

Not all cellular reprogramming is created equal

December 1 2011

Tweaking the levels of factors used during the reprogramming of adult cells into induced pluripotent stem (iPS) cells greatly affects the quality of the resulting iPS cells, according to Whitehead Institute researchers.

"This conclusion is something that I think is very surprising or unexpected—that the levels of these reprogramming factors determine the quality of the iPS cells," says Whitehead Founding Member Rudolf Jaenisch. "We never thought they'd make a difference, but they do."

An article describing this work is published in the December 2 issue of *Cell Stem Cell*.

iPS cells are made by introducing specific reprogramming genes into [adult cells](#). These factors push the cells into a pluripotent state similar to that of embryonic stem (ES) cells. Like ES cells, iPS cells can become any cell type in the body, a characteristic that could make them well-suited for therapeutic cell transplantation or for creating cell lines to study such diseases as Parkinson's and Alzheimer's.

Since the creation of the first iPS cells in 2006, researchers using various reprogramming techniques have reported a broad spectrum of efficiency rates and quality of resulting iPS cells. Although researchers have shown iPS cells can fulfill all developmental tests applied to ES cells, recent reports have identified molecular differences that can influence their developmental potential and render them less-than-equivalent partners to ES cells. These inconsistencies have tarnished the promise of iPS cells,

dampened enthusiasm, and fueled speculation that they may never be used therapeutically.

In one example reported last year, a lab created iPS cells using a cutting-edge technique in which a piece of DNA containing four reprogramming genes is safely integrated in the genome of adult mouse cells. In this highly publicized study, the resulting iPS cells performed poorly in tests of pluripotency and failed to produce adult mice, which is the most stringent test of pluripotency. Yet again this called into question the fidelity by which reprogramming factors could consistently generate fully reprogrammed cells equivalent to [ES cells](#). Many in the field saw this as another nail in the coffin of iPS cells.

To Bryce Carey, first author of the Cell Stem Cell paper and a graduate student in Jaenisch's lab at the time, this death knell seemed premature. He repeated the experiment, changing a few details, including the order in which the reprogramming factors were placed on the inserted piece of DNA. Surprisingly, such small alterations had a profound effect—more adult cells were converted to high-quality iPS cells than in the earlier, nearly identical study.

"We are trying to show that the [reprogramming](#) process is not as flawed as some have thought, and that you can isolate these fully pluripotent iPS cells that have all of the developmental potential as embryonic stem cells at a pretty high frequency," says Carey, who is now a postdoctoral associate at Rockefeller University. "A lot of times these parameters are very difficult to control, so while the approach first described by [Shinya] Yamanaka back in 2006 is still the most reliable method for research purposes, we should be cautious in concluding there are inherent limitations. We show recovery of high-quality [cells](#) doesn't have to be the exception."

More information: "Reprogramming factor stoichiometry influences

the epigenetic state and biological properties of induced pluripotent stem cells," Cell Stem Cell, December 2, 2011

Provided by Whitehead Institute for Biomedical Research

Citation: Not all cellular reprogramming is created equal (2011, December 1) retrieved 9 April 2024 from <https://phys.org/news/2011-12-cellular-reprogramming-equal.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--