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Effects of Concentration on Synergistic Hyaluronan-PRG4 Cartilage Boundary Lubrication

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Abstract

Introduction: Proteoglycan 4 (PRG4) and hyaluronan (HA) are constituents of synovial fluid (SF) that act synergistically to contribute to the boundary lubrication of articular cartilage in a dose-dependent manner[1]. However, the potential concentration dependency of this HA-PRG4 synergism remains to be elucidated. The objective of this study was therefore to evaluate the in vitro cartilage boundary lubricating ability of PRG4+HA at varying concentrations of each.

Methods: Cartilage boundary lubricating ability was assessed using bovine osteochondral samples in a cartilage-on-cartilage friction test, as previously described[1]. Test sequences were as follows: Test 1 (PRG4 dose response, + constant HA = 3.33 mg/mL, n=6): PBS, 150μg/mL PRG4 + HA, 450μg/mL PRG4 + HA, 1500μg/mL PRG4 + HA, SF. Test 2 (HA dose response, + constant PRG4 = 450 μg/mL, n=5): PBS, 0.3mg/mL HA + PRG4, 1.0mg/mL HA + PRG4, 3.33mg/mL HA + PRG4, SF. Static, μstatic,N_{eq}, and kinetic, $<\mu_{kinetic}$,$N_{eq}>$, friction coefficients were then calculated[2].

Results: In all tests, μstatic,N_{eq} values were consistently highest in PBS and lowest in SF, with all PRG4+HA combinations tested being similar to SF. Test 1: $<\mu_{kinetic}$,$N_{eq}>$ values in varying PRG4 concentrations + constant HA were not significantly different from each other, nor from SF. Test 2: $<\mu_{kinetic}$,$N_{eq}>$ values in varying HA concentrations + constant PRG4 were not significantly different from each other, nor from SF.

Discussion: These results demonstrate that HA+PRG4 lubrication synergism is maintained provided that either PRG4 or HA is present at a physiologically normal concentration, and that these combinations provide lubricating ability approaching that of SF. Intra-articular PRG4 has been shown to be chondroprotective in animal injury models of osteoarthritis[3–6]. Therefore, clarifying the PRG4+HA synergism will contribute to the potential application of PRG4, with or without HA, as an improved biotherapeutic treatment. (Acknowledgements: AI, CAN, NSERC (CREATE), TAS).

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