Promoting Functional Fiber-Reinforced Tissue Formation with Dynamic Mechanical Loading

Fibrocartilaginous tissues such as the meniscus and annulus fibrosus serve critical load-bearing roles, relying on arrays of highly organized collagen fibers to resist tensile loads experienced with normal physiologic activities [1]. As these specialized structures are often injured, there exists great demand for engineered tissues for repair or replacement. Towards recreating the structural and mechanical features of these anisotropic tissues *in vitro,* we fabricate scaffolds composed of co-aligned, ultra-fine biodegradable polymer fibers. These 3D micro-patterns direct cell orientation and the subsequent formation of organized extracellular matrix (ECM) [2]. As this matrix develops with time in culture, the mechanical properties of the construct gradually increase, but thus far have not reached parity with native tissues. Mechanical forces are essential to the development and maintenance of musculoskeletal tissues. Given this, we are interested in how mechanical loading impacts cells living in a nanofibrous microenvironment. In previous studies, we have observed morphological and transcriptional changes with scaffold deformation (A) [3]. Additionally, we have examined how long-term cyclic tensile loading of MSC-laden nanofibrous constructs enhances their *in vitro* maturation. In one recent study, samples were precultured for 6 weeks and either cyclic loaded daily or maintained as nonloaded controls. Four weeks of cyclic loading induced a 16% increase in the tensile modulus over nonloaded controls (B). While the collagen content of controls plateaued by week 10, loaded constructs continued to accrue collagen where by the terminal time point, loaded constructs contained more collagen controls (C). Consistent with load induced increases in properties and matrix content, real-time RT-PCR analysis showed that loading triggered an increase in collagen I, lysyl oxidase, and fibronectin gene expression (D). Taken together, these results shows that dynamic tensile loading increases the mechanical properties of MSC-laden engineered nanofiber-based constructs. Results from this study have bearing on strategies for engineering tissues, but may also serve as a model system for understanding how cells in organized tissues respond to external mechanical stimuli and maintain their microenvironment.

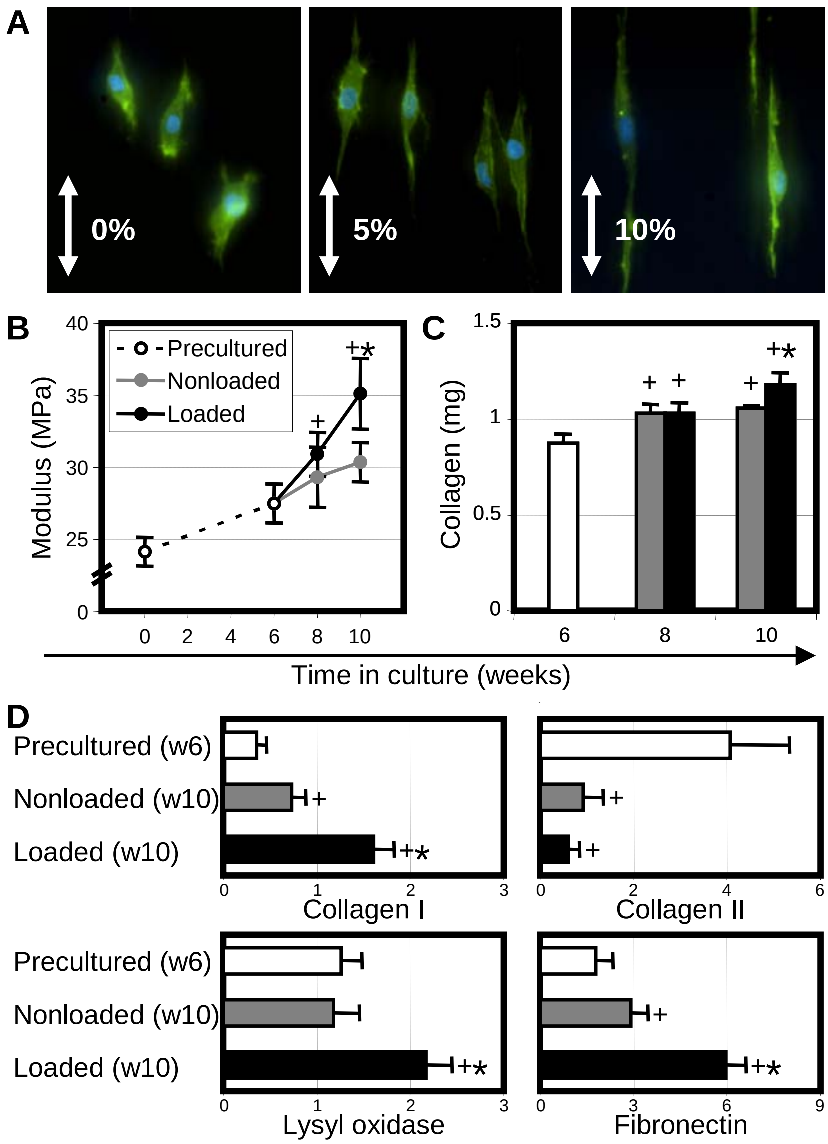

Figure 1. A) Meniscus fibrochondrocytes on nanofibrous scaffolds under 0, 5, and 10% strain. B) Tensile modulus of constructs (note break in axis). C) Total collagen content content (n=6, +: p<0.05 vs. precultured values (w6), *: p<0.05 vs. nonloaded at same time point). D) mRNA expression of collagen I, collagen II, lysyl oxidase, and fibronectin normalized to GAPDH in precultured samples at week 6 and loaded/nonloaded constructs at 10 weeks (n=6, +: p<0.05 vs. precultured values, *: p<0.05 vs. nonloaded).

Recent publications:

1. Mauck RL, Baker BM, Nerurkar NL, Burdick JA, Li WJ, Tuan RS, Elliott DM. “Engineering on the Straight and Narrow: The Mechanics of Nanofibrous Assemblies for Fiber-Reinforced Tissue Regeneration,” 2009, Tissue Engineering: Part B, 15(2):171-93.
2. Baker BM, Mauck RL. “Alignment Enhances the Maturation of Nanofiber-Based Engineered Meniscus Constructs,” 2007, Biomaterials, 28(11):1967-77.

3. Nathan AS, Baker BM, Nerurkar NL, Mauck RL. “Time-Dependent and Anisotropic Nuclear Deformations on Aligned Nanofibrous Scaffolds,” Transactions of the 56th Annual Meeting of the Orthopaedic Research Society, New Orleans, LA, March 6-9, 2010, submitted.
4. Baker BM, Shah RP, Silverstein AM, Mauck RL. “Dynamic Tension Improves the Mechanical Properties of Nanofiber-Based Engineered Meniscus Constructs,” Transactions of the 56th Annual Meeting of the Orthopaedic Research Society, New Orleans, LA, March 6-9, 2010, submitted.

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