Co-culture of mesenchymal stromal (stem) cells and meniscal cells in type I collagen hydrogel for meniscal tissue regeneration

SUMMARY

Menisci of the knee have a fundamental role in the biomechanics of the joint. Partial meniscectomy was the golden standard treatment for meniscal tears regarding the inner zone of the menisci, however recent studies demonstrated its correlation with increasing risks of early OA. As a solution, the implantation of Collagen Meniscus Implant (CMI) for regeneration of meniscal tissue after partial meniscectomy is currently clinically available. Although follow up studies until 12.5 years showed positive remodeling and tissue regeneration, this device presents the drawback of shrinking in size after implantation. A feasible and cost effective solution to this problem could be to seed the construct with a combination of autologous meniscal cells and allogeneic human mesenchymal stromal cells (hMSCs) during CMI implantation in a single stage operation. The objective of this study was to evaluate if co-culture of human meniscal cells (MEN) and hMSCs would result in meniscus like ECM formation and to study the best performing MEN:hMSC ratio.

Our hypothesis was that co-culture of meniscal cells and hMSCs would result in enhanced ECM production when compared with only meniscal cells or hMSCs. For this experiment meniscal cells from 3 donors and hMSCs from one donor were mixed in ratios of 100:0, 50:50, 20:80, 10:90 and 0:100 MEN:hMSCs. In order to mimic a collagenous environment, cells were seeded in three-dimensional type I collagen hydrogels and cultured for 28 days. The outcomes were evaluated through macroscopic size analysis, biochemical assays, gelatinase activity assay, histology, immunohistochemistry, and mechanical indentation. In this study, the co-cultures of MEN and hMSCs, and particularly the condition 20:80 MEN:hMSCs, resulted in higher GAGs content and production, collagen release in the medium and gelatinase activity compared to mono-cultures. Higher collagen content and production was related to higher hMSCs ratios. Even though meniscal cell monocultures resulted in higher mechanical properties with thicker collagen fibers when compared with the other conditions, they showed to have lower collagen content and reduction in size. On the other hand, the ratio 20:80 mechanically outperformed all the remaining conditions, presenting similarities to hydrogels containing only meniscal cells. These data demonstrated that, overall, the ratio 20:80 MEN:hMSCs results in an optimal combination for meniscal tissue regeneration due to active (functional) matrix production and remodelling resulting in enhanced mechanical properties. While the underlying cell-cell interaction mechanism remains unknown and further evaluation of the cell combination and the CMI are needed, we conclude that 20:80 MEN:hMSCs in collagenous environment is the optimal ratio for a potential clinical testing for meniscal tissue regeneration.