Press Book

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Technical Summary of Research Activities:

Generous support from various funding agencies including the Department of Veterans Affairs, National Institutes of Health, and several private foundations have allowed the Stubbs lab to pursue our ***primary research interests focused on developing novel therapeutic strategies for the clinical management of neuropathies.*** One such strategy being developed in the Stubbs lab utilizes a novel nanoparticle-based local drug delivery platform for the treatment of Guillain-Barré Syndrome (GBS), a prominent and debilitating acute inflammatory demyelinating disorder of the peripheral nervous system (AIDP). Our recently published experimental studies demonstrate that peri-neural administration of lovastatin-encapsulating PLGA nanoparticles significantly attenuate the clinical severity of EAN, an established animal model of AIDP/GBS. Statin-associated neuroprotection was found to significantly limit transendothelial trafficking of autoreactive leukocytes into peripheral nerve by disrupting isoprenylation of Rho GTPases. Statins similarly were found to alter Rho GTPase signaling in primary human trabecular meshwork (TM) cells. Human TM cells play a key role in regulating aqueous humor (AH) outflow / intraocular pressure. For reasons that remain unclear, AH outflow through the trabecular meshwork is impaired in patients with primary open angle glaucoma (POAG) leading to elevated intraocular pressure and ultimately glaucomatous neuropathy. Using our nanoparticles as a platform, we are able to deliver deep within the TM various encapsulated therapeutic agents, including novel mitochondrial-targeted antioxidants. It is here where these agents may have the greatest therapeutic impact for the management of POAG by minimizing or preventing oxidative-injury associated increases in outflow resistance. A third neuropathic disorder that the Stubbs lab studies in association with clinical colleagues is diabetic neuropathy, a very common metabolic neuropathy that significantly alters the quality of life for millions of people worldwide. Bringing together specialists in neurology and exercise physiology, we successfully conducted a VA-funded single site randomized clinical trial looking at the impact that moderate-intensity aerobic or strength-training exercise elicits on the progression of polyneuropathy among glycemic-controlled type 2 diabetic Veterans. Qualitative findings from this study suggest that a short-term (12-week) course of aerobic physical exercise may very well improve sensory, but not motor, nerve fiber function independent of glycemic control. Although the mechanism for this remains speculative, our experimental studies show that aerobic exercise can significantly delay the onset of neuropathic pain, in part, by attenuating calcium channel function within small diameter DRG neurons by altering opioidergic tone.

Non-Technical Summary of Research Activities:

The Stubbs lab is actively engaged in the development of novel therapeutic strategies for the treatment of various types of diseases that selectively affect the bodies peripheral nerves as well as those that are responsible for helping us perceive our visual world. Using nanotechnology, the lab capitalizes on biomedical engineering advancements to produce microscopic sized particles that are then used to deliver novel therapeutic agents directly to the site of nerve injury thereby minimizing undesirable side-effects often observed with systemic delivery of the same agents. Patients with metabolic disorders such as diabetes

often develop serious complications that impair nerve function more uniformly throughout the body. To help these individuals, a different therapeutic approach is needed that has a more wide-spread effect. Physical exercise is well known as an effective adjunctive strategy by which to manage blood glucose levels among diabetic patients. As an already established and proven therapeutic strategy, we are advancing this approach clinically to determine whether a non-invasive program of physical exercise type will prove just as effective at slowing or halting the progression of nerve injury among patients affected by this common metabolic-associated nerve disorder.

Training Opportunities in the Stubbs Lab:

Motivated graduate students seeking advanced Master or Doctorate level degrees in biochemistry, neurochemistry, cellular or molecular biology who join the Stubbs lab can expect to receive hands-on one-on-one training in the neurosciences using state of the cellular and molecular quantitative approaches. Students in training will be develop and master critical skills in experimental design, assay development, data analysis and data interpretation using appropriate parametric or non-parametric statistical measures. Students will learn how and when to evaluate programmatic progress and develop critical skills in implementing alternative design strategies while recognizing progress-delaying pitfalls. While in the Stubbs lab, students will develop and master vital interpersonal communication skills including how to best market and present original research findings at local, national, and international scientific meetings. Students of the Stubbs lab can expect to complete their training by learning first-hand how to prepare and disseminate original research findings not only through the production of a high-quality faculty reviewed and approved thesis/dissertation but also publishing their findings in high-impact peer-reviewed scientific journals. The student can be assured that masterful completion of these and other skill within the Stubbs lab will lead to professional advancement opportunities at and beyond the postgraduate level in the biomedical sciences.