Progress is reported on repairing spinal cords
Scientists at UCSD link up nerve cells

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LA JOLLA — Moving one step closer to developing a possible therapy for repairing spinal cord injuries, scientists at the University of California San Diego say they have successfully guided regenerating nerve axons to cell targets, where they re-establish connections essential to any recovery.

“It was a breakthrough a few years ago to finally get axons to regenerate,” said Dr. Mark Tuszynski, a professor of neurosciences and part of a team of scientists from UCSD, the San Diego Veterans Affairs Medical Center and UCLA that reported the achievement in yesterday's online edition of the journal Nature Neuroscience.

“With this advance, we've shown it's possible to direct an axon to find the correct target from among potentially millions of incorrect ones in the spine and brain and make the right connection.”

Axons are long, fragile fibers connecting nerve cells. They are the conduits through which electrical signals pass between neurons, from stimulus to brain and back. In spinal cord injuries, axons are damaged and severed, cutting off neural communications. The result is sensory loss and possible paralysis.

A survey this year by the Christopher & Dana Reeve Foundation found 1.275 million Americans have suffered a spinal cord injury and more than 5.6 million Americans live with some form of paralysis. Stroke was the leading cause of paralysis (29 percent), followed by spinal cord injuries (23 percent) and multiple sclerosis (17 percent).

Tuszynski and colleagues were able to restore severed neural connections in laboratory rats through a painstaking combination of therapies. They injected a benign virus carrying a natural growth factor called neurotrophin-3, a type of chemical hormone, into the targeted tissue site. The growth factor behaves like a magnet, attracting growing axons to it.

At the same time, the researchers placed a graft or bridge of cells across the injury site to support axon growth and stimulated genes in the affected nerves to turn up axon growth.

“What this work dramatically shows is that it will take a combination of things to effectively repair spinal cord injuries,” said Naomi Kleitman, a program officer at the National Institute of Neurological Disorders and Stroke who is familiar with the UCSD research.

“It's one important step in a long process of many steps. There are still many things we don't know. There are likely more elements that will be needed before it's possible to translate this research to humans. The process, even now, sounds like a lot. But compared to being paralyzed for the rest of your life, maybe it's not asking too much."

Tuszynski's research focused on sensory neurons, which convey information about touch, position and pain. He and his colleagues are now investigating whether the same combination works with motor neurons, which govern movement and are tougher to manipulate.

UCSD's success was not complete. Although the regenerated axons could be precisely guided to their targets and form obvious synapses with other cells, the resulting connections were not electrically active. They did not work.

The problem, Tuszynski theorizes, may be that the regenerated axons lack a myelin sheath – a fatty coating that serves the same function that rubber insulation does for electrical wiring. Myelin sheathing focuses and speeds electrical impulses through axons.

"Just as an electrical circuit needs insulation so it doesn't short-circuit, it appears that these regenerating axons require restoration of the myelin sheath to ultimately restore function," Tuszynski said.

The solution, Tuszynski said, might be to introduce another element to the therapeutic combination: a cell, perhaps, that triggers or produces myelin formation at the injury site.

This year, first-phase clinical trials were approved for one such possible approach. Geron, a biotechnology company based in Menlo Park, will conduct first-phase safety trials for a procedure involving the injection of embryonic stem cells into human patients with spinal cord injuries. The hope is that the stem cells will mature into oligodendrocytes, a kind of spinal cord cell that produces myelin.