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Another step forward in cell reprogramming

Chemical used in place of two cancer genes in reprogramming process

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Imagine, if you can, a day within the next decade when a physician-scientist could remove a skin cell from your arm, and with a few chemicals turn that fully formed adult cell into a dish of stem cells genetically matched to you.

That day came a step closer to reality Oct. 12 with the publication in Nature Biotechnology of a report in which Harvard Stem Cell Institute researchers describe successfully having used a chemical in place of half the gene cocktail currently used to reprogram adult cells into induced pluripotent stem (iPS) cells.

"This study demonstrates there's a possibility that instead of using genes and viruses to reprogram cells, one can use chemicals," said Doug Melton, HSCI co-director and senior author of the study, whose first author is Danwei Huangfu, a postdoctoral fellow in Melton's lab.

"The exciting thing about Danwei's work is you can see how one might be able to sprinkle chemicals on cells and make stem cells," said Melton, a Howard Hughes Medical Institute investigator, giving his postdoc credit for the experiment.

This publication marks Huangfu's second success using chemicals in reprogramming – last year, working with mouse cells, Huangfu used a chemical to improve the efficiency of the gene-induced reprogramming process.

Eliminating the use of genes, and the viruses being used to insert them

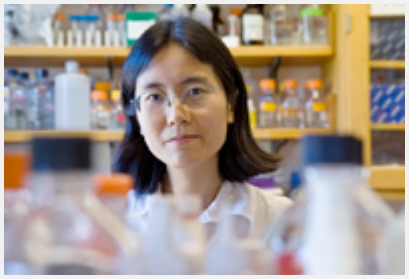

PHOTO BY JON CHASE/HARVARD NEWS OFFICE

Danwei Huangfu. "The exciting thing about Danwei's work is you can see for the first time that you could sprinkle chemicals on cells and make stem cells," said Doug Melton, a Howard Hughes Medical Institute investigator, giving his postdoc credit for the experiment.

into target cells, is a goal of scientists doing reprogramming work, because the genes become integrated into the genome of the target cells and may change them in ways not yet understood or anticipated.

In the latest experiment – using human cells – Huangfu, Melton, and colleagues took a major step by using a chemical to eliminate the need for two of the four genes now routinely used in reprogramming experiments. What is even more significant in terms of hastening the day when stem cells may be used to treat disease is that the two genes Huangfu eliminated were c-Myc and K1f4, both of which are cancer genes.

Valproic acid, the chemical used in the reprogramming experiment, has been used for a number of years as a medication to treat seizure disorders. "On at least a superficial level, it appears to be safe," which cancer genes are not, Huangfu said.

"The chemical has a transient effect on the cells we treat," the researcher, who came to Melton's lab three years ago after earning her Ph.D. at Cornell, said, while the genes used in cellular reprogramming are incorporated into the cells. The chemical loosens up the chromatin – the packaging of the cellular chromosome – so that the state of the cell can be altered.

What is not known at this point is whether chemicals can replace all the genes used in reprogramming, because it is the genes that instruct the cell to reprogram itself back to a stem cell state, said Melton, co-director of the Department of Stem Cell and Regenerative Biology.

"We may need two types of chemicals, " Huangfu explained, "one to loosen the chromatin structure, and another to activate a genetic program for the stem cell state. We are looking for that reprogramming chemical, and it should be possible to find."