

Gene therapy improves limb function following spinal cord injury

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Delivering a single injection of a scar-busting gene therapy to the spinal cord of rats following injury promotes the survival of nerve cells and improves hind limb function within weeks, according to a study published April 2 in *The Journal of Neuroscience*. The findings suggest that, with more confirming research in animals and humans, gene therapy may hold the potential to one day treat people with spinal cord injuries.

The [spinal cord](#) is the main channel through which information passes between the brain and the rest of the body. Most [spinal cord injuries](#) are caused by damage to the axons, the long extensions that [brain cells](#) use to send these messages. Once these injuries take place, scar tissue forms and prevents the damaged nerves from re-growing.

Previous animal studies show that one way to promote the growth of injured spinal nerve [cells](#) is to administer the enzyme chondroitinase ABC (ChABC), which digests scar-forming proteins, to the site of injury. However, because ChABC breaks down quickly, maintaining these beneficial effects for a long period of time requires invasive and repeated administration of the enzyme to the spinal cord. To get around this hurdle, in recent years, scientists began exploring gene therapy as a method to efficiently coax spinal cord cells to produce the enzyme.

In the current study, a group of researchers led by Elizabeth Bradbury, PhD, of King's College London used a single injection to deliver the ChABC gene therapy into the spinal cord of injured adult rats. The

treatment not only led the spinal cord cells to produce and secrete ChABC in large quantities over areas spanning the injury epicenter, it helped to maintain the overall health of the damaged spinal cord and restored hind limb function in the animals within 12 weeks.

"These findings provide convincing evidence that gene therapy with chondroitinase not only encourages the sprouting of injured axons, but also imparts significant protection to nerve cells," said Mark Tuszynski, MD, PhD, who studies how nerve cells recover following injury at the University of California, San Diego, and was not involved in this study. "These are new and important findings that could lead to the development of testable therapies for spinal cord injury in people," he added.

Bradbury's team delivered the ChABC gene into the matrix of the spinal cord (the space between [spinal cord cells](#)). Twelve weeks later, the animals that received the therapy had more surviving spinal [nerve cells](#) and fibers present through and around the scar compared with animals that did not receive the treatment. ChABC gene therapy also led to the recovery of hind limb function in the animals, allowing them to navigate the rungs of a horizontal ladder.

Additional analysis revealed that ChABC gene therapy changed the way that inflammatory cells in the region respond following injury. Normally, after injury, immune cells invade the spinal cord and cause destructive and irreparable tissue damage. However, ChABC [gene therapy](#) decreased the presence of these cells and increased the presence of other immune cells called M2 macrophages that help to reduce inflammation and enhance tissue repair.

"This scar-busting therapy represents an important advance since it reveals a novel interaction between the supportive matrix and the [immune cells](#) following an injury," Bradbury said. The ability to treat

large areas of the spinal cord for extended periods of time in animals "will be important for scaling up to the larger human spinal cord for future translation of this therapy to the clinic," she added.

Provided by Society for Neuroscience

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