The aim of the project is to determine the role of stearoyl-CoA desaturase 1 (SCD1) in the epigenetic control of lipolysis in the state of normoxia as well as hypoxia in the heart. SCD1 catalyzes the synthesis of monounsaturated fatty acids, which are an important energetic substrate for the heart. The conducted studies have shown that, SCD1 may influence lipolysis, i.e. decomposition of triacylglycerols (TAG) into glycerol and free fatty acids. Two enzymes play an important role in the lipolysis pathway: adipose triglyceride lipase (ATGL) and hormone-sensitive lipase (HSL) that hydrolyze TAG and diacylglycerols (DAG). The proper activity of the lipolysis pathway is very important for the functioning and heart work. Disruptions in the lipolysis pathway lead to: accumulation of lipids (TAG and DAG), lipotoxicity, disorders in the heart work and can even contribute to myocardial infarction. The studies also showed that lipid metabolism can be controlled by epigenetic modifications, i.e. changes introduced into the body through biochemical modifications in DNA sequences or histone proteins, which consequently affect gene expression. Epigenetic modifications are also an important factor controlling the metabolism and work of the heart. Interestingly, SCD1 may also cause epigenetic changes, such as a change in the level of DNA methylation in non-coding sequences found at the beginning of genes (i.e. promoter sequences) of pro-inflammatory interleukins.

In the proposed project we will check what role plays SCD1 in the epigenetic control of the lipolysis process. We will investigate, which epigenetic mechanisms, i.e. changes in DNA methylation, or histone acetylation and methylation, will be associated with SCD1 expression. More importantly, we will check how epigenetic changes affect the metabolism of cardiomyocytes in a reduced oxygen content (hypoxia), conditions similar to those prevailing in the heart after myocardial infarction. We will also investigate, whether SCD1 affects the methylation level of promoter sequences of *HSL* and ATGL activator - *CGI-58* genes. We will also check, whether the inhibition of ATGL and HSL activity will affect epigenetic modifications in cardiomyocytes. We will also determine, how epigenetic changes due to overexpression/silencing of SCD1 will affect the physiology and metabolism of cardiomyocytes by measuring the level of reactive oxygen species (ROS), autophagy and HIF-1α hypoxia inducible factor which causing changes in the expression and activity of many proteins in hypoxia.

Understanding the epigenetic mechanisms involved in the control of heart work and heart function is very important because cardiovascular diseases are the most common cause of death in the world. Research performed in this project will contribute to the creation of new therapies for heart diseases related to disorders in lipid metabolism and hypoxia.