Our work is centred on endothelial and vascular pathologies where the effort is in identifying novel targets and restoring functionality. Our translational approach ranges from cellular to tissue and animal models through to human and patient cohorts in vitro and in vivo.

Research Brief
We work on the luminal and abluminal influences of the endothelium on vessel reactivity and inflammation with a focus in coronary artery disease (CAD), atherosclerosis, hypertension and peripheral arterial occlusive disease (PAOD). The successful research paradigm upon which we work includes academic-industrial links underpinned by a strong basic-clinical interface. Our research is aimed at 3 deliverables: 1) novel therapy focused on inflammation and exploiting the original findings that soluble P-selectin has potent inflammatory effect, that HDL has potent monocytic anti-inflammatory effects as well as potential macrophage differentiation influence and the high intraluminal pressure per se induces vascular inflammation. We recently made the original finding that caveolin-1 has a critical role for monocytic differentiation into macrophages successfully manipulating intracellular L-arginine concentrations for restoration of endothelium function in vascular disease. Most recently we demonstrated that arginase, and in particular arginase II, can critically influence cardiovascular related outcomes identifying new biomarkers and mediators in cardiovascular disease (CVD). We showed for the first time the circulating fibrocyte levels (CD45(+)/CD34(+)/collagen I(+) measured by flow cytometry was slower in patients with acute myocardial infarction compared with healthy controls or patients with stable angina.

Methodologies
- Pharmacological studies in vitro, in vivo and in man
- Imaging leukocyte-endothelium interactions in real time
- Flow Cytometry
- Small animal models and experimentation

Selected Publications
Caveolin-1 Plays a Critical Role in the Differentiation of Monocytes into Macrophages

Mouse PBMCs from wild type (WT) or caveolin-1 KO (KO) mice were treated with GM-CSF (50ng/ml) for 7 days. (A) Images show the morphology of different types of cells under 7-day GM-CSF treatment (X100). (B) The gene expression of CD68 was measured by real-time PCR. Graph shows the relative quantitative ratios of CD68 to 18s, and control groups are set as 1. (C) CD115 and F4/80 were detected on CD11b+ PBMCs by flow cytometry (Red Curve: WT; Green Curve: KO). (D) Graph shows the group data of PE geo-means from 3 independent experiments. The fluorescence geo-means of control (untreated) groups are set as 100%.

Endothelial Arginase II Overexpression induces Hypertension & Atherosclerosis

hArgII overexpression mice (A) systolic blood pressure (systolic BP), (B) mean arterial pressure (MAP) and (C) diastolic BP showing increase in blood pressure and (D) plaque lesion area in control aorta and (E) aorta from hArgII x ApoE -/- mouse showing increase.

Decreased Fibrocyte # Is Associated with Atherosclerotic Plaque Instability in Man

Representative flow cytometric analysis of circulating fibrocytes: (a) Total cells acquired; (b) CD45+ cells; (c) Isotype control for collagen I and CD34 set on CD45+ cells; (d) Positive staining for collagen I and CD34 set on CD45+ cells; (e) CD14+ monocytes determined by CD14 PE staining. Scatter plot shows circulating fibrocytes in patients with acute myocardial infarction (MI, n=22), patients with stable angina (SA, n=20) and healthy controls (Ctrl, n=22).