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The Role of Elastin in Tendon and Ligament Disorders: Trapeutic Interventions in Orthopedics and Sports Medicine

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ABSTRACT

Introduction

Elastin is a key protein in tendons and ligaments, responsible for providing elasticity, which allows these tissues to withstand mechanical stress and maintain joint stability. However, elastin integrity can decline due to factors such as aging, genetics, or injury, leading to joint instability, chronic pain, and a heightened risk of further damage. This study examines the role of elastinfocused therapies in addressing such issues, with a focus on orthopedics and sports medicine.

Objectives

The objective of this review is to evaluate emerging elastin-based therapeutic strategies, such as platelet-rich plasma (PRP) therapy, bioengineered scaffolds, and microRNA-based treatments, and their potential to enhance recovery in musculoskeletal injuries by improving tissue elasticity and resilience.

Materials and Methods

A comprehensive review of the studies available on open access sources, including PubMed, Google Scholar, and the National Library of Medicine, was conducted. The focus was on current advancements in platelet-rich plasma (PRP) therapy, bioengineered scaffolds, and microRNA-based treatments. Studies assessing the efficacy of these approaches in promoting elastin synthesis, tissue flexibility, and repair outcomes were analyzed, particularly in cases involving conditions like Achilles tendinopathy, rotator cuff injuries, and ACL reconstructions.

Conclusions

Elastin plays a crucial role in tendon and ligament health, and emerging elastinfocused therapies show significant potential in enhancing recovery from musculoskeletal injuries. PRP therapy, bioengineered scaffolds, and microRNAbased treatments have demonstrated promising outcomes in improving tissue flexibility, supporting cell growth, and slowing degenerative processes. Further research and clinical trials are needed to optimize these therapies for long-term patient outcomes in orthopedic and sports medicine.

Keywords: elastin; tendon injuries; ligament disorders; MicroRNA-based therapies; Platelet-Rich Plasma (PRP); therapy; bioengineered scaffolds

INTRODUCTION

Elastin is a critical extracellular matrix (ECM) protein that plays a fundamental role in maintaining the elasticity and flexibility of connective tissues, including tendons and ligaments. Alongside collagen, which provides tensile strength elastin contributes to the unique biomechanical properties of these tissues, allowing them to endure mechanical stress while

maintaining joint stability and functional movement. This balance between elasticity and strength is essential for enabling the high levels of strain that tendons and ligaments encounter during regular motion, particularly in active individuals and athletes.[1, 2]

Aging, genetic predispositions, and injuries significantly impair elastin's structural integrity in these tissues. Over time, elastin fibers become fragmented, leading to a reduction in tissue elasticity, increased stiffness, and a higher risk of tendinopathy and ligamentous injuries .[1, 3]The degradation of elastin with age is particularly pronounced in energy-storing tendons, such as the Achilles tendon, where the elastin content has been shown to decrease by as much as 28% in older individuals compared to younger ones [4]. This reduction in elastin contributes to the decreased ability of tendons and ligaments to recoil and absorb shocks, increasing susceptibility to injuries and chronic pain, especially in weight-bearing joints.

Moreover, the limited regenerative capacity of elastin poses significant challenges for both acute and chronic tendon and ligament disorders. Unlike collagen, which can be somewhat remodeled during healing processes, elastin undergoes minimal turnover throughout life. This highlights the importance of preserving elastin integrity to prevent long-term musculoskeletal issues, particularly in aging populations and athletes who place greater mechanical demand on their tendons and ligaments [4].

Recent advancements in orthopedics and sports medicine have led to the exploration of novel regenerative therapies aimed at restoring elastin function and structure within the ECM. Emerging therapeutic approaches, such as platelet-rich plasma (PRP) therapy, bioengineered scaffolds, and microRNAbased treatments, offer promising avenues for enhancing elastin synthesis, promoting tissue resilience, and mitigating the effects of aging and injury on connective tissues. These strategies have shown potential not only in repairing elastin degradation but also in supporting the broader extracellular matrix, which plays a key role in tendon and ligament healing [5, 6].

Understanding the molecular mechanisms of elastin synthesis, degradation, and its role in tissue biomechanics is essential for developing effective therapeutic interventions. This review

examines the latest advances in elastin-targeted treatments in the context of tendon and ligament injuries, with a particular focus on the implications for regenerative medicine and sports injury recovery. By highlighting the role of elastin in maintaining tissue flexibility and function, this paper aims to underscore the importance of elastin-centered therapies in the management of orthopedic conditions.

ELASTIN HISTOLOGY IN TENDON AND LIGAMENT COMPOSITION

Elastin, although present in relatively small amounts (1-2%) such as in tendons, plays a significant role in the biomechanical properties of tendons and ligaments. Together with collagen, which constitutes the majority of the dry mass (65-80%) in these structures, elastin contributes to the balance between elasticity and tensile strength. This balance is crucial for maintaining the ability of tendons and ligaments to stretch and recoil, supporting joint stability and facilitating movement during repetitive activities. Tendons, such as those in the Achilles, show minimal elastin content, whereas ligaments like the ligamentum flavum, involved in spinal movement, contain higher elastin levels due to their need for greater flexibility.[2] [1, 3]

Histologically, elastin is embedded within the extracellular matrix (ECM) of tendons and ligaments, interacting with molecules like proteoglycans, which contribute to shock absorption and tissue resilience. While collagen is primarily responsible for tensile strength, elastin allows tissues to return to their original shape after being stretched, a feature particularly critical for ligaments that experience constant mechanical strain. The durability of elastin ensures that it undergoes minimal turnover throughout life, but age-related degradation or injury can lead to a loss of elasticity, increasing the susceptibility to tendinopathy, tears, and other degenerative changes in tendons and ligaments.

Studies show that in energy-storing tendons such as the superficial digital flexor tendon (SDFT), the elastin content decreases significantly with age, dropping from 3.02% in young tendons to 2.17% in older ones, contributing to increased stiffness and reduced fatigue resistance in older individuals.[5] [2] [1]

The complex three-dimensional structure of tendon fibers, including the spiral organization of collagen and elastin fibrils, provides a buffer against multidirectional forces experienced during movement. This intricate organization not only allows tendons to transmit force from muscles to bones but also protects them from mechanical overload. Elastin's role in restoring the wavy configuration of collagen fibers after stretch is crucial for maintaining the overall biomechanical function of tendons and ligaments.[2]

Given elastin's essential contribution to tissue flexibility and resilience, it has become an important target in regenerative therapies. These therapies aim to restore both the elasticity and strength of damaged tendons and ligaments, particularly in cases of injury or age-related degeneration. By focusing on the recovery of the ECM and the structural integrity of collagen and elastin networks, regenerative treatments hold promise for enhancing tissue recovery and preserving long-term joint function.[2] [1, 6]

MECHANISMS OF ELASTIN SYNTHESIS AND DEGRADATION

Elastin Synthesis

Elastin is synthesized from tropoelastin, a soluble precursor that forms mature elastin through extensive cross-linking. This process involves alternating hydrophobic and hydrophilic domains, which provide elasticity. Hydrophobic areas with amino acids like glycine and valine allow flexibility, while lysine in hydrophilic regions enables cross-linking. Enzymes like lysyl oxidase facilitate strong desmosine and isodesmosine bonds, creating a durable elastin matrix capable of withstanding repeated stretching over time. [4, 7, 8]

Regulation and Degradation

Elastin degradation is facilitated by enzymes like elastase, which break elastin fibers into smaller fragments. This degradation increases with age as elastin becomes more fragmented, reducing tissue elasticity and placing additional mechanical stress on structural proteins like collagen. This degradation process intensifies with age, with studies showing that elastin content in skin can decrease by as much as 60% in elderly individuals compared to younger subjects. [9, 10]

External factors, such as reactive oxygen species (ROS), inflammation, and UV radiation, also accelerate elastin breakdown. For example, ROS can oxidize elastin, making it more vulnerable to enzymatic cleavage and leading to a 30% decrease in elastin's tensile strength over time. [11].

Furthermore, advanced glycation end products (AGEs), which build up with aging and oxidative stress, contribute to elastin degradation by promoting crosslinking within its structure, thus diminishing elasticity. Additionally, calcification and lipid binding stiffen elastin fibers, further reducing their functional capacity.

Lysyl oxidases (LOXs), enzymes that cross-link collagen and elastin, contribute to ECM stabilization but can lead to increased tissue stiffness when overactivated. LOXL-1, in particular, plays a role in elastin deposition, and disruptions in its function have been linked to conditions like tendinopathy, where reduced elasticity impairs tendons' shock absorption and force transmission capabilities. These changes often lead to conditions like tendinopathy, where compromised elasticity and tensile strength in tendons and ligaments impair their shock absorption and force transmission capabilities. [4, 12].

IMPLICATIONS FOR THERAPEUTIC INTERVENTIONS

Understanding the molecular mechanisms of elastin synthesis and degradation is key to developing effective orthopedic therapies. Targeted treatments that stimulate elastin production or inhibit its breakdown, such as those using growth factors like TGF-β and micro-RNA modulation, offer potential for restoring tissue elasticity in aging or damaged tissues. [11] [7]

Research shows that healing tendons contain significantly higher levels of elastin compared to intact tendons, with elastin content nearly doubling during the healing process. This increase in elastin is particularly important for enhancing tendon compliance, which is essential for preventing re-injuries during early locomotion. The broader distribution of elastin throughout the extracellular matrix in healing tendons further underscores its critical role in supporting the viscoelastic properties of the tissue, contributing to overall tissue resilience and flexibility during recovery. [13]

These insights into elastin regulation highlight the importance of protecting and potentially replenishing elastin to support tendon and ligament health, offering avenues for advanced therapeutic strategies in managing both acute and degenerative musculoskeletal conditions. [11]

Elastin-based therapies for tendon and ligament disorders have garnered significant interest in orthopedics and sports medicine due to their potential to restore elasticity and improve tissue resilience. These treatments aim to enhance elastin synthesis, provide structural support, and promote cellular regeneration, all crucial for optimizing healing outcomes.

1. Platelet-Rich Plasma (PRP) therapy

One prominent approach is Platelet-Rich Plasma (PRP) therapy, which utilizes a patient's own blood, rich in growth factors such as TGF-β and PDGF, to stimulate tissue repair and cell regeneration. [14]

PRP is particularly valuable for enhancing elastin levels, supporting the structural integrity and flexibility of tendons and ligaments, and offering substantial benefits in treating injuries like Achilles tendinopathy. Despite promising findings, the effectiveness of PRP can be inconsistent due to variations in PRP preparation methods and patient-specific factors.

Metaanalyses and clinical trials reveal mixed results, with some reporting significant improvements in pain reduction and function, while others show negligible differences compared to control treatments. In a study on the use of PlateletRich Plasma (PRP) for ACL reconstruction, 60 patients were analyzed to assess PRP's effect on tendon-bone healing and graft maturation. Results indicated that while PRP did not significantly reduce bone tunnel widening or expedite tendon healing, it showed a trend toward improved graft maturation.

The study concludes that while PRP has some potential, further research is necessary to determine its long-term impact on ACL recovery. Overall, PRP therapy offers a promising avenue for addressing both acute and chronic musculoskeletal injuries by enhancing elastin synthesis and strengthening tissue, positioning it as a tool in regenerative sports medicine.

Studies also highlight the variability of PRP's effects based on its composition. For instance, leukocyte-rich PRP can have a more potent inflammatory response compared to pure PRP, which influences the healing process differently. While leukocyte-rich PRP may promote a stronger initial inflammatory response, pure PRP has been associated with reduced inflammation and better tissue regeneration in some cases.[15-17]

2. Bioengineered Scaffolds

Synthetic and bioengineered scaffolds, like those made with poly(lactic- coglycolic acid) (PLGA), are designed to mimic the flexibility and strength of elastin in tendon and ligament repair. PLGA is a biodegradable polymer that provides a framework for cells to grow and differentiate. The study from BMC Sports Science, Medicine and Rehabilitation showed that PLGA scaffolds can boost tissue resilience by 30% and decrease degradation by 40% under repetitive strain, replicating the natural elasticity needed for long-lasting repairs in areas like the rotator cuff and ACL, where strength and flexibility are critical for recovery.

Elastin-based scaffolds, including those made from tropoelastin and elastin-like peptides (ELPs), have been shown to enhance tissue regeneration by supporting cell proliferation and mimicking the mechanical properties of native tissues.

When combined with PLGA, elastin-based scaffolds can further improve tissue strength and flexibility, providing an optimal environment for long-term recovery in load-bearing tissues like tendons and ligaments.[18, 19].

3. MicroRNA

MicroRNA (miRNA)-based therapies are increasingly recognized for their potential in treating tendon and ligament injuries due to their role in regulating key cellular processes such as inflammation, cell proliferation, and extracellular matrix (ECM) remodeling, which are vital for tissue repair. In conditions like Achilles tendinopathy, specific miRNAs like the let-7 family modulate genes responsible for ECM synthesis and cellular proliferation, improving tendon resilience and reducing chronic pain.[20]. Additionally, miRNAs like miR-135a delay cellular senescence in tendon stem/progenitor cells (TSPCs), preserving their regenerative capacity,

which is crucial for preventing age-related tendon degeneration. [21] Another significant function of miRNAs is their regulation of apoptotic pathways under oxidative stress, as seen with miR-28 and the miR- 1792 cluster, which balance pro- and anti-apoptotic proteins to reduce cell death and preserve tendon structure in conditions like patellar tendinopathy. miRNAs play a crucial role in tendon healing, particularly across its three stages: inflammatory, proliferative, and remodeling phases. For instance, miR-210 enhances angiogenesis during early tendon healing, while miR-29b reduces tendon adhesions by modulating ECM remodeling.

Moreover, these miRNAs regulate critical aspects of bone metabolism, including osteogenesis and bone resorption. Studies highlight that miR-140 delivered via exosomes can promote fibrocartilage regeneration and osteogenesis at the tendon-bone junction, making miRNA therapies a promising tool for regenerative medicine aimed at improving long-term functional outcomes in patients with tendon injuries.[22] [20, 21].

miRNA	Role in Tendon Healing
let-7 family	Modulates genes responsible for ECM synthesis and cellular proliferation in conditions like Achilles tendinopathy
miR-135a	Delays cellular senescence in tendon stem/progenitor cells, promoting regenerative capacity
miR-28	Regulates apoptotic pathways under oxidative stress by inhibiting sirtuin 3, influencing p53 and Bim proteins
miR-17-92	Regulates apoptotic pathways, reducing cell death in conditions like patellar tendinopathy
miR-210	Enhances angiogenesis, promoting blood vessel formation and improving tendon repair
miR-29b	Reduces tendon adhesions by modulating ECM remodeling during tendon healing

4. Growth Factor-Based Treatments

Growth factors such as transforming growth factor-beta (TGF-β) and fibroblast growth factor (FGF) play a crucial role in tendon and ligament repair by promoting the synthesis of essential extracellular matrix (ECM) components and regulating cell behavior. TGF-β stimulates collagen production while inhibiting matrix metalloproteinases (MMPs), which helps preserve the extracellular matrix during healing, ensuring the tissue maintains its strength and structure. It also drives fibroblast differentiation into myofibroblasts, important for tissue remodeling. However, excessive TGF-β activity can lead to fibrosis and excessive scar tissue, necessitating careful regulation. FGF, particularly FGF-2, enhances fibroblast proliferation and promotes

elastin production, crucial for restoring elasticity in tendons and ligaments, as well as angiogenesis, which improves nutrient supply to the injured tissue. Both TGF-β and FGF can be delivered locally through platelet-rich plasma (PRP) or scaffold systems, offering sustained release of these growth factors to promote healing. In conditions like rotator cuff injuries and patellar tendinopathy, these growth factors help enhance tendon-to-bone healing, reduce inflammation, and improve collagen organization, contributing to stronger, more resilient tissues.

In addition, injectable hydrogels have gained attention in tendon and ligament tissue engineering as carriers for growth factors. These hydrogels can be loaded with TGF-β, FGF, or other growth factors, such as platelet-derived growth factor (PDGF), to enhance the repair process. PDGF-BB has been shown to promote collagen synthesis and ECM remodeling, as well as support the healing of medial collateral ligaments and tendons. A study demonstrated that PDGFBB- impregnated hydrogels significantly improved tendon healing in a rat model of rotator cuff repair by increasing collagen fiber organization and mechanical strength. Furthermore, bone morphogenetic proteins (BMPs), especially BMP-2 and BMP-7, have been employed in hydrogels to accelerate tendon-bone healing by stimulating fibrocartilage formation at the tendon-bone interface.

These hydrogels allow for controlled release of growth factors, ensuring localized and sustained therapeutic effects [23].

The development of biodegradable scaffolds combined with growth factors offers a promising approach for tissue regeneration. Hydrogels based on natural materials, such as collagen, gelatin, fibrin, and hyaluronic acid, are often used for their biocompatibility and ECM-mimicking properties, which support cell adhesion, proliferation, and differentiation.

Despite their potential, these hydrogels face challenges such as rapid degradation and limited mechanical strength, highlighting the need for improved formulations that balance degradation rates with the tissue healing process.

Combining hydrogels with synthetic polymers like polyethylene glycol (PEG) can enhance mechanical stability and control the release of growth factors over time, thus improving their application in long-term tissue repair.[24]

In conclusion, growth factor-based therapies, especially when combined with advanced scaffold and hydrogel technologies, offer an effective strategy for promoting tendon and ligament healing. By enhancing ECM production, modulating inflammation, and facilitating tendon-to-bone integration, these therapies hold significant promise for improving functional recovery in musculoskeletal injuries.[18, 20, 25]

5. Stem Cell and Tissue Engineering

Advanced tissue engineering approaches incorporate stem cells to promote elastin regeneration in tendon and ligament repair. Mesenchymal stem cells (MSCs) can differentiate into tenocytes or ligamentocytes, which are cell types that produce elastin and other extracellular matrix proteins. These cells can be seeded onto elastin-enriched scaffolds or used in conjunction with growth factors to improve the structural and functional recovery of damaged tissues.

This method is being explored in a variety of applications, including ACL repair, where the restoration of elastin is critical for long-term joint stability. [1, 26, 27]

The exploration of these treatment approaches reflects the growing recognition of elastin's importance in maintaining the structural and functional integrity of tendons and ligaments. As research progresses, these elastin-based therapies have the potential to become integral parts of regenerative medicine, offering effective solutions for managing both acute and chronic orthopedic injuries in sports medicine and beyond.

SUMMARY

Therapeutic Approach	Description	Advantages
Platelet-Rich Plasma (PRP) Therapy	Uses growth factors like TGF-β and PDGF to promote elastin synthesis, enhancing tissue flexibility and structural integrity in tendons and ligaments.	Effective for Achilles tendinopathy and lateral epicondylitis, promoting flexibility and repair.
Bioengineered Scaffolds	Synthetic scaffolds made from materials like PLGA and collagen provide mechanical support and mimic elastin, promoting cellular attachment and proliferation for tissue repair.	Supports cellular growth; beneficial for rotator cuff repair and ACL reconstruction by maintaining elasticity.
Micro-RNA Therapies	Targets genes involved in elastin production and degradation, enhancing elastin synthesis and slowing degradation, beneficial for degenerative joint conditions.	Preserves joint elasticity; helpful in managing conditions like osteoarthritis.

Growth Factor-Based Treatments	Local administration of growth factors such as TGF-β and FGF stimulates elastin synthesis, enhancing resilience and supporting tissue healing.	Creates a supportive healing environment, improving outcomes for conditions like rotator cuff injuries.
Stem Cell and Tissue Engineering	Incorporates MSCs to promote elastin regeneration; cells seeded on elastin-enriched scaffolds aid in structural and functional recovery of tendons and ligaments.	Improves recovery in ACL repair; restores long-term stability in ligaments and tendons.

CONCULSIONS

Elastin plays a crucial role in the structure and function of tendons and ligaments, providing these tissues with the necessary elasticity to withstand daily mechanical stress. When elastin is compromised—due to factors like aging, genetic conditions, or injuries—tissue integrity can be reduced, leading to issues such as joint instability, chronic pain, and an increased risk of further injury. Recognizing the significance of elastin in musculoskeletal health, recent advancements in regenerative medicine have focused on therapies that aim to enhance or restore elastin function in tendons and ligaments.

Various therapeutic approaches show promise in addressing elastin deficiencies in orthopedic and sports-related conditions. PRP therapy, for instance, uses growth factors to promote elastin synthesis, thereby improving tissue flexibility and supporting recovery from injuries like Achilles tendinopathy and rotator cuff tears. Bioengineered scaffolds, which mimic elastin's structural properties, provide a supportive environment for cellular growth and have been particularly effective in high-stress injuries, such as ACL reconstructions. Moreover,

microRNA-based therapies offer targeted intervention by modulating specific genes involved in elastin production, potentially slowing tissue degradation in conditions like osteoarthritis. The combined potential of these therapies underscores the growing recognition of elastin's role in maintaining the structural and functional integrity of tendons and ligaments. By focusing on elastin, these regenerative strategies could lead to more effective treatment options for both acute and chronic injuries. As research continues, elastin-based therapies may become a cornerstone in the field of sports medicine, improving recovery outcomes and supporting long-term musculoskeletal health for diverse patient populations.

Disclosure

Author's contribution

Conceptualization: W.Górska; methodology: K.Bochen; F. Jasiński; software: K. Wojtach; check: F. Banyś, F. Jasiński;
formal analysis: K. Bochen, J. Szałajska; investigation: A. Łukawski, I. Wiak;
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Conflict of interest

The authors deny any conflict of interest.

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