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Nerve Cells Successfully Regenerated Following Spinal Cord Injury

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Using a combination of therapies and cell grafts, a team of University of California, San Diego (UCSD) School of Medicine researchers has promoted significant regeneration of nerve cells in rats with spinal cord injury.

The therapeutic approach successfully stimulated new nerve fibers called axons to grow and extend well beyond the site of the injury into surrounding tissue, following surgically induced spinal cord damage.

These results prove that combinational therapy can promote the vigorous growth of new axons even after a complete lesion of the spinal cord cells, with the new growth extending through implanted tissue grafts, and into the spinal cord and healthy tissue surrounding the injury site, according to Mark Tuszynski, M.D., Ph.D., professor of neurosciences at UCSD and senior author of the study. The paper is published in the July 14 issue of the *Journal of Neurosciences*.

"Previous studies have demonstrated reduced lesion and scarring, tissue sparing and functional recovery after acute spinal cord injury," said Tuszynski, who also has an appointment with the Veterans Affairs Medical Center, San Diego. "This study shows unequivocally that axons can be stimulated to regenerate into a cell graft placed in a lesion site, and out again, into the spinal cord -- the potential basis for putting together a practical therapy."

The successful regeneration followed complete lesion of the nerve site. The study, which targeted sensory axons, was not designed to test functional improvement.

Axon regeneration is one of the many challenges confronting spinal cord researchers. The axon is a critical communication path from the nerve cell, with many sensory axons extending from the spine to the brain. When the spine is severely damaged that connection is lost, and gaps form in the healed spine that fill with fluid, an environment that complicates regeneration efforts since axons can't grow across the lesion cavity. Therefore, to be successful, regeneration therapy must stimulate growth and provide a scaffold that creates an appropriate environment to support axonal growth.

The most dramatic axonal growth seen in the UCSD study was in rats pre-treated with cyclic AMP (cAMP). The team injected cAMP, an important cellular messenger that regulates various metabolic processes, directly into the nerve cell nucleus before creating the lesions. After surgical severance of the spine, the injury site was implanted with a tissue bridge of bone marrow stromal cells and treated with neurotrophins (growth factor). In these rats, over a three-month period significant growth of axons was noted, extending into and beyond the tissue graft. Pre-treatment with cAMP could be a practical approach for treating patients with established, chronic spinal cord injuries, a possibility that is the subject of current study by the UCSD group.

Co-authors of the paper are Paul Lu, Ph.D., UCSD Department of Neurosciences; Leonard Jones Ph.D., UCSD Department of Neurosciences and Veterans Affairs Medical Center, San Diego; and Marie T. Filbin, Ph.D., Biology Department, Hunter College, New York.

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