Scientists discover marker indicating the developmental potential of stem cells

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Researchers in China are reporting that they have found a way to determine which somatic cells -- or differentiated body cells -- that have been reprogrammed into a primordial, embryonic-like state are the most viable for therapeutic applications.

In a paper published online last week by the Journal of Biological Chemistry, two collaborating teams from institutes at the Chinese Academy of Sciences point to a marker they found in induced-pluripotent stem cells, or iPS cells, taken from mice. That marker is a cluster of small RNA whose expression appears strictly correlated with levels of pluripotency, or "stemness." (The more pluripotent, the more likely a stem cell will develop into the desired tissue, organ or being.)

"We identified a genomic region encoding several genes and a large cluster of microRNAs in the mouse genome whose expression is high in fully pluripotent embryonic stem cells and iPS cells but significantly reduced in partially pluripotent iPS cells, indicating that the Dlk1-Dio3 region may serve as a marker," said Qi Zhou, a researcher at the CAS Institute of Zoology and co-author of the paper. "No other genomic regions were found to exhibit such clear expression changes between cell lines with different pluripotent levels."

After the creation of the first iPS cells in Japan in 2006, Zhou and others set out to determine whether the reprogrammed adult cells are versatile enough to generate an entire mammalian body, as embryonic stem cells can.

Then, last summer, Zhou announced that his team had reprogrammed somatic cells of mice, injected them into embryos and created 27 live offspring, which clearly demonstrated that iPS cells can, like embryonic stem cells, produce healthy adults. Though lauded as a huge step forward, they also found not all iPS cells were perfect: Many of the iPS cell lines used did not produce mice, and some of the mice that were produced had abnormalities.

"The success rate of obtaining iPS cells with full pluripotency was still extremely low, which significantly hindered the application of iPS cells in therapeutics and other aspects," Zhou said.

Believing that there might be some intrinsic gene expression difference between the lines of iPS cells with varying levels of pluripotency that could be identified at early culture stages, so that less viable lines could be abandoned and more viable lines focused on, Zhou teamed up with bioinformatics specialist Xiu-Jie Wang, who works at the Chinese academy's Institute of Genetics and Developmental Biology.

Together, their groups profiled the small RNA expression patterns of ES and iPS cell lines from different genetic backgrounds and with different pluripotent levels using Solexa technology.

"There are nearly 50 miRNAs encoded in this region, and those expressed miRNAs all exhibited consistent and significant expression differences between stem-cell lines with different pluripotency levels," Wang said. "With this discovery, iPS cells with different pluripotency can be distinguished in their early phases, which will, thus, significantly improve the production of full pluripotent iPS cells and promote their application in disease therapy," Wang said.

As stem cells can be applied in the treatment of many diseases related to tissue replacement or organ implantation, Zhou said, if the team's

findings also are true for humans, "it will cause a revolution in stem-cell research and the application of it in the very near future."

More information: The paper can be found at www.jbc.org/content/early/2010 … 4/13/jbc.M110.131995

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