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.

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 Schlager 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 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 in hypertension and chronic stress. We are also using the sympathetic recording in rabbits to unravel the mechanisms driving neurogenic hypertension in the early phases of obesity where central leptin signalling is 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**

Photomicrographs of coronal sections of medulla from an AT1A 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.

**Schlager Hypertensive Mice Are Resistant To The Effects Of Diazepam**

Hypertensive mice (BPH) are insensitive to Diazepam but normotensive mice have a reduced response to stress.

In BPH hypertensive mice many neurons expressing GABA<sub>A</sub> receptors (orange) were also immunoreactive for NPY (red) and each of these were triple labelled with Fos (yellow) in the paraventricular nucleus (PVN) and medial amygdala (MeAm).

**y 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.