Seminar Title:
“Late sodium current, a mechanism for angina, heart failure, and arrhythmia, is controlled by nitrosylation mechanisms within the cardiac sodium channel complex.”

Abstract:
Late sodium current is a residual flow normally representing less than 1% of the peak current, but increasing to 3% or more under many conditions such as heart failure, ischemia, and long QT arrhythmia (LQT) mutations. Despite the small size, it affects action potential duration and calcium loading, and plays a role in the pathogenesis of the clinical manifestations of angina, heart failure, and arrhythmia, and therefore represents an attractive therapeutic target. Sodium current flow through a multiprotein complex that regulates the channel. Mutations in two of these interacting proteins, syntrophin alpha 1 and caveolin 3 cause LQT syndromes LQT12 and LQT9 respectively. Studies of these mutations showed that the mechanism for increased late sodium current involved direct nitrosylation of the sodium channel pore protein caused by a loss of function of nitrosylation inhibition. Although LQT12 and LQT9 are rare syndromes, these “experiments of nature” have revealed general regulatory mechanisms acting through regulation of late sodium current and affecting cellular electrophysiology and calcium homeostasis that have wider implications for patients with acquired heart disease.