New concoction reprograms differentiated cells into pluripotent stem cells

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In the new issue of the journal *Cell Stem Cell*, Singapore scientists report the surprising discovery that a novel transcription factor, Nr5a2, can replace one of the classical reprogramming factors, Oct 4, to significantly increase the efficiency of reprogramming differentiated stem cells into induced pluripotent stem cells (iPS cells).

Previous research revealed that the reprogramming of differentiated cells into induced iPS cells could be achieved by the three transcription factors, Oct4, Sox2 and Klf4.

In this latest finding, which is potentially relevant to cell therapy-based medicine, Genome Institute of Singapore (GIS) and National University of Singapore (NUS) scientists determined that Nr5a2 can replace Oct4. Thus, a new combination of Nr5a2, Sox2 and Klf4 can reprogram differentiated cells into iPS cells.

"This is a very exciting moment," said GIS Senior Group Leader Ng Huck Hui, Ph.D. "Fundamental research in embryonic stem cells is extremely important for us to harness the full potentials of these cells, and this study provides valuable and crucial insights into the mechanism of reprogramming.

"Given Oct4's critical role in embryonic stem cells and reprogramming, we were very surprised with the discovery that Nr5a2 could replace Oct4," added Dr. Ng, senior author of the paper. "This study highlights the prospect of finding more surprises in the field of reprogramming."

"This paper represents significant addition to the very active field of cellular reprogramming," added Davor Solter, M.D., Ph.D., Senior Principal Investigator at Singapore's Institute of Medical Biology (IMB).

Both GIS and IMB are part of Singapore's A*STAR (Agency for Science, Technology and Research).

"The authors show that gene coding for nuclear receptor Nr5a2 can replace one of the classical reprogramming factors Oct 4," Dr. Solter said. "In addition they presented evidence that this and another nuclear receptor can significantly increase the efficiency of reprogramming. These results have great basic and practical significance."

The reprogramming of differentiated cells into iPS cells is one of the most important breakthroughs in stem cell research, because iPS cells can give rise to all other differentiated cell types that make up the human body.

Because they behave like embryonic stem cells, iPS cells are important starting points for the creation of organs for replacement or transplantation.

The *Cell Stem Cell* paper, published on Jan. 21, 2010, is the second research report on iPS cell science by Dr. Ng's research group. In Jan. 2009, Dr. Ng and his colleagues reported in *Nature Cell Biology* that the transcription factor Esrrb could replace Klf4 in the combination of Oct4, Sox2 and Klf4 for iPS cell creation.

More information: The paper titled, "The Nuclear Receptor Nr5a2 can replace Oct4 in the Reprogramming of Murine Somatic Cells to Pluripotent Cells," will be published in the Jan. 21, 2010 online issue of Cell Stem Cell.

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