

ENGINEERING ASTROCYTES TO PROMOTE WOUND REPAIR AND MODULATE FOREIGN BODY RESPONSES IN THE CNS



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ABSTRACT

Astrocytes are the predominant glial cells in the mammalian central nervous system (CNS) and play essential roles in maintaining neural circuit activity and tissue homeostasis. In response to CNS insult, including traumatic injury or implantation of a medical device, astrocytes undergo a conserved, temporally regulated reprogramming that reshapes their prioritized functions to protect adjacent neural tissue. The nature and extent of astrocyte reprogramming critically influences outcomes after CNS insult. For example, regeneration after traumatic CNS injury in adult mammals is limited by local responding astrocytes lacking sufficient self-renewal capacity. By contrast, the CNS of neonate (newborn) mammals possesses exceptional parenchymal repair capacity owing to immature astrocytes with elevated proliferative and migratory potential. In the context of an implanted medical device, the spatial extent of astrocyte reprogramming and how impacted astrocytes respond to any further device micromotion, latent infection, or other persistent device-derived stimuli, dictates device performance and longevity. Engineering astrocyte responses to promote targeted functional gains while preserving key capabilities of healthy neural tissue astrocytes will be critical to enabling effective neural regeneration therapies and improving long-term performance of implanted devices. In this talk, I will outline our emerging understanding of how adult astrocytes adaptively reprogram in response to CNS injury and implanted foreign bodies, drawing insights from innovative astrocyte-specific transcriptomic bioassays. I will also provide an overview of biomaterial and cell-grafting strategies that we are exploring to direct astrocyte responses in preclinical models of stroke, spinal cord injury, and foreign body responses.

BIO

Dr. Timothy O'Shea, PhD is an Assistant Professor in the Biomedical Engineering department at Boston University (BU). Tim grew up in Brisbane, Australia and completed a Bachelor of Medical Engineering (First Class Honours) and a Masters in Engineering Management at Queensland University of Technology (QUT) before moving to the US for graduate school. He completed his PhD study in Medical Engineering and Medical Physics within the collaborative Health Sciences and Technology program of the Harvard Medical School and the Massachusetts Institute of Technology where we conducted PhD thesis research with Institute Professor Robert Langer. As a Postdoctoral Fellow in Neurobiology at UCLA, he worked with Professors Michael Sofroniew (Neurobiology) and Timothy Deming (Bioengineering) developing and testing novel bioengineering tools to study biological mechanisms involved in CNS injury and repair as well as the CNS foreign body response to implants. Since Fall 2020 he has been leading the Glia Engineering Lab at BU where he has received numerous awards including the Maximizing Investigators' Research Award (MIRA) from NIH and grants from several spinal cord injury research foundations such as Craig H Neilsen, Paralyzed Veterans of America, Bryon Reisch, and Wings for Life.