

Reprogramming Glial Cells into Functional Neurons to Treat SCI

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Background/Objective:

Spinal cord injuries (SCI) disrupt descending neural pathways that are required for motor function. Among these tracts, the most important for forelimb function is the corticospinal tract (CST). Mature CNS neurons typically fail to regenerate after injury due to an extrinsic inhibitory environment and an intrinsic incapability to grow. After SCI, a major inhibitory component at the lesion site consists of NG2 glial cells. Decreasing the amount of NG2 around the lesion should create a more permissive environment for CST regeneration. We hypothesize that NG2 glial cells at the lesion site can be reprogrammed into functional neurons, which can then facilitate CST regeneration and synapse formation, leading to functional recovery.

Methods:

Dorsal hemisections of the spinal cord at C5 were performed on 29 adult mice in three groups. Reprogramming of glial cells was completed using a Lenti-SOX2 virus. BrdU and AAV8-GFP were administered to each mouse to trace the proliferating cells and CST, respectively. After sacrificing, the spinal cord tissue was harvested, cryosectioned, and mounted on slides. NeuN and BrdU immunofluorescence staining were performed and high-quality images were obtained using a NeuroLucida microscope system equipped with fluorescence.

Results:

We successfully stained proliferating cells using BrdU and neurons using NeuN. Imaging collection is carried out in a blinded fashion and is not yet complete. However, initial data on a subset of obtained images have shown signs of CST regenerating through the lesion site rather than retracting from it.

Conclusion/Impact:

Preliminary data suggests that reprogramming of NG2 glial cells into functional neurons is an effective method of promoting CST regeneration after SCI. With the annual incidence of SCI of approximately 17,810 new cases, further studies are required to determine if this approach would promote motor functional recovery and, if so, can be translated to treatments to improve quality of life for those who suffer from SCI.