Single factor converts adult stem cells into embryonic-like stem cells

5 February 2009

The simple recipe scientists earlier discovered for making adult stem cells behave like embryonic-like stem cells just got even simpler. A new report in the February 6th issue of the journal Cell, a Cell Press publication, shows for the first time that neural stem cells taken from adult mice can take on the characteristics of embryonic stem cells with the addition of a single transcription factor. Transcription factors are genes that control the activity of other genes.

The discovery follows a 2006 report also in the journal Cell that showed that the introduction of four ingredients could transform differentiated cells taken from adult mice into "induced pluripotent stem cells" (iPS) with the physical, growth, and genetic characteristics typical of embryonic stem cells. Pluripotent refers to the ability to differentiate into most other cell types. The same recipe was later shown to work with human skin cells as well.

Subsequent studies found that the four-ingredient recipe could in some cases be pared down to just two or three essential ingredients, said Hans Schöler of the Max Planck Institute for Molecular Biomedicine in Germany. "Now we've come down to just one that is sufficient. In terms of the biology, it's really quite amazing."

The discovery sheds light on centuries-old questions about what distinguishes the embryonic stem cells that give rise to egg and sperm from other body cells, Schöler said. It might also have implications for the use of reprogrammed stem cells for replacing cells lost to disease or injury.

Other researchers led by Shinya Yamanaka showed that adult cells could be reprogrammed by adding four factors - specifically Oct4, Sox2, Klf4, and c-Myc. Recently, Schöler and his colleagues demonstrated that Oct4 and Klf4 are sufficient to induce pluripotency in neural stem cells.

By omitting Klf4 in the new study, they have now established that Oct4 is the "driving force" behind the conversion of the neural stem cells into iPS cells. The lone transcription factor is not only essential, but it is also sufficient to make neural stem cells pluripotent.

Those cells, which Schöler's team calls "1F iPS" can differentiate into all three germ layers. Those primary germ layers in embryos eventually give rise to all the body's tissues and organs. Not only can those cells efficiently differentiate into neural stem cells, heart muscle cells, and germ cells, they show, but they are also capable of forming tumors when injected under the skin of nude mice. Those tumors, or teratomas, contain tissue representing all three germ layers. When injected into mouse embryos, the 1F iPS cells also found their way into the animals' developing organs and were able to be transmitted through the germ line to the next generation, they report.

The results show that adult stem cells can be made pluripotent without c-Myc and Klf4, both of which are "bona fide" oncogenes that can help turn normal cells into cancer cells, Schöler said. Limiting the number of factors is also a bonus because it means fewer genes must be inserted into the genome, where they can potentially have detrimental effects.

"Strikingly, Oct4 alone is sufficient to induce pluripotency in neural stem cells, which demonstrates its crucial role in the process of reprogramming…" the researchers concluded. "Future studies will show whether other sources of neural stem or progenitor cell populations such as mouse or human bone marrow-derived mesenchymal stem cells or dental pulp can be reprogrammed to iPS cells and whether expression of Oct4 can be induced by non-retroviral means, a prerequisite for the generation of iPS cells of therapeutic value."

Source: Cell Press

APA citation: Single factor converts adult stem cells into embryonic-like stem cells (2009, February 5) retrieved 26 September 2021 from https://phys.org/news/2009-02-factor-adult-stem-cells-embryonic-like.html

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