CHAPTER **31**

Tendon Orthobiology

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INTRODUCTION

In the US roughly 32 million musculoskeletal injuries occur per year. This represents 30-50% of all sporting injuries accumulating a US financial burden of $13.5 billion a year (1). Tendon injuries account for the majority of yearly musculoskeletal injuries. Overuse causes tendon injury and induces micro trauma, creating an environment of local inflammation and oxidative stress (2). Due to the recurrent, cyclic nature of overuse, in the majority of affected tendons, 97%, have undergone some type of degenerative process.

Anatomically, the rotator cuff, Achilles, tibialis posterior, and patellar tendons are the most frequently injured tendons in the body requiring surgical intervention. Approximately 300,000 operative tendon repairs occur per year and the Achilles tendon represents 40% of all operated tendons (1). With surgical repair, the primary goals are to reestablish native tendon architecture and retain as much inherent mechanical strength as possible. Towards this goal the use of biologics to enhance tendon repair has been employed.

STRUCTURE

Tendons are organized in units comprised of tenocytes, fibrils, fibers, and fascicles, which when grouped comprise a tendon unit. The tendon unit is also housed with blood vessels, lymphatics, and nerves. This highly-organized structure allows the tendon to have elevated tensile force under mechanical stress.

Type I collagen is the most abundant molecule in tendon extracellular matrix, accounting for almost 60% of the dry mass of the tissue and 95% of the total collagen (3). Type III is the next most abundant collagen. It is found to a lesser extent in normal undamaged tendon but is abundantly present in pathologic tendons. Other collagen fibers include types V, VI, XII, XIV, and XV. Other tendon molecules include elastin fibers, ground substance, and inorganic components.

HEALING

Tendon healing occurs in 3 phases that overlap. Their durations vary with the severity of the injury or disease. Healing begins with the inflammatory phase, which starts immediately after the initial injury. Notable cellular processes in this phase include the signaling and gathering of macrophages, neutrophils, monocytes, and fibroblasts. Angiogenesis or the development of new blood vessels is also initiated. Inflammation lasts for several days before leading into the reparative phase, which is characterized by the proliferation of fibroblasts. These cells predominately synthesize collagen type III, which is laid in a haphazard fashion. This is different from type I, which is highly organized. After approximately 6-8 weeks, the tendon's repair phase begins to decelerate.

Lastly, the remodeling phase occurs, which lasts for several months to years. It is characterized by decreased cellularity due to resolution of inflammation and proliferation. In addition, there is an increase of type I collagen deposition. More of the extracellular matrix is also produced. Components of the extracellular matrix such as hyaluronan, proteoglycans, and glycoproteins add to the tendon's deformability and viscoelasticity. Any tendon biologic used must be able to accommodate all components of healing.

ORTHOBIOLOGICS

Current biologics for tendons include use of either a human-based collagen material/graft or xenograft. All of the grafts currently in use serve as a scaffold and contain many or all of the following properties: 1) biocompatibility; 2) supportive for cell adhesion and growth; 3) high surface area; 4) promote tendon differentiation; 5) not to induce host inflammatory responses; and 6) when not biodegradable to mimic native tendon architecture and mechanical properties (4).

Scaffolds formed by tendon matrices would ideally retain both the normal biomechanic and biochemical properties; however, these properties are usually compromised during the processing phase. In order to be utilized, the native cells are removed to prevent disease transmission and immune responses (4). These processes utilize mechanical forces such as ultrasonication, repeated freeze-thaw cycles, and chemical detergents (1). Despite this process, approximately 93% of extracellular matrix proteins and growth factors are preserved. The use of decellularized tendon appears to be an interesting approach for the treatment of tendon ruptures and tears. This is the most adequate structure available to guide the regeneration of the injured tissue. It does so by preserving the complex matrix architecture (4). Grafts currently in clinical use are degradable and offer little to no additional mechanical advantage. They are typically wrapped around or sutured over the repair site and serve to provide support rather than strengthen the repaired construct.

Xenografts of both equine and porcine linage are clinically available. Notably porcine dermis, small intestine submucosa, and pericardium serve as scaffolds. Similar to their human counterparts they possess low mechanical properties unable to support the physiologic loading required to be used as tendon substitutes.

Many in vivo studies for augmenting tendon repair exist. They typically involve the incorporation of various growth factors and stem cells. The most clinically relevant is platelet rich plasma (PRP), which is a centrifuged collection of blood. Its contents include growth factors, chemokines, and interleukins, which work in cell signaling (5). The final product of PRP is considered to have anti-inflammatory properties (6). In the literature some studies suggest that the use of PRP results in faster tendon healing/recovery and less pain while others dismiss its use as a placebo treatment. Proving the definitive efficacy of PRP remains challenging due to the inability to prepare a PRP formulation of standard reproducible composition, which would be amenable to randomized control trials.

FUTURE DIRECTIONS

The future of tendon tissue bioengineering is promising. Multiple challenges remain when translating research bench work to clinical usage. Nevertheless on-going research continues in areas of growth factors, stem cells, and tissue regeneration.

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