

# SFB Guest Lecture Series

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## **What drives the heart to fail in metabolic disorders?--Uncovering molecular mechanisms and therapeutic targets**

Metabolic disorders are increasingly recognized as major drivers of heart failure. Notably, the association between diabetes and heart failure was first documented more than 150 years ago, yet therapeutic strategies remain suboptimal. The limited efficacy of current interventions, including anti-diabetic agents, largely reflects an incomplete understanding of the molecular and cellular mechanisms underlying cardiac dysfunction in metabolic disease.

Heart failure is a multifaceted syndrome characterized by interconnected abnormalities at the molecular, cellular, and organ levels, each contributing to impaired myocardial performance. This presentation will highlight our recent investigations into the pathogenic pathways linking metabolic disorders to heart failure, with particular emphasis on the genetic regulation of cardiomyocyte organelle homeostasis, including mitochondrial and endoplasmic reticulum function, the molecular control of intracellular lipid homeostasis in cardiomyocytes, and the intercellular communication networks within the myocardium.

By elucidating the genetic determinants and mechanistic pathways that drive cardiac dysfunction in metabolic disease, our work also assesses the therapeutic effects. Interventions targeting the genes or pathways studied have been, or are being, evaluated in preclinical models of metabolic disorders, providing proof-of-concept evidence for the development of more precise and mechanism-based therapies for heart failure.