Abstract

Type 1 diabetes (T1D) is an autoimmune disease, whose incidence is rising every year, and its prevention or a cure does not exist. T1D is influenced by multiple genetic factors but environmental factors represent the major contributor to the recent almost epidemic increase of T1D incidence worldwide, primarily in developed countries. Amongst these factors belong for example enteroviral infections, microbiota dysbiosis or gluten-free diet (GFD). GFD has been proven to have a protective effect in NOD mice, which is a spontaneous model of T1D, and a beneficial effect on glycemic control in humans, when administered after T1D onset. This diploma thesis examined changes of regulatory and potentially regulatory T-cells and their cytokines in peripheral blood mononuclear cells (PBMC) of T1D children, who underwent 12-month intervention trial of GFD. Secondly, the thesis assessed if the influence of GFD on immune regulatory functions can be transferred by colonization of germ-free NOD mice with gut microbiota of these children. We have found that intervention with GFD increases percentage of Tr1 cells and IL-10 producing $CD4^+$ T-cells in PBMC of T1D children. Furthermore, the beneficial effect on immune regulation can be at least partially transferred to NOD mice by the colonization with human microbiota because this also increased the percentage of regulatory, potentially regulatory T-cells and IL-10 producing $CD4^+$ T-cells. Thus, this diploma thesis brings novel findings about the influence of GFD on immune regulatory functions in the context of human T1D and indicates a possibility that this influence may be, at least from a part, mediated by a diet shaping of microbiota composition.

Key words: type 1 diabetes, T-cells, regulatory cells, gluten-free diet, human, microbiome transfer, NOD mouse, gnotobiotic