Project Title: A Combined Cell and Gene Therapy for Retrograde Delivery of Neurotrophic Payloads for Neuromuscular Disease
Principal Investigator: Michael Hicks, PhD

Imagine in the future receiving a shot in your shoulder muscle to cure neurological disorders. Transport from the skeletal muscle to the central nervous system is a natural occurring process for some viruses, and my proposal seeks to lay the groundwork for re-envisioning gene delivery to the spinal cord and brain for scientific discovery and human health benefits. Skeletal muscle is multinucleated and readily accepts new myonuclei through fusion of muscle stem cells. The fusion of even one transgenic muscle stem cell with a diseased myofiber could provide transgene expression to hundreds of myonuclei within that myofiber. Skeletal muscles are also innervated by motoneurons, providing direct access to the CNS by retrograde transmitting viruses.

My expertise is in creating skeletal muscle from human pluripotent stem cells (hPSCs) that can engraft and fuse with patient muscles for personalized cell therapies. My proposal seeks to be the first to synthesize next-generation neurotrophic gene therapies customized for hPSC muscle progenitors that can be transplanted into patient muscles to provide controlled, unique, and new avenues for personalized neural therapeutics.

I am seeking pilot funding to gather preliminary data for this new direction in my laboratory. My workflow aims to differentiate hPSCs to skeletal muscle progenitor cells, infect muscle progenitor cells with custom-designed viruses containing Cas9+gRNA, and transplant the cell+gene therapy into the skeletal muscle of mice to gather proof-of-concept for bio-distribution and timing of retrograde transport into the spinal cord and CNS. This proposal is not currently funded.