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MEETING REPORT

2012 Annual Meeting of the Orthopaedic Research Society: tendon and ligament biology and development

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Meeting Report from the Orthopaedic Research Society Annual Meeting 2012, San Francisco, CA, USA, 4–7 February 2012

The mechanisms driving tendon and ligament development and homeostasis have received relatively little attention in the musculoskeletal community. Six studies on tendon and ligament biology and development were described at a session of the 2012 Annual Meeting of the Orthopaedic Research Society. New insights were presented on the role of mechanical loading on tendon and tendon-to-bone insertion site development, the importance of small leucine-rich proteoglycans on tendon development, a link between exercise and tendon stem cell behavior, and the application of progenitor cell populations for enhanced tendon-to-bone healing.

Meeting Highlights

Huang *et al.*[1] demonstrated that the development of the flexor digitorum sublimis (FDS) tendon depends on muscle translocation. In the study, the authors showed a remarkable finding: the sublimis muscles of mice first form as myofibers in the autopod before moving to their final location in the zeugopod. It was also demonstrated that the development of the FDS tendon and muscle is tightly coordinated. In mice with defects in tendon formation, the FDS muscle failed to translocate; this suggests that tendon is required for muscle movement. In mice with defects in muscle contraction, the muscle failed to translocate and the tendons failed to form; this suggests that muscle contraction is necessary for both processes.

Schwartz *et al.*[2] showed that muscle loading is necessary for the postnatal development of a functional tendon. Shoulder muscles were paralyzed in neonatal mice using botulinum toxin A. The removal of muscle load led to significant defects in tendon structural and mechanical properties. Specifically, collagen fiber orientation distributions were less organized when muscle loading was removed. The strength and modulus of the tendon were also reduced when muscle loading was removed. Mechanical cues are therefore necessary for the postnatal development of a mechanically robust tendon. Muscle unloading severely compromised the functional development of the tendons and their bony insertions in a murine model.

In an *in vitro* study, Brown *et al.*[3] showed that mechanical stimuli direct the formation of elastic fibers by tendon and ligament cells. Tendon- and ligament-specific cells were isolated and mechanically loaded in tension. Cell responses to mechanical loading depended on developmental stage: relative to unloaded cells, E15 limb cells upregulated their expression of elastic fiber genes, E17 limb cells did not change their expression pattern for elastic fiber genes and P0 and P7 limb cells downregulated their expression of elastic fiber genes. Interestingly, opposite trends were noted in axial cells. The study highlighted the complexity in temporal and spatial expression patterns for elastic fiber-related genes during tendon and ligament development.

Dourte *et al.*[4] examined the roles of the proteoglycans decorin and biglycan on the mechanics, composition and structure of tendon. Patellar tendons from decorin and biglycan heterozygous and null mice were isolated and mechanically tested. Tendons were also examined for total collagen, biglycan and decorin gene expression, and collagen fiber diameter and spread. Decreased levels of decorin or biglycan led to increases in the dynamic modulus of the patellar tendon, despite few changes in total collagen and collagen fiber diameters. These proteoglycans may therefore have a direct role in tendon viscoelasticity that is independent of their role in collagen fibrillogenesis.

Zhang *et al.*[5] studied potential links between tendon stem cells, mechanical loading and aging. Aging in mice led to accumulation of fatty tissues; increased loading via treadmill running reduced fatty tissue content. When examining tendon stem cell populations in these groups, higher numbers and increased proliferation capacity was evident in the exercise group. These results have important implications for understanding aging and mitigating degeneration of tendons. Moderate exercise may be effective in maintaining tendon stem cell populations and their activities, leading to prevention of the degenerative changes typically seen because of aging.

In a study by Chen *et al.*,[6] periosteum cell sheets were used to enhance tendon-to-bone healing in a rabbit animal model. Successful anterior cruciate ligament reconstruction

requires integration of a tendon graft with bone. Periosteum progenitor cells, which have pluripotent differentiation capacity, were formed into sheets *in vitro* and then implanted at the repair site during anterior cruciate ligament reconstruction. Histologically and mechanically, healing was dramatically improved in the treated group. This novel approach for improving tendon-to-bone healing has translational potential for a number of clinical scenarios that require soft-tissue integration into bone.

In summary, the session presented new data elucidating a number of mechanisms related to tendon development, aging and healing. A better understanding of tendon development may help to drive new therapies to prevent age-related degeneration or to enhance healing.

Conflict of Interest

The author declares no conflict of interest.

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