

Project 1.12 Stearoyl-CoA desaturase as a novel regulator of cardiomyocyte maturation

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Background:

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 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 palmitoleate, which are used as substrates for the synthesis of triglycerides, 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.

Aim:

The main objective of the proposed project is to determine the role of SCD in structural and functional heart maturation with special emphasis on AMP-activated protein kinase (AMPK)-mediated metabolic reprogramming and the role of affected signaling pathways in the acquisition of adult heart phenotype.

Requirements:

- MSc degree in biomedical sciences, biotechnology, biology or related field,
- experience in laboratory work and knowledge of basic molecular biology and biochemistry techniques,
- good knowledge of English and ability to work in a team,
- experience in working with animals will be an additional advantage.