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Signal explains why site of origin affects fate of postnatal neural stem cells

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New research may help to explain why the location of postnatal neural stem cells in the brain determines the type of new neurons that are generated. The research, published by Cell Press in the July 28 issue of the journal *Neuron*, demonstrates that a signaling pathway which plays a key role in development also actively regulates the fate of neural stem cells in the adult brain. Manipulation of this signaling pathway redirected the fate of adult stem cells, a finding that may impact the design of future strategies for creating stem cell therapies.

Recent research has led to a shift in the long-standing theory that neurons of the central nervous system are produced only during embryonic development. It is now clear that several types of neurons continue to be produced in the adult brain. These new neurons arise from special locations that contain neural stem cells and continue to generate neurons throughout adulthood. "Research has shown that the subventricular zone, the largest germinal zone in the adult brain, is arranged as a mosaic, with stem cells in different locations producing different kinds of neurons," says senior study author Dr. Arturo Alvarez-Buylla from the University of California, San Francisco. "However, the molecular mechanisms responsible for this positional specification in the adult subventricular zone remain unknown."

Using a mouse model system, Dr. Alvarez-Buylla and colleagues discovered that sonic hedgehog (Shh) signaling occurs in the ventral portion of the subventricular zone and is associated with the production of specific types of neurons. Shh belongs to the hedgehog family of

signaling molecules that play a key role in patterning the developing nervous system. Neurons residing close to the ventral portion of the subventricular zone were identified as a potential source of Shh signaling molecules. The researchers went on to show that in the absence of Shh, production of ventrally derived neuron types decreased while activation of the Shh pathway in dorsal neural stem cells in the adult mouse brain was sufficient to redirect their fate.

"Our results are the first to identify a signaling pathway that is sufficient to determine neuronal cell fate in adult subventricular zone neural stem cells," explains Dr. Rebecca Ihrie, the lead author of the study. "Importantly, our findings demonstrate that adult neural stem cells may be reprogrammed if the relevant specification signals are identified and suggest that reprogramming of neural stem cells for therapeutic purposes may depend, at least in part, on the identification of signaling pathways involved in the generation of desired cell types."

Provided by Cell Press

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