Autologous matrix induced chondrogenesis combined with Epiphyseal Chondro-Progenitor Cells for the Treatment of Full Thickness Cartilage Injuries – An Experimental GLP-grade Safety Study in Goats

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Introduction

Bone marrow stimulation or microfracture (MF) is the most widely used surgical technique to repair cartilage tissue injuries. While repair tissue is built relatively quickly, the MF procedure leads to the formation of a fibrocartilaginous scar tissue. Another major pitfall of MF is the instability of the mesenchymal blood clot formed. Autologous Matrix Induced Chondrogenesis (AMIC) aims stabilize the blood clot with a membrane, which can be glued in place using tissue sealant. The clinical superiority of AMIC compared to standard MF however has not yet been determined by randomized trials. As such, we have endeavored to combine the matrix-stabilizing technique with bioactive factors, namely therapeutic cells, which may effectively interact with reparative cells from the bone marrow and transform the repair response to a regenerative response. We have previously reported the reliable expansion and characterization of a clinical-grade human epiphyseal chondro-progenitor (ECP) cell bank from a single tissue donation. Aimed for allogenic off-the-shelf implantation, ECPs exhibited remarkable homogeneity and stability in expansion [1].

We have conducted a GLP-grade pre-clinical safety study in goats to assess the effect of implanted ECPs in a full thickness chondral defect. ECPs were delivered within a collagen-based matrix. The cell-laden construct is delivered in combination with MF to direct new tissue repair and remodeling. We present here the findings from our 3-months pre-clinical study, focusing on the safety of ECPs, the feasibility of the proposed treatment protocol as well as early indications of repair.

Materials and Methods

This study was performed in compliance with Principles of Good Laboratory Practice (OECD, C(97)186/Final). All animal experiments were conducted according to Swiss laws of animal protection and welfare and authorized by the cantonal ethical committee (license 174/2012). Eight female Saanen goats were randomized to two treatment groups. Six goats in the ECP group received ECPs seeded in Chondro-Gide® collagen matrix (Geistlich, Switzerland) over MF in full thickness chondral defects. Two goats in the control group received saline soaked Chondro-Gide® matrix over MF. Full thickness chondral defect were performed in medial and lateral condyles of the stifle joint. Animals were sacrificed 3 months after the surgery. Organ and tissue samples were processed to screen for traces of human cells as well as potential histological abnormalities. Magnetic Resonance Imaging was performed on operated stifles to detect subchondral bone sclerosis and bone marrow edema. Macroscopic, histological and immunohistochemical assessments were performed to evaluate the quality of early repair as well as that of the surrounding cartilage and subchondral bone.

Results

At the early 3-month time point, the macroscopic state of repair as well as subsequent subchondral bone sclerosis and bone marrow edema showed no statistically detectable difference compared to control. A trend was however observed in cartilage tissue surrounding the defects with the ECP group exhibiting healthier, better preserved surrounding cartilage compared to controls. Tracking ectopically engrafted human cells did not reveal pathological observations of any kind.

Discussion and Conclusions

ECP implantation in combination with AMIC may provide necessary protective cues to maintain joint homestasis during repair. Whether ECPs are more likely to work as chaperones of repair or builders of new tissue, results from the 3-months study highlights their safety. The proposed implantation protocol provides the operating room staff with enough flexibility without requiring much pre-planning or the need for additional expensive equipment in the operating room. The results obtained will help inform the design of a long-term investigation attempting to achieve functional cartilage regeneration.

References


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