Nerve-cell regeneration quest is fast tracke

Microchip technology rapidly identifies compounds for regrov nerves, in live animals.

Anne Trafton, MIT News Office

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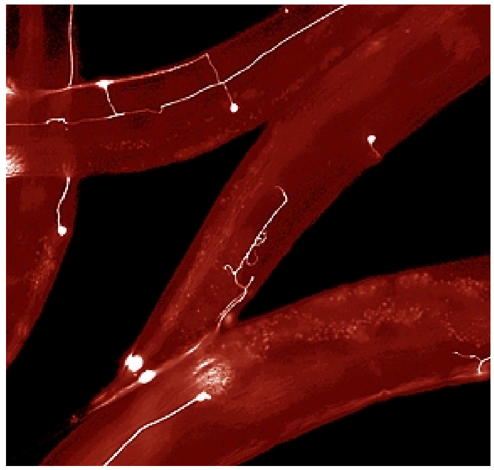

MIT engineers have developed a way to rapi surgery on single nerve cells in the worm C. The white lines represent axons — long exte nerve cells that carry messages to other cel Image: Craig Millman and Yanik Lab

Scientists have long sought the ability to regenerate nerve cells, or neurons, which could offer a new way to treat spinal-cord damage as well as neurological diseases such as Alzheimer's or Parkinson's. Many chemicals can regenerate neurons grown in Petri dishes in the lab, but it's difficult and time-consuming to identify those chemicals that work in live animals, which is critical for developing drugs for humans.

Engineers at MIT have now used a new microchip technology to rapidly test p drugs on tiny worms called C. elegans, which are often used in studies of the system. Using the new technology, associate professor Mehmet Fatih Yanik a colleagues rapidly performed laser surgery, delivered drugs and imaged the neuron regrowth in thousands of live animals.

"Our technology helps researchers rapidly identify promising chemicals that tested in mammals and perhaps even in humans," says Yanik. Using this tec researchers have already identified one promising class of neuronal regener

The paper will appear in the online edition of the *Proceedings of the Nationa of Sciences* the week of Oct. 11.

Lead authors of the paper are postdoctoral associate Chrysanthi Samara an students Christopher Rohde and Cody Gilleland, and collaborating chemists Haggarty and Stephanie Norton. Development of the new technology and the regeneration screen was funded by the NIH Director's New Innovator Award P Packard Fellowship in Science and Engineering, an Alfred Sloan Award in Ne an NSF Graduate Fellowship and a Merck Graduate Fellowship.

Rapid analysis

C. elegans is a useful model organism for neuron regeneration because it is transparent, and its entire neural network is known. Yanik and colleagues ha developed a femtosecond laser nanosurgery technique which allowed them t observe regeneration of individual axons — long extensions of neurons that to neighboring cells. Their femtosecond laser nanosurgery technique uses ti focused infrared laser pulses that are shorter than billionth of a second. This laser to penetrate deep into the animals without damaging the tissues on its

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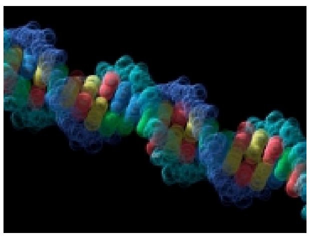

In a new book, prominent historian of science dismisses the 'unanswerable' question of whether heredity or the environment matter more in human development.

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the laser beam hits its final target.

In the PNAS study, the researchers used their microchip technology to rapidl axons of single neurons that sense touch. Moving single worms from their inc to an imaging microchip, immobilizing them and performing laser surgery take about 20 seconds, which allows thousands of surgeries to be performed in a of time.

After laser surgery, each worm is returned to its incubation well and treated v different chemical compound. C. elegans neurons can partially regrow withou which allowed Yanik's team to look for drugs that can either enhance or inhib regrowth. After two or three days, the researchers imaged each worm to see had any effect.

The MIT team found that a compound called staurosporine, which inhibits ce enzymes known as PKC kinases, had the strongest inhibitory effect. In a follo they tested some compounds that activate these kinases, and found that one stimulated regeneration of neurons significantly. Some of Yanik's students ar testing those compounds on neurons derived from human embryonic stem ce

The new technology represents a significant advance in the level of automat be achieved in C. elegans studies, says Michael Bastiani, professor of biolog University of Utah. "Using 'classical' handling techniques you can cut and ass 100 animals per day," he says. "Yanik's automated system seems like it coul throughput by at least 10-fold over that number." He points out that one pote limitation of the system is that it might not pick up the effects of neural regen can't penetrate the worm's cuticle, a thick outer layer that surrounds the skin

However, chemicals can still be taken up through the worms' digestive tract, v important test for checking whether chemicals would work on live animals, sa