SPRING 2024

SEMINAR FOR NEUROTRAUMA AND DISEASES

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PRESENTS

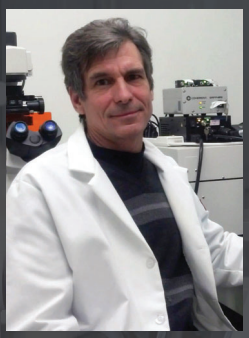
REHABILITATION INDUCES ADAPTATION OF MOTOR CONTROL PATHWAYS AFTER SCI

Date: April 24, 2024 **Time:** 4:00 p.m. - 5:00 p.m. EST

Location: DLR 131 **Zoom Link**: http://bit.ly/42hhhJG

Meeting ID: 923 5486 2062 **Passcode:** CPR

FEATURED SPEAKER



GEORGE SMITH, PhD

Professor and Vice Chair, Department of Neural Sciences; Interim Director, Shriners Children Hospitals Pediatric Research Center; Professor of Bioengineering, Lewis Katz School of Medicine at Temple University

After graduating with my BS in Chemistry, I moved to Case Western Reserve University and completed my graduate studies in the Department of Developmental Genetic and Neurosciences under the mentorship of Dr. J Silver. During this time, I worked on the changing role of astrocytes from growth promoting (immature) to scar forming (mature). I also participated in the founding of Gliatech, Inc. with Dr. Silver. In 1991, I started my first laboratory at UT Southwestern Medical Center as an Assistant Professor studying the role of neurotrophins in regeneration of sensory afferents into the spinal cord. I also began collaborations with Robert Eberhart in the BME program developing filamentous nerve growth conduits. We were the first groups to examine the use of bioresorbable filaments to guide axons across the conduit. In 2001, I was recruited as an Associate Professor to the Spinal cord and Brain Injury Research Center (SCoBIRC) at the University of Kentucky continuing my work on neurotrophins in spinal cord injury and Parkinson's disease. Where we furthered our work constructing and producing various recombinant virus systems to examine regeneration and targeting of transplanted neurons. In 2011, I moved to Philadelphia to study pediatric spinal cord injury. There I changed my research direction from neurotrophins to motor control. The primary goal of my laboratory is to enhance axon regeneration and circuit reformation of the spinal cord after injury or in neurodegenerative disorders, with the long-term goal of developing and transferring treatments to human patients.

ABSTRACT

Approximately 18,000 patients each year are affected by spinal cord injury causing motor, sensory and autonomic dysfunction. Children 16 years of age or younger account for 5% of cases with the majority being cervical level that effect forelimb function. To improve their current lifestyle, patients affected by SCI desire return of hand and digit function. However, most spinal cord injury studies examined recovery of locomotion after thoracic lesions in adults and not goal-directed or skilled forelimb movements after cervical injuries, especially in younger animals. In general, the corticospinal tract drives skilled forelimb movements with support from indirect brainstem regions. After lesions to the corticospinal tract there is a significant loss of forelimb function. Our data shows good recovery in juvenile rats when modulated by altering the excitation of the forelimb motor cortex using chemogenetic channels during play which provided a form of physical and social enrichment. Here expression of Designer Receptors Exclusively Activated by Designer Drugs (Dreadds) showed a hierarchy of recovery of forelimb function. Excitatory Dreadds showed the best recovery with significant increases in recovery above control levels, whereas reduced recovery below control levels was observed when inhibitory Dreadds were expressed within the motor cortex of lesioned CST axons. Likewise, we saw a similar recovery in forelimb kinematics and muscle activity, in which expression of excitatory Dreadds in cortical motor neurons showed the best recovery, followed by mCherry controls with expression of inhibitory Dreadds showing the poorest outcome. We hypothesize that cortical activity modulates axonal sprouting of the lesioned CST, while physical play shapes the connects to promote circuit adaptation rerouting motor commands through brainstem and propriospinal motor systems. We further show that these brainstem and propriospinal networks are involved in relaying the motor command around the spinal cord lesions. Following these circuits, we have developed a novel approach to motor control theory and circuits involved in motor learning supporting rehabilitation.

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