# Research reveals development of the glial cell

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A vast majority of cells in the brain are glial, yet our understanding of how they are generated, a process called gliogenesis, has remained enigmatic. Researchers at Baylor College of Medicine have identified a novel transcripitonal cascade that controls these formative stages of gliogenesis and answered the longstanding question of how glial cells are generated from neural stem cells.

The findings appear in the current edition of *Neuron*.

"Most people are familiar with neurons, cells that process and transmit information in the brain. Glial cells, on the other hand, make-up about 80 percent of the cells in the brain and function by providing trophic support to neruons, participating in neurotransmission, myelin sheaths for axons, and comprise the blood brain barrier," said Dr. Benjamin Deneen, assistant professor of neuroscience at BCM. "Importantly, glia have been linked to numerous CNS pathologies, from brain tumors and spinal cord injury and several neurological disorders including, Retts Syndrome, ALS, and Multiple Sclerosis. Therefore deciphering how glial cells are generated is key to understanding brain function during health and disease."

As researchers began investigating glial development in chicks they started by going backwards – examing what steps were needed before the glial cells matured. They discovered that glial cells are specified in neural stem cells when the transcription factor NFIA is induced.

Taking another step back in the transcriptional cascade, they looked for

what triggered NFIA induction.

"By comparing mouse and chick regulatory sequences we were able to perform enhancer screening in the chick to identify regulatory elements with activity that resembled NFIA induction. This method allowed us to pinpoint Sox9," said Peng Kang, postdoctoral associate in the Center for Stem Cell and Regenerative Medicine at BCM. "Subsequently, we found that Sox9 doesn't just induce NFIA expression, it also associates with NFIA, forming a complex."

Just after the initiation of gliogenesis this complex was discovered to co-regulate a subset of genes that play important roles in mitochondria energy metabolism and glial precursor migration.

"Sox9 induces NFIA expression during glial initiation and then binds NFIA to drive lineage progression by cooperatively regulating a genetic program that controls cell migration and energy metabolism, two key processes associated with cellular differentiation," said Deneen. "We now need to ask what other proteins contribute to this process, and how does the nature of this complex evolve during astro-glial lineage progression."

Additionally, these findings may also help researchers to understand how certain brain tumors might begin to form, as these same developmental processes and proteins are found in both adult and pediatric brain tumors . A more comprehensive understanding how this regulatory cascade operates during development, could eventually lead to better treatment targets for brain tumors.

Provided by Baylor College of Medicine

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