

Master regulator found for regenerating nerve fibers in live animals

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Researchers at Children's Hospital Boston report that an enzyme known as Mst3b, previously identified in their lab, is essential for regenerating damaged axons (nerve fibers) in a live animal model, in both the peripheral and central nervous systems. Their findings, published online by *Nature Neuroscience* on October 25, suggest Mst3b - or agents that stimulate it - as a possible means of treating stroke, spinal cord damage and traumatic brain injury. Normally, neurons in the central nervous system (the brain and spinal cord) cannot regenerate injured nerve fibers, limiting people's ability to recover from brain or spinal cord injuries.

The study, led by Nina Irwin, PhD and Larry Benowitz, PhD, of the Laboratories for Neuroscience Research in Neurosurgery and the F.M. Kirby Neurobiology Center at Children's, builds on previous discoveries in the lab. In 2002, they showed that a naturally occurring small molecule, inosine, stimulates axon regeneration, later showing that it helps restore neurological functions in animal models of injury. In 2006, Benowitz and colleagues reported a previously unknown growth factor, oncomodulin, to have dramatic effects on axon growth.

Investigating the mechanisms of action of inosine and oncomodulin, Irwin and Benowitz discovered that both compounds activate Mst3b, an enzyme that appears to be a master regulator of a cell-signaling pathway controlling axon growth. Mst3b, a protein kinase, in turn activates signals that switch on the genes necessary for axons to grow.

Working with live rats whose optic nerve was damaged (a common model of [central-nervous-system](#) injury), Irwin, Benowitz and colleagues show that in the absence of Mst3b, axons show very little regeneration, even in the presence of factors known to enhance axon growth. In cell cultures, axon growth increased when activated Mst3b was expressed in the neurons.

"All the growth factors we've tested - oncomodulin, inosine, brain-derived neurotropic factor, nerve growth factor - act through Mst3b," says Benowitz. "In fact, activating Mst3b by itself is enough to cause growth even if there are no growth factors around. In terms of basic understanding of nerve cells, this is a very exciting finding."

Further studies examining how Mst3b exerts this growth-promoting effect may open up new avenues for treating brain and [spinal cord injuries](#), Benowitz says. While this study explains why growth factors work - because they stimulate Mst3b - it's not yet known whether Mst3b is the best stimulator of axon growth from a practical drug-development standpoint, he adds.

Irwin is now working on possible gene therapy approaches involving Mst3b. Activating Mst3b may help overcome some natural "brakes" in the cell-signaling system that prevent nerve regeneration under normal conditions.

Source: Children's Hospital Boston ([news](#) : [web](#))

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