Cardiomyopathies represent a collection of conditions with decreased cardiac contractility that can lead to heart failure (HF) and death. The molecular mechanisms that result in cardiac dysfunction are presently unknown, but inappropriate signaling cascades likely underlie critical functional impairment of cardiac cells. My research focus has been on the discovery of novel molecular biochemistry pathways, therapeutics and diagnostics for cardiovascular (CV) disease. Scientifically, protein kinases and signaling factors have been implicated in cardiac remodeling and disease progression, including well-known regulators of cell growth, proliferation, differentiation and survival. Our central hypothesis is that additional critical regulatory pathways that determine patient outcomes remain to be discovered. We have focused on analysis of cardiac cell surface receptors and global protein phosphorylation states in healthy and diseased human and mouse cardiac tissue using unbiased global proteomics and quantitative mass spectrometry phosphoproteotyping. By systematically identifying and measuring changes in the activity, modification states and abundance of critical signaling factors, from regulatory kinases to downstream transcriptional effectors, our goal is to understand, and alter, the molecular mechanisms that drive progression to HF. In translational studies, we are examining human plasma and myocardial tissue excised from HF patients and various comparator control groups. Our long-term goal is to develop more effective markers for the earlier detection of HF, and where appropriate, novel therapeutics in disease. In this talk, I will highlight our recent developments together with discussing our ongoing direction.

"Analysis of mouse and human cardiovascular tissues using global and phosphoproteomic approaches"