The heart is the first organ formed in embryogenesis to provide the developing fetus with nutrients. The last stage of cardiomyocyte differentiation occurrs from the late prenatal period until youth. During this stage, called maturation, cardiomyocytes undergo a series of highly regulated changes from metabolic to electrophysiological, which grant the adult phenotype of the heart to provide efficient blood circulation through the organism. Relatively little is known about factors that drive maturations and their mechanisms of action. Among known factors which promote maturation are glucocorticoids and thyroid hormones. Moreover, biophysical factors: substrate rigidity, pacing and growth in cardiospheres; biochemical: glucose ablation and fatty acids supplementation; pharmacological: inhibition of HIF-1 and activation of PPARs promotes induced cardiomyocytes maturation. Nevertheless, there is still a lack of description of factors that drive cardiomyocyte maturation *in vivo*, especially cell-autonomously.

To maintain efficient energy supply for contraction metabolism switches from anaerobic with preferable utilization of lactate and glucose in neonatal to oxidative with fatty acids as a primary substrate in mature cardiomyocytes. Activation of glucose uptake and oxidation or inhibition of fatty acid oxidation promotes cardiomyocyte proliferation and slowdown maturation rate. Activation of fatty acid utilization promotes the opposite effect – it accelerates maturation. Importantly, fatty acid treatment of induced cardiomyocytes led to inhibition of *de novo* lipogenesis, with stearoyl-CoA desaturase (SCD) being the most downregulated gene. SCD is the rate limiting enzyme catalyzing the biosynthesis of monounsaturated fatty acids, mainly oleate and palmitoleoate, which are used as substrates for the synthesis of triglycerides, wax esters, cholesteryl esters, and phospholipids. In the heart, the lack of SCD1 enhances glucose transport and metabolism at the expense of fatty acid uptake and oxidation. Disruption of the SCD1 gene improves cardiac function in obesity by correcting the systolic and diastolic dysfunction. However, the role of SCD-dependent signaling in controlling cardiomyocytes maturation is unknown. Based on our preliminary data and the facts that *de novo* lipogenesis is downregulated during heart maturation and SCD is a crucial factor that regulates lipogenesis in cardiomyocytes and affects heart metabolism and function, we hypothesize that SCD and lipid signaling networks controlled by this enzyme are involved in cardiomyocytes transition from neonatal to adult phenotype. Thus, the main objective of the proposed project is to define the role of SCD, in particular ubiquitously expressed SCD1 and heart-specific SCD4 isoforms, in structural and functional heart maturation with special emphasis on AMPK-mediated metabolic reprogramming and the role of affected signaling pathways in the acquisition of adult cardiac phenotype. Our second priority is to examine to what extent SCD is involved in the switch of cardiomyocytes energy metabolism occurring in the maturing heart.

The research area addressed by this project is one of the highest priorities worldwide. Preterm birth occurs in humans with a frequency of 1/10 of pregnancies, and preterm born adults have an increased risk of ischemic heart disease and heart failure due to the oversoon heart maturation. Therefore, understanding of the mechanisms of *in vivo* heart maturation will provide new data for the treatment of such patients and possibly improved outcomes. In addition, SCD inhibitors are currently considered promising metabolic syndrome and cancer therapeutic agents and undergoing clinical trials, and results obtained during project realization will provide info for limitations for such therapy in pregnant and pediatric patients.