Researchers identify key mechanism that regulates the development of stem cells into neurons

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Researchers at the University of Southern California (USC) have identified a novel mechanism in the regulation and differentiation of neural stem cells.

Researchers found that the protein receptor Ryk has a key role in the differentiation of neural stem cells, and demonstrated a signaling mechanism that regulates neuronal differentiation as stem cells begin to grow into neurons. The study will be published in the Nov. 11 issue of the journal *Developmental Cell*, and is now available online.

The findings could have important implications for regenerative medicine and cancer therapies, says Wange Lu, Ph.D., assistant professor of biochemistry and molecular biology at the Keck School of Medicine of USC, and the principal investigator on the study.

"Neural stem cells can potentially be used for cell-replacement therapy for neurodegenerative diseases such as Alzheimer's and Parkinson's Disease, as well as spinal cord injury," Lu says. "Knowledge gained from this study will potentially help to generate neurons for such therapy. This knowledge can also be used to inhibit the growth of brain cancer stem cells."

During brain development, neural stem cells respond to the surrounding environment by either proliferation or differentiation, but the molecular

mechanisms underlying the development of neural stem cells and neurons are unclear, Lu notes.

Ryk functions as a receptor of Wnt proteins required for cell-fate determination, axon guidance and neurite outgrowth in organisms. Researchers at the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC analyzed sections of the forebrain in animal model embryos to investigate Ryk's function in vivo.

They found that during neurogenesis, when neural stem cells start to grow into neurons, Ryk protein is cleaved and translocates to the cell nucleus to regulate neuronal differentiation.

This finding is extremely important for understanding the regulation of self-renewal and differentiation of neural stem cells, Lu says. Previous research has shown that Ryk functions as a receptor of Wnt proteins. However, the role of Ryk in neural stem cells and the molecular mechanism of Ryk signaling have not previously been known.

"This study will help in our efforts to produce nerve cells from embryonic stem cells, and may lead to the development of new strategies for the repair of the nervous system, using protein or small molecule therapeutic agents," says Martin Pera, Ph.D., director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC.

Further research is needed to explore how Ryk regulates neuronal gene expression, Lu says. Researchers are now expanding their research to studies of differentiation of human embryonic stem cells into neural stem cells and neurons. These studies are very important for regenerative medicine and drug discovery for therapy of neurodegenerative diseases.

Source: University of Southern California