Proceedings of the Nutrition Society (2010), **69 (OCE1)**, E31 doi:10.1017/S0029665109992199

Over- and undernutrition: challenges and approaches. 29 June–2 July 2009

Effects of *Lactobacillus casei* Shirota on immune function

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Modulation of host immunity is an important potential mechanism by which probiotics confer health benefits[(1)]. The present study was designed to investigate the effect of a probiotic strain *Lactobacillus casei* Shirota (LcS) on the immune function using human peripheral blood mononuclear cells (PBMC) *in vitro*.

PBMC were obtained from eleven healthy adults. LcS were grown in MRS broth (CD0359; Oxoid Ltd, Basingstoke, Hants., UK) anaerobically and harvested in the exponential phase. PBMC (2×10^6 cells/ml) were exposed to three different concentrations of viable LcS for 24 h with or without 2.5 μg concanavalin A (ConA)/ml. The activation markers, CD69 and CD25, on T-cell subsets were assessed by flow cytometry[(2)]. Whole blood (WB) or PBMC were stimulated for 24 h by three different concentrations of viable LcS with or without 1 μg lipopolysaccharide (LPS)/ml and cytokines were measured by ELISA[(3)].

In the absence of ConA LcS induced expression of both CD69 and CD25 on CD8+ T-cell subset, but had less effect on CD4+ T-cells and LcS had no further effect on ConA-stimulated cultures (Fig 1). The maximal effect was seen with 10^6 CFU/ml, representing an LcS:PBMC of 1:1. LcS alone induced production of IL-1β, IL-6, TNFα, IL-12 and IL-10, but greatly inhibited LPS-induced IL-10 and IL-6 production (Fig 2). Cytokine production was also measured in WB. Production of cytokines in response to LcS and/or LPS by PBMC and WB was highly correlated (r 0.69–0.83, $P<0.01$).

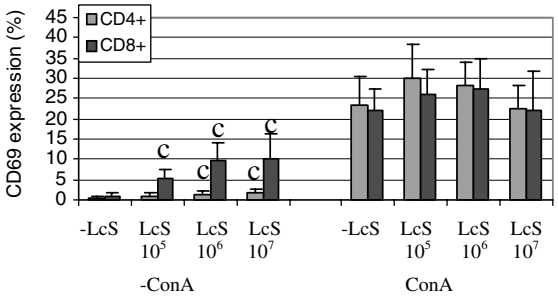

Fig. 1. Effect of LcS on CD69 expression by lymphocyte subsets in the presence or absence of ConA.
Mean values were significantly different from those for unstimulated cultures (− LcS, − ConA cultures): $^cP<0.001$.

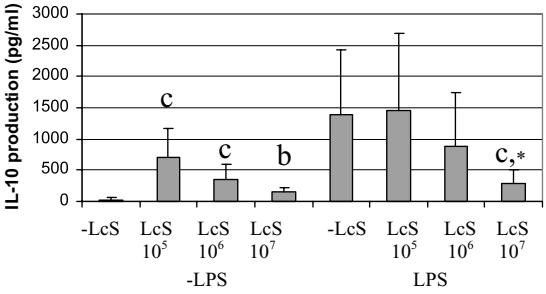

Fig. 2. Effect of LcS on IL-10 production in supernatants of PBMC cultures with or without LPS.
Mean values were significantly different from those for unstimulated cultures (− LcS, − ConA cultures): $^bP<0.01$, $^cP<0.001$. Mean values were significantly different from those for LPS-stimulated cultures: $^*P<0.05$.

In the absence of mitogenic stimulation LcS enhances lymphocyte activation, particularly that of cytotoxic T lymphocytes (CD8+ T-cells). The present study is the first to show such an effect of LcS and suggests that LcS could potentiate the destruction of infected cells in the body. LcS also induces both pro-inflammatory and anti-inflammatory cytokine production in the absence of LPS, indicating that LcS could promote cell-mediated immunity and also down regulate inflammation. Further research to investigate the mechanisms is required and human trials are needed to confirm immunomodulation of LcS *in vivo*.

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3. Shida K, Suzuki T, Kiyoshima-Shibata J *et al*. (2006) *Clin Vaccine Immunol* **13**, 997–1003.