Description for the general public

Diabetes mellitus (DM) represents a chronic metabolic disorder, and is considered as a disease of XXI century in the world. Lack of insulin or lack of insulin activity in patients suffering from diabetes results in an elevated level of blood glucose, which in turn leads to a number complications among them the most lifethreatening is diabetic cardiomyopathy (diabCM). This term includes pathological and functional changes that occur in the heart during diabetes, caused by chronic hyperglycemia. These changes lead to an impairment of heart function and heart failure and involve disturbance in microcirculation, cardiac hypertrophy, lipid deposition within cardiac cells, heart fibrosis. Microcirculatory changes play an important role in the development of cardiomyopathy. Scientific literature offers a very extensive knowledge on the structure and function of blood vessels during development of metabolic diseases, including diabetes and diabetic cardiomyopathy. Another type of heart vessels, which are responsible for draining excess fluid, electrolytes and proteins from tissue to circulatory system and transport of immune cells, is the lymphatic system. For many years lymphatic system of the heart was considered to be unimportant in the normal function of the heart, and therefore, it was disregarded as a subject of research studies. However, the role of the lymphatic vessels is equally important and cannot be ignored in the study of cardiomyopathy. Normal morphology and integrity of the lymphatic vessels, providing a constant flow of lymph, is crucial for ensuring proper function of the heart. We assume that during development of diabetic cardiomyopathy, lymphatic vessels will undergo unfavourable changes, that contribute to the impairment of heart function. Therefore, the objective of this project is characterisation of lymphatic vessels in diabetic heart, demonstration their morphology, phenotypes of lymphatic endothelial cells, the extracellular matrix positioned adjacent to lymphatic vessel walls and pattern of intercellular junctions. Research will be conducted in animal models type 2 diabetes – transgenic mice db/db, that mimic the symptoms of diabetes in humans, and in the healthy control mice for the comparison. Markers specific to the lymphatic vessels, as well as extracellular matrix, both those that should be present in normal conditions and those whose presence can be expected due to the pathological conditions, will be stained on the whole hearts and sections. Confocal microscopy would allow to analyze the vessels demonstrated as multi-color images of the myocardial lymphatics. In addition lymphatic endothelial cells will be isolated from mouse hearts and then characterized using flow cytometer, which simultaneously allow to assess quantity of cells. Sorted lymphatic endothelial cells will be studied by molecular method (qPCR), to find out which genes are upregulated. This analysis will provide information on the biological potential of lymphatic endothelial cells (i.e. whether they are able to perform their function, whether they multiply, whether they possess survival potential, and whether they are able to create new lymphatic vessels). Knowledge about the alterations occuring in the cardiac lymphatic vessels during development of cardiomyopathy will form the basis for innovative therapies in the future that will allow to repair and improve the adverse changes in the lymphatic system, and can also be crucial for effective prevention of the lymphatic complications in diabetic cardiomyopathy.