

# WAYNE STATE UNIVERSITY

## The WSU Program for Traumatic Brain Injury Research

presents a Special Topic Seminar

### Thomas Hudson Sanderson, PhD

#### “Modulation of Cytochrome c Oxidase Activity with Specific Infrared Light Wavelengths: Non-invasive Therapeutic Applications for Reperfusion Injury”

**Abstract:** Reperfusion injury plays a major role in tissue damage in multiple pathologies, including stroke, cardiac arrest/resuscitation, and myocardial infarction. The toxic effect of reperfusion has been attributed to mitochondrial reactive oxygen species (ROS), which are generated at high mitochondrial membrane potentials ( $\Delta\Psi_m$ ). Traditional attempts to scavenge ROS have failed, due to inherent difficulties in sub-cellular delivery within the early minutes of reflow. Accordingly, in these studies we developed a non-pharmacologic therapy that targets cytochrome c oxidase (CcO) using infrared light (IRL). We discovered 4 specific IRL wavelengths that reduce the activity of CcO. We proposed that inhibitory IRL should stabilize  $\Delta\Psi_m$  during pathologic stress, by partially inhibiting CcO and preventing high  $\Delta\Psi_m$ . We tested this hypothesis in a rat model of global brain ischemia/reperfusion. All single, double, triple, and quadruple wavelength combinations that reduce CcO activity were evaluated for neuroprotection using a randomized and blinded study design (n = 8-12/group, 15 treatments). After 14 days, brains were stained for neuron counting. In animals subjected to ischemia there was an 88% loss of neurons. Strikingly, for the 15 IRL-combination groups, loss of neurons ranged from only 11% with the best treatment regimen to 58% with the least efficacious regimen (n = 153). The neurologic protection in IRL treated rats also coincided with preservation of neurologic function, as demonstrated by a 40% improvement in spatial learning deficits. We next utilized in situ detection of mitochondrial superoxide generation to gain preliminary mechanistic insight. In untreated animals, reperfusion induced a 7-fold increase in MitoSOX fluorescence, indicative of mitochondrial ROS production, whereas animals treated with IRL showed fluorescence similar to controls. These data demonstrate a neuroprotective effect of non-invasive reduction of CcO activity with specific IRL wavelengths.

**Date:** Thursday July 12<sup>th</sup>, 2012

**Time:** 12:00pm – 1:00 pm

**Location:** Scott Hall – Green Hall

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