Gene that improves quality of reprogrammed stem cells identified by Singapore scientists

February 7 2010

In the 7 Feb. 2010 issue of the journal *Nature*, scientists at the Genome Institute of Singapore (GIS), report that a genetic molecule, called Tbx3, which is crucial for many aspects of early developmental processes in mammals, significantly improves the quality of stem cells that have been reprogrammed from differentiated cells.

Stem cells reprogrammed from differentiated cells are known as induced pluripotent stem cells or iPS cells.

By adding Tbx3 to the existing reprogramming cocktail, GIS scientists successfully produced iPS cells that were much more efficient in recapitulating the entire developmental process.

The capability of iPS cells for germ-line transmission represents one of the most stringent tests of their ESC-like quality. This test requires that iPS cells contribute to the formation of germ cells that are responsible for propagating the next generation of offspring.

"This represents a significant milestone in raising the current standards of iPS cell research. With this new knowledge, we are now able to generate iPS cells which are, or approach, the true equivalent of ESCs," said Lim Bing, M.D., Ph.D., lead author of the Nature paper and Senior Group Leader at GIS, one of the research institutes of Singapore's A*STAR (Agency for Science, Technology and Research).

"When applied to the area of cell therapy-based medicine, we have a

better inkling of what we might aim for before differentiating iPS cells to clinically useful cell types. The finding also adds to our insight into the fascinatingly, unchartered but rapidly moving field of reprogramming," Lim added.

George Q. Daley, M.D., Ph.D., Director, Stem Cell Transplantation Program, HHMI/Children's Hospital Boston, Harvard Medical School, added, "This paper highlights the rapid progress towards optimized reprogramming strategies. The Singapore group has made an important advance in the production of high quality iPS cells. I would like to congratulate them on this important contribution."

Embryonic stem cells (ESCs) are undifferentiated master stem cells that are developmentally important because they give rise to all other differentiated cell types in the human body. It has been shown that with the introduction of a few genetic factors into differentiated cells, these master stem (undifferentiated) cells can be re-created through a process known as reprogramming into iPS cells.

Converting adult cells to embryonic cells such as iPS cells represents one of the most astounding breakthrough technologies in biological research. These cells look and behave like normal embryonic stem cells (ESCs) that can generate all other tissue types. Hence the great excitement over iPS potential impact on tissue regeneration and development of therapeutics.

Previous studies have demonstrated how scientists can make iPS cells by using different cocktails of genetic factors, as well as improve this efficiency via the addition of chemical supplements. However, not all iPS cells generated with different cocktails resemble true ESCs; that is, the quality of the iPS cells is highly varied.

"The ability to produce iPS cells has the potential to accelerate advances

in human medicine. To achieve this objective, it is important to establish iPS cells that most closely resemble authentic embryo-derived pluripotent stem cells," said Azim Surani, Ph.D., Professor of Physiology and Reproduction at the Wellcome Trust /Cancer Research UK Gurdon Institute, University of Cambridge.

"The new study by Bing Lim and colleagues shows that the inclusion of Tbx3 as one of the reprogramming factors significantly improves the quality of iPS cells. These iPS cells were superior since viable adults composed entirely of these iPS cells could be generated," said Surani. "These iPS cells also showed superior ability for contribution and transmission through the germ line, which is one of the critical criteria for assessing the quality of iPS cells."

More information: The research findings are published in the 7 Feb. 2010 advance online issue of Nature in a paper titled, "Tbx3 improves the germ-line competency of induced pluripotent stem cells".

Provided by Agency for Science, Technology and Research (A*STAR), Singapore