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Integartional behavior of tissue engineered chondrocyte/MSC-laden hydrogel constructs in an in vitro bovine cartilage defect model

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Introduction:

The success of matrix-based autologous cell implantation for the treatment of articular cartilage defects is dependent on the lateral integration and the deposition of cartilage specific extracellular matrix components. Due to the limited availability of healthy chondrocytes and dedifferentiation during expansion culture, the need for an alternative cell is obvious. In this study, using a bovine in vitro integration model, agarose constructs laden with MSCs, differentiated and dedifferentiated chondrocytes were compared concerning their applicability in matrix-based cartilage repair strategies.

Materials and Methods:

Circular native cartilage rings with a centred 4mm hole were fabricated from knee cartilage of calves. In the first group cell-laden agarose constructs (10x106cells/ml) seeded with either de-/differentiated chondrocytes (0, 2, 5 or 8 population doublings), or MSCs were implanted into the cartilage rings. These hybrid constructs were cultured for 28 days in a chemically defined, serum free medium (CM-). In a second group, constructs were initially kept as free-swelling culture in CM-supplemented with TGF-s3 (CM--+) for 21 days and then implanted. Four weeks after implantation lateral integration, biomechanical properties and accumulated glycosaminoglycans/bulk collagen were assessed within the constructs.

Results:

Untreated scaffolds seeded with dedifferentiated chondrocytes or MSCs revealed significant lower integration compared to differentiated chondrocytes. In comparison, in the pre-treated group MSC-seeded cell-carriers showed stronger integration into the surrounding native cartilage than those seeded with de-differentiated chondrocytes. Remarkably, pre-treated MSC-seeded constructs showed distinct matrix deposition, mechanical properties and integration that were significantly higher compared to constructs seeded with dedifferentiated chondrocytes.

Discussion:

These results show that chondrocytes lose their ability to deposit cartilage specific extracellular matrix components within the implant with increasing number of population
doublings, resulting in inferior mechanical properties and integration. In addition, de-differentiated chondrocytes exhibit inferior responsiveness to anabolic factors, such as TGF-s3. MSCs are able to undergo chondrogenic differentiation during the pretreatment with CM+ and show superior accumulation of cartilage specific extracellular matrix after implantation, supporting their applicability in matrix-based cartilage repair strategies.

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