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[8] The Effect of Mesenchymal Stem Cells in Stimulating Intervertebral Disc Cells: A Comparative Study Towards Disc Regeneration

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INTRODUCTION: Intervertebral disc (IVD) degeneration is suggested to begin from the nucleus pulposus (NP). Evidence from various studies highlights mesenchymal stem cells (MSC), in most cases using bone marrow derived MSC, as a potential stem cell source for NP regeneration. However there are indications that fetal or close to fetal tissue sources contain MSC with relatively undifferentiated phenotype with respect to MSC from adult sources. Moreover, umbilical cord (C)-MSC may have better chondrogenic differentiation potential than bone marrow (B)-MSC. We hypothesize CMSC are more efficient than BMSC in stimulating NP regeneration.

OBJECTIVES AND METHODS: The aim of this research is to analyse the paracrine effect of MSC on degenerated human NP cells, and compare the effect of MSC from human bone marrow and human umbilical cord. Conditioned media (CM) was collected from confluent MSC monolayer, and used for stimulation of NP cells. Cell proliferation were assessed by MTT assay. Proteoglycan content were measured by DMMB assay. Gene expression of degeneration related molecules, including CDH2, CD55, FBLN1, SOX9, KRT19, KRT18, MGP, were determined by realtime RT-PCR. All results were normalized to the control cells in basal medium.

RESULTS: MTT readings of NP cells in MSC-CM were significantly enhanced than that in control basal medium, especially in CMSC-CM. CMSC-CM promoted GAG/total protein production more strongly than BMSC-CM. Among all the genes investigated, the expression levels of KRT19 and MGP in NP cells showed significant changes upon MSC-CM treatment. MGP expression was down-regulated in MSC-CM, especially in CMSC-CM. MMP12 expression were decreased by 30% in BMSC-CM compared to that in control medium, while a even bigger drop (70%) was detected in CMSC-CM. KRT19 expression in NP cells was significantly up regulated to 170% by stimulation with BMSC-CM, and by CMSC-CM the expression is 200% compared to control. Both changes in MGP and KRT19 suggested the degenerative NP cells acquired a phenotype resembling a non-degenerative state.

DISCUSSION: This is the first study revealing how the soluble factors secreted by MSC affect the biological activities and the expression of NP marker genes of cultured human NP. Our study suggested that MSC-CM increased the overall metabolic activities of degenerative NP cells in vitro. In addition, MSC-CM was also effective in promoting NP cells towards a non-degenerative phenotype. In all aspects tested, CMSC was more potent than BMSC, indicating CMSC as a promising and superior source of MSC for disc regeneration.