Researchers engineer cartilage from pluripotent stem cells

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A team of Duke Medicine researchers has engineered cartilage from induced pluripotent stem cells that were successfully grown and sorted for use in tissue repair and studies into cartilage injury and osteoarthritis.

The finding is reported online Oct. 29, 2012, in the journal the Proceedings of the National Academy of Sciences, and suggests that induced pluripotent stem cells, or iPSCs, may be a viable source of patient-specific articular cartilage tissue.

"This technique of creating induced pluripotent stem cells – an achievement honored with this year's Nobel Prize in medicine for Shimya Yamanaka of Kyoto University - is a way to take adult stem cells and convert them so they have the properties of embryonic stem cells," said Farshid Guilak, PhD, Laszlo Ormandy Professor of Orthopaedic Surgery at Duke and senior author of the study.

"Adult stems cells are limited in what they can do, and embryonic stem cells have ethical issues," Guilak said. "What this research shows in a mouse model is the ability to create an unlimited supply of stem cells that can turn into any type of tissue – in this case cartilage, which has no ability to regenerate by itself."

Articular cartilage is the shock absorber tissue in joints that makes it possible to walk, climb stairs, jump and perform daily activities without pain. But ordinary wear-and-tear or an injury can diminish its effectiveness and progress to osteoarthritis. Because articular cartilage

has a poor capacity for repair, damage and osteoarthritis are leading causes of impairment in older people and often requires joint replacement.

In their study, the Duke researchers, led by Brian O. Diekman, PhD., a post-doctoral associate in orthopaedic surgery, aimed to apply recent technologies that have made iPSCs a promising alternative to other tissue engineering techniques, which use adult stem cells derived from the bone marrow or fat tissue.

One challenge the researchers sought to overcome was developing a uniformly differentiated population of chondrocytes, cells that produce collagen and maintain cartilage, while culling other types of cells that the powerful iPSCs could form.

To achieve that, the researchers induced chondrocyte differentiation in iPSCs derived from adult mouse fibroblasts by treating cultures with a growth medium. They also tailored the cells to express green fluorescent protein only when the cells successfully became chondrocytes. As the iPSCs differentiated, the chondrocyte cells that glowed with the green fluorescent protein were easily identified and sorted from the undesired cells.

The tailored cells also produced greater amounts of cartilage components, including collagen, and showed the characteristic stiffness of native cartilage, suggesting they would work well repairing cartilage defects in the body.

"This was a multi-step approach, with the initial differentiation, then sorting, and then proceeding to make the tissue," Diekman said. "What this shows is that iPSCs can be used to make high quality cartilage, either for replacement tissue or as a way to study disease and potential treatments."

Diekman and Guilak said the next phase of the research will be to use human iPSCs to test the cartilage-growing technique.

"The advantage of this technique is that we can grow a continuous supply of cartilage in a dish," Guilak said. "In addition to cell-based therapies, iPSC technology can also provide patient-specific cell and tissue models that could be used to screen for drugs to treat osteoarthritis, which right now does not have a cure or an effective therapy to inhibit cartilage loss."

Provided by Duke University Medical Center