

Distinguished Lecture Series in Physiology

Mariajose Metcalfe, Ph.D.

Project Scientist
Department of Anatomy and Neurobiology
University of California, Irvine

“Consequences of AAV-retro mediated deletion of PTEN following cervical spinal cord injury in mice.”

Spinal cord injury (SCI) causes damage to cells and nerves that send and receive signals to and from the brain and the rest of the body. The corticospinal tract (CST), which controls skilled movements in mammals, is a prominent target after SCI. Cre-driven deletion of phosphatase and tensin homolog (PTEN) in neurons that give rise to the CST reliably enables axon regeneration after SCI. We tested the efficacy of an approach using AAV/Cre vectors that are transported retrogradely from an injection site in the spinal cord, to the majority of neurons that give rise to spinal tracts. Following SCI, PTEN^{ff};Rosa^{tdTomato} mice were injected with AAV-retro/Cre and forelimb motor function was assessed over time using a grip strength meter. PTEN-deleted mice exhibited greater recovery than respective controls. Despite initial recovery, grip strength began to decline at around 1 month post injury in PTEN-deleted mice and at 2-3 months post-injury, 35-50% of the mice began to exhibit incessant scratching and hindlimb dystonia. In addition to retrograde transduction of cells of origin of spinal pathways in the brain, some dorsal root ganglia (DRG) neurons in ganglia near the injection site were also transduced. However, co staining for tdTomato and calcitonin gene-related peptide (CGRP) revealed no transduction of CGRP-positive neurons that give rise to C-afferents that mediate nociception. We conclude that, although intra-spinal injections of AAV-retro/Cre in mice can lead to initial improvements in forelimb motor recovery after SCI, there are late-developing functional abnormalities with the experimental conditions used here. The mechanisms underlying late-developing pathophysiologies remain to be defined.

Thursday, January 12, 2022
GBSF & Zoom
12 p.m.

January
12



Mariajose Metcalfe, Ph.D.
Project Scientist
Department of Anatomy and Neurobiology
University of California, Irvine



Host: Theanne Griffith
tgriffith@ucdavis.edu