

Reprogrammed mouse fibroblasts can make a whole mouse

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In a paper publishing online July 23 in *Cell Stem Cell*, a Cell Press journal, Dr. Shaorong Gao and colleagues from the National Institute of Biological Sciences in Beijing, China, report an important advance in the characterization of reprogrammed induced pluripotent stem cells, or iPSCs.

Scientists working with iPSCs have been eager to find out if these cells are fully pluripotent, as this would tell us to what extent they have in fact been truly reprogrammed and resemble normal embryonic stem cells (ESCs).

The generally accepted "gold standard" for determining whether a mouse iPSC line has been fully reprogrammed is to show that when injected into an early embryo (or blastocyst), the iPSCs can contribute to many different tissues in the resulting chimeric mouse, including the germline. However, unlike bona fide mouse ESCs, until now mouse iPSCs have not been able to pass a more stringent test of true pluripotency termed "tetraploid complementation," which uses a hybrid embryo method to generate full-term mice entirely comprised of ESC-derived cells.

In their current report, Gao and his colleagues used established methods to reprogram mouse cells to isolate five new iPSC lines, and then found that, using one of these lines, they were able to make by tetraploid complementation embryos that survived until birth, and one embryo that also survived to adulthood.

The authors decided to test this specific iPSC line in the tetraploid complementation experiment because it gave an unusually high level of chimerism when injected into blastocysts and thus might have unique characteristics not found in many other iPSC lines. As emphasized by Gao, "Although these findings are an important proof of principle, it would be premature to make claims about whether iPSCs in general are functionally equivalent to normal ESCs." As the authors remark in their paper, it will be interesting to determine if there are specific reasons why this particular line succeeded where others have failed.

The demonstration that mouse iPSCs can, in fact, pass the most stringent test of pluripotency offers added hope that the process of reprogramming may indeed one day overcome the need for embryo destruction in order to derive pluripotent cells for research and potential therapies. However, it remains to be seen whether lessons obtained from these findings can be applied to human cells and thus whether human iPSCs will be a viable alternative to human ESCs in all circumstances.

Source: Cell Press

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