Researchers Demystify a Fountain of Youth in the Adult Brain
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Duke University Medical Center researchers have found that a Â“fountain of youthÂ” that sustains the production of new neurons in the brains of rodents is also believed to be present in the human brain.
The existence of a vital support system of cells around stem cells in the brain explains why stem cells by themselves canÂ't generate neurons in a lab dish, a major roadblock in using these stem cells for injury repair.

Â“We believe these findings will have important implications for human therapy,Â” said Chay Kuo, MD, PhD, George Brumley Jr. Assistant Professor of Cell Biology, Pediatrics, and Neurobiology, and senior author of the study.

The study is the cover story in the July issue of Neuron, published online July 14.

The scientists found that neighboring Â“epithelial-likeÂ” ependymal cells -- not stem cells themselves -- maintain a special structure that keeps neural stem cells Â“neurogenic,Â” able to make new neurons.

Currently, when neural stem cells are harvested for growth in culture, however, the ependymal cells are not removed along with them, and this can be a problem.

Â“Neural stem cells in a lab dish donÂ't continue to make neurons as they do inside the brain,Â” Kuo said. Â“Instead, they often produce astrocytes, a cell type that may not be helpful to re-implant into a brain.Â” He said that uncontrolled astrocyte growth can lead to brain tumors.

In a series of experiments, the researchers found that the generation of new neurons depended on what he calls the Â“ugly siblingÂ” of the stem cells, the ependymal cell that has long, moving, hair-like cilia that cover its surface.

Kuo decided to study these cells because the lateral ventricles in the brain, where adult neural stem cells reside, are also the last area of a developing brain that grows ependymal cells.

Â“The common radial glial progenitors in the developing nervous system prior to birth give rise to both the ependymal cells and the adult stem cells,Â” Kuo said. Â“So it made sense to study these niche cells as well as the stem cells.Â”

Â“There is this fountain of youth inside the adult brain that actively makes new neurons,Â” Kuo said. Â“Yet we donÂ't know how this fountain is constructed or maintained.Â”

Kuo and his colleagues found that the Foxj1 transcription factor, a class of master proteins that turn other genes on and/or off, is critical to instruct ependymal cells to change shape and assemble into pinwheel-like architecture surrounding stem cells. He said the lateral membranes of mature ependymal cells are shaped like machine cogs or fingers that lace together.

The researchers determined that the structural protein Ankyrin 3 was turned on by Foxj1 in these ependymal cells to provide structural support for the delicate neural stem cells. Signals generated by this structural support will probably be important for instructing introduced neural stem cells to make neurons in therapeutic settings, he said.

Kuo said he would not have examined the role of ependymal cell Foxj1 in relation to neural stem cells if not for his Cell Biology chair, Brigid Hogan, PhD, whose lab next door is a world leader in understanding adult lung and airway stem cell function.

Likewise, Kuo said pioneering work on ankyrins by Duke Cell Biology and Howard Hughes Medical Institute Investigator Vann Bennett, MD, PhD, a co-author on the paper, paved the way for study of these proteins in the neural stem cell environment.

Future studies will look closely at the details of the niche environment to learn more. Â“Understanding the environmental control of neuron production in the adult brain will be crucial for future therapeutic strategies using human stem cells to replace neurons,Â” Kuo said.

Other authors include lead author Patricia Paez-Gonzalez, Khadar Abdi, Dominic Luciano, Yan Liu, Mario Soriano-Navarro, Emma Rawlins, and Jose Manuel Garcia-Verdugo.

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