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Injured nerves regrow when fidgetin enzyme is suppressed

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Suppressing the enzyme fidgetin promotes the re-growth of experimentally injured nerve cells and their connections, according to research with laboratory rats that will be presented Tuesday, Dec. 17, at the American Society for Cell Biology (ASCB) annual meeting in New Orleans.

If additional studies confirm these results, fidgetin inhibition could be a potential new therapeutic approach to promote tissue regeneration and repair of the broken cell connections that occur in a wide range of conditions including myocardial infarction, or heart attack, chronic cutaneous wounds and spinal cord injury.

To explore the enzyme's role in neurons, Peter Baas, Ph.D., Lanfranco Leo and colleagues at Drexel University in Philadelphia collaborated with David Sharp, Ph.D., of Albert Einstein College of Medicine in Bronx, NY.

Dr. Sharp was the first scientist to determine that during growth and development, fidgetin prunes unstable microtubule scaffolding in cells. Microtubules hold up a cell's cytoskeleton.

Fidgetin also prunes unneeded connections in the neuronal network as it grows in complexity and size during childhood and adolescence.

The ability of nerves to grow and prune diminishes as individuals mature. As a result, neurons of adults have lost most of the power to

reshape themselves. This characteristic is good for the hard wiring of the nervous system but a bitter pill because adult nerves that are badly injured or severed will not regenerate.

To determine whether fidgetin prevents nerve regrowth in the adult brain, the researchers used a novel nanoparticle technology to block the enzyme in the injured nerves of adult rats. By blocking fidgetin, they were able to restart growth in the animal model, a finding with potential implications for many types of human nerve injury, including the most difficult challenge, spinal cord injury.

The nanoparticle technology was developed by Joel Friedman, M.D., Ph.D., and Adam Friedman, M.D., of Albert Einstein College of Medicine. The tiny nanoparticles were infused with siRNA, small interfering RNA, that bound the messenger RNA (mRNA) transcribed from the fidgetin gene. The siRNA binding caused the mRNA to be tagged for destruction. As a result, the mRNA for fidgetin was not translated, and the fidgetin enzyme was not produced by the cell.

This study builds on Dr. Sharp's other research that showed that inhibiting fidgetin might help the healing of wounds, such as skin burns as well as heart tissue damaged by a heart attack.

"Depleting novel microtubule-related proteins represents a new and proprietary approach," according to the researchers, who have formed a biotech company, MicroCures Inc., to commercialize their approach. Among its potential uses, they said, would be "tissue regeneration and repair in a wide range of therapeutic contexts including: spinal cord injury, myocardial infarction, and acute and chronic cutaneous wounds."

The enzyme fidgetin is the protein product of the fidgetin gene, which was first identified in a mutant strain of "fidget" mice, first bred in 1943 by Hans Grüneberg and named for their fidgety behavior.

More information: Author will present, "Fidgetin restrains axonal growth during neuronal maturation by a microtubule-based mechanism and provides a means for therapeutically enhancing regeneration of injured adult axons," on Tuesday, Dec. 17, during the 12 noon to 1:30 p.m. poster session, "Neuronal Cytoskeleton II."

Provided by American Society for Cell Biology