Biomarker could help scientists choose the right cell line when conducting stem cell experiments

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According to researchers at Boston Children's Hospital, stem cells that strongly express a gene called WNT3 are biased to develop into cells and tissues including pancreas, liver and bladder. This discovery suggests that other genes may serve as biomarkers for selecting stem cells with a preference for turning into different tissue types. Such markers would make it easier for stem cell scientists to choose the right cell line to start with when generating specific tissues for study.

The researchers, led by Wei Jiang, PhD, and Yi Zhang, PhD, of the Program in Cellular and Molecular Medicine at Boston Children's, published their findings June 6 in the inaugural issue of the journal *Stem Cell Reports*.

All human embryonic (hESC) and induced pluripotent (iPSC) cell lines can develop or differentiate into any kind of cell or tissue in the body. However, differentiation potential—the ability to develop into particular cell types—is not equal across all hESC and iPSC lines. Rather, each line is biased to develop into one of the three major tissue lineages: endoderm (e.g., digestive tract, liver, pancreas), mesoderm (e.g., cartilage, circulatory system, kidneys) and ectoderm (e.g., cornea, nervous system, teeth).

That bias can significantly impact stem cell studies.

"If you want to differentiate stem cells into pancreas cells, for instance, you want to start with a line with a high differentiation potential for endoderm," says Zhang. "It's like athletes and sports. Some athletes are built for football, some for baseball, some for swimming. Every cell line has its own strengths, and the challenge is knowing what those strengths are."

Currently, investigators must resort to testing several lines with the same differentiation process—which can cost a great deal of time and effort—and then using the one that turns out to be the most efficient at producing cells of the type they need.

What they would like to be able to do, Zhang says, "is select the most appropriate cell line without having to carry out full differentiation experiments first."

The discovery of WNT3's role as an endoderm differentiation marker grew out of work by Jiang on pancreatic cell development. "Wei was testing different lines to find ones that we could use to generate pancreatic beta cells," Zhang explains. "He noted the correlation between WNT3 expression and endoderm differentiation efficiency in the lines he was testing and suggested that it might work well as a biomarker."

From there, the pair went on to show—in collaboration with researchers at Duke University—that they could use WNT3 expression levels in hESCs to predict the potential of hESC lines for differentiating into endoderm.

In addition, Jiang and Zhang found they could change particular hESC lines' differentiation potential by manipulating WNT3 expression. Increasing or reducing WNT3 activity made hESC lines more or less likely, respectively, to develop into endoderm.

How WNT3 affects endoderm differentiation potential is not yet clear, and is something Zhang wants to understand. But he believes that other genes may possibly serve as markers for selecting lines primed for mesoderm and ectoderm development.

"We would like to find other markers and develop a scoring system," he continues. "There are many hESC and iPSC lines, and we need a simple way to tell which to use in order to produce particular cell types."

Provided by Children's Hospital Boston

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