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DIABETIC ATHEROSCLEROSIS

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
- Blood pressure measurements and metabolic cage collections
- Analysis of molecular pathways of the renin-angiotensin system, Urotensin II and CDA-1 (by Western blotting, siRNA). Protein staining in vessels using immunohistochemistry
- Use of cultured cells to explore involvement of the above systems

Selected Publications

Pathway To Diabetic Atherosclerosis And Nephropathy

**Metabolic**
- Glucose
- Advanced Glycation
- Oxidative Stress

**Haemodynamic**
- Flow/Pressure
- Renin-Angiotensin, AT2R
- Urotensin II/III receptor

**Intracellular signalling molecules**

**Growth factors and cytokines**
- Eg CDA1/CDABP1

**Diabetic atherosclerosis** and nephropathy