New 'control knobs' for stem cells identified

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Natural changes in voltage that occur across the membrane of adult human stem cells are a powerful controlling factor in the process by which these stem cells differentiate, according to research published by Tufts University scientists.

Tufts doctoral student Sarah Sundelacruz, Professor of Biology Michael Levin, and Chair of Biomedical Engineering David L. Kaplan (corresponding author) published their paper "Membrane Potential Controls Adipogenic and Osteogenic Differentiation of Mesenchymal Stem Cells" in the November 17, 2008, issue of *PLoS ONE* (http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0003737).

"We have found that voltage changes act as a signal to delay or accelerate the decision of a stem cell to drop out of a stem state and differentiate into a specific cell type. This discovery gives scientists in regenerative medicine a new set of control knobs to use in ongoing efforts to shape the behavior of adult stem cells," said Levin. "In addition, by uncovering a new mechanism by which these cells are controlled in the human body, this research suggests potential future diagnostic applications."

Harnessing the potential of stem cells for applications such as wound healing and tissue regeneration is a tantalizing yet daunting task. Although many studies indicate that electrophysiology plays a crucial role in cell proliferation and differentiation, its functional role in stem

cell biology is poorly understood.

The Tufts researchers studied the changes in membrane potential (voltage across the membrane) shown by human mesenchymal stem cells (hMSCs) obtained from donor bone marrow as the hMSCs were differentiating into fat and bone cells. They found that hyperpolarization (increased difference between the voltage in the interior and exterior of a cell) was characteristic of differentiated cells compared with undifferentiated cells and that hMSCs show different membrane potential profiles during bone vs. fat differentiation.

To determine whether hyperpolarization was functionally required for differentiation, the scientists depolarized the hMSCs by exposing them either to high levels of extracellular potassium ions or to ouabain, a compound that blocks the transfer of ions in and out of cells. Both treatments disrupted the normal increase in negative voltage that occurs during differentiation and suppressed fat and bone cell differentiation markers.

In contrast, treatment with hyperpolarizing reagents up-regulated bone cell markers – indicating that voltage changes are not merely permissive for differentiation but can act as an instructive signal to either induce or inhibit differentiation.

More study is needed to determine whether hyperpolarization also determines which specific type of cell stem cells will differentiate into, according to the Tufts researchers.

Source: Tufts University