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NEW PROCESS FOR EMBRYONIC STEM CELL DIFFERENTIATION DISCOVERED

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In a novel approach to the study of embryonic stem cells, researchers at Brigham and Women's Hospital (BWH) have discovered a potential means of controlling differentiation into desired cell types, by demonstrating that sugars play a major role in modulating stem cell differentiation into tissues. These findings appear online on October 26, 2009 in *Circulation*.

The potential for enabling the differentiation of stem cells holds tremendous implications in organ growth and regeneration. "Repairing or replacing damaged organs requires proper direction of vessel growth to support organ function and we now know that sugars play a key role determining this direction," said Dirk Hentschel, MD, of the Renal Division at BWH.

Differing from previous studies that focused on the role of growth factors in controlling differentiation, BWH researchers investigated the role sugars play. "Finding a way to control differentiation with sugars has the crucial advantage of reducing oncogenic risks associated with growth factor therapy in clinical settings," said Rania Harfouche, PhD, research fellow in the Renal Division at BWH.

Using sugar sequencing techniques, researchers discovered that as embryonic stem cells differentiate into endothelial cells, the sugars on the cell surface change in composition to become more sulfated. Inhibiting this process prevents the formation of blood vessels. By knocking down the enzyme responsible for sulfation of sugars in a developing zebrafish embryo, the researchers observed abnormal vascular development that could be recovered using defined sulfated sugars. "This is a simpler solution to differentiation, compared to determining the exact combination of growth factors that a cell requires," explains Shiladitya Sengupta, PhD of the Department of Medicine at BWH.

"The next step in this research is to determine specific sugar sequences that can promote efficient differentiation of stem cells into endothelium," said Stephanie Piecewicz, a graduate student at MIT. The researchers believe that by providing the appropriate extracellular 'net,' the cell can capture the appropriate combination of physiological molecules that it needs to proceed through differentiation.

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