Connecting links to musculoskeletal: tendons & ligaments

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Abstract

The bones, muscles, and connective tissues (such as cartilage, tendons, and ligaments) that bind tissues and organs together make up the musculoskeletal system. This system's main functions are to give the body structure and support, as well as to protect essential organs and allow movement. Tendons and ligaments allow locomotion by providing connections between muscle and bone or bone and bone. A common cause of impairment is damage to tendons and ligaments caused by acute or chronic injury, as well as ageing and arthritis. A greater understanding of tendon and ligament development, cell biology, and pathophysiology is required to improve therapeutic options for these disorders. Despite the fact that tendons and ligaments play a distinct and crucial role in musculoskeletal function and disease, research in this field is not as advanced as it is in other skeletal tissues. This is due in part to the fact that the transcription factors required for the creation and maintenance of these tissues were unknown until recently.

Keywords: connecting tissues, tendons, ligaments

Ligaments and tendons are two separate but related structures. Although the developmental processes of tendon and ligament tissues differ from the phenotypes of mice with genetic deletion of essential transcription factors, the basic architecture of these tissues and the gene expression profiles of their major cell type (tenocytes) are very similar. Recent research has discovered a shared basis between tendons and ligaments, and it uses Anterior Cruciate Ligament (ACL) injuries as an example of tendon and ligament injuries.

Tendon and ligament damage is a common clinical problem caused by accident or overuse, as well as ageing and arthritis. Damaged tissues heal slowly and seldom fully recover. Damage to the glenohumeral ligaments and rotator cuff tendons of the shoulder joint, which can cause shoulder pain and functional restrictions, is extremely common, affecting more than half of those over the age of 60. Surgical treatment has a low success rate, with up to 50% of rotator cuff repair treatments failing.

In humans, the Achilles tendon is the most often torn tendon. Injury and aging-related changes in the ECM of tendon and ligament in the knee joints, particularly the ACL, are key risk factors for Osteoarthritis (OA). The ACL serves as an anterior/posterior stabilizer and is important for knee kinematics, particularly in rotation. Articular cartilage and menisci are more prone to arthritic alterations in the presence of an ACL deficit. ACL deficiency is seen in a high proportion of OA patients without a history of ligament damage at the time of total knee arthroplasty, and there is a link between the radiologic OA grade and the histological grade of ACL degeneration in end-stage OA. In addition, ACL rupture is more common among people with symptomatic knee OA than in those without. It has been found that fewer than half of people with ACL rupture recall a knee injury, suggesting that this risk factor for knee OA is under-recognized. These findings suggest that tendons and ligaments in arthritic knees undergo significant alterations that are not induced by massive trauma, but rather by mediators in the arthritic joints that impact tendon and ligament cells and the ECM, such as cytokines or matrix degrading enzymes. Tenocytes or ligament fibroblasts, which are positioned between parallel chains of collagen fibrils, are the most common cell types in tendon and ligament. Tendon and ligament cells are assumed to be dormant and have low rates of proliferation under normal circumstances, whereas ECM synthesis is responsive to changes in mechanical load. Types I, III, IV, V, and VI collagen, which are also synthesized during embryogenesis to build tendon and ligament tissues, are among the elevated genes in tendon and ligament cells. While these matrix genes aren't exclusive to tendon and ligament cells, Tenomodulin (Tnmd) is specifically expressed in mature tendon and ligament cells. However, its role in tendons and ligaments is unknown, and Tnmd knockout mice appear to be completely normal.

Small subsets of progenitor cells can be found in tendon and ligament cell populations. Biglycan and fibromodulin deficiency in mice results in the loss of tendon progenitor cells, implying that these extracellular matrix components provide a home for stem cells. The discovery of distinct molecular markers for tendon progenitor cells in adult tissues will aid in understanding how this subgroup contributes to tendon homeostasis and regeneration. New mechanisms that control tendon and ligament cell differentiation and activation have been discovered as a result of recent developments in tendon and ligament cell biology research, particularly the identification and functional studies of tissue-specific transcription factors. Important concerns, such as how tenocytes build the hierarchal structure of tendon and ligament tissue and how precise and robust tissue integration occurs between tendon and ligament and bone or muscle, remain unanswered. In the foreseeable future, novel methods like as mechano-transduction or knockout rat models should also bring fresh insights. Improvements in serial block face-scanning electron microscopy techniques have given fresh insight on how the tendon anlage grows into a mature tendon structure with tenocytes embedded in collagen fibers.

Progress in tendon and ligament biology research will also offer information on its potential therapeutic applications in musculoskeletal injuries and disorders in the future. Correcting aberrant Mkx expression, for example, could be a novel way to address tissue repair after damage and during chronic diseases like OA.

Pharmacological techniques, such as employing Mkx expression as a criterion while screening for drug candidates, can be used to address aberrant differentiation by inhibiting inflammatory signals or enhancing differentiation cues. To develop effective treatments for tendon and ligament pathologies, more research is needed in basic tendon and ligament biology as well as animal models of injury and disease.

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