To maintain optimal oxygen delivery to tissues, there is constant regulation of respiratory and cardiovascular systems by mechanisms that act on different time scales. On a fast time scale, a small chemosensory organ in mammals called the carotid body senses decreases in blood oxygen to increase breathing within seconds. The carotid body is important for normal physiological adaptation to low environmental oxygen, such as at high altitude, and to increased oxygen demand, like in exercise and pregnancy. In pathological conditions, carotid body hyperactivity can contribute to disease progression in sleep-disordered breathing, hypertension, heart failure, and metabolic syndrome. Using the mouse as our primary model, we aim to identify the molecular mechanisms that mediate the carotid body’s ability to detect changes in blood oxygen as well as other metabolic signals, such as carbon dioxide and acid. One long term goal is to apply this knowledge to manipulating carotid body activity in the treatment of cardiovascular disease and metabolic syndrome.