After brain injury, new astrocytes play unexpected role in healing

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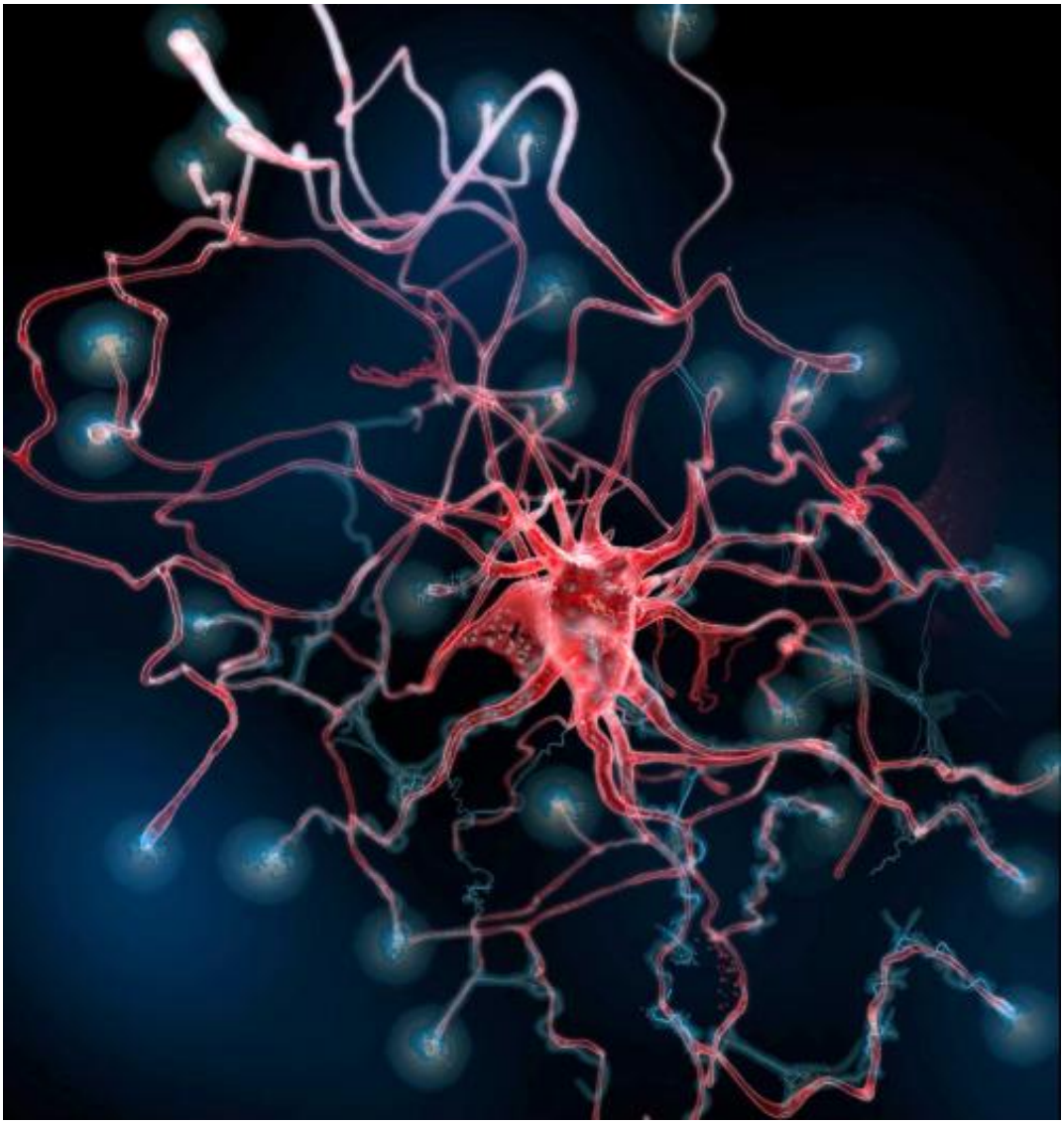

This is an artist's rendition of a special astrocyte. Credit: Andrew Swift

The production of a certain kind of brain cell that had been considered an impediment to healing may actually be needed to staunch bleeding and promote repair after a stroke or head trauma, researchers at Duke Medicine report.

These cells, known as astrocytes, can be produced from stem cells in the brain after injury. They migrate to the site of damage where they are much more effective in promoting recovery than previously thought. This insight from studies in mice, reported online April 24, 2013, in the journal *Nature*, may help researchers develop treatments that foster brain repair.

"The injury recovery process is complex," said senior author Chay T. Kuo, M.D., PhD, George W. Brumley Assistant Professor of Cell Biology, Pediatrics and Neurobiology at Duke University. "There is a lot of interest in how new neurons can stimulate functional recovery, but if you make neurons without stopping the bleeding, the neurons don't even get a chance. The brain somehow knows this, so we believe that's why it produces these unique astrocytes in response to injury."

Each year, more than 1.7 million people in the United States suffer a traumatic brain injury, according to the Centers for Disease Control and Prevention. Another 795,000 people a year suffer a stroke. Few therapies are available to treat the damage that often results from such injuries.

Kuo and colleagues at Duke are interested in replacing lost neurons after a brain injury as a way to restore function. Once damaged, mature neurons cannot multiply, so most research efforts have focused on inducing brain stem cells to produce more immature neurons to replace them.

This strategy has proved difficult, because in addition to making

neurons, neural stem cells also produce astrocytes and oligodendrocytes, known as glial cells. Although glial cells are important for maintaining the normal function of neurons in the brain, the increased production of astrocytes from neural stem cell has been considered an unwanted byproduct, causing more harm than good. Proliferating astrocytes secrete proteins that can induce tissue inflammation and undergo gene mutations that can lead to aggressive brain tumors.

In their study of mice, the Duke team found an unexpected insight about the astrocytes produced from stem cells after injury. Stem cells live in a special area or "niche" in the postnatal/adult brain called the subventricular zone, and churn out neurons and glia in the right proportions based on cues from the surrounding tissue.

After an injury, however, the subventricular niche pumps out more astrocytes. Significantly, the Duke team found they are different from astrocytes produced in most other regions of the brain. These cells make their way to the injured area to help make an organized scar, which stops the bleeding and allows tissue recovery.

When the generation of these astrocytes in the subventricular niche was experimentally blocked after a brain injury, hemorrhaging occurred around the injured areas and the region did not heal.

Kuo said the finding was made possible by insights about astrocytes from Cagla Eroglu, PhD, whose laboratory next door to Kuo's conducts research on astrocyte interactions with neurons.

"Cagla and I started at Duke together and have known each other since our postdoctoral days," Kuo said. "To have these stem cell-made astrocytes express a unique protein that Cagla understands more than anyone else, it's just a wonderful example of scientific serendipity and collaboration."

Additionally, Kuo said first author Eric J. Benner, M.D., PhD, a former postdoctoral fellow who now has his own laboratory at Duke, provided key clinical correlations on brain injury as a physician-scientist and practicing neonatologist in the Jean and George Brumley Jr. Neonatal-Perinatal Research Institute.

"We are very excited about this innate flexibility in neural stem cell behavior to know just what to do to help the brain after injury," Kuo said. "Since bleeding in the brain after injury is a common and serious problem for patients, further research into this area may lead to effective therapies for accelerated brain recovery after injury."

More information: Research paper: dx.doi.org/10.1038/nature12069

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