Heart failure occurs when the cardiac muscle cannot provide an adequate blood supply to all tissues and organs. This is caused by impeded systolic and diastolic heart function, which can result from any long-term heart disorder, such as atherosclerosis, coronary disease, valve dysfunction, high blood pressure, as well as other systemic illnesses, such as viral inflammation. One of the most serious outcomes of coronary artery disease is myocardial infraction that represent an acute event, being the last stage of this disease and the most dramatic by considering its high consequences. Up to now it is known that many factors related to our habits (e.g. dyslipidemia, hypertension, diabetes, obesity, smoking, diet, physical activity, alcohol consumption and psychosocial stress) are directly linked with the evolution of coronary artery disease. In this regards, it has been demonstrated that from the above mentioned factors, the changes in our dietary habits have the most important impact to the incidence of mortality due to atherosclerosis and heart failure and have shown an increasing trend over the years. Moreover, altered lipid metabolism resulted from diet reach in fatty acids as well as endogenous fatty acid metabolism were identify as involved in heart injury associated with atherosclorosis.

Adipose tissue accumulated around the heart and coronary artery evokes pathological changes in cardiac and coronary arteries structure and function. Our previous studies showed that stearoyl-CoA desaturase (SCD) is a key factor regulating cardiac metabolism and function, and is likely to represent critical step in the maintenance of the proper heart structure. 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, cholesterol 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 pericardial and pericoronary adipose tissue accumulation and function, coronary plaque formation and angiogenesis in murine models of lipotoxic heart disease and atherosclerosis is unknown. Taken into consideration presented above data and the performed by us preliminary study, we hypothesize that metabolic pathway networks controlled by SCD are likely to represent critical steps in the regulation of coronary artery angiogenesis and in regulation of perivascular and pericardial adipose tissue metabolism in obesity and atherosclerosis. Therefore, **the main objective** of the proposed project is to provide solid foundation for knowledge about the role of SCD and lipid mediators in pericoronary adipose tissue and coronary artery dysfunction in obesity and atherosclerosis. If our hypotheses come true, while pursuing this project, we will be able to (1) determine a novel add-on to understanding the role of intracellular lipid-signaling involved in the regulation of differentiation and function of pericardial and coronary perivascular adipose tissue, (2) identify local SCD-dependent signaling that is driving the cells along a proper differentiation/proliferation program and ischemia-induced coronary angiogenesis, and (3) provide an explicit support to the concept that pericoronary adipose tissue: (*i*) is involved in the pathogenesis of vascular dysfunction in obesity/the metabolic syndrome and atherosclerosis, and (*ii*) is a feasible target of therapies designed to restore its function in order to improve vascular function in these diseases.

The research area addressed by this project is one of the highest priorities world-wide. Cardiovascular disease is a major public health and economic problem in Western countries and is one of the most common causes of hospitalization and death. Understanding how SCD-dependent signaling regulates pericardial and pericoronary adipose tissue metabolism and function, and vascular homeostasis in cardiomyopathy caused by lipids and atherosclerosis will not only gain insight into basic mechanisms governing vascular biology in health and disease, but it will also provide opportunities for development of new treatment strategies to augment cardiac vascular function and heart remodeling.