Tendons and Ligaments

This issue is largely devoted to a topic seldom discussed by this and many other journals dealing with orthopaedic and connective tissue research. A total of 8 papers have analyzed in the form of review, perspective or original research on basic structure and biochemistry of tendons, and the structural, biochemical and biomechanical changes tendons undergo with development, age or activity. Tendons (and ligaments) are an integral, though less studied, part of the musculoskeletal system. They are generally considered to be dull, somewhat lifeless ropes attaching muscles to bones in the case of tendons or, in the case of ligaments, connecting two bones. This notion is akin to that one held about bones some eons ago: they were thought to be rigid, unchanging supporting structures. Today we know that bones are very metabolically active undergoing constant remodeling that depends to a large extent on their mobility status. Similarly, there are constant and reciprocal interactions between tendon structure and biochemistry on one side, and tendon mechanical function on the other.

To understand the basis of tendon development and growth-dependent modeling and remodeling one has to be familiar with collagen fibrillogenesis and its regulation. The first paper by Zhang et al. does just that. This group of authors (David Birk and his colleagues) summarizes the wealth of data on collagen fibrillogenesis, a lot of which comes from their laboratory. They review collagen fibrillogenesis beginning as an assembly of collagen molecules in a series of extracellular compartments, progressing through post-depositional maturation leading to thicker and longer fibrils and ending in their coalescence in the final stages of fiber production. Zhang et al. discuss data indicating that at least in chicken embryos the growth of fibrils occurring from pre-formed fibril intermediates depends on mechanical loading of tendons through active movement of the embryonal chick limb.

Tendon fibrillogenesis is regulated by several mechanisms. The initial fibril assembly is in part regulated by the heterotypic interaction between two different (I and III) fibrillar collagen types. The roles of other collagen types in fibrillogenesis are also discussed, with a focus on the so-called FACIT or fibril-associated collagens (types IX, XII, XIV, XVI, XIX, and XX).

Work with mice deficient in leucine-rich repeat proteoglycans provides us with better insight into proteoglycan regulation of fibrillogenesis. The implications of deficiency in one or two leucine-rich repeat proteoglycans (fibromodulin, lumican, decorin and biglycan) in mice in regulation of tendon fibrillogenesis are discussed here as well as in another paper by Yoon and Halper in this issue. These studies established that in addition to decorin and biglycan, fibromodulin and lumican play important roles in fibrillogenesis, confirming that loss of even one of the proteoglycans alters the mechanical properties of tendons.

The following paper by Doschak and Zernicke should be of particular interest to readers of this Journal. It reviews the structure and function of the types of insertion or entheses between bone-tendon and bone-ligament, and thus complements the first paper. Authors also discuss the time-dependent properties of viscoelastic materials such as tendons, ligaments and their entheses and how their transition through different zones of increasing stiffness in surrounding tissues may offer a mechanical advantage. The primary function of the enthesis is reduction of strain concentrations at the interface of compositionally distinct tissues during loading. For example, fibrocartilage (located in regions of tendons subjected to compression) interdigitates with the underlying bone and, through an increase in the cross-sectional area of interface between the more compliant tendon and the bone mediates as decrease in stress concentrations during load transmission from the tendon or ligament to the bone. Finally they summarize data, mostly from their laboratory, pertinent to pathogenesis of enthesopathies and their repair using several methods, including short-term anti-resorptive therapy with bisphosphonates and surgical procedures.

Banes et al. have documented that mechanical load stimulates expression of numerous genes in avian flexor tendon cells. Two papers in this issue deal with several aspects of collagen turnover and changes in gene expression, one by Kjaer et al. and the second by Halper et al. Kjaer et al. provide a comprehensive review of tendon response to loading and exercise. The accelerated formation and degradation of connective tissue in both muscle and tendon as a result of exercise have been well documented by many groups, including theirs. Kjaer et al. address and provide plausible explanations for apparent contradictions. For example, to explain increase both in collagen synthesis and in matrix metalloproteinases with mechanical loading, they hypothesize that this reflects both physiological adaptation and repair of damage of extracellular matrix structures during exercise. They discuss increased gene transcription and especially post-translational modifications of proteins of the extracellular matrix and growth factors following exercise as preceding stimulation of synthesis of collagen and other extracellular matrix proteins, and as pre-requisites for changes in biomechanical properties as well as the structural properties modifications in collagen. They highlight the differences between the in vitro and in vivo models of properties of tendons. The main advantage of in vivo studies on humans is that they allow continuous measurements in environmental blood flow, tissue oxy-

Foreword
References


