

Debra Schwinn, Pharmacology and Cancer Biology



Our laboratory is involved in elucidating mechanisms underlying regulation of human adrenergic receptors (ARs) in health and disease. Since AR tissue distribution is highly species dependent, one of our areas of research includes determination of 5'-regulatory sequences directing AR subtypes to specific human tissues using the α 1a-AR as a model. Results from these studies should facilitate tissue-specific targeting of gene expression in human gene therapy.

In addition to demonstrating species-specific tissue expression, α 1aARs are upregulated by agonist in rat neonatal myocyte cultures, whereas most G protein-coupled receptors are desensitized (dampened signaling) with agonist exposure. We are characterizing human α 1aAR desensitization, trafficking, and transcriptional regulation in order to determine under what conditions and by what mechanism these receptors continue signaling in the presence of agonist. Alterations of these processes by naturally occurring α 1aAR genetic polymorphisms are also being examined. These studies are important in understanding diseases such as myocardial hypertrophy, benign prostatic hyperplasia, and hypertension.

The last major project in our laboratory focuses on perioperative genomics. The impact of pre-existing genetic polymorphisms on clinical outcomes such as myocardial, renal, and neurocognitive functions during heart surgery as well as premature labor, are being investigated. A team of investigators with expertise in statistical genetics, clinical trials, genetics, molecular pharmacology, genomics, and proteomics is working together to define genetic variants that predict response(s) to acute stress and perioperative outcomes, as well as identifying new mechanisms of disease identified from these studies. Such approaches should enhance development of personalized medicine.