Immunomodulatory properties of probiotic bacteria: Effects on dendritic cells and their interactions with NK cells and T cells

Certain lactic acid bacteria (LAB) are part of the commensal intestinal flora and considered beneficial for health, as they compete with pathogens for adhesion sites in the intestine and ferment otherwise indigestible compounds. Another important property of these so-called probiotic bacteria is the ability to modulate the immune response. This thesis describes the immunomodulatory properties of gut-derived bacterial strains on different antigen-presenting cells, and the effector cell responses elicited by bacterially stimulated antigen-presenting cells in natural killer (NK) cells and T cells. Autologous NK cells and mature dendritic cells (DC) mutually activate each other and this interaction is believed to be important for NK cytotoxic activity against cancer cells and for T cell polarisation. The first study included in this thesis establishes that LAB, as potent stimulators of monocyte-derived DC, are capable of directing NK cell responses. All tested strains increased NK cell proliferation and cytotoxic activity via maturation of DC, whereas only IL-12-inducing LAB induced IFN-gamma production in NK cells. Specific LAB, capable of inhibiting IL-12 production in DC also inhibited IFN-gamma production in NK cells. Secondly, it was investigated whether the strain-dependent induction of IL-12 by LAB and E. coli strains observed in monocyte-derived DC also occurred in freshly isolated blood myeloid DC and monocytes. Both types of blood antigen-presenting cells produced cytokines when stimulated with bacteria, and the cytokine pattern induced by specific bacteria resembled the pattern induced in MoDC, except for TNF-alpha and IL-6, which were induced in response to different bacteria in blood DC/monocytes and monocyte-derived DC. Autologous NK cells produced IFN-gamma when cultured with blood DC, monocytes and monocyte-derived DC and IL-12-inducing bacteria, whereas only DC induced IFN-gamma production in allogeneic T cells. In vitro-generated DC is a commonly used model of tissue DC, but they differ in certain aspects from intestinal DC, which are in direct contact with the intestinal microbiota. In the last study, we isolated DC from Peyer’s patches, mesenteric lymph nodes, and spleens of mice, and stimulated these cells with strains of LAB and E. coli. Spleen and mesenteric lymph node DC responded to stimulation with cytokine production comparable to in vitro-generated DC. Peyer’s patch DC produced only IL-6. Cells from spleen and mesenteric lymph nodes enriched in DC rapidly produced IFN-gamma when stimulated with the bacteria that induce IFN-gamma production in NK and T cells via in vitro-generated DC. Especially mesenteric lymph node cells produced large amounts of IFN-gamma, which may indicate that mesenteric lymph node NK cells have a strong potential for cytokine-production in response to commensal bacteria.