Abstract

The use of probiotics has emerged in the last decades as a promising strategy when it comes to the treatment of inflammatory diseases. Through modulation of composition of the intestinal microbiota and the signalling it provides, probiotics can favourably tune the immune system. Beneficial effects of probiotic treatment have been documented in multiple animal inflammatory disease models. The effect of probiotic treatment on uveitis—a sight-threatening disease—has however not yet been described. In our study, we have tested two commercially available probiotics—*Escherichia coli* Nissle 1917 (EcN) and *Escherichia coli* O83:K24:H31 (EcO)—in the treatment of experimental autoimmune uveitis (EAU).

The disease severity was assessed by ophthalmoscopy and histology, proportions of leukocyte populations and intracellular expression of cytokines were evaluated by flow cytometry and the gut immune environment was analysed by tissue culture and ELISA. We found that prophylactic and early oral treatment with EcN reduces the severity of EAU. However, EcO treatment does not. The effects were accompanied by immune changes including a lowered production of inflammatory cytokines in Peyer´s patches, a shift in macrophage populations in ileum and mesenteric lymph nodes or a reduced IRBP-specific response of $CD4^+$ T cells in the lymph nodes. To describe the immune background further, this thesis has aimed to assess the differences in capacities of immunomodulation provided by EcO and EcN, which could determine their potential to reduce the severity of EAU.

Using RT-PCR we have assessed the colonization abilities of each microbe. We found, there are no differences in the time period microbes persist in the host. However, the data suggested that colonization could be affected by microbiota context determined by animal facility. To assess whether antigen-presenting cells could be involved in the immune effects induced by EcN *in vivo*, we tested the response of bone-marrow derived macrophages (BMDMs) and dendritic cells (BMDDCs) to lysates and cultivation filtrates derived from each microbe. The production of IL-1β, IL-10 and IL-12 was analysed by ELISA, respiratory burst was evaluated by Griess reaction and surface markers involved in co-stimulation and antigen-presentation were assessed by flow cytometry. EcN-derived lysate, compared to EcO lysate, induced lower production of NO and IL-1β by BMDMs and an increased expression of CD103 and an elevated production of IL-10 by BMDDCs.

Our study provides the first data documenting a reduction of EAU severity by treatment with EcN. This thesis offers additional data assessing the immune effects of EcN and EcO, which could determine their distinct effects in the treatment of EAU.