Lab-made skin cells will aid transplantation, cancer, drug discovery research

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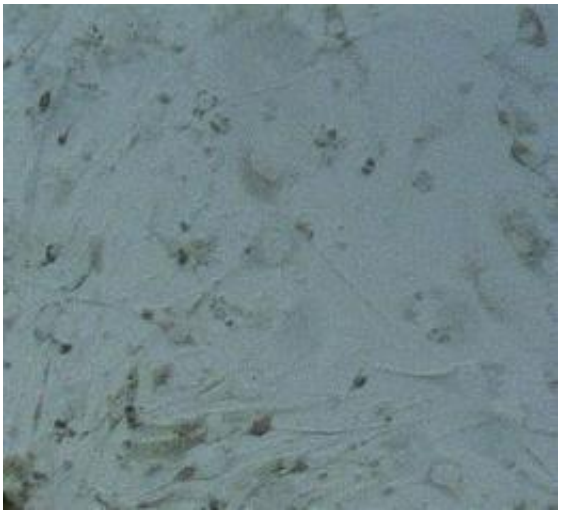

These are pigmented melanocytes derived from induced pluripotent stem cells. Credit: Xiaowei Xu, MD, PhD, Perelman School of Medicine, University of Pennsylvania

The pigmented cells called melanocytes aren't just for making freckles and tans. Melanocytes absorb ultraviolet light, protecting the skin from the harmful effects of the sun. They also are the cells that go haywire in melanoma, as well as in more common conditions as vitiligo and albinism.

Naturally, researchers would love to study melanocytes in the laboratory. There's just one problem -- melanocytes from adult skin don't grow very

well in the lab. Now, researchers at the Perelman School of Medicine at the University of Pennsylvania have found a way to create melanocytes from mouse tail cells using embryonic stem cell-like intermediates called inducible pluripotent (iPS) cells.

Xiaowei Xu, MD, PhD, associate professor of Pathology and Laboratory Medicine, is senior author the study, which appears online in the Journal of Investigative Dermatology ahead of the December print issue. Xu and his team converted mouse tail-tip fibroblasts into iPS cells using four genes, which were first described by Shinya Yamanaka in 2006, producing pluripotent cells similar to embryonic stem cells, but without the concomitant ethical issues.

According to Xu, these lab-made melanocytes promise benefits in areas from tissue transplantation to drug discovery. "This method really has lots of clinical implications," says Xu. "We are not quite there yet, but this is an early step."

For example, by collecting a tissue sample from patients with, say, vitiligo, and converting it to iPS cells, researchers can study what goes wrong as those cells differentiate into melanocytes. Or, they can study the development and possible treatment of melanoma.

Xu's new study is the first to report creating melanocytes from iPS cells in mice, and builds on his previous work. Xu's lab was involved in the first study to work out the conditions for differentiating human embryonic stem cells to melanocytes in 2006. Earlier this year, a Japanese team became the first to differentiate human iPS cells to melanocytes.

Transformation of Cells

Initially, the researchers from Xu's lab introduced the four Yamanaka

genes into mouse cells by infecting the cells with transgenic viruses. Between 0.5% to 0.8% of fibroblasts treated in this way converted to iPS cells in Xu's lab – a rate that is consistent with other researchers' findings, he says. But his team also could achieve the same result (albeit at lower efficiency, 0.01%) using a non-viral "transposon" called piggyBac. Finally, the researchers showed they could differentiate both iPS cell populations into melanocytes in about two weeks by feeding the cells a defined cocktail of growth factors.

According to Xu, the growth factor cocktail used in the present study differs somewhat from the formulation his lab worked out several years ago for human embryonic stem cells. Among other things, it works in the absence of the growth factor Wnt3a and the carcinogen TPA, both of which are required for human melanocyte differentiation. TPA, especially, could be problematic for possible cell-based therapies, in that it is tumorigenic. It remains to be seen, however, whether human iPS cells can also be differentiated in the absence of this compound, Xu notes.

His study's implementation of piggyBac in creating the iPS cells (a technique first published by Canadian researchers in 2009) could possibly extend the technique's clinical value, he adds. Unlike viruses, which insert their genetic cargo into the host genome, thereby raising concerns of genetic alterations in the infected cells, piggyBac delivers genes without permanently altering the host genome.

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