Abstract

Type 1 diabetes mellitus (T1D) is an organ-specific autoimmune disease characterised by autoimmune destruction of insulin-producing beta cells in the islets of Langerhans. It is a long-term process initiated months or even years prior to the clinical onset. The main role in the pathogenesis is played by T lymphocytes but other cell types are involved as well. The presence of autoantibodies in the circulation is typical even before the disease onset. Nowadays, intensive research is focused on finding individuals at risk and developing an effective prevention.

During my postgraduate studies I was involved mainly in the research of T1D prediction and prevention. We investigated the relationship of established autoimmune markers – autoantibodies – and the cellular reactivity to GAD65 and IA2 autoantigens. We discovered that the reaction to autoantigens is very individual and it is influenced by the patient‘s autoantibody profile. These results could be relevant in planning antigen-specific immunointervention studies and improving their efficacy. We also made an attempt to improve specificity and sensitivity of a beta cell destruction marker (specifically demethylated DNA), which would enable better understanding of the beta cell decline and identification of individuals at risk of T1D development. In order to develop efficient prevention of the disease it is important to understand its pathogenesis. We therefore studied changes in B lymphocyte subpopulations in peripheral blood of patients at disease onset, long-term treated and their healthy relatives. The most distinct differences were seen in in the early developmental stages of B lymphocytes. We also addressed the interconnection of immune system and metabolic changes that accompany T1D.

Despite the intensive research, all the attempts to prevent T1D made up to date were more or less unsuccessful. Unspecific inhibition of the immune system causes adverse effects and antigen-specific treatment is as yet inefficient. Better knowledge of dynamics and pathogenesis of the autoimmune process and personalization of the therapy is vital for successful prevention of T1D.