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HEALTH

Indian researchers develop 3D bioprinted cartilage

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MAY 27, 2017 18:40 IST
UPDATED: MAY 27, 2017 18:43 IST

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It is the first time that permanent cartilage similar to natural ones has been developed

Millions of people around the world suffer from degenerative joint diseases such as arthritis. Despite attempting for the last 30 years, scientists across the world have not been able to produce in the lab cartilage-like tissues that are functionally and structurally similar to cartilages seen in human knees and have load-bearing capacity. For the first time, Indian researchers have been able to achieve a measure of success in developing cartilages that are molecularly similar to the ones seen in human knees.

While scientists attempting to tissue-engineer cartilage have focussed on growing cells on porous scaffolds, in a paradigm shift, a team led by Prof. Sourabh Ghosh from the Department of Textile Technology at the Indian Institute of Technology (IIT) Delhi has been successful in 3D bioprinting of cartilage using a bioink.

The bioink has high concentration of bone-marrow derived cartilage stem cells, silk proteins and a few factors. The chemical composition of the bioink supports cell growth and long-term survival of the cells. The cartilage developed in the lab has remained physically stable for up to six weeks. The results of the study were published in the journal *Bioprinting.*

“This is the first study from India where any 3D bioprinted tissue has been developed in a lab,” says Shikha Chawla from the Department of Textile Technology at IIT Delhi and the first author of the paper.

“The silk protein has different amino acids that closely resemble the amino acids present in human tissues. Just like cells are surrounded by proteins inside our body, the cells in the engineered cartilage are also surrounded by bioink that has a similar composition,” says Prof. Ghosh, who is one of the corresponding authors of the paper.

Transient cartilage

While the cartilage found in the knee is an articular cartilage that is typically sponge-like and has a huge load-bearing capacity, the ones produced in the lab so far are of a different kind — transient cartilage. Unlike articular cartilage, transient cartilage becomes bone cells and, therefore, brittle within a short time. As a result, the engineered cartilage loses its capacity to bear huge load that is typically encountered in the knee.

But the 3D bioprinting approach adopted by the team allows the high concentration of bone-marrow derived cartilage stem cells present in the bioink to gradually convert to chondrocyte-like cells (specialised cells which produce and maintain the extracellular matrix of cartilage).

“We have succeeded in stopping this conversion of chondrocyte-like cells or stem cells into bone cells so that they remain as stable articular cartilage,” says Prof. Ghosh. This was done by optimising the bioink composition, 3D bioprinting process, and by using a combination of growth factors. The optimisation of the silk-gelatin bioink was done in such a manner that it activated two important signalling pathways that are responsible for minimising or inhibiting the conversion of the cartilage into bone-like tissue.

“All earlier work never evaluated for the production of articular or permanent cartilage, while we assessed and found that our strategy leads to the production of permanent cartilage in the lab,” says Prof. Amitabha Bandyopadhyay of Department of Biological

Sciences and Bioengineering, Indian Institute of Technology (IIT) Kanpur, and a corresponding author.

Stem-cell like nature

The team was able to achieve this by combining the tissue engineering and 3D bioprinting expertise at IIT Delhi with developmental biology expertise at IIT Kanpur. Prof. Bandyopadhyay's laboratory developed a well characterised, novel cell line from bone-marrow stem cells. The cell line retained its stem cell-like nature even after months of culturing under laboratory conditions.

"As a next step, we would implant this 3D bioprinted cartilage into the knee joints of animals to see if it remains stable in the knee joint and is able to integrate with the surrounding cartilage tissue," says Prof. Ghosh. This study also opens up platforms to use 3D bioprinted cartilage on in vitro model system for assessing drug delivery and pharmaceutical studies.