Our team investigates the various pathways involved in diabetic atherosclerosis. The main areas we focus on are the Renin Angiotensin System in particular the AT2 receptor and low salt diets, the Urotensin II system as well as CDA-1. We also specialise in assisting others in a division with murine models of diabetic atherosclerosis and nephropathy.

Research Brief

We have previously studied the diabetic ApoE knockout mouse and found increased accumulation of RAGE and AGEs in large blood vessels; and found that when AGEs were inhibited/ blocked, there was a significant reduction in atherosclerosis formation. Activation of RAGE induces a response that leads to inflammation and blood vessel injury ultimately leading to blockage of the blood vessel causing heart attack, stroke and/or gangrene. It is unknown whether these responses are mediated by blood vessel RAGE or immune cell RAGE. The first aim of the laboratory is to determine which is the detrimental source of RAGE.

Recent advances in diabetic research indicate that the renin angiotensin system (RAS) plays a pivotal role. Drugs such as ACE inhibitors and angiotensin receptor antagonists which block this system may have cardioprotective effects. The second aim of the laboratory is to investigate the cellular and molecular pathways linking the angiotensin receptor with pro-inflammatory and pro-atherosclerotic effects in diabetes. This research may lead to a deeper understanding of the development of diabetes induced atherosclerosis.

Methodologies

- Murine models of diabetes-associated atherosclerosis; includes en face and aortic sinus evaluation of lesions
- New model of aortic aneurysms in diabetes.
- Analysis of molecular pathways of the renin-angiotensin system, Urotensin II and CDA-1 (by Western blotting, siRNA).
- Immunohistochemistry. Bone marrow transplantation.
- Use of cultured cells to explore involvement of the above systems.

Selected Publications

The role of haemopoietic versus stromal cells

This work involves the use of bone marrow transplantation in diabetic ApoE KO mice. Some preliminary data from this study are shown below. This depicts the plaque staining for control and diabetic mice in the aortic arch area with and without RAGE from the bone marrow (BM):

![Image of plaque staining]

The role of the Angiotensin II AT2 receptor in diabetic atherosclerosis

Although initially considered the “good guy” in the renin angiotensin system our work suggests that this may not be a good receptor to activate in the diabetic population. Indeed in preliminary plaque area findings, the AT2 agonist, C21 may worsen diabetes related atherosclerosis.

![Graph of plaque area findings]

A new model of diabetes associated aortic aneurysms (AAA)

This work is in collaboration with Dr Zhonglin Chai who is also in Diabetic Complications. The picture to the left depicts an example of aneurysms found in this new model.

![Image of aortic aneurysm]