

Immune-modulation by *Lactobacillus acidophilus* in Murine Model of Breast Cancer Induces Enhanced Systemic Anti-tumour Immune Responses

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Background & Objectives: Cancer immune-therapy is an interesting avenue of studying the effects of deviating immune system responses to achieve the desired result, through many strategies which are focusing on one thing that is built naturally by active immune responses. *Lactobacilli* are inhabitants of the GI tract which have shown beneficial health effects on various ailments including malignancies. Their mechanisms of action comprise a very intense area of research. Although their mucosal actions are local, the effects are systemic and therefore in this study we evaluated the immunomodulatory effects of *Lactobacillus acidophilus* in in vivo model of breast cancer.

Methods: *Lactobacillus acidophilus* (L.a) used, was isolated from traditional home-made yogurt and also from neonatal stool by aerobic overnight culture at 37°C in MRS broth. Delayed Type Hypersensitivity (DTH) assay was performed to find the best immunostimulant dose. 4T1 breast cancer cell line was used in this study as the breast cancer model. Mice were treated with 2×10⁸ cfu of isolated *L. acidophilus* and 20 mg/kg Cyclophosphamide as positive control for 15 consecutive days. Tumour volume was measured using a digital vernier calliper (Mitutoyo, Japan). Mononuclear cell was separated from spleen. Lymphocyte proliferation was done using MTT proliferation assay. Splenocyte cytokine production was assessed in the presence of purified tumour antigen. IFN γ , IL-4 and TGF- β concentrations were measured using R&D DuoSet ELISA Development kit.

Results: According to results administration of L.a induced a significant decrease in tumour growth pattern (P value=0.00) comparable to anti-proliferative effects of Cyclophosphamide. Significant alterations in splenocyte production of IFN- γ , IL-4 and TGF- β (P values<0.05) and also lymphocyte proliferation in L.a treated animals was evident (P value<0.05).

Conclusion: This study indicated that oral administration of L.a is able to alter the cytokine production in tumour bearing mice into a Th1 protective pattern, favourable to anti tumour immunity. Reduced tumour growth rate and increased lymphocyte proliferation are also supportive evidences of protective actions of L.a as a therapeutic probiotics in cancer therapy via mechanisms including modulating the responses of immune system. Further studies are required to elucidate the exact mechanism by which local actions of probiotics affect the systemic immune responses against transformed cells.

Keywords: *Lactobacillus acidophilus*; 4T1 Breast Cancer Cell Line; Immune Modulation; Cyclophosphamide