Title:

Differential Regulation of Articular Cartilage Tensile Properties by IGF-1 and TGF-β1 during *In Vitro* Growth

Authors & affiliations:

M.E. Stender[1], N.T. Balcom[1], B. Berg-Johansen[1], K.J. Dills[1], D. Dyk[1], S.J. Hazelwood[1], A.C. Chen[2], R.L. Sah[2], S.M. Klisch[1]

[1] *California Polytechnic State University, San Luis Obispo, USA,*
[2] *University of California at San Diego, USA*

Abstract: (Your abstract must use **Normal style** and must fit in this box. Your abstract should be no longer than 300 words. The box will 'expand' over 2 pages as you add text/diagrams into it.)

Introduction: Articular cartilage (AC) undergoes biomechanical changes during growth and maturation *in vivo*. Regulation of immature AC by growth factors *in vitro* can lead to distinct growth phenotypes. The study objectives were to test the hypotheses that (1) TGF-β1 and IGF-1 differentially regulate the tensile modulus of immature AC during *in vitro* growth and (2) tensile properties of immature AC depend on anatomical location.

Methods: Immature bovine knee superficial (S) and middle (M) layer AC explants were prepared from the groove of the trochlea. Samples were analyzed fresh (D0) or after 12 days of culture (D12) in medium with 10ng/ml TGF-β1 or 50ng/ml IGF-1. Additional D0 explants were harvested from the trochlea ridge. Explants were tested to 5% and 10% tensile strain and equilibrium tensile modulus (E) was determined from stress relaxation data. The effects of treatment or location were analyzed using ANOVA with post-hoc Tukey testing ($p<0.05$).

Results: Compared to D0, D12 TGF-β1 explants had maintained or increased E (Figure 1a,b). In contrast, D12 IGF-1 explants had decreased E. Groove explants had higher E than ridge explants at 5% strain (Figure 1c) with a similar trend at 10% strain.

Discussion: These findings elucidate the differential biomechanical consequences of TGF-β1 and IGF-1 regulation of AC growth, which may occur through alteration of the collagen network and may help guide *in vitro* growth of native or tissue-engineered cartilage. Variational properties of tensile modulus across layer and location are important considerations for AC tissue engineering.

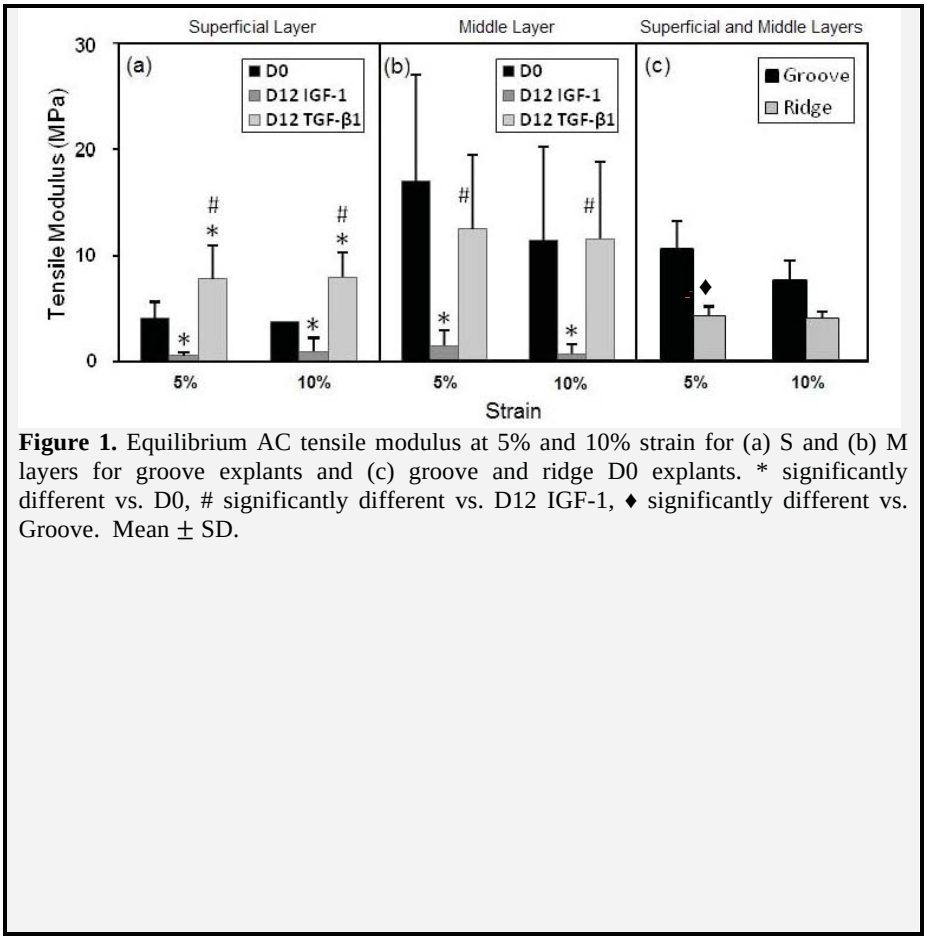

Figure 1. Equilibrium AC tensile modulus at 5% and 10% strain for (a) S and (b) M layers for groove explants and (c) groove and ridge D0 explants. * significantly different vs. D0, # significantly different vs. D12 IGF-1, ♦ significantly different vs. Groove. Mean ± SD.