The Heart Failure Research Group seeks to improve the quality of life and outcomes for patients with established and advanced cardiovascular disease.

Research Brief

The research activities of the Heart Failure Research Group are motivated by a desire to improve the quality of life and outcome for patients with advanced cardiovascular disease including heart failure and atrial fibrillation their precursors. In particular, the laboratory provides a unique basis for research in both the ‘bench to bedside’ and ‘bedside to bench’ directions, based upon the strong portfolio of clinical and laboratory based methodologies and the opportunity it provides for interaction between clinical and basic researchers.

Our research focuses on the role of several fundamental pathogenic processes that contribute to the progressive nature of heart failure (HF), and which might may manipulated for therapeutic purposes. Cardiac fibrosis: Altered cardiac matrix is a key feature of HF. We have conducted a range of clinical and laboratory based studies to identify novel mechanisms of cardiac fibrosis and particularly their implication in HFPEF. Cardiac ‘regeneration’: Improving myocardial performance is a major goal of HF therapy. We have demonstrated the potential for enhanced myocardial function using a range of approaches including gene therapy, augmentation of cardiomyocyte division and by drug development. HF & Arrhythmia: Frequently occurring together, the combination of HF and AF is associated with deleterious outcome. Insights for combined large animal and cellular studies have identified new targets for therapeutic intervention. Endothelial dysfunction: is a key feature of many forms of cardiac and renal disease. We have developed novel insights into the role of the L-arginine:nitric oxide system in HF, hypertension and renal dysfunction and are currently investigating the role of new mechanisms. Cardiac device development: Based upon on expertise in large animal studies we have developed several novel devices that have formed the basis of 2 medical device companies, both now with active clinical programs.

Methodologies

- Clinical cath lab: haemodynamics inc. exercise physiology, regional blood sampling (particularly transcardiac), P-V loops, vascular physiology
- Large animal models – multiple models HF, MI, AF, with detailed physiology (echo, P-V loops), gene delivery
- Transgenic animals
- Langendorff perfused hearts
- Cellular/Mitochondrial Studies

Selected Publications

Strategies for the Regeneration of the Failing Heart

Gene Therapy

A Favorable effects of AAV2/1-SERCA gene therapy on cardiac function in ovine HF model. A. PV loop pre and post gene delivery using a novel recirculating delivery system developed in the Heart Failure Research Gp. B. Group data. C. Nerve growth factor stimulates cardiomyocyte division in a zebrafish model of HF. D. BrdU positive cardiomyocytes in cmrl2-GFP zebrafish.

Understanding the causes and consequences of cardiac fibrosis

A The SDF-1 antagonist AMD3465 attenuates cardiac fibrosis in DOCA treated mice. B SDF-1 is released from the failing human heart. C. Bone marrow derived cells (GFP+) are recruited to the heart and may develop into myofibroblasts. D. SDF-1 mRNA induction in cardiac myocytes.