

The effect of different probiotic strains on immune function *in vitro*

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Lactobacilli and bifidobacteria are two major probiotic species used in the food industry. The modulation of immune function by probiotics has become a hot topic in the recent years. The immune response to probiotics is generally regarded to be strain-dependent. However, evidence for this is rather limited, particular with regard to the cellular immune response. The aim of the current study was to compare the immunomodulatory properties of different probiotic strains in a human blood mononuclear cell model *in vitro*.

Live cells of four *Lactobacillus* strains (*Lactobacillus casei* Shirota, *Lactobacillus rhamnosus* GG, *Lactobacillus plantarum* NCIMB 8826, *Lactobacillus reuteri* NCIMB 11951/ATCC23272) and two *Bifidobacterium* strains (*Bifidobacterium longum* SP 07/3, and *Bifidobacterium bifidum* MF 20/5) were individually incubated with human peripheral blood mononuclear cells from seven healthy older subjects at a ratio of 1:1 for 24 h. Expression of the activation markers, CD69 and CD25, and natural killer cell activity were assessed by flow cytometry. Supernatants were collected for cytokine measurement (flow cytometry or ELISA).

All six strains stimulated CD69 expression on CD3⁺CD8⁺ (cytotoxic T cells; Tc) and CD3⁻CD56⁺ (natural killer; NK cells) subsets, but increased CD25 expression only on NK cells. All strains also increased the level of expression (mean fluorescence intensity; MFI) of CD69 on CD4⁺ (Th) and CD3⁺CD56⁺ (NKT cells) subsets, and all strains, except for *L. casei* Shirota and *L. reuteri* NCIMB 11951, induced CD25 expression (MFI) by NKT cells. NK cell activity was significantly increased by all six strains, without any difference between strains. All of the strains increased the production of IL-1β, IL-6, IL-10, TNF-α, GM-CSF, MIP-1α to different extents, but had no effect on IL-2, IL-4, IL-5, or TNF-β production. Four of the cytokines/chemokines analysed were differentially regulated by the probiotics; these were interferon-γ (IFN-γ), regulated upon activation, normal T-cell expressed and secreted (RANTES), IL-12 and MCP-1. Table 1 summarises the effects of the six strains on these mediators. IFN-γ and RANTES production was stimulated by all strains except for *L. rhamnosus* GG and LPS (*P* = 0.062–0.05). IL-12 production was only increased by *L. casei* Shirota and *L. plantarum* NCIMB 8826 (*P* < 0.001). IL-8 production was induced by all *lactobacillus* strains except for *L. reuteri* NCIMB 11951 (*P* = 0.083–0.05). MCP-1 production was only induced by bifidobacteria and LPS (*P* = 0.075–0.05). In addition, bifidobacteria and LPS were more potent inducers of IL-10 than lactobacilli. All strains, except for *L. reuteri* NCIMB 11951, induced more IL-1β and TNF-α production than LPS.

The results suggested that there was little evidence of strain-specific effects on T cell activation or natural killer cell activity, while the production of some cytokines and chemokines was differentially influenced by probiotic strains. The biological importance of these selected strain-specific effects remains to be determined.

Cytokine production	Probiotic strains						
	LPS	<i>L. casei</i> Shirota	<i>L. rhamnosus</i> GG	<i>L. plantarum</i> NCIMB 8826	<i>L. reuteri</i> NCIMB 11951	<i>B. longum</i> SP 07/3	<i>B. bifidum</i> MF 20/5
IFN-γ	-	↑	-	↑	↑	↑	↑
RANTES	-	↑	-	↑	↑	↑	↑
IL-12	-	↑	-	↑	-	-	-
IL-8	-	↑	↑	↑	-	-	-
MCP-1	↑	-	-	-	-	↑	↑

↑ increase, - no change compared with the negative control.

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