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Karyotyping of human chondrocytes in scaffold-assisted cartilage tissue engineering

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ABSTRACT

Scaffold-assisted autologous chondrocyte implantation (ACI) is an effective clinical procedure for cartilage repair. The aim of our study was to evaluate the chromosomal stability of human chondrocytes subjected to typical cell culture procedures needed for regenerative approaches in polymer-scaffold-assisted cartilage repair. Chondrocytes derived from post mortem donors and from donors scheduled for ACI were expanded, cryopreserved and re-arranged in polyglycolic acid (PGA)–fibrin scaffolds for tissue culture. Chondrocyte redifferentiation was analyzed by electron microscopy, histology and gene expression analysis. Karyotyping was performed using GTG banding and fluorescence in situ hybridization on a single cell basis. Chondrocytes showed de- and redifferentiation accompanied by the formation of extracellular matrix and induction of typical chondrocyte marker genes like type II collagen in PGA–fibrin scaffolds. Post mortem chondrocytes showed up to 1.7% structural and high numbers of numerical (up to 26.7%) chromosomal aberrations, while chondrocytes from living donors scheduled for ACI showed up to 1.8% structural and up to 1.3% numerical alterations. Cytogenetically, cell culture procedures and PGA–fibrin scaffolds did not significantly alter chromosomal integrity of the chondrocyte genome. Human chondrocytes derived from living donors subjected to regenerative medicine cell culture procedures like cell expansion, cryopreservation and culture in resorbable polymer-based scaffolds show normal chromosomal integrity and normal karyotypes.

1. Introduction

Traumatic or focal degenerative articular cartilage defects are often accompanied by pain, loss of mobility and considerable limitations in quality of life and may lead to severe osteoarthritis (OA) and total knee replacement. Frequently applied first and second-line cartilage repair procedures comprise for example bone marrow stimulating techniques like drilling or microfracturing, osteochondral autograft transfer and autologous chondrocyte implantation (ACI) [1–3].

In ACI, a cartilage biopsy is taken from the less weight-bearing area of the knee joint, and chondrocytes are isolated enzymatically and grown in vitro in the presence of autologous serum. In a second surgery, the cartilage defect is debrided, leading to a self-contained compartment with an intact cartilage rim surrounding the defect. After covering of the defect with a periosteal flap or a collagen sheet, sutured onto the healthy cartilage, the expanded chondrocytes are injected into the defect. Meanwhile, a variety of clinical studies showed the efficacy of implantation of in vitro expanded chondrocytes for cartilage repair [4–6], but the superiority of the ACI procedure to other cartilage repair techniques in the treatment of full-thickness cartilage defects is still discussed controversially [7–10].

To overcome inherent technical disadvantages of ACI, like for example loss of cells into the joint cavity, ablation and periosteal hypertrophy that may lead to re-operations in up to 40% of the cases [11], matrix- or scaffold-assisted cartilage tissue engineering grafts were developed that use expanded chondrocytes embedded in resorbable, three-dimensional (3-D) scaffolds. These scaffold-based approaches have been shown to be pre-clinically and clinically effective for hyaluronan [12,13], collagen [14,15] and polymer-gel (polyglycolic/polylactic acid–fibrin) scaffolds [16–18].

From the regulatory point of view, the approval of these cell-based cartilage repair approaches has implications in the

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