Our research focus is on key pathological substrates in the heart that drive disease progression and lead to the development of heart failure. We explore mechanisms of these pathological changes and conduct research to test novel therapeutic interventions in vivo and to validate in human patients findings from animal models of heart disease.

Research Brief

Research conducted in this laboratory has been centered on mechanisms and therapeutic intervention of cardiovascular remodeling, particularly inflammation, myocardial hypertrophy and fibrosis, as well as β-adrenergic signaling known to contribute to remodeling. We have been particularly interested in identifying major factors that contribute to cardiac inflammation with consequent adverse remodeling after myocardial infarction. Our recent studies have identified the inflammatory cytokine macrophage migration inhibitory factor (MIF) and platelets as pivotal factors contributing to initiation of cardiac and systemic inflammatory responses and related complications after acute myocardial infarction. Joint experimental and clinical studies are on-going to further these findings and to explore the potential clinical significance of MIF in the setting of ischemic and hypertensive heart diseases. Our therapeutic studies have also provided promising results indicating both factors are potential therapeutic targets for inflammation. Our long-term research on the peptide hormone relaxin has contributed to the consensus that relaxin is a specific and potent anti-fibrotic drug. Relaxin has been shown to effectively reduce established fibrosis in a series of animal models of cardiovascular diseases. We are conducting relaxin therapeutic testing in aged animals with cardiovascular diseases to better simulate clinical situations. Sympatho-β-adrenergic signaling is a known factor contributing to cardiac remodeling and development of heart failure. We are investigating novel signaling mechanisms by which β-adrenergic activation mediate biological consequences including oxidative stress, cardiomyocyte apoptosis, interstitial fibrosis and angiogenesis.

Methodologies

- Microsurgery for induction of heart diseases in mice and in vivo drug delivery
- Echocardiography (non-invasive functional assessment)
- Micromanometry (hemodynamics)
- Immunohistochemistry and quantitative histology
- Radiotelemetry for assessment of conscious in vivo CV parameters
- Flow cytometry
- Routine cellular and biochemical assays

Selected Publications

Heart Research in Mice with our Established Mouse Cardiology Platform

Heart research using genetically modified mice requires subjecting animals under diseased conditions, such as myocardial infarct (MI) or transverse aortic constriction (TAC) (A) and detailed functional phenotyping either by non-invasive echocardiography (B) or invasive micromanometry (C).

MIF Contributes to Innate Immunity after Acute Myocardial Infarction

A. myocardial infarction (MI) was induced in mice by coronary artery occlusion (top), biochemical staining depicts the infarct myocardium (bottom). B. CAO for 60 min induces release of MIF into the circulation indicated by a reciprocal change of MIF levels in plasma and the left ventricle. C. MIF gene knock-out (KO) mice with MI had reduced cardiac rupture and improved survival. D & E. Knock out of MIF gene also significantly attenuated cardiomyocyte apoptosis (top) and neutrophil infiltration (bottom) when compared to that in wild type (WT) control mice.

Anti-fibrotic Action of Relaxin in Various Cardiovascular Disease Models

Recent research has shown that the reproductive peptide hormone relaxin has potent anti-fibrotic action. Our series of research have shown reversal of large artery (A) and cardiac fibrosis (B) by relaxin therapy. In relaxin knockout mice, there is an age-dependent development of cardiac fibrosis (B). Our current research is to test efficacy of relaxin on aged animals with cardiovascular fibrosis.