Abstract

Type 1 diabetes is characterized by chronic hyperglycaemia leading to life-threatening complication. The pathogenetic mechanism of T1D is the abnormal immune reaction destroying β-cell mass in pancreas. The current therapy is based on the administration of subcutaneous insulin. However, this therapy can not prevent the episodes of transient hyperglycaemia. Thus, the high blood glucose influences negatively cellular metabolism and progressively leads to tissue damage. The cellular therapy brings the new strategy allowing the direct modulation of the abnormal autoimmune reaction. This strategy promises more targeting therapy with less adverse effects. In this thesis we discuss two types of immune-suppressive cells which are candidates for cellular therapy in autoimmune diseases. The first part describes the tolerogenic dendritic cells (tDC) and their stable suppressive phenotype in proinflammatory condition. tDC maintain their stable inhibitory phenotype and are able to suppress antigen-specific T-cell proliferation together with the induction of T-regulatory cells. These properties of tDC are very important for potential clinical application. The thesis also reveals the relation between laboratory parameters of T1D patients and suppressive properties of tDC. The second part of the thesis is focused on myeloid-derived suppressive cells (MDSC). These cells are expanded in T1D patients and their first-degree relatives. MDSC likewise exhibit the suppressive phenotype and are able to inhibit the proliferation of T-lymphocytes due to cell-cell contact and production of TGF-β. Last but not least we discuss the problem of hyperglycaemia-induced proinflammatory changes in immune system and the role of cellular therapy in the context of current immune-interventional strategies.