MedicalXpress

Study identifies specific gene network that promotes nervous system repair

February 19 2016, by Mark Wheeler

Whether or not nerve cells are able to regrow after injury depends on their location in the body. Injured nerve cells in the peripheral nervous system, such as those in the arms and legs, can recover and regrow, at least to some extent. But nerve cells in the central nervous system—the brain and spinal cord—can't recover at all.

A UCLA-led collaboration has identified a specific network of genes and a pattern of gene expression mice that promote repair in the peripheral nervous system in a mouse model. This network, the researchers found, does not exist in the central nervous system. The researchers also found a drug that can promote nerve regeneration in the central nervous system.

The study appears in the online edition of the journal *Neuron*.

Nerve cells throughout the body are responsible for transmitting and receiving electrical messages to cells and tissues in other organ systems. "We know this transmission of messages can be impaired by injury, and the recovery of nerve cells after injury largely depends on their location," said Vijayendran Chandran, a project scientist in the department of neurology at UCLA and the study's first author.

"Understanding these molecular differences in injured nerve cells in the limbs, where regeneration happens, versus injured nerve cells in the spinal cord, where regeneration fails, would open up the possibility to design treatment to enhance neuron regeneration in the central nervous

system after injury."

The researchers measured the response of gene regulation at the level of messenger RNA, or mRNA, in each instance of injury. Gene regulation is the process of turning genes on and off, ensuring that genes are expressed at the right times. Messenger RNA carries information from a gene that, in a long molecular cascade, ultimately tells a protein what to do.

The researchers developed a unique set of algorithms to look at the interactions of various groups of genes and the order in which they were expressed.

"That allowed us to find common patterns that correlated with regeneration in the peripheral nervous system, and within those patterns we were able to identify several genes not previously known that enhanced repair," said Dr. Dan Geschwind, the study's senior author and a professor of neurology, psychiatry and human genetics at UCLA.

"But we did not find these patterns in the central nervous system. That was the major advance—identifying, in an unbiased way, the entire network of pathways turned on in the peripheral nervous system when it regenerates, key aspects of which are missing in the central nervous system."

Next, as a proof of principle that global patterns of gene expression could be used to screen for drugs that mimic the same pattern, the researchers used a publicly available database at the Broad Institute to look for such a drug. That led them to one called Ambroxol, which significantly enhanced central nervous system repair.

"We're excited about this study because there are a number of firsts that came out of it," Geschwind said. "While we still have a long way to go

from a mouse study to humans, we present a novel paradigm that has never been applied to the nervous system."

More information: A Systems-Level Analysis of the Peripheral Nerve Intrinsic Axonal Growth Program. DOI: dx.doi.org/10.1016/j.neuron.2016.01.034

Provided by University of California, Los Angeles