

## **Restoring blood flow in cardiovascular disease – collaterals as keys to therapy.**

Cardiovascular disease results not just from occlude vessels, but from impaired ability of the vessels to circumvent those occlusions by developing collateral vessels. The mechanisms of this impaired angiogenesis are now beginning to be elucidated, with the contribution of vascular growth factors, angiopoietins, and other angiogenic factors being dysregulated in some patients, particularly in diabetics. This project will focus on the molecular mechanisms underlying defects in collateral formation in patients, in animal models, and in cells in culture. It will investigate why some patients never get symptoms of cardiovascular disease (painful legs, ulcers, necrosis and gangrene, or angina, and coronary ischemia followed by myocardial infarction), while others have poor symptoms despite minor disease progression. It will use in vitro and in vivo models, including transgenic and viral mediated gene transfer to investigate the mechanisms underlying regulation of angiogenic molecules, using our state of the art cardiac and peripheral limb imaging modalities (including MRI, PET, and laser Doppler spectral imaging), and collaborate with partners across Europe.

Primary Supervisor: David Bates

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High Cost, Lab based Research