How far are we from repairing cartilage tissue with tissue-engineered products?

'An Editorial for Bioreactor manufactured cartilage grafts repair acute and chronic osteochondral defects in large animal studies: doi:10.1111/cpr.12653'

Cartilage defects due to sports injury, tumour recession or age-related abrasion usually resulted in constant pain and functional limitations of joints, thus leading to serious medical consequences. It was believed that even small defects in cartilage could set off chronic inflammation in joints and started the progression of osteoarthritis. Current treatments such as allogenic cartilage transplantation and bone marrow stimulation often lead to insufficient cartilage regeneration. With the development of tissue engineering technology, cartilage tissue can be engineered in the laboratory to mimic the properties of hyaline cartilage. Thus, tissue-engineered cartilage was considered to be the ultimate treatment for cartilage defects.

1 | WHAT IS CARTILAGE ENGINEERING?

Cartilage tissue engineering is the technology to grow cartilage tissue using live chondrocytes usually combined with biodegradable scaffolds. Autologous chondrocyte implantation (ACI) could be considered as the first generation of cartilage engineering. This procedure often required a two-step surgery—the first harvested cartilage tissue from a non-weight-bearing site of the patient, followed by weeks of cell expansion in laboratory and the second implanted the expanded chondrocytes at the defect site. Now, the technique had evolved to the third generation: matrix-induced autologous chondrocyte implantation. The format of implanted tissue, which included cells seeded on scaffold, had met almost every criterion as a tissue engineering product. However, these therapies were highly personalized and hard to standardize during manufacturing. The ideal tissue engineering product for cartilage regeneration should be manufactured with unified industrial standards.

2 | WHY DO WE GROW CARTILAGE IN A BIOREACTOR?

With the rapid development of stem cell-based therapies, people from both academia and industry started to realize that manufacturing a cell or tissue product needs industrial standardization. Growing tissues in a bioreactor would fulfill these criteria perfectly. With a good bioreactor design, the culture conditions such as medium exchange and mechanical loading can be precisely and steadily controlled. In this issue of Cell Proliferation, we have an article by Prof Ivan Martin, Prof David Wendt and colleagues from the University of Basel who have contributed to this topic with their design of a bioreactor that can be operated in a GMP facility. In this study, the authors evaluated the efficacy of cartilage grafts engineered in a perfusion bioreactor system to repair osteochondral defects in two different large animal models. The results demonstrated that grafts produced in the system accelerate cartilage regeneration in a chronic defect sheep model, which was considered to be more clinically relevant. By demonstrating the safety and efficacy of bioreactor-generated grafts in two large animal models, this work is the first of its kind that represents a bioreactor-based manufacturing strategy for producing clinically applicable implants of human cartilage tissue. It advances bioreactor technology from the laboratory to the clinic.

Notably, nasal cartilage was used as the source for chondrocytes in this study. Prof Martin is a pioneer in the movement of utilizing nasal chondrocytes for cartilage engineering. As early as 2002, he and Prof Anthony Hollander had proposed using nasal cartilage as a source of chondrocytes for cartilage engineering. From then on, Martin’s group has published a series of papers to support this idea. In 2014, autologous nasal cartilage tissues were reported to have been engineered and used clinically for functional restoration of alar lobules. In 2016, hyaline-like cartilage tissues were reported to have been engineered from autologous nasal chondrocytes to repair articular cartilage defects in the human knee joints. Nasal cartilage was proven to be a reliable source of chondrocytes.

3 | WHAT CAN WE EXPECT IN THE FUTURE?

In the early years of the automotive industry, manufacturing of cars was highly innovative and complex. For many years, the prosperity of the industry was bottle-necked by the number of skilled experts who were well trained on the novelty and complexity of car
manufacturing. It was only when Henry Ford’s mass production line was invented that manufacturing of automobiles could be performed by ordinary workers. This not only brought down the cost to an affordable level, but it also increased the quality of cars to industrial standards. Bioreactors can be the same to cartilage engineering as mass production lines are to automobile manufacturing. With the advances in this technology, we believe that in 10-20 years’ time, tissue-engineered cartilage will be easily accessible in ordinary clinics.

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