Immune system discovery could lead to better spinal injury treatments

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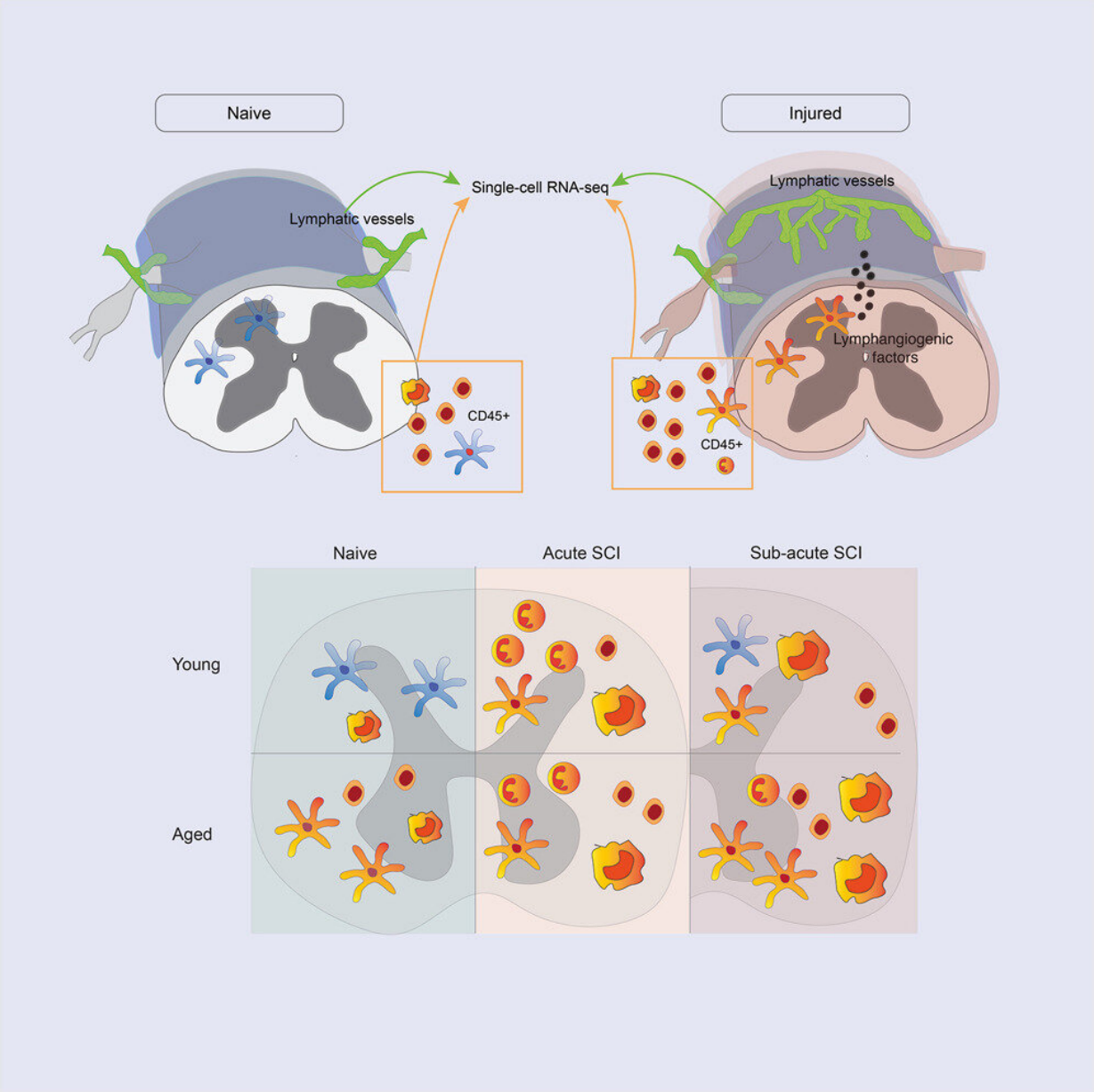

Credit: *Neuron* (2023). DOI: 10.1016/j.neuron.2023.04.011

New research suggests that the immune system's ability to respond to spinal-cord injuries diminishes with age, and identifies potential avenues to improve that response and help patients heal.

The findings offer insight into how the immune system responds to spinal-cord injuries, and why that response becomes blunted with the passing years. It also reveals an important role for membranes surrounding the spinal cord in mounting an immune response to injury. With this information, doctors one day may be able to bolster the body's immune response to improve patient outcomes, particularly among older adults.

"Our findings suggest in aging, there is an impairment in how the immune response is initiated and resolved, compared to young people," said researcher Andrea Francesca M. Salvador, who just received her doctorate from the University of Virginia School of Medicine. "Hopefully, our results can help identify points of intervention and druggable targets that can improve recovery and address long-term consequences of injury, such as pain."

The researchers have published their findings in the journal *Neuron*.

Understanding spinal-cord injuries

Spinal-cord injuries can have devastating, lifelong effects. Depending on the severity and location of the injury, they can leave patients unable to move or unable to control their bowels. They can cause pain, sexual dysfunction or uncontrollable spasms. Better understanding how the body responds to spinal-cord injuries is important to develop better

treatment methods.

The findings are the latest from the lab of Jonathan Kipnis, who made a stunning discovery while at UVA in 2015 that the brain was connected to the immune system by vessels thought not to exist. Prior to that, it was believed the brain was essentially walled off from the immune system.

The discovery of the vessels in the brain membrane, or meninges, rewrote textbooks and opened a new frontier in neurological research. Today, "neuroimmunology," or the study of the nervous system's relationship to the immune system, is one of the hottest areas of neuroscience research, and it is poised to transform understanding of the brain and the ability to treat a vast array of neurological diseases.

In their recent research, Salvador, Kipnis and collaborators determined that the meninges surrounding the spinal cord play an essential role in the immune response to spinal-cord injury. They discovered that previously unknown meningeal lymphatic "patches" form above the site of spinal-cord injuries.

More research is needed to determine exactly what these structures do, but their formation speaks to an important role for the spinal-cord meninges in the immune response to injury.

Salvador and her collaborators also quantified how immune cells respond to spinal-cord injuries. They found the response was much stronger in young lab mice than in older ones, suggesting that scientists may be able to target certain immune cells to improve recovery after spinal-cord injuries.

Together, the findings identify the spinal-cord meninges and their interactions with other components of the central nervous system as new areas for researchers to explore.

"This is an exciting finding and one which may indeed lead to new therapeutic approaches for spinal cord-injury patients," said Kipnis, now a professor at Washington University School of Medicine in St. Louis and director of its Brain Immunology and Glia Center (BIG Center). "We are now collaborating with clinicians in a hope to better understand what is happening in human patients and how our findings could be translated to make a real difference."

The research team consisted of Salvador, Taitea Dykstra, Justin Rustenhoven, Wenqing Gao, Susan M. Blackburn, Kesshni Bhasiin, Michael Q. Dong, Rafaela Mano Guimarães, Sriharsha Gonuguntla, Igor Smirnov, Kipnis and Jasmin Herz.

More information: Andrea Francesca M. Salvador et al, Age-dependent immune and lymphatic responses after spinal cord injury, *Neuron* (2023). DOI: 10.1016/j.neuron.2023.04.011

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