B. breve ATCC 15698*, *Eubacterium rectale L15*) on TNFα-induced secretion of IL-8 (ELISA) or of various other epithelial molecules (chemokines, cytokines, growth factors, others) using a cytokine microarray, were assessed in the intestinal epithelial cell line HT29-Cl.19A. The effects of *Bb*-CM on NF-κB) and activator protein 1 (AP-1) pathways were assessed by electrophoretic mobility shift assay, confocal microscopy and Western Blot (inhibitory subunit of NF-κB (IκBα), p38-mitogen-activated protein kinase (MAPK)). Living or latent bacteria were exposed on HT29-Cl.19A monolayers that were mounted in Ussing chambers to assess their effects on carbachol-stimulated chloride secretion.

Bb or *Bb*-CM, in contrast to other bacteria strains, induced a time- and dose-dependent inhibition of IL-8 secretion by epithelial cells ($\leq 73\%$) and increased the release of epithelial transforming growth factor β and of various growth factors. The inhibition of IL-8 secretion was shown to involve a decrease in nuclear translocation of the two transcription factors NF-κB and AP-1. Accordingly, the phosphorylation of p38-MAPK and IκBα was also decreased, suggesting that *Bb* targets both IL-8 signal transduction pathways. Carbachol-stimulated chloride secretion was inhibited in a dose-dependent manner by living *Bb* but not by the other bacterial strains. The inhibitory effect on IL-8 and on chloride secretion was not the result of a bacteria-induced decrease in the viability of HT29-Cl.19A cells, as attested by transepithelial electrical resistance, cytokeratin cleavage or lactate dehydrogenase release.

These results allow a better understanding of the mechanisms by which the bacterial strain *B. breve* C50 can moderate intestinal inflammation *in vitro* and suggest that the inhibitory effect on fluid and electrolyte secretion may be beneficial in secretory diarrhoea.