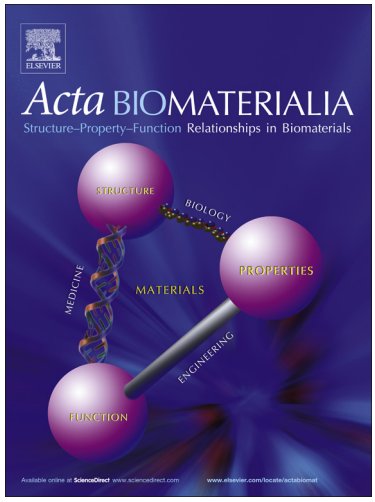


Full length article

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# Focal adhesion signaling affects regeneration by human nucleus pulposus cells in collagen- but not carbohydrate-based hydrogels

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## Abstract

Hydrogel-based 3D cell cultures are an emerging strategy for the regeneration of cartilage. In an attempt to regenerate dysfunctional intervertebral discs, nucleus pulposus (NP) cells can be cultured in hydrogels of various kinds and physical properties. Stiffness sensing through focal adhesions is believed to direct chondrogenesis, but the mechanisms by which this works are largely unknown. In this study we compared focal adhesion formation and glycosaminoglycan (GAG) deposition by NP cells in a range of hydrogels. Using a focal adhesion kinase (FAK) inhibitor, we demonstrated that focal adhesion signaling is involved in the response of NP cells in hydrogels that contain integrin binding sites (i.e. methacrylated gelatin (gelMA) and type II collagen), but not in hydrogels deplete from integrin binding sites such as alginate and agarose, or CD44-binding hydrogels based on hyaluronic acid. As a result of FAK inhibition we observed enhanced proteoglycan production in gelMA, but decreased production in type II collagen hydrogels, which could be explained by alteration in cell fate as supported by the increase in the adipogenic marker peroxisome proliferator-activated receptor gamma (PPARγ). Furthermore, GAG deposition was inversely proportional to polymer concentration in integrin-binding gelMA, while no direct relationship was found for the non-integrin binding gels alginate and agarose. This corroborates our finding that focal adhesion formation plays an important role in NP cell response to its surrounding matrix.