Genes that aid spinal cord healing in lamprey also present in humans

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Jennifer Morgan and Ona Bloom with juvenile lamprey in the MBL Whitman Center. Credit: Amanda R. Martinez

Many of the genes involved in natural repair of the injured spinal cord of the lamprey are also active in the repair of the peripheral nervous system in mammals, according to a study by a collaborative group of scientists

at the Marine Biological Laboratory (MBL) and other institutions. This is consistent with the possibility that in the long term, the same or similar genes may be harnessed to improve spinal cord injury treatments.

"We found a large overlap with the hub of transcription factors that are driving regeneration in the mammalian peripheral nervous system," says Jennifer Morgan, director of the MBL's Eugene Bell Center for Regenerative Biology and Tissue Engineering, one of the authors of the study published this week in *Scientific Reports*.

Lampreys are jawless, eel-like fish that shared a common ancestor with humans about 550 million years ago. This study arose from the observation that a lamprey can fully recover from a severed spinal cord without medication or other treatment.

"They can go from paralysis to full swimming behaviors in 10 to 12 weeks," says Morgan.

"Scientists have known for many years that the lamprey achieves spontaneous recovery from spinal cord injury, but we have not known the molecular recipe that accompanies and supports this remarkable capacity," says Ona Bloom of the Feinstein Institute for Medical Research and the Zucker School of Medicine at Hofstra/Northwell, a former MBL Whitman Center Fellow who collaborated on the project.

"In this study, we have determined all the genes that change during the time course of recovery and now that we have that information, we can use it to test if specific pathways are actually essential to the process," Bloom says.

The researchers followed the lampreys' healing process and took samples from the brains and spinal cords at multiple points in time, from the first hours after injury until three months later when they were healed. They

analyzed the material to determine which genes and signaling pathways were activated as compared to a non-injured lamprey.

As expected, they found many genes in the spinal cord that change over time with recovery. Somewhat unexpectedly, they also discovered a number of injury-induced gene expression changes in the brain. "This reinforces the idea that the brain changes a lot after a spinal cord injury," says Morgan. "Most people are thinking, 'What can you do to treat the spinal cord itself?' but our data really support the idea that there's also a lot going on in the brain."

They also found that many of the genes associated with spinal cord healing are part of the Wnt signaling pathway, which plays a role in tissue development. "Furthermore, when we treated the animals with a drug that inhibits the Wnt signaling pathway, the animals never recovered their ability to swim," says Morgan. Future research will explore why the Wnt pathway seems particularly important in the healing process.

The paper is the result of a collaboration between Morgan, Bloom and other scientists including Jeramiah Smith of University of Kentucky and Joseph Buxbaum of Icahn School of Medicine at Mount Sinai, both former Whitman Center Fellows. The collaboration was made possible by the MBL Whitman Center Fellowship program.

"[This study] involved several different labs located in different parts of the country with different types of expertise, but it absolutely could not and would not have been done without the support of the MBL that allows us to to work collaboratively in a shared laboratory setting," says Morgan.

More information: Paige E. Herman et al (2018) Highly conserved molecular pathways, including Wnt signaling, promote functional

recovery from spinal cord injury in lampreys. *Scientific Reports*, 2018.

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