Oct-Nov-Dec 2010
Volume 11, Issue 4

Targeting Trends

Reporting the latest news in Molecular Surgery

Inside this issue:

Newsletter Highlights

Denise Higgins, Editor

ADVANCED TARGETING SYSTEMS

Targeted Ablation of Sympathetic Neurons Reduces Ventricular Arrhythmias and Autonomic Dysreflexia

Contributed by Heidi L. Lujan and Stephen E. DiCarlo,
Department of Physiology, Wayne State University School of Medicine, Detroit, MI 48201

Excessive sympathetic activity is responsible for, and/or contributes to, the morbidity and mortality associated with cardiovascular diseases (e.g. hypertension, stroke, heart failure, ischemic heart disease, ventricular arrhythmias). For example, myocardial ischemia provokes a powerful reflex increase in cardiac sympathetic efferent activity that directly promotes ventricular arrhythmias. Similarly, spinal cord injuries above thoracic level 6 (T6) are associated with episodic bouts of life-threatening hypertension as part of a condition known as autonomic dysreflexia (AD). Physiologically, AD is caused by a massive reflex sympathetic discharge triggered by a stimulus originating below the level of the spinal cord injury.

Importantly, interventions that reduce sympathetic activity protect against ventricular arrhythmias and AD. Accordingly, efforts to reduce sympathetic activity are the first-line therapy for these cardiovascular disorders. However, despite favorable effects, adverse complications (due to generalized sympatho-inhibition, e.g. fatigue, impotence; or specific sympatho-inhibition, e.g. Horner's syndrome, paraesthesia, disruption of sexual, bladder or bowel function) limit compliance and patient satisfaction with these treatments.

However, targeted ablation of cardiac sympathetic neurons reduced the susceptibility to ventricular arrhythmias (2) and targeted ablation of mesenteric projecting sympathetic neurons reduced AD (1) while avoiding these complications.

Specifically, CTB-SAP (cholera toxin B conjugated to saporin; Cat. #IT-14), injected into the stellate ganglia, reduced the number of left ventricular sympathetic fibers (Figure 1), the number of sympathetic post-ganglionic neurons in the stellate ganglia, and virtually eliminated sympathetic pre-ganglionic neurons (SPNs) of spinal cord segments T1-T5 without altering

(continued on page 6)

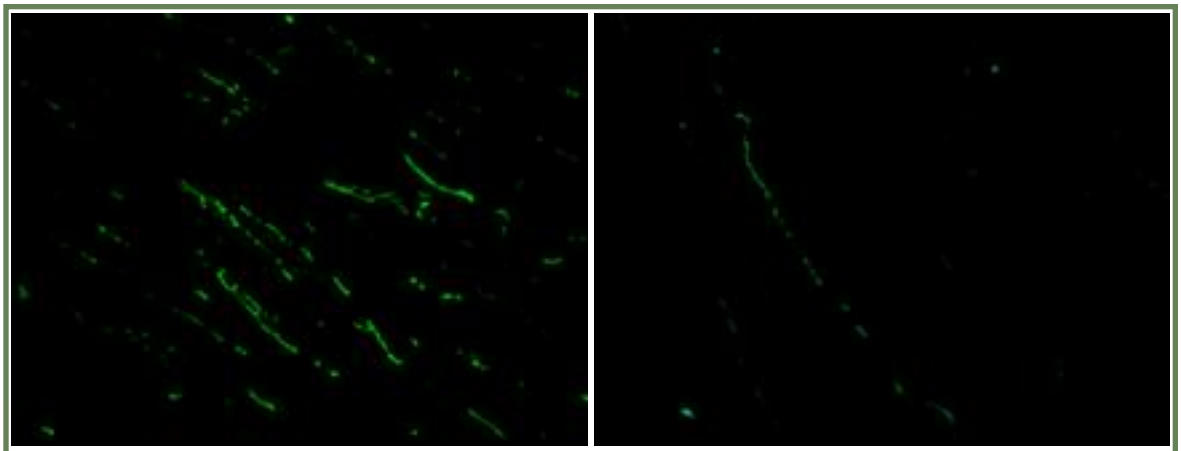

Figure 1 presents tyrosine hydroxylase-immunoreactive sympathetic nerve fibers from the left ventricular free wall of rats that had CTB (left panel) or CTB-SAP (right panel) injected into both stellate ganglia. The CTB-SAP group showed a significant reduction in sympathetic nerve fibers compared to the CTB group.