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WORKING TOWARDS A REGENERATIVE THERAPY FOR OSTEOARTHRITIS: INFLUENCE OF STEM CELLS

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Background: Osteoarthritis is incurable and a leading cause of disability worldwide. Mesenchymal stem cells (MSCs) have recently been used to treat osteoarthritis due to their anti-inflammatory and pro-regenerative characteristics. Interestingly, the few clinical trials utilising MSCs to treat knee osteoarthritis have not demonstrated consistent benefits[1]. This study aims to understand the variable efficacy of stem cell therapy using an in vitro model of a human osteoarthritic joint.

Methods: MSCs were co-cultured with human synovial fibroblasts (HSFs) isolated from osteoarthritic tissues, for 21 days in growth, osteogenic and chondrogenic media (simulating relevant conditions in the joint). Cell interactions were assessed using RT-PCR (n=4) and histology (n=2).

Results: MSCs co-cultured with osteoarthritic HSFs showed increased inflammation (MMP2, ADAMTS5) and impaired ability to form new bone (reduced BSP, SPP1 expression and calcium deposition) and cartilage (reduced COL2A1, ACAN expression and proteoglycan deposition) at 21 days, suggesting that the osteoarthritic joint is an inhibitory environment that reduces the therapeutic effects of MSCs. Furthermore, short-term (3 days) exposure of the osteoarthritic HSFs to MSCs ('pre-conditioning') was insufficient for sustained modifications to their diseased phenotype. The osteoarthritic HSFs, whether previously exposed to MSCs or not, had similar expression profiles of inflammatory markers, and also similar negative effects on MSCs, including inflammatory marker upregulation (e.g. IL-8, ADAMTS4) and impaired chondrogenesis.

Conclusion: Diseased cells in an osteoarthritic joint can create an inhibitory environment that negatively affects the therapeutic effects of MSCs following injection. Future regenerative therapies for osteoarthritis may benefit from using the secreted products of stem cells.

References

1. McIntyre JA, Jones IA, Han B, Vangsness CT. Intra-articular mesenchymal stem cell therapy for the human joint: a systematic review. *Am J Sports Med.* 46, 3550, 2017