Obesity and stress induced hypertension is a major global burden of disease. Our laboratory explores the role of the sympathetic nervous system in the development and maintenance of hypertension with a particular emphasis on the central pathways and neurotransmitters which contribute to the long term adaptive changes which lead to hypertension in obesity and during chronic stress.

Research Brief
The main theme of our research is the understanding of the short and long term regulation of blood pressure by the central nervous system through the sympathetic nervous system. We use a number of animal models and are able to directly measure blood pressure in conscious freely moving mice, rats and rabbits as well as directly record sympathetic nerve activity in rabbits using implanted telemetry devices. A major focus is mechanisms underlying neurogenic hypertension in genetic hypertensive mice with a focus of limbic and hypothalamic stress activated pathways. We are now using genetically modified mice and viral delivery of angiotensin receptors to determine the role of the central renin/angiotensin/aldosterone system in blood pressure regulation. We are using our chronic sympathetic recordings in rabbits to more precisely determine the long term contribution of the brain renin/angiotensin system to hypertension and in mediating the cardiovascular impact of chronic stress. We are also using the sympathetic recording in rabbits to unravel the mechanisms driving obesity hypertension in the early phases where central leptin and insulin signalling are critical. In each case we are able to determine the specific CNS pathways involved using immuno-histochemical analysis of brain regions. Commercial: We are developing a novel natriuretic peptide to treat heart failure. Translation: Development of novel analysis of 24 hour ambulatory blood pressure measurements to quantify the morning surge in blood pressure in hypertensive patients.

Methodologies
- Telemetry recording of blood pressure in conscious mice, rats and rabbits
- Direct recording of sympathetic nerve activity in conscious rabbits
- Testing cardiovascular function (baroreflexes, hypoxia, stress)
- Immuno-histochemical analysis to determine areas of brain activation
- Clinical ambulatory blood pressure studies

Selected Publications
Transfection of Angiotensin Receptors into the Medulla Oblongata in Mice

Photomicrographs of coronal sections of medulla from an AT<sub>1a</sub>-/- mouse microinjected with Lv-PRSx8-GFP showing immunofluorescent localization of tyrosine hydroxylase (TH, red), green fluorescent protein (GFP, green) and the merged image (yellow).

Baroreflex gain from cross spectral analysis is reduced 5 weeks after transfecting AT1 receptors.

Genetic hypertension in mice is neurogenic and largely abolished by discrete cell body lesions in the Medial Amygdala, a region involved in integrating the response to stress.

Hypertensive mice (BPH) have 60% lower BP after lesions of the medial amygdala. The lesions had no effect on BP in normotensive BPN mice.

In BPH and BPN the lesions destroyed 77% of the active neurons in the medial amygdala.

The Role of Leptin in Obesity Related Hypertension

Elevated blood pressure is associated with increased sympathetic nerve activity and plasma leptin in fat fed rabbits.

CNS administration of a leptin antagonist reduces sympathetic activation and normalises BP in rabbits fed a high fat diet.