Research team discovers cell in zebrafish critical to brain assembly, function

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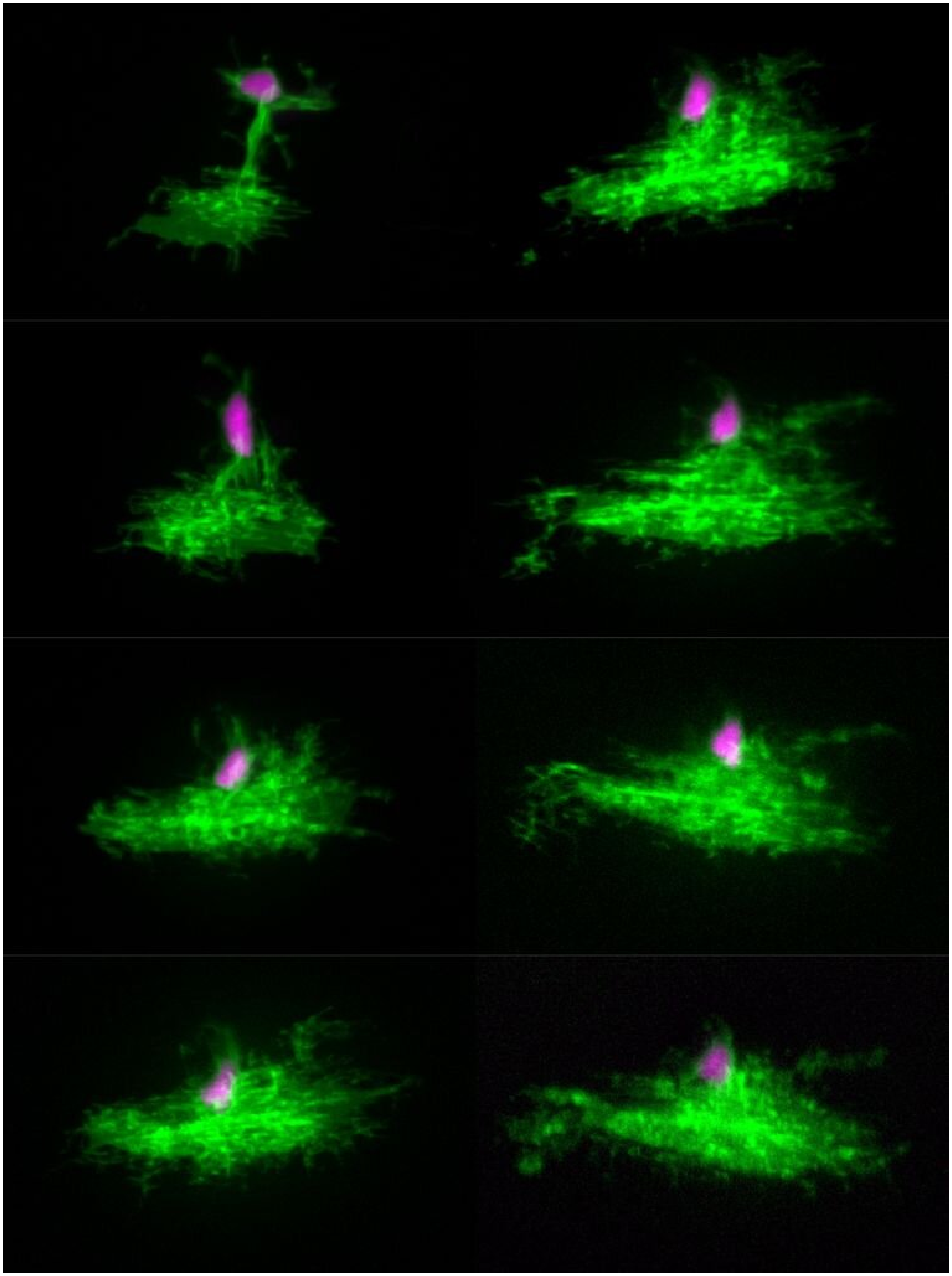

This series of photos shows the development of a single astrocyte in the zebrafish spinal cord, starting from a progenitor cell in a fish two-days old, ending with a fish at nine days old. Credit: OHSU

New research from Oregon Health & Science University for the first time documents the presence of astrocytes in zebrafish, a milestone that will open new avenues of research into a star-shaped type of glial cell in the brain that is critical for nearly every aspect of brain assembly and function.

The research was published this week in the journal *Nature Neuroscience*.

With their transparent bodies, zebrafish larvae provide a unique opportunity to gaze into the inner workings of the central nervous system, including the brain, even in living animals. The identification of astrocytes and the generation of tools to work with them in zebrafish will enable researchers around the world to open new lines of research to advance scientific understanding of how astrocytes function.

Astrocytes, it turns out, are the most abundant and mysterious cell type in the human brain, and OHSU is becoming a hub for research into their roles in development, brain function and disease.

"There is no neurodegenerative disease that I know of where astrocytes are not profoundly affected in some way," said senior author Kelly Monk, Ph.D., professor and co-director of the Vollum Institute at OHSU. "This gives us a powerful tool to get a handle on what these cells do and how they do it."

Monk and co-author Marc Freeman, Ph.D., credit lead author Jiakun

Chen, Ph.D., a post-doctoral researcher in the Monk and Freeman labs, with developing a panoply of tools, including a cell-specific approach using the gene editing tool CRISPR to label and manipulate astrocyte precursors and incisively study their development and functions.

"He was able to capture the birth of an astrocyte from a stem cell and its entire development, which has never been visualized before in a vertebrate animal," Monk said.

Kelly Monk, Ph.D., in her lab at the Vollum Institute. Credit: OHSU/Kristyna Wentz-Graff

Freeman said the discovery will dramatically enhance the study of how glia regulate brain development and physiology.

"This opens the door to experiments that you can't do in any other organism," Freeman said. "Zebrafish is the only animal in which you can now live-image all types of vertebrate glial cells—astrocytes, microglia, oligodendrocytes and OPCs—along with any neuron in intact neural circuits, from the earliest stages of development. Zebrafish is also the only vertebrate in which you can image the entire brain in live, behaving animals to figure out how it works. Understanding the role of these cells (astrocytes) in brain development will be key to understanding devastating neurodevelopmental disorders like autism spectrum disorder and schizophrenia.

"It's a major step forward and should power a lot of exciting work in the coming years."

More information: Jiakun Chen et al, Live-imaging of astrocyte morphogenesis and function in zebrafish neural circuits, *Nature Neuroscience* (2020). DOI: 10.1038/s41593-020-0703-x

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