

Summary of Research

Diabetic patients have a two- to three-fold greater risk of developing heart failure. Despite recent improvements made in heart failure survival, the death rate remains high and approaches 50% at 5 years after initial diagnosis. While hyperglycemia and insulin resistance are well-known risk factors for cardiovascular diseases, the molecular alterations caused by both factors in the heart have been far less well investigated than in other insulin sensitive organs.

Our research is investigating the molecular mechanisms by which nutrient oversupply leads to contractile dysfunction of the heart. Our strategy is based on the identification of metabolic networks and specific proteins affected by dietary manipulations in rodents. The identified proteins are then targeted *in vivo* and *in vitro* to determine their role in the global regulation of myocardial metabolism and contractile function under physiological and pathological conditions.

Current research in our laboratory focuses on: a) the role of glucose and of its metabolites as regulators of gene expression in the heart; b) the consequences of altered insulin signaling on myocardial adaptation to stress conditions such as an increase in workload or ischemia; c) the role of mitochondrial UCP3 in the control of energy providing substrate selection by the heart.