Cartilage Catabolism Induced by Metalloproteinases or Inflammatory Cytokines Are inhibited by Alpha-2-Macroglobulin (A2M) and Platelet-Rich Plasma

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Disclosures

Scuderi is the founding board member of Cytonics Corporation

Golish has received consulting fees and stock options from Cytonics Corporation

Hanna, Weiser and Carballo are employees of Cytonics Corporation
Osteoarthritis known to involve inflammatory mediators and proteases

- Pro-Inflammatory Cytokines Degrade Cartilage (i.e. IL-1, IL-6, TNFα, INFγ, MIP, MCP, etc...)

- Metalloprotease Enzymes Breakdown Cartilage (i.e. MMP’s 1,3,9,13, etc...)

- Disintegrin Proteins Cleave Cartilage (i.e. ADAMTS 4,5, 13, etc...)
Background

- Alpha-2-Macroglobulin (A2M) is a plasma glycoprotein
- A2M is a naturally potent protease inhibitor
- A2M “baits” and “traps” proteases like MMPs
- A2M normally not found in high concentration in intra-articular space

Hypothesis:

- An A2M-enriched autologous product will inhibit cartilage catabolism by interfering with proteases.
A2M Blocks Cytokine-induced Cartilage Degradation

- To more closely mimic cartilage that is already in the process of degrading, BCE were treated with cytokines for 24 hrs followed by Component treatment for 48 hrs.
Methods

- Attempted inhibition of cartilage degradation with:
  - Purified human A2M
  - A2M enriched plasma (APIC)
  - PRP alone

Protease degradation model: ADAMTS-5, MMP 7, MMP 12
Inflammatory degradation model: TNFa, IL-1β, LR-PRP
Results
Results
Results

A. BCE APIC Blood PRP

BCE APIC PRP

C. BCE A2M PRP
Conclusions

• A2M and plasma-enriched with A2M (APIC) inhibit cartilage catabolism by MMPs and inflammatory cytokines
• PRP induces cartilage catabolism, attenuated by A2M or APIC
• A2M and APIC inhibition of cartilage degradation is dose-dependent