ABSTRACT

During treatment of diabetes mellitus by immunointervention or transplantation, it is necessary to monitor the markers of immune destruction or rejection of surviving insulin producing cells. An aim of this thesis is to improve the possibilities of following autoimmunity and to detect the survival of transplanted pancreatic islet in vivo.

Partial aims included vitality testing of isolated islets for transplantation by measurement of respiration activity, observing the process of in vitro labeling of isolated islets with superparamagnetic iron oxide (SPIO) contrast agent for subsequent magnetic resonance imaging (MRI) of islets and observing SPIO particles transport after transplantation. We also studied a new dual paramagnetic contrast agent combined with fluorescein intended for identification of the MRI contrast agent in samples for histology. Further, we assessed autoimmune reaction by evaluation of cytokine response to specific stimulation with auto-antigens. We tried to affect beta-cells destruction by polyclonal anti-thymocyte antibodies in a mouse experimental model.

A new method of the islet respiration measurement correlated with other methods of islet quality testing and it was suggested as a diagnostic test before clinical transplantation. Results obtained studying the intercellular transport of SPIO particles showed that the particles are incorporated into all islet cell types during islet labeling. After transplantation, the particles were translocated into tissue macrophages, they persisted there in the case of immune tolerance but they were eliminated from the liver during rejection. We showed that a new dual contrast agent enables both islet imaging by MRI and localization by fluorescence microscopy. We found differences in cytokine reaction profiles after stimulation of lymphocytes with specific auto-antigens in groups of recent onset diabetic patients and their healthy relatives. This pointed to activation of inflammatory reaction in this group of patients. By flow cytometry we found an increase of regulatory T-lymphocytes population after the anti-thymocyte globulin treatment.

The new findings helped to solve long-term projects of the working group and were published in impacted journals.