Commonly Used Orthopaedic Clinical Therapeutics Affect the Cytokine Activity of Culture-Expanded Mesenchymal Stem Cells

Jacob G Calcei MD, Tracey L Bonfield PhD, Ryan J Furdock MD, Andrew Moyal MD, David Fletcher BA, Evan Rudo BA, James E Voos MD

Assistant Professor of Orthopedic Surgery
University Hospitals Cleveland Medical Center
Case Western Reserve University SOM
Jacob.Calcei@UHhospitals.org





Disclosures

One of the authors (JEV) is a paid consultant for Arthrex Inc.

One of the authors (TLB) receives research support from Rooster Biologicals





Non-Operative Osteoarthritis (OA) Management

Weight loss, physical therapy, NSAIDs

Injectable therapeutics

- Hyaluronic acid (HA)
- Platelet-rich plasma (PRP)
- Methylprednisolone (MP)

Do not reverse OA progression







Stem Cell Therapy



Human bone marrow derived mesenchymal stem cells (BM-MSCs) may be able to restore articular cartilage

Reverse OA



Work via two mechanisms:

- 1. Differentiation into chondrocytes
- 2. Production of cytokines

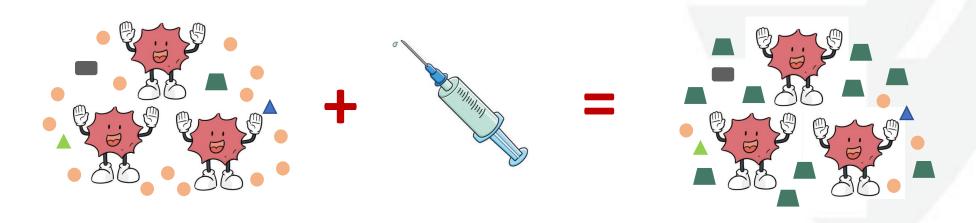






Clinical Question

Do HA, PRP, and MP affect the cytokine profile of BM-MSCs?



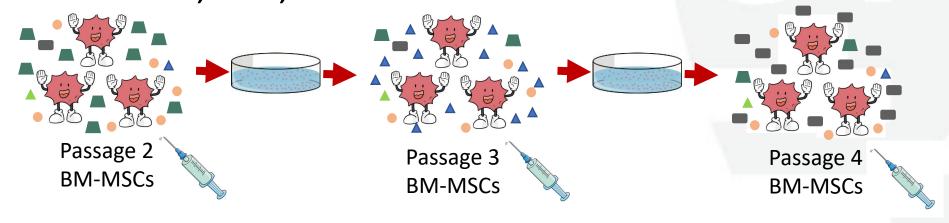




Methods

BM-MSCs grown from passage 2 -> passage 4

Levels of OA related cytokines were evaluated 24 hours after exposure to HA, PRP, or MP



Luminex multiplex assays used to measure cytokine levels







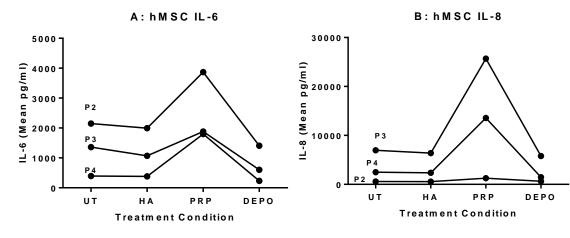
Results

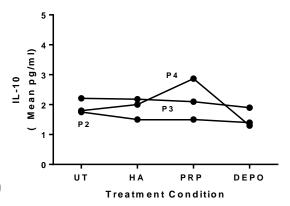
HA reduced BM-MSC expression of SCF, SDF- α , VEGF, CCL20, and adiponectin (p<.05)

PRP did not affect IL-10, but increased the following:

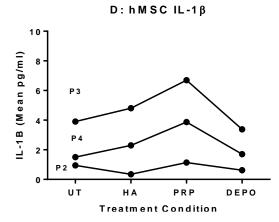
- IL-1 levels in P2 and P3
- IL-6 in P2
- IL-8 in P3

MP did not affect cytokine expression (p>.05)





C: hMSC IL-10

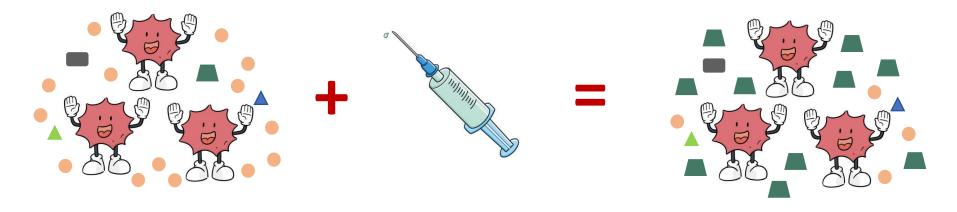






Conclusion

Orthopaedic adjuvants influence the inflammatory cytokine profile of BM-MSCs at multiple stages of culture expansion



These therapeutics may be used with BM-MSCs to create an optimal cytokine environment for OA treatment





Thank You







