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The role of synovial fluid constituents in the lubrication of collagen-glycosaminoglycan scaffolds for cartilage repair

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ABSTRACT

Extracellular matrix (ECM)-derived scaffolds have shown promise as tissue-engineered grafts for promoting cartilage repair. However, there has been a lack of focus on fine-tuning the frictional properties of scaffolds for cartilage tissue engineering as well as understanding their interactions with synovial fluid constituents. Proteoglycan-4 (PRG4) and hyaluronan (HA) are macromolecules within synovial fluid that play key roles as boundary mode lubricants during cartilage surface interactions. The overall objective of this study was to characterize the role PRG4 and HA play in the lubricating function of collagen-glycosaminoglycan (GAG) scaffolds for cartilage repair. As a first step towards this goal, we aimed to develop a suitable *in vitro* friction test to establish the boundary mode lubrication parameters for collagen-GAG scaffolds articulated against glass in a phosphate buffered saline (PBS) bath. Subsequently, we sought to leverage this system to determine the effect of physiological synovial fluid lubricants, PRG4 and HA, on the frictional properties of collagen-GAG scaffolds, with scaffolds hydrated in PBS and bovine synovial fluid (bSF) serving as negative and positive controls, respectively. At all compressive strains examined ($\varepsilon = 0.1$–0.5), fluid depressurization within hydrated collagen-GAG scaffolds was >99% complete at ½ minute. The coefficient of friction was stable at all compressive strains (ranging from a low 0.103 ± 0.010 at $\varepsilon = 0.3$ up to 0.121 ± 0.015 at $\varepsilon = 0.4$) and indicative of boundary-mode conditions. Immunohistochemistry demonstrated that PRG4 from recombinant human (rh) and bovine sources adsorbed to collagen-GAG scaffolds and the coefficient of friction for scaffolds immersed in rhPRG4 (0.067 ± 0.027) and normal bSF (0.056 ± 0.020) solution decreased compared to PBS (0.118 ± 0.21, both $p < 0.05$, at $\varepsilon = 0.2$). The ability of the adsorbed rhPRG4 to reduce friction on the scaffolds indicates that its incorporation within collagen-GAG biomaterials may enhance their lubricating ability as potential tissue-engineered cartilage replacements. To conclude, this study reports the development of an *in vitro* friction test capable of characterizing the coefficient of friction of ECM-derived scaffolds tested in a range of synovial fluid lubricants and demonstrates frictional properties as a potential design parameter for implants and materials for soft tissue replacement.

1. Introduction

Tissue-engineered cartilage aims to regenerate or replace damaged tissues through a combination of cells, signaling molecules, and scaffolds (Langer, 2000). Three-dimensional scaffolds, typically fabricated using synthetic or natural polymers, are designed to possess both the biological and biomechanical specifications of native components. Biologically, scaffolds should promote cellular integration, chondrogenic differentiation, and synthesis of new matrix before finally degrading into non-toxic bi-products (O'Brien, 2011). Biomechanically, scaffolds must remain structurally intact within the complex joint loading environment until full tissue-integration and repair is complete (Lee et al.,

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