Biological Response of Human Chondrocytes to Shear Loading Following Changes to Hydrogel Surface Properties

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Introduction: Articular cartilage provides a nearly frictionless surface with remarkable capacity to bear and distribute loads in a synovial joint. Nevertheless, alterations to the articular surface may lead to altered loads and increased catabolism, and ultimately to the development of osteoarthritis (OA), a degenerative joint disorder affecting millions of people worldwide. Due to the complexity of identifying the biophysical phenomena that occur during cartilage loading in vivo, the regulatory mechanisms are not fully understood. In this study, we established a hydrogel-based cartilage model mimicking the range of friction from healthy to pathological conditions and investigated the biological response of encapsulated chondrocytes to dynamic shear loading.

Methods: Hydrogels to mimic the varying surface properties of cartilage were formed by altering the concentration of styrene sulfonic acid in a photo-crosslinkable poly(ethylene glycol) (PEG)-based hydrogel. Frictional properties of the hydrogels were assessed using an Instron microtester. Human chondrocytes were encapsulated in alginate-methacrylate and combined with a pre-cross-linked surface gel by further UV cross-linking. Constructs were cultured under free-swelling conditions for 21 days, followed by 11 days of static compression (SC control) or dynamic shear loading (1 hr/day at 1Hz and 1.0 mm extension) in a custom bioreactor. The biological response of the chondrocytes was assessed by measuring expression of genes related to matrix production and degradation and immunostaining for collagen type II and aggrecan.

Results: The dynamic coefficient of friction varied significantly between hydrogels (p < 0.01), decreasing from 0.085 to 0.045 with increasing styrene sulfonic acid content. The application of long-term intermittent shear loading significantly increased chondrogenic gene expression in constructs with low frictional properties over SC controls (18.5-fold increase for COL2A1, and 2.5-fold increase for ACAN; both p < 0.01). While chondrogenic marker gene transcription remained at SC level for high-friction constructs, expression of matrix degrading MMP3 was significantly up-regulated by dynamic shear loading (1.7-fold over SC; p < 0.05). Immunofluorescence indicated an increased collagen type II and aggrecan accumulation in low friction constructs compared to SC and high-friction constructs following long-term shear loading.

Conclusions: These results demonstrate that chondrocyte response to dynamic shear loading varies with frictional properties of the construct surface, suggesting the usefulness of this model for further investigations into mechanisms of cartilage degeneration and OA.

‘Real World’ Implications: This research project will provide new insights into the early molecular mechanisms of cartilage pathology and might therefore identify target molecules for drugs against the development and progression of OA.