Chondrocyte

Chondrocytes are the only cells found in healthy cartilage.

Function

They produce and maintain the cartilaginous matrix, which consists mainly of collagen and proteoglycans. Although the word chondroblast is commonly used to describe an immature chondrocyte, the term is imprecise, since the progenitor of chondrocytes (which are mesenchymal stem cells) can differentiate into various cell types, including osteoblasts.

From least- to terminally-differentiated, the chondrocytic lineage is:

Colony-forming unit-fibroblast (CFU-F)

Mesenchymal stem cell / marrow stromal cell (MSC)

Chondrocyte

Hypertrophic chondrocyte

When referring to bone, or in this case cartilage, the originally undifferentiated mesenchymal stem cells lose their pluripotency, proliferate and crowd together in a dense aggregate of chondrogenic cells (cartilage) at the location of chondrification. These chondrogenic cells differentiate into so-called chondroblasts, which then synthesize the cartilage extra cellular matrix (ECM), consisting of a ground substance (proteoglycans, glycosaminoglycans for low osmotic potential) and fibers. The chondroblast is now a mature chondrocyte that is usually inactive but can still secrete and degrade the matrix, depending on conditions.

BMP4 and FGF2 have been experimentally shown to increase chondrocyte differentiation.

Chondrocytes undergo terminal differentiation when they become hypertrophic, which happens during endochondral ossification. This last stage is characterized by major phenotypic changes in the cell.

Autologous chondrocyte implantation (ACI, ATC code M09AX02 (WHO)) is a biomedical treatment that repairs damages in articular cartilage. ACI provides pain relief while at the same time slowing down the progression or considerably delaying partial or total joint replacement (knee replacement) surgery. The goal of ACI is to allow people suffering from articular cartilage damage to return to their old lifestyle; regaining mobility, going back to work and even practicing sports again.

ACI procedures aim to provide complete hyaline repair tissues for articular cartilage repair. Over the last 20 years, the procedure has become more widespread and it is currently probably the most developed articular cartilage repair technique.

The surgical technique was first performed in Sweden in 1987; the results of the 9 year follow up are available in Lars Peterson et al. 2000. Brittberg published the first description of the technique on humans in 1994. He reported good and promising results with 23 patients for defects on the femoral

condyles .The technique also seems promising with regard to long-term results.

NOVOCART® Disk plus, an autologous cell compound for autologous disk chondrocyte transplantation, was developed to reduce the degenerative sequel after lumbar discectomy or to prophylactically avoid adjacent segment disease, if present.

The NDisc trial is an ongoing multi-center, randomized study with a sequential phase I study within the combined phase I/II trial with close monitoring of tolerability and safety. Twenty-four adult patients were randomized and treated with the investigational medicinal product NDisc plus or the carrier material only. Rates of adverse events in Phase I of this trial were comparable with those expected in the early time course after elective disk surgery. There was one reherniation 7 months after transplantation, which corresponds to an expected reherniation rate. Immunological markers like C reactive protein and IL6 were not significantly elevated and there were no imaging abnormalities. No indications of harmful material extrusion or immunological consequences due to the investigational medicinal product NDplus were observed. Therefore, the study appears to be safe and feasible. Safety analyses of Phase I of this trial indicate a relatively low risk considering the benefits that patients with debilitating degenerative disk disease may gain [1)].

1)

Tschugg A, Diepers M, Simone S, Michnacs F, Quirbach S, Strowitzki M, Meisel HJ, Thomé C. A prospective randomized multicenter phase I/II clinical trial to evaluate safety and efficacy of NOVOCART disk plus autologous disk chondrocyte transplantation in the treatment of nucleotomized and degenerative lumbar disks to avoid secondary disease: safety results of Phase I-a short report. Neurosurg Rev. 2017 Jan;40(1):155-162. doi: 10.1007/s10143-016-0781-0. Erratum in: Neurosurg Rev. 2017 Jan;40(1):177. PubMed PMID: 27567635.