Effect of Inflammatory Cytokines on Chondrogenic Progenitor Cells

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INTRODUCTION:
Chondrogenic progenitor cells (CPCs) are pluripotent cells which are active in chondral regeneration and may be affected by inflammatory cytokines. The study purpose was: 1) evaluate effect of inflammatory cytokines on in vitro CPC gene expression, and 2) compare gene expression from pilon fracture patients CPCs to in vitro CPCs.

METHODS: CPCs activated from harvested human donor tibial plafond cartilage were incubated in either standard media (control), IL-1β (pro-inflammatory), or SDF-1 (pro-chondrogenic) supplemented media. After culture, CPCs were isolated, and gene expression was evaluated by RT-PCR. Target gene expression was then compared to non-reconstructable cartilage samples harvested from pilon fracture patients. Fold change was calculated by the 2-ΔΔCt method using average expression levels from control samples. One-way ANOVA and Bonferroni post hoc correction were used to compare mean expression values.

RESULTS: Twenty-three donor samples (8 standard, 7 IL-1β, and 8 SDF-1) and six pilon patient samples were analyzed. COL2A1 and Aggrecan expression were significantly lower in both IL-1β and pilon CPCs compared to SDF-1. PRG4 and SOX9 (chondrogenic) expression were similarly decreased in the pro-inflammatory samples and the pilon samples. IL-1β, IL-8, and IL-6 expression were significantly greater in IL-1B media as compared to pilon and SDF-1 samples. There was no difference in expression of osteogenic RUNX2, TGFβ, or SMAD3. MMP expression was not different between groups, although ADAMTS-4 was significantly higher in pilon CPCs.

DISCUSSION AND CONCLUSION: In CPCs from both IL-1β media and pilon fracture samples, several pro-inflammatory genes were upregulated and chondrogenic genes were down-regulated. Future investigation should focus on interventions to disrupt the pro-inflammatory cascade that may contribute to dysregulation of CPCs and development of posttraumatic osteoarthritis.