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Optogenetic Control of a Neuromuscular Junction Model on a Chip

Currently, more than 300,000 people in the United States live with spinal cord injuries (SCIs). Such damage to the central nervous system frequently results in paralysis, impairing a patient's ability to function independently. In one downstream effect of SCI, motor neurons, which control voluntary and involuntary movement, die and fail to properly synapse on muscles at neuromuscular junctions (NMJs). No treatment effectively reverses the damage of an SCI. Pluripotent stem cells (PSCs) are an attractive candidate for post-injury cell replacement therapy because they can differentiate into the three germ layers responsible for forming all adult tissue. Optogenetics, or light control of cells, provides a groundbreaking means to stimulate neurons without electrical or pharmacological agents. Microfluidics devices serve as a high throughput investigative tool to demonstrate the therapeutic potential of PSCs. These apparatus provide an optimal setting to mimic three-dimensional microenvironments within the body previously limited to animal model investigations.

In this study, we utilized a microfluidic approach to demonstrate functional optogenetic neuronal control of NMJs. We differentiated a line of PSCs constitutively expressing the optogenetic protein channel rhodopsin-2 (ChR2) into optically excitable motor neurons within a 3D aggregate. We co-cultured these aggregates with muscle strips in the microfluidics device to form NMJs.

Our NMJ-on-a-chip will serve as model for cell replacement therapy. The selective activation of specific muscle sets with optogenetic control could be used to retrain an SCI patient to walk again.