ABSTRACT

Type 1 Diabetes (T1D) results from autoimmune destruction of insulin-producing pancreatic ß-cells. This disease, with a peak incidence in childhood, causes the lifelong need for insulin injections and necessitates careful monitoring of blood glucose levels. However, despite the current insulin therapies, it still shortens life expectancy due to complications affecting multiple organs. Recently, the incidence of T1D in childhood has increased by 3 – 5% per year in most developed Western countries. The heterogeneity of the disease process is supported by the findings of follow-up studies started early in infancy. The development of T1D is usually preceded by the appearance of autoantibodies targeted against antigens expressed in the pancreatic islets. The risk of T1D increases significantly with an increasing number of positive autoantibodies. The order of autoantibody appearance affects the disease risk. Genetic susceptibility, mainly defined by the human leukocyte antigen (HLA) class II gene region and environmental factors, is important in the development of islet autoimmunity and T1D. Environmental factors, mainly those linked to the changes in the gut microbiome as well as several pathogens, especially viruses, and diet are key modulators of T1D.

The aim of this doctoral dissertation is to expand the understanding of the aetiology and pathogenesis of T1D in childhood by detailed description and study of factors affecting the progression from the islet autoimmunity to T1D in children.

KEYWORDS: Type 1 diabetes; T1D prediction; Islet autoantibodies; HLA; Gut microbiome