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RESEARCH NEWS

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Opening the Way for Nerve Regeneration Studies in Worms

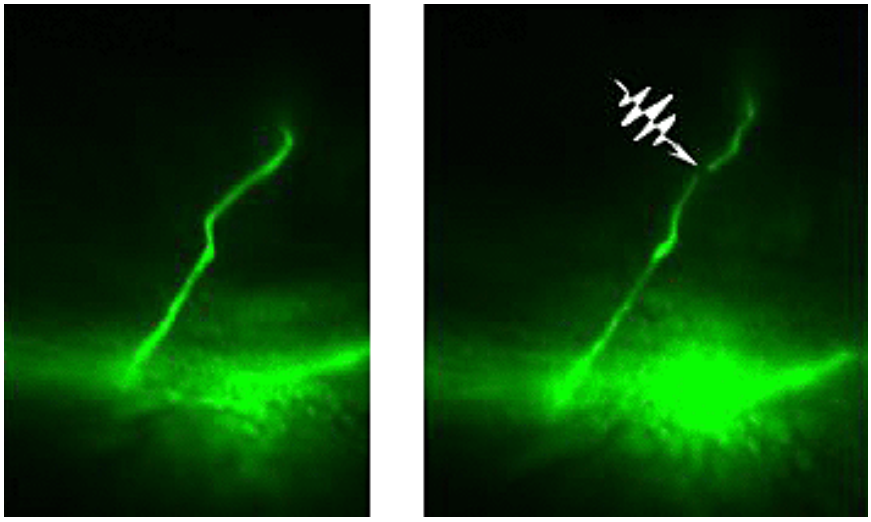

Image Title: The two images depicted show enlarged views of an uncut axon (left) from the roundworm *C. elegans* and an axon cut (right) by laser. - Courtesy of Yishi Jin, also published in December 16, 2004, issue of Nature.

Using a precisely targeted laser, researchers have snipped apart a single neuron in the roundworm *C. elegans* — an achievement that opens a new avenue for studying nerve regeneration in this genetically manipulable animal. Indeed, their initial studies have demonstrated that the severed nerves of worms are capable of regenerating and regaining full function.

According to the researchers, studying nerve regeneration in the worm could provide answers to questions that are not accessible currently by doing experiments in more complex animals, including mice and zebrafish.

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— Yishi Jin

A research team that included Yishi Jin, a Howard Hughes Medical Institute investigator at the University of California, Santa Cruz (UCSC), Andrew Chisholm, also of UCSC, and Adela Ben-Yakar, who was at Stanford University and is now at the University of Texas at Austin, reported its achievement in the December 16, 2004, issue of the journal *Nature*. Other co-authors are from Stanford University and UCSC.

The researchers used a laser that produces energy pulses of 200-quadrillionths of a second in a beam focused to less than one-hundredth the diameter of a human hair. The laser can vaporize tissue precisely without causing extensive heat or damage that would compromise the viability of the targeted cell or surrounding tissue, said the researchers.

“This new capability of cutting individual nerves offers the opportunity to use the well-characterized genetics of *C. elegans* to study the basic mechanisms of nerve regeneration," said Jin. “Until now there has been little study of nerve regeneration using genetic methodology, because most studies have been done on higher vertebrate organisms, where following the consequences of genetic manipulation is not yet readily accessible." Such studies, said Jin, would involve making mutations in genes believed to be involved in nerve regeneration and studying the effects on regeneration following laser severing of the nerves.

In the experiments reported in *Nature*, the researchers first introduced a gene that produced a green fluorescent protein in the target nerve, in this case, one that controls a particular muscle movement in the worm. When they directed the laser at the cable-like axon that snaked away from the nerve-cell body, they found they could precisely sever the axon. They observed that both ends of the severed nerve axon immediately retracted, but that in about half the cases, the nerve regrew in about a day. By doing dye-uptake experiments, the researchers could see that the laser had actually cut the axons, and had not simply bleached the region hit by the beam.

The researchers also noticed an intriguing and potentially important result: The worms that had been operated on showed evidence that the nerves had regrown and also regained the ability to move the muscle served by the neuron. This observation indicated that the regrowth of the nerve caused functional changes.

Among the immediate questions raised by the new experiments is how the nerves regrow after cutting, said Jin. “We see that the proximal end, nearest the cell body, appears to begin regrowth, and the distal end seems to hang around for a while. Depending on how fast the proximal end regrows, it might attach to the distal end. Otherwise, the distal end seems to deteriorate, and the nerve regeneration will proceed from the proximal end. However, we will need to do more detailed studies to determine whether regeneration is of the two cut axons, or due to a complete regrowth," she said.

According to Jin, the laser they used had a custom-built apparatus to permit the precise focus of laser on biological samples, but the laser itself is available commercially. Thus, the technique can be readily adopted by other laboratories, she said. And with its proven ability to cut individual nerves, Jin said she could envision the laser being used for other applications, such as selective ablation of subcellular structures, to explore their role in nerve regeneration.