Protein is key to embryonic stem cell differentiation

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Investigators at Burnham Institute for Medical Research (Burnham) have learned that a protein called Shp2 plays a critical role in the pathways that control decisions for differentiation or self-renewal in both human embryonic stem cells (hESCs) and mouse embryonic stem cells (mESCs).

The research, led by Gen-Sheng Feng, Ph.D., differs with some earlier findings that suggested hESCs and mESCs differentiate as a result of different signaling mechanisms. The discovery that Shp2 has a conserved role between mice and humans suggests an interesting common signaling mechanism between mESCs and hESCs, despite the known distinct signaling paths and biological properties between the two types of pluripotent stem cells. The study was published online in the journal PLoS ONE on March 17, 2009.

Embryonic stem cells (ESCs) are pluripotent cells that can differentiate to become more than 200 different cell types. Because of their plasticity, ESCs have been suggested as potential therapies for numerous diseases and conditions, including neurodegenerative diseases, spinal cord injury and tissue damage. Development of such therapies is largely dependent on fully understanding and controlling the processes that lead to differentiation of hESCs into specialized cell types.

"There are many signaling pathways that help embryonic stem cells decide their fate," said Dr. Feng. "We found that the Shp2 protein acts as a coordinator that fine-tunes the signal strength of multiple pathways

and gives us a better understanding of the fundamental signaling methods that determine whether a stem cell's fate will be self-renewal or differentiation."

In the study, the Feng lab created mutant Shp2 mESCs and showed that differentiation was dramatically impaired as the cells self-renewed as stem cells. The researchers also demonstrated small interfering RNAs in hESCs reduce Shp2 expression and subsequent cell differentiation. Feng and colleagues screened chemical libraries and identified a small-molecule inhibitor of Shp2 that, in small doses, partially inhibits differentiation in both mESCs and hESCs. Taken together, these results suggest a conserved role for Shp2 in ESC differentiation and self-renewal in both mice and humans.

"This opens the door for new experimental reagents that will amplify the self-renewal process to create more stem cells for research and potential clinical use in the future," Dr. Feng added. "This research also suggests that comparative analysis of mouse and human embryonic stem cells will provide fundamental insight into the cellular processes that determine 'stemness,' a critical question that remains to be answered in the stem cell biology field."

Source: Burnham Institute