6 years ago

#astrocytes

#spinal cord injury

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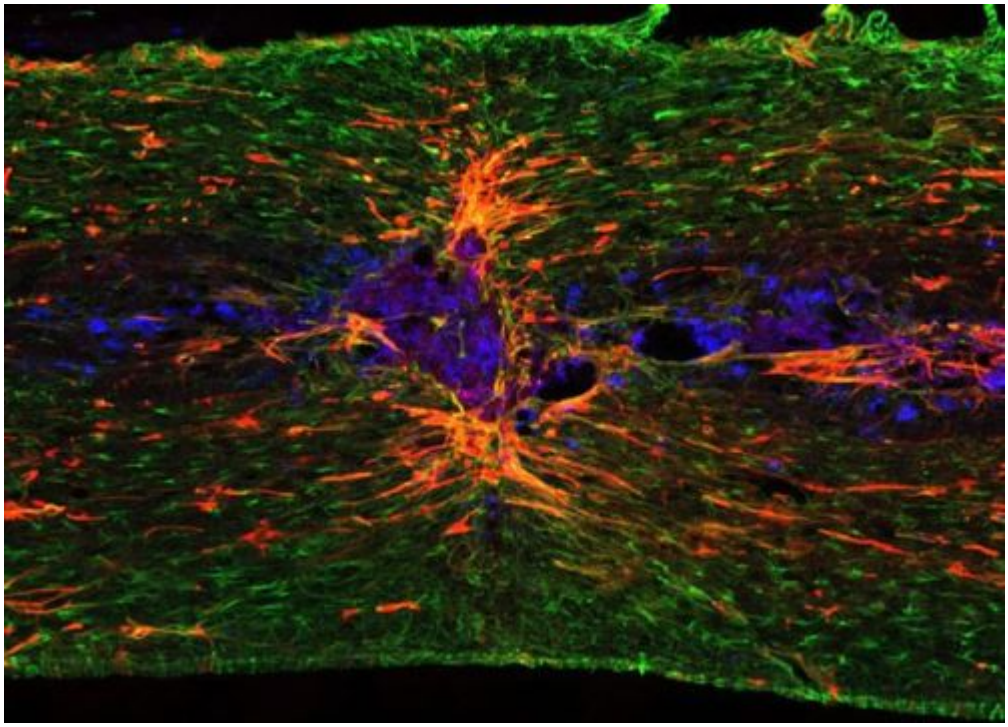
Bring in the Astrocytes

By manipulating levels of the enzyme LZK, researchers can dial up or down the repair response to spinal cord injury in mice

Binhai Zheng, PhD, and his research team at UC San Diego School of Medicine typically study how neurons regenerate, particularly after a spinal cord injury. But they recently turned their attention to another cell type that helps make up the central nervous system (CNS): astrocytes. These star-shaped cells help provide nutrients to other cells and have other vital functions. When the CNS is injured, they form a barrier between the CNS and the rest of the body.

“The rush of astrocytes to an injury site — astrogliosis — is similar to the response of immune and other cells to a skin wound,” said Zheng, professor of neurosciences. “It’s meant to be beneficial and protective, but at the same time can have a detrimental effect. For example, astrogliosis and the subsequent scar formation can inhibit neuronal plasticity.”



In this horizontal section of an injured mouse spinal cord LZK-overexpressing (red), astrocytes home in and confine the injury site. Immune cells are shown in blue.

Zheng's team, in collaboration with Yishi Jin, PhD, professor of neurobiology and neurosciences at UC San Diego, previously found that an enzyme called LZK (a.k.a. MAP3K13) promotes growth of axons — the long arms of a neuron — in lab-grown cells. In mice, they've now unexpectedly discovered that spinal cord injuries boost LZK levels in astrocytes.

The research team headed by Zheng and Jin generated two mouse models — one in which LZK is overexpressed in astrocytes and one in which the enzyme has been removed specifically from those cells. In mice with lots of astrocytic LZK, astrogliosis was widespread even without injury. After spinal cord injury, LZK-enhanced astrogliosis helped contain the injury site, making it more compact. In contrast, the mice lacking LZK in their astrocytes had larger injury sites. Though it's not totally clear yet, Zheng thinks LZK-driven astrogliosis is likely beneficial for injury repair.

"In any case, this is exciting because there are not many molecules we know of that we can target to manipulate the repair process at the site of a spinal cord injury," Zheng said. "LZK will make a good tool for future studies of astrogliosis and its role in spinal cord injuries and other situations — information we need to aid in the design of new therapeutic interventions to promote recovery and repair following CNS injury and disease."

The study published March 27 in *Cell Reports*.

Next Zheng and colleagues want to find ways to fine tune LZK, since too much of its activity could be just as harmful as too little. Eventually, LZK could make a feasible drug target since it's a kinase, a type of enzyme frequently targeted by therapeutic drugs.

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