

## **New Technologies for Repairing Spinal Cord Injuries: Suppressing scar formation and bridging injury sites.**

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When nerve fibers (called axons) are severed by traumatic injury to the adult spinal cord, the surviving cut ends often sprout but ultimately fail to regenerate across the site of injury, resulting in a loss of nervous system function. Traumatic spinal cord injuries also result in the loss of support cells (collectively called glia) that are vitally important for maintaining the structure and function of the nervous system. One type of glia called astrocytes (“star cells”), are thought to account for ~70% of all cells in the human spinal cord and brain. The injured spinal cord often reacts to inflammation and the loss of glia at sites of injury by rapidly forming a meshwork of dense scar tissue containing molecules that are actively inhibitory to axon growth. Our research has clearly demonstrated that scar tissue presents a combined physical and molecular barrier to axon regeneration in the injured spinal cord.

**1. Controlling scar formation with Decorin:** In collaboration with Integra LifeSciences, my research team has shown that a naturally occurring suppressor of scar formation, a molecule called Decorin, is highly effective at suppressing the formation of both misaligned scar tissue and the levels of axon growth inhibitors at sites of spinal cord injury. More importantly we observed the rapid growth of sensory axons across decorin treated spinal cord injuries in just 4 days. We have also shown that decorin can induce the spinal cord to make an enzyme called Plasmin that has the ability to break down scar tissue. Working with Integra LifeSciences we have already developed pharmaceutical grade human decorin and are now actively testing its ability to promote axon regeneration and functional recovery in chronically injured rat spinal cords. I am pleased to say that our work with decorin won the 2006 American Spinal Injury Association Prize for breakthrough in spinal cord injury research.

**2. GRP-derived Astrocytes for bridging spinal cord injuries:** It has long been known that the embryonic spinal cord does not form inhibitory scar tissue and supports axon regeneration across sites of injury. My research team, in collaboration with the University of Rochester NY, have therefore developed a novel technology that allows us to make large numbers of a subtype of embryonic astrocyte that is highly effective at promoting axon regeneration and functional recovery in adult spinal cord injured rats. By treating embryonic glial restricted precursors (stem cell-like cells) with the correct signaling molecules we can generate a subtype of early astrocyte (called GDAs) that promote a ~40% efficiency of sensory axon regeneration in just 8 days when transplanted into adult rat spinal cord injuries. In addition, GDA cells were also able to suppress scar formation, protect injured neurons in the brain and promote robust recovery of locomotor function in spinal cord injured rats. We are now developing the human form of GDA cells and investigating whether these cells can also be made from adult stem cells.

In summary Decorin and GDA cells are two highly promising novel therapies for repairing human spinal cord injuries, that given sufficient funding we are hoping to take to clinical trial in the US within the next 3 years. The support of the Christopher and Dana Reeve Paralysis Act by Congress will help ensure that we are able to meet this goal and provide new and truly effective therapies to alleviate the suffering of those with severe spinal cord injuries.