Review Article

The Role of Decorin in Autoimmune and Inflammatory Diseases

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Decorin is an extracellular matrix protein that belongs to the family of small leucine-rich proteoglycans. As a matrix protein, the first discovered role of decorin is participating in collagen fibril formation. Many other functions of decorin in various biological processes have been subsequently identified. Decorin is involved in an extensive signaling network and can interact with other extracellular matrix components, growth factors, receptor tyrosine kinases, and various proteases. Decorin has been shown to be involved in wound repair, cell cycle, angiogenesis, tumor metastasis, and autophagy. Recent evidence indicates that it also plays a role in immune regulation and inflammatory diseases. This review summarizes the characteristics of decorin in immune and inflammatory diseases, including inflammatory bowel disease (IBD), Sjögren’s syndrome (SS), chronic obstructive pulmonary disease (COPD), IgA nephropathy, rheumatoid arthritis (RA), spondyloarthritis (SpA), osteoarthritis, multiple sclerosis (MS), idiopathic inflammatory myopathies (IIM), and systemic sclerosis (SSc) and discusses the potential role in these disorders.

1. Introduction

Autoimmune and inflammatory diseases are major health problems affecting over 200 million people worldwide [1]. The search for new therapeutic approaches is not only to help understand the process of disease occurrence and development but also to alleviate patients’ symptoms and reduce the economic burden on society. The extracellular matrix is a well-organized complex collection of different proteins, including collagen, elastin, proteoglycan, and glycosaminoglycan [2]. Proteoglycans, which consist of one or more sulfated glycosaminoglycan chains and core proteins, include large proteoglycans and small leucine-rich proteoglycans (SLRPs) [3, 4]. SLRPs can be divided into five distinct classes based on their number of LRRs, amino acid residues at the N-terminus, and their chromosomal organization. Decorin belongs to the first class of SLRPs. In humans, the core protein of decorin is made up of 10–12 repeating leucine-rich motifs, and the GAG chain covalently attaches to the amino terminus via a serine residue [5]. The GAG side of decorin is usually dermal sulfate (DS) or chondroitin sulfate (CS), depending on the tissue. Skin, tendons, and intima arteriae are mainly DS, while bone and cartilage are mainly CS [6]. Decorin has multiple functions and is not only localized to the extracellular matrix and dense connective tissues such as tendons and ligaments but also exists in the body fluid, including plasma and aqueous humor [7–13]. In addition to interacting with collagen, soluble decorin is also involved in various biological processes, including inflammation, autophagy, angiogenesis, cell cycle, wound healing, and fibrosis [14–20]. Previous studies focused on its inhibitory effect on fibrosis and tumor. As an endogenous antagonist of transforming growth factor β (TGF-β), decorin can physically interact with TGF-β, interfere with TGF-β signaling, and form decorin/TGF-β complexes in the extracellular matrix, thereby significantly attenuating the profibrotic effect of TGF-β [21]. In tumors, decorin has been shown to inhibit metastasis, tumor cell proliferation, and angiogenesis and regulate autophagy and inflammation [22]. In addition to these characteristics, decorin, as one of the damage-associated molecular patterns (DAMPs), can initiate aseptic inflammation and induce the activation of innate immune cells, which provides the basis for its involvement in autoimmune and inflammatory diseases [11, 23]. This review article
summarizes the characteristics of decorin in immune and inflammatory diseases and discusses the potential role of decorin in autoimmune diseases.

1.1. The Structural Characteristics of Decorin. Decorin, also known as PG40, is a member of the small leucine-rich proteoglycan (SLRPs) family [24, 25]. Mature decorin contains a 42 kDa protein core with a sulfated glycosaminoglycan chain attached to its N-terminal [24]. The protein core contains twelve leucine-rich repeats (LRR) flanked by a cysteine-rich region [26, 27] (Figure 1). The decorin has a horseshoe-shaped appearance, with fourteen β-sheets at the concave surface and many α-helices at the convex surface [26, 28]. In physiologic conditions, decorin exists as a dimer; however, this process is reversible, which is mediated by the concave surfaces of decorin, and the dimerization of decorin prevents its core region from binding to other substrates, implying that monomeric decorin accounts for most of the interactions [29, 30]. Furthermore, decorin can generate complex context-dependent interactions with many ligands through GAG chains and core proteins [24]. Despite its complex function, decorin knockout mice were fertile and viable. No significant morphological abnormalities were observed, except reduced skin and tendon mechanics, suggesting a role of decorin in collagen fiber formation [6]. On the other hand, the study also found that the function of decorin overlaps with other SLRPs such as biglycan and asporin, which relieves the symptoms after decorin knockout [31, 32].

1.2. The Source and Expression of Decorin. Decorin is mainly expressed in fibrous connective tissue and primarily involves collagen fiber formation in the dermis, cornea, tendons, and cartilage. Decorin is typically synthesized and secreted by fibroblasts, maintaining the dynamic balance of the extracellular matrix. However, epithelial cells and endothelial cells can also synthesize decorin; although, they do not constitutively express it [9]. Many factors can modulate the expression of decorin. Among them, the effect of inflammation and cytokines on the decorin expression is interesting. Decorin is significantly induced in inflammation-related angiogenesis in vivo but not in noninflammation-dependent angiogenesis. However, inflammatory cytokines failed to directly induce decorin synthesis in endothelial cells, suggesting that decorin may act on endothelium through paracrine processes [9, 33]. Recent studies have also shown that decorin can be released early after ferroptosis and participate in the proinflammatory responses [34]. Cytokines interleukin-6 (IL-6) and IL-10 have been shown to upregulate the expression of decorin in smooth muscle cells and endothelial cells, whereas tumor necrosis factor α (TNF-α) and TGF-β inhibit the transcription of decorin [35–37].

1.3. Signaling Network Initiated by Decorin. Decorin has been linked to several biological functions. It can directly participate in collagen formation, act as a ligand to bind relevant receptors to mediate downstream signal transduction, and block specific cytokines and growth factors to inhibit downstream signal transduction. Decorin binds to various collagen fibers (including I, II, III, IV, V, VI, XII, and XIV) which type I collagen is the most widely studied [30, 42]. It has been demonstrated that the triple helix of type I collagen has a site in both “D” and “E” bands that can bind to the core protein of decorin. Such a structure can prevent abnormal fusion between collagen molecules [26]. The core protein of decorin binds to collagen fibrils at a uniform spacing of 65 nm, and the charged GAG chain is perpendicular to the collagen fibrils and connects adjacent fibrils, regulating the distance between fibrils. Furthermore, the GAG chain may attach to tenascin-X, modulating its effects on collagen and ECM integrity, and decorin can act as a bridging molecule binding different collagens [5]. These are important for the accurate arrangement and localization of collagen fibrils in the ECM. So, the lack of decorin leads to variations in the diameter of fibril, and the spacing and biomechanics are impaired. In addition, decorin can interact with other extracellular matrix components such as matrilin-1, tenascin-X, microfilament-associated protein (MFAP-2), and fibrillins, which are involved in tissue cell adhesion and migration to maintain the mechanical strength of connective tissue [43–45].

Decorin can also act directly on receptors on the cell surface. Met, encoded by protooncogene c-Met, is a tyrosine kinase receptor that plays an essential role in cell migration, apoptosis, proliferation, and differentiation. Studies showed that decorin could bind to Met on the surface of tumor cells, leading to rapid receptor phosphorylation and degradation in the endosomes, and could also induce mitochondrial autophagy by activating Met [46–48]. Decorin could also target insulin-like growth factor 1 receptor (IGF1R) on the surface of cancer cells and inhibit its downstream signaling or target vascular endothelial growth factor receptor 2 (VEGFR2) on the surface of endothelial cells to promote autophagy [49, 50]. Decorin can also inhibit tumor growth by blocking epidermal growth factor receptor (EGFR) and ErbB4 dimerization [51]. Decorin could also serve as a reservoir for TGF-β, myostatin, connective tissue growth factor (CTGF), fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), and TNF-α to maintain their homeostasis, which requires complex feedback mechanisms and strict regulatory networks [30] (Figure 2).

1.4. Decorin and Inflammation. Decorin, as endogenous ligands, binds to TLR2 and TLR4 on the surface of macrophages with an affinity comparable to that of pathogen ligands, triggering an acute inflammatory response, leading to rapid activation of P38, ERK1/2, and NF-κB pathways and the synthesis of proinflammatory factors TNF-α and IL-12p70 [52]. In addition, by signaling through TLR2/4, decorin also acts as a transcriptional inducer of the tumor
suppressor programmed cell death 4 (PDCD4), a specific translational suppressor of IL-10, maintaining a proinflammatory environment [52]. However, the core protein alone may play a role in inhibiting inflammation in a triple-negative orthotopic breast cancer xenograft model by competitive inhibition of other DAMP molecules bound to TLR2 and TLR4 [53]. In addition to immune cells, Toll-like receptors were also expressed in some tissue cells, such as annulus fibrosus cells and salivary gland epithelial cells, which both expressed TLR4 [54, 55]. The former can produce MIP-2 in response to decorin stimulation, and the latter can increase TNF-α transcription level in response to decorin stimulation, and both of them can be inhibited by TAK-242 (TLR4 inhibitor). Furthermore, the regulation of decorin in the inflammatory response is complicated and depends on the context of inflammation. In ischemia-reperfusion injury, TGF-β is involved in the aggravation of tissue damage after perfusion, and decorin has a potentially protective effect by inactivating TGF-β [59]. In addition, intraperitoneal injection of decorin after traumatic brain injury significantly reduced caspase 3 activity, increased superoxide dismutase levels, and protected brain tissue and neurons [60].

1.5. Decorin and Autophagy. Autophagy is a self-degrading process that degrades damaged organelles and misfolded and aggregated proteins through the lysosomal pathway [61]. Physiological autophagy is essential for normal cell

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**Figure 1:** The structure of decorin. Decorin consists of amino-terminal domains, glycosaminoglycan chains, core protein domains, and carboxy-terminal domains. The binding site of the GAG (glycosaminoglycan) chain exists in the amino-terminal domain. The core protein domain contains leucine repeats (LRR) and N-linked-oligosaccharides. The remainder is the carboxy-terminal domain.

**Figure 2:** The biological signaling network of decorin. Decorin binds to collagen fibers (including I, II, III, IV, V, VI, XII, and XIV). In addition, decorin can interact with other extracellular matrix components such as matrilin-1, tenasin X, MFAP-2, and fibrillins. Decorin can bind to receptors on the surface of tumor cells (such as Met, IGF1R, EGFR, or VEGFR2). Moreover, decorin also acts as a reservoir for cytokines (TGF-β, myostatin, CTGF, FGF, PDGF, and TNF-α).
function, signal transduction, and proliferation, but pathological autophagy is involved in various diseases, including autoimmune diseases [62]. Decorin is the first extracellular matrix component identified to influence cellular metabolic processes. The role of decorin in mitochondrial autophagy in epithelial-derived tumors and endothelial cells has been widely reported [22]. Decorin induced the expression of mitostatin in breast cancer, leading to mitochondrial ultrastructural changes [63, 64]. Decorin could also trigger mitochondrial depolarization and cause the translocation of Parkin from the cytoplasm to mitochondria, leading to the ubiquitination of mitochondrial proteins [65, 66]. Decorin stimulated polyethylene glycol 3 (PEG3) synthesis in endothelial cells by interacting with VEGFR2. Decorin could also inhibit the upregulation of mTOR after VEGFA binding to VEGFR2, which resulted in enhanced expression of TGF-βR1 [11, 23, 70]. However, decorin can activate other receptors as well. Recent studies showed that extracellular decorin bound to advanced glycosylation end product-specific receptor (AGER) on macrophages triggers proinflammatory cytokine production in an NF-κB dependent manner [34] (Figure 3). Decorin also indirectly affected the foxp3 gene expression through the TGF-β signaling pathway [71]. In DCN-/- mice, the biological activity of TGF-β, CD4+CD25+Foxp3+ T lymphocytes, and IL-10 levels were increased, which inhibited the Th2 cell immune response in allergic asthmatic mice [71].

2. Decorin in Autoimmune and Inflammatory Diseases

Decorin is a multifunctional protein that plays a vital role in various biological processes. Decorin may be involved in immune-related diseases for several important reasons. First, as one of the DAMPs, it can activate pattern recognition receptors such as TLR on innate immune cells. Secondly, as an endogenous TGF-β blocker, it reduces the level of anti-inflammatory factor IL-10 and maintains the persistence of inflammation. Finally, it can induce autoantibodies against decorin; although, its significance has not been elucidated [70]. Previous studies on autoimmune and inflammatory diseases have focused on the interactions between immune cells and immune cells and between immune cells and parenchymal tissue cells. Still, there has been limited research on the interaction between immune cells and extracellular matrix. The extracellular matrix is one of the most abundant tissue components in the body. Although its role in disease has not been fully elucidated,
TABLE 1: The role of decorin in autoimmune and inflammatory diseases.

| Disease | The role of decorin in disease pathogenesis | References |
|---------|--------------------------------------------|------------|
| IBD     | The levels of decorin, Belrin1, and LC3b in the intestinal wall of IBD mice were increased; the overexpression of decorin in human colon epithelial cells resulted in increased autophagosomes and decreased apoptosis. Degradation products of decorin in the exocrine gland of NOD mice were increased; in a pSS model (NOD.B10), decorin was found to induce TNF-α production in spleen tissues via TLR4 and reduce MIP-1α and MCP-1 levels in spleen cells; in a pSS model (NOD.B10), autoantibodies against decorin were significantly elevated, and decorin was strongly expressed in salivary gland tissues, lung, and kidney tissues. Decorin was significantly elevated in the salivary glands both in the experimental Sjögren’s syndrome model and pSS patients. Decorin induced the apoptosis of A253 cells and polarization of macrophages towards the M1 phenotype. The level of decorin secreted by fibroblasts from patients with severe COPD was decreased; using extracellular matrix components and cytokines stimulated PBMC in COPD patients, more antidecorin IgG was produced; immunizing mice with extracellular matrix components induced a specific immune response to decorin; decorin could act as a predictor of acute disease exacerbation in patients with COPD. | [69] [54], 77–79 |
| SS      | The transcriptional level of decorin was increased and was mainly located in sclerotic glomeruli and fibrotic sites in patients with IgA nephropathy. Decorin could promote podocyte autophagy and maintain cell homeostasis; podocytes may be a source of decorin. | [85–88] |
| COPD    | The frequency of IgM antibodies against decorin was the highest among all matrix molecules in RA; these antibodies may interfere with the binding of decorin to C1q complement to regulate inflammatory processes. | [96] |
| IgAN    | Autoantibodies against decorin were significantly higher in SpA synovial fluid than in OA patients. Serum decorin levels were elevated in patients with OA and could be a risk factor for OA; Li et al. found that decorin had a protective effect on cartilage regeneration in posttraumatic osteoarthritis by regulating the fibrogenesis of the cartilage surface; the articular cartilage matrix showed higher stiffness and resistance to OA after decorin deletion. In perivascular fibrotic tissues of MS, Mohan et al. found the upregulation of decorin, which interacted with fibrillar collagens. Decorin was involved in perivascular fibrosis, which had positive implications for limiting inflammatory cell infiltration and lesion progression. Decorin could bind and inhibit myostatin from promoting the proliferation and differentiation of myogenic cells. | [96] |
| RA      | The role of decorin in autoimmune and inflammatory diseases. | [99–101] |
| SpA     | Decorin could also attach to TGF-β2 and positively affect skeletal muscle production; the injection of decorin into the injured muscle could induce muscle regeneration. | [104, 105] |
| OA      | Decorin was significantly increased at both transcriptional and protein levels in SSc. | [112] |
| MS      | The levels of decorin, Belrin1, and LC3b in the intestinal wall of IBD mice were increased; the overexpression of decorin in human colon epithelial cells resulted in increased autophagosomes and decreased apoptosis. | [107–109] |
| SSc     | Decorin could also attach to TGF-β2 and positively affect skeletal muscle production; the injection of decorin into the injured muscle could induce muscle regeneration. | |

Abbreviation: IBD: inflammatory bowel disease; SS: Sjögren’s syndrome; COPD: chronic obstructive pulmonary disease; IgAN: IgA nephropathy; RA: rheumatoid arthritis; SpA: spondyloarthritis; OA: osteoarthritis; MS: multiple sclerosis; IIM: idiopathic inflammatory myopathy; SSc: systemic sclerosis; pSS: primary Sjögren’s syndrome; TNF-α: tumor necrosis factor α; TLR4: Toll-like receptor 4; MIP-1α: macrophage inflammatory protein-1 α; MCP-1: monocyte chemotactrant protein 1; PBMC: peripheral blood mononuclear cell; TGF-β2: transforming growth factor β2.

it has significant therapeutic potential. This review summarizes the role of decorin in diseases including IBD, SS, COPD, IgA nephropathy, MS, IIM, RA, and osteoarthritis (Table 1).

2.1. IBD. Inflammatory bowel disease (IBD) is a nonspecific chronic inflammatory disease, including Crohn’s disease (Th1 dominant immune response) and ulcerative colitis (Th2 dominant immune response) [72]. The role of decorin in IBD has been explored only in mouse models and in vitro cell lines. The study found increased levels of decorin and autophagy-related proteins Beclin1 and LC3b in the intestinal wall of IBD mice. The overexpression of decorin in human colon epithelial cells resulted in increased autophagosomes and decreased apoptosis, suggesting that decorin may play a protective role in inflammatory bowel disease by increasing the autophagy of epithelial cells and decreasing apoptosis [69]. However, further research is needed to clarify the relationship between decorin and inflammation disease, for example, whether there is a clear interaction between decorin and the immune cells or is there a long-term effect of epithelial autophagy and whether this could lead to dysfunction of epithelial cells.

2.2. SS. Sjögren’s syndrome (SS) is a common autoimmune disease involving exocrine glands (salivary and lacrimal). About 40% of patients develop exocrine symptoms, including muscle arthralgia, interstitial lung disease, and central nervous system involvement, and about 5% develop lymphoma [73]. The roles of epithelial cells and immune cells in Sjögren’s syndrome have been extensively studied. However, the treatment selection of Sjögren’s syndrome is still limited [74–76]. The evidence of the involvement of decorin in SS is growing. An earlier study found an increased MMP activity and an enhanced decorin degradation in the exocrine glands of NOD mice. However, given the limited activities of cleaved decorin, the role of decorin in SS is not precisely clarified [77]. In a primary Sjögren’s syndrome mouse model (NOD.B10), decorin was found to induce TNF-α production and reduce MIP-1α and MCP-1 in the spleen via TLR4 rather than TLR2 [78]. This indicates that decorin may have a different effect on different cytokines/chemokines and immune cells in SS. Further studies showed that although circulating levels of decorin were not different between NOD.B10 mice and control mice, autoantibodies against decorin were significantly elevated in pSS mice, and decorin was highly expressed in the salivary gland, lung,
and kidney tissues of pSS mice [79]. Our study also found that decorin was significantly elevated in the salivary glands in the experimental Sjögren’s syndrome model and pSS patients, and decorin induced the apoptosis of A253 cells and polarization of macrophages towards the M1 phenotype [54]. Current evidence supports the ECM degradation products as a new source of B cell activation in SS. However, more evidence is needed to clarify whether decorin can be used as an early therapeutic target in SS.

2.3. COPD. Chronic obstructive pulmonary disease (COPD) is a chronic airway disease with restricted airflow. There is increasing evidence that COPD is associated with immune abnormalities, and some patients present with autoimmune reactions [80]. These abnormalities are characterized by the formation of B cell lymphoid follicles in the lung tissue and the presence of anti-HEP-2 epithelial cells and antielastin and antidecorin autoantibodies in the serum of patients with COPD [81–85]. The level of decorin secreted by fibroblasts from patients with severe COPD was decreased, and the expression of decorin was also reduced in pulmonary mesenchymal stem cells (LMSCs) from COPD patients [86]. More antidecorin IgG was produced when PBMCs from COPD patients were stimulated by a combination of extracellular matrix components and cytokines [85]. However, when the mice were immunized with extracellular matrix and exposed to cigarette smoke, an immune response specific to decorin was induced; although, it did not enhance smoke-induced inflammation. However, it cannot be ruled out that autoantibodies against decorin may cause tissue damage over a longer time [87]. In addition, decorin in the peripheral blood of patients with COPD has recently been reported as a predictor of acute disease exacerbation [88]. The current evidence supports that decorin has some immunogenicity. However, more evidence is needed to support the involvement of decorin in COPD.

2.4. IgA Nephropathy. IgA nephropathy is a common primary glomerular disease caused by the deposition of immune complexes in the mesangial region, resulting in mesangial cell proliferation [89]. Decorin is mainly secreted by renal fibroblasts in the normal kidneys and located in the renal tubule interstitium [90]. In IgA nephropathy, the transcriptional level of decorin was increased and was mainly located in sclerotic glomeruli and fibrotic sites. These results suggest that decorin is involved in the pathogenesis of IgA nephropathy [91]. A recent study investigated the effects of TGF-β1 and decorin on podocyte autophagy. The results showed that TGF-β1 could activate the mammalian target of rapamycin complex 1 (mTORC1) to inhibit podocyte autophagy and participate in podocyte apoptosis [92]. In addition, this study also found that podocytes may be a source of decorin [92]. However, it is exciting and necessary further to investigate the mechanism of decorin in IgA nephropathy.

2.5. RA, SpA, and Osteoarthritis. Rheumatoid arthritis (RA) is characterized by synovial hyperplasia, pannus formation, and bone/cartilage damage [93]. Lymphoid follicles and ectopic germinal centers were found in the synovial tissues, suggesting that the cartilage matrix may be a potential component of autoantigens in RA [94]. It was reported that the frequency of IgM antibodies against decorin was the highest among all matrix molecules. Decorin binds C1q to inhibit the classical pathway of complement under normal conditions, while autoantibodies bind decorin and activate the classical pathway of complement, which has a potential pro-inflammatory effect [95]. In addition, decorin normally inhibits TGFβ, and autoantibodies may affect this process, but the effect on the disease phenotype is complex and unknown [96]. Seronegative spondyloarthropathies (SpA) are chronic inflammatory diseases involving the spine, peripheral joints, ligaments, and tendons [97]. Autoantibodies against decorin were significantly higher in SpA synovial fluid than in OA patients, suggesting that matrix proteins are involved in the chronic inflammatory environment of local joints [96]. Osteoarthritis is a chronic degenerative cartilage disease characterized by joint pain and stiffness [98]. The role of decorin in osteoarthritis is complex. It was reported that serum decorin levels were elevated in OA and could be a risk factor for OA [99]. However, studies in mouse models showed different results. Li et al. found that decorin had a protective effect on cartilage regeneration in posttraumatic osteoarthritis by regulating the fibrogenesis of the cartilage surface [100]. Another study found that the articular cartilage matrix showed higher stiffness and resistance to OA after decorin deletion [101]. These also indirectly illustrate the complexity of decorin in disease, and more studies are still needed.

2.6. MS. Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease related to immune dysfunction, often accompanied by sensory, motor, and visual impairment [102]. Decorin in MS is rarely studied, and its function is complex, but it is believed that it has some protection function. In part because it inhibits TGF-β, and in the EAE model, inhibition of TGF-β signaling may have benefits in the treatment of the acute phase [103]. On the other hand, it is involved in the formation of perivascular fibrosis, which is a typical feature of chronic lesions and can limit the recruitment of immune cells and the expansion of MS lesions [104, 105]. However, more evidence is needed to support whether it can be used as a therapeutic target.

2.7. Other Diseases. Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of autoimmune diseases characterized by muscle weakness, inflammatory cell infiltration, and overexpression of MHC1 molecules in muscle fibers [106]. Polymyositis (PM) is mainly infiltrated by CD8+ T cells in the endomysium, while dermatomyositis (DM) is primarily infiltrated by CD4+ T cells in the epimysium. It was reported that decorin could bind and inhibit myostatin from promoting the proliferation and differentiation of myogenic cells [107]. Decorin could also attach to TGF-β2 and promote skeletal muscle production [108]. Moreover, the injection of decorin into the injured muscle could induce muscle regeneration [109]. Therefore, decorin can be a potential target in IIM [110].
Systemic sclerosis (SSc) is an autoimmune disease with localized or diffuse skin thickening and fibrosis [111]. Studies have shown that proteoglycan secretion in fibroblasts of SSc patients was significantly increased. Among them, decorin was significantly increased at both transcriptional and protein levels. It is speculated that these changes may affect the composition of the stroma and the course of the disease [112].

3. Discussion

Decorin is a versatile protein that interacts with various receptors, enzymes, and cytokines. Decorin is involved in autophagy, cell cycle, inflammation, angiogenesis, and other biological processes. The role of decorin in autoimmune and inflammatory diseases is based on several essential parts. Firstly, decorin, as one of the DAMPs, can participate in the activation of innate immune cells through interacting with TLRs or ARGE receptors. Secondly, the immune system can produce autoantibodies against decorin, which may interfere with the normal function of soluble decorin. Thirdly, decorin is thought to mediate autophagy in endothelial cells or epithelial cells. Finally, decorin can suppress the effects of TGF-β, especially in fibrosis. These results suggest that decorin plays a role in developing and progressing autoimmune and inflammatory diseases. Therefore, it is crucial to elucidate the role of decorin in the dynamics of disease development to guide treatment more precisely.

4. Conclusion

Decorin has been extensively studied in the process of anti-fibrosis and antitumor. However, its role in autoimmune and inflammatory diseases is not fully understood. Although several studies have indicated an involvement of decorin in autoimmune and inflammatory disease, the underlying mechanisms remain to be elucidated due to the complexity of decorin in these conditions.

Data Availability

The data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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References

[1] W. H. Wu, D. F. Zegarra-Ruiz, and G. E. Diehl, "Intestinal microbes in autoimmune and inflammatory disease," *Frontiers in Immunology*, vol. 11, article 597966, 2020.

[2] A. D. Theocharis, D. Manou, and N. K. Karamanos, “The extracellular matrix as a multitasking player in disease,” *The FEBS Journal*, vol. 15, no. 286, pp. 2830–2869, 2019.

[3] L. Schaefer and R. M. Schaefer, "Proteoglycans: from structural compounds to signaling molecules," *Cell and Tissue Research*, vol. 339, no. 1, pp. 237–246, 2010.

[4] R. V. Iozzo, "Matrix proteoglycans: from molecular design to cellular function," *Annual Review of Biochemistry*, vol. 67, no. 1, pp. 609–652, 1998.

[5] R. R. Mohan, J. C. Tovey, R. Gupta, A. Sharma, and A. Tandon, "Decorin biology, expression, function and therapy in the cornea," *Current Molecular Medicine*, vol. 11, no. 2, pp. 110–128, 2011.

[6] K. G. Danielson, H. Baribault, D. F. Holmes, H. Graham, K. E. Kadler, and R. V. Iozzo, "Targeted disruption of decorin leads to abnormal collagen fibril morphology and skin fragility," *The Journal of Cell Biology*, vol. 136, no. 3, pp. 729–743, 1997.

[7] R. V. Iozzo and L. Schaefer, "Proteoglycan form and function: a comprehensive nomenclature of proteoglycans," *Matrix Biology*, vol. 42, pp. 11–55, 2015.

[8] C. J. Handley, T. Samircir, and M. Z. Ilic, "Structure, metabolism, and tissue roles of chondroitin sulfate proteoglycans," *Advances in Pharmacology*, vol. 53, pp. 219–232, 2006.

[9] M. G. Kinsella, S. L. Bressler, and T. N. Wight, "The regulated synthesis of versican, decorin, and biglycan: extracellular matrix proteoglycans that influence cellular phenotype," *Critical Reviews in Eukaryotic Gene Expression*, vol. 14, no. 3, pp. 203–234, 2004.

[10] S. P. Evanko, E. W. Raines, R. Ross, L. I. Gold, and T. N. Wight, "Proteoglycan distribution in lesions of atherosclerosis depends on lesion severity, structural characteristics, and the proximity of platelet-derived growth factor and transforming growth factor-beta," *The American Journal of Pathology*, vol. 2, no. 152, pp. 533–546, 1998.

[11] R. Merline, K. Moreth, J. Beckmann et al., "Signaling by the matrix proteoglycan decorin controls inflammation and cancer through PDCD4 and MicroRNA-21," *Science Signaling*, vol. 4, no. 199, 2011.

[12] M. Schneider, R. Pawlak, G. R. Weber et al., "A novel ocular function for decorin in the aqueous humor outflow," *Matrix Biology*, vol. 97, pp. 1–19, 2021.

[13] T. Hosoya, G. Oda, T. Nakagawa et al., "Plasma levels of decorin increased in patients during the progression of breast cancer," *Journal of Clinical Medicine*, vol. 23, no. 10, 2021.

[14] C. Bocian, A. K. Urbanowitz, R. T. Owens, R. V. Iozzo, M. Gotte, and D. G. Seidler, "Decorin potentiates interferon-gamma activity in a model of allergic inflammation," *The Journal of Biological Chemistry*, vol. 18, no. 288, pp. 12699–12711, 2013.

[15] S. Buraschi, T. Neill, and R. V. Iozzo, "Decorin is a devouring proteoglycan: remodeling of intracellular catabolism via autophagy and mitophagy," *Matrix Biology*, vol. 75-76, pp. 260–270, 2019.

[16] H. Jarvelainen, A. Sainio, and T. N. Wight, "Matrix proteoglycans orchestrate receptor crosstalk during inflammation," *Science Signaling*, vol. 43, pp. 15–26, 2015.

[17] K. Moreth, R. V. Iozzo, and L. Schaefer, "Small leucine-rich proteoglycans orchestrate receptor crosstalk during inflammation," *Cell Cycle*, vol. 11, no. 11, pp. 2084–2091, 2012.
growth by activating the epidermal growth factor receptor,” *The Journal of Clinical Investigation*, vol. 101, no. 2, pp. 406–412, 1998.

[19] H. Jarvelainen, P. Puolakkainen, S. Pukkainen et al., “A role for decorin in cutaneous wound healing and angiogenesis,” *Wound Repair and Regeneration*, vol. 14, no. 4, pp. 443–452, 2006.

[20] K. Baghry, R. V. Iozzo, and I. Kovalszky, “Decorin-TGFbeta axis in hepatic fibrosis and cirrhosis,” *The Journal of Histochemistry and Cytochemistry*, vol. 4, no. 60, pp. 262–268, 2012.

[21] T. A. Jarvinen and E. Ruoslahti, “Targeted antiscarring therapy for tissue injuries,” *Advances in Wound Care*, vol. 2, no. 2, pp. 50–54, 2013.

[22] V. Diehl, L. S. Huber, J. Trebicka, M. Wygrecka, R. V. Iozzo, and L. Schaef er, “The role of decorin and biglycan signaling in tumorigenesis,” *Frontiers in Oncology*, vol. 11, article 801801, 2021.

[23] R. Merline, R. M. Schaef er, and L. Schaef er, “The matricellular functions of small leucine-rich proteoglycans (SLRPs),” *Journal of Cell Communication and Signaling*, vol. 3-4, no. 3, pp. 323–335, 2009.

[24] R. V. Iozzo and L. Schaef er, “Proteoglycans in health and disease: novel regulatory signaling mechanisms evoked by the small leucine-rich proteoglycans,” *The FEBS Journal*, vol. 19, no. 277, pp. 3864–3875, 2010.

[25] T. Krusius and E. Ruoslahti, “Primary structure of an extracellular matrix proteoglycan core protein deduced from cloned cDNA,” *Proceedings of the National Academy of Sciences of the United States of America*, vol. 20, no. 83, pp. 7683–7687, 1986.

[26] I. T. Weber, R. W. Harrison, and R. V. Iozzo, “Model structure of decorin and implications for collagen fibrillogenesis,” *The Journal of Biological Chemistry*, vol. 30, no. 271, pp. 31767–31770, 1996.

[27] T. A. Jarvinen and S. Prince, “Decorin: a growth factor antagonist for tumor growth inhibition,” *BioMed Research International*, vol. 2015, Article ID 654765, 11 pages, 2015.

[28] P. G. Scott, P. A. McEwan, C. M. Dodd, E. M. Bergmann, P. N. Bishop, and J. Bella, “Crystal structure of the dimeric protein core of decorin, the archetypal small leucine-rich repeat proteoglycan,” *Proceedings of the National Academy of Sciences of the United States of America*, vol. 44, no. 101, pp. 15633–15638, 2004.

[29] M. Islam, J. Gor, S. J. Perkins, Y. Ishikawa, H. P. Bachinger, and E. Hohenester, “The concave face of decorin mediates reversible dimerization and collagen binding,” *The Journal of Biological Chemistry*, vol. 49, no. 288, pp. 35526–35533, 2013.

[30] M. A. Gubbiotti, S. D. Vallet, S. Ricard-Blum, and R. V. Iozzo, “Decorin interacting network: a comprehensive analysis of decorin-binding partners and their versatile functions,” *Matrix Biology*, vol. 55, pp. 7–21, 2016.

[31] A. Corsi, T. Xu, X. D. Chen et al., “Phenotypic effects of biglycan deficiency are linked to collagen fibril abnormalities, are synergized by decorin deficiency, and mimic Ehlers-Danlos-like changes in bone and other connective tissues,” *Journal of Bone and Mineral Research*, vol. 7, no. 17, pp. 1180–1189, 2002.

[32] S. Kalama jski, A. Aspberg, K. Lindblom, D. Heinegard, and A. Oldberg, “Asporin competes with decorin for collagen binding, binds calcium and promotes osteoblast collagen mineralization,” *The Biochemical Journal*, vol. 423, no. 1, pp. 53–59, 2009.

[33] L. Nelinmarkka, H. Salminen, T. Kuopio et al., “Decorin is produced by capillary endothelial cells in inflammation-associated angiogenesis,” *The American Journal of Pathology*, vol. 2, no. 158, pp. 345–353, 2001.

[34] J. Liu, S. Zhu, L. Zeng et al., “DCN released from ferroptotic cells ignites AGER-dependent immune responses,” *Autophagy*, pp. 1–14, 2021.

[35] A. Mauviel, M. Santra, Y. Q. Chen, J. Uitto, and R. V. Iozzo, “Transcriptional regulation of decorin gene expression. Induction by quiescence and repression by tumor necrosis factor-alpha,” *The Journal of Biological Chemistry*, vol. 19, no. 270, pp. 11692–11700, 1995.

[36] I. J. Edwards, W. D. Wagner, and R. T. Owens, “Macrophage secretory products selectively stimulate dermatan sulfate proteoglycan production in cultured arterial smooth muscle cells,” *The American Journal of Pathology*, vol. 3, no. 136, pp. 609–621, 1990.

[37] I. J. Edwards, H. Xu, M. J. Wright, and W. D. Wagner, “Interleukin-1 upregulates decorin production by arterial smooth muscle cells,” *Arteriosclerosis and Thrombosis*, vol. 7, no. 14, pp. 1032–1039, 1994.

[38] K. Kuroda and H. Shinkai, “Downregulation of decorin expression in dermal fibroblasts by interleukin-4,” *Archives of Dermatological Research*, vol. 289, no. 8, pp. 476–480, 1997.

[39] Y. Wegrzowska, V. Paltot, P. Gillery, B. Kalis, A. Randoux, and F. X. Maquart, “Stimulation of sulphated glycosaminoglycan and decorin production in adult dermal fibroblasts by recombiant human interleukin-4,” *Biochemical Journal*, vol. 307, no. 3, pp. 673–678, 1995.

[40] E. Tufvesson and G. Westergren-Thorsson, “Alteration of proteoglycan synthesis in human lung fibroblasts induced by interleukin-1beta and tumor necrosis factor-alpha,” *Journal of Cellular Biochemistry*, vol. 2, no. 77, pp. 298–309, 2000.

[41] J. Chatterjee, S. Sanapala, O. Cobb et al., “Asthma reduces glioma formation by T cell decorin-mediated inhibition of microglia,” *Nature Communications*, vol. 12, no. 1, p. 7122, 2021.

[42] G. Nareyeck, D. G. Seidler, D. Troyer, J. Rautenberg, H. Kresse, and E. Schonherr, “Differential interactions of decorin and decorin mutants with type I and type VI collagens,” *European Journal of Biochemistry*, vol. 16, no. 271, pp. 3389–3398, 2004.

[43] C. Wiberg, A. R. Klatt, R. Wagener et al., “Complexes of matrilin-1 and biglycan or decorin connect collagen VI microfibrils to both collagen II and aggrecan,” *The Journal of Biological Chemistry*, vol. 39, no. 278, pp. 37698–37704, 2003.

[44] F. Elefteriou, J. Y. Exposito, R. Garrone, and C. Lethias, “Binding of tenasin-X to decorin,” *FEBS Letters*, vol. 495, no. 1-2, pp. 44–47, 2001.

[45] B. C. Trask, T. M. Trask, T. Broekelmann, and R. P. Mecham, “The microfibrillar proteins MAGP-1 and fibrillin-1 form a ternary complex with the chondroitin sulfate proteoglycan decorin,” *Molecular Biology of the Cell*, vol. 5, no. 11, pp. 1499–1507, 2000.

[46] S. Buraschi, N. Pal, N. Tyler-Rubinstein, R. T. Owens, T. Neill, and R. V. Iozzo, “Decorin antagonizes Met receptor activity and down-regulates [beta]-catenin and Myc levels,”
The Journal of Biological Chemistry, vol. 53, no. 285, pp. 42075–42085, 2010.

S. Goldoni, A. Humphries, A. Nyström et al., “Decorin is a novel antagonistic ligand of the Met receptor,” The Journal of Cell Biology, vol. 185, no. 4, pp. 743–754, 2009.

T. Neill and R. V. Iozzo, “The role of decorin proteoglycan in mitophagy,” Cancers (Basel), vol. 3, no. 14, 2022.

A. Morcavallo, S. Buraschi, S. Q. Xu et al., “Decorin differentially modulates the activity of insulin receptor isoform A ligands,” Matrix Biology, vol. 35, pp. 82–90, 2014.

T. Neill, A. Torres, S. Buraschi, and R. V. Iozzo, “Decorin has an appetite for endothelial cell autophagy,” Autophagy, vol. 10, no. 9, pp. 1626–1628, 2013.

S. Goldoni and R. V. Iozzo, “Tumor microenvironment: modulation by decorin and related molecules harboring leucine-rich tandem motifs,” International Journal of Cancer, vol. 11, no. 123, pp. 2473–2479, 2008.

H. Frey, N. Schroeder, T. Manon-Jensen, R. V. Iozzo, and L. Schaef er, “Biological interplay between proteoglycans and their innate immune receptors in inflammation,” The FEBs Journal, vol. 10, no. 280, pp. 2165–2179, 2013.

S. Buraschi, T. Neill, R. T. Owens et al., “Decorin protein core affects the global gene expression profile of the tumor microenvironment in a triple-negative orthotopic breast cancer xenograft model,” PLoS One, vol. 7, no. 9, article e45559, 2012.

R. Gao, J. Tang, Y. Dong et al., “The aberrant levels of decorin induce damages of human salivary gland epithelial cells and polarization of macrophages,” Modern Rheumatology. 2022.

D. P. Zwambag, S. Molladavoodi, M. J. Guerreiro, S. J. DeWitte-Orr, and D. E. Gregory, “Immuno-stimulatory capacity of decorin in the rat tail intervertebral disc and the mechanical consequence of resultant inflammation,” European Spine Journal, vol. 7, no. 29, pp. 1641–1648, 2020.

J. Koning, N. A. Giese, M. Bartel et al., “The ECM proteoglycan decorin links desmoplasia and inflammation in chronic pancreatitis,” Journal of Clinical Pathology, vol. 59, no. 1, pp. 21–27, 2006.

H. Jin, L. Kumar, C. Mathias et al., “Toll-like receptor 2 is important for the I$_{11}$ response to cutaneous sensitization,” The Journal of Allergy and Clinical Immunology, vol. 123, no. 4, pp. 875–882.e1, 2009.

C. Soria-Valles, A. Gutiérrez-Fernández, M. Guiu et al., “The anti-metastatic activity of collagenase-2 in breast cancer cells is mediated by a signaling pathway involving decorin and miR-21,” Oncogene, vol. 23, no. 33, pp. 3054–3063, 2014.

C. Alan, H. Kocoglu, R. Almintas, B. Alici, and E. A. Resit, “Protective effect of decorin on acute ischaemia-reperfusion injury in the rat kidney,” Archives of Medical Science, vol. 2, no. 2, pp. 211–216, 2011.

R. Özyaz, E. Türkoglu, B. Gürer et al., “Does decorin protect neuronal tissue via its antioxidant and antiinflammatory activity from traumatic brain injury? An experimental study,” World Neurosurgery, vol. 97, pp. 407–415, 2017.

D. J. Klionsky, G. Petroni, R. K. Amaravadi et al., “Autophagy in major human diseases,” The EMBO Journal, vol. 19, no. 40, article e108863, 2021.

H. Yin, H. Wu, Y. Chen et al., “The therapeutic and pathogenic role of autophagy in autoimmune diseases,” Frontiers in Immunology, vol. 9, p. 1512, 2018.

T. Neill, A. Torres, S. Buraschi et al., “Decorin induces mitophagy in breast carcinoma cells via peroxisome proliferator-activated receptor gamma coactivator-1alpha (PGC-1alpha) and mitostatin,” The Journal of Biological Chemistry, vol. 8, no. 289, pp. 4952–4968, 2014.

Y. Chen and G. N. Dorn, “PINK1-phosphorylated mitofusin 2 is a Parkin receptor for culling damaged mitochondria,” Science, vol. 6131, no. 340, pp. 471–475, 2013.

J. I. Castillo-Quan, “Parkin’s control: regulation of PGC-1α through PARIS in Parkinson’s disease,” Disease Models & Mechanisms, vol. 4, no. 4, pp. 427–429, 2011.

J. H. Shin, H. S. Ko, H. Kang et al., “PARIS (ZNF746) Repression of PGC-1α Contributes to Neurodegeneration in Parkinson’s Disease,” Cell, vol. 144, no. 5, pp. 689–702, 2011.

A. Torres, M. A. Gubbiotti, and R. V. Iozzo, “Decorin-inducible Peg3 evokes beclin 1-mediated autophagy and thrombospondin 1-mediated angiostasis,” The Journal of Biological Chemistry, vol. 12, no. 292, pp. 5055–5069, 2017.

T. Neill, C. Sharpe, R. T. Owens, and R. V. Iozzo, “Decorin-evokedaternally expressed gene 3 (PEG3) is an upstream regulator of the transcription factor EB (TFEB) in endothelial cell autophagy,” The Journal of Biological Chemistry, vol. 39, no. 292, pp. 16211–16220, 2017.

H. Zhao, H. Xi, B. Wei et al., “Expression of decorin in intestinal tissues of mice with inflammatory bowel disease and its correlation with autophagy,” Experimental and Therapeutic Medicine, vol. 6, no. 12, pp. 3885–3892, 2016.

J. Zeng-Brouwers, S. Pandey, J. Trebicka, M. Wygrecka, and L. Schaef er, “Communications via the small leucine-rich proteoglycans: molecular specificity in inflammation and autoimmune diseases,” The Journal of Histochemistry and Cytochemistry, vol. 68, no. 12, pp. 887–906, 2020.

M. C. Borges, V. Narayanan, R. V. Iozzo, and M. S. Ludwik, “Deficiency of decorin induces expression of Foxp3 in CD4+CD25+ T cells in a murine model of allergic asthma,” Respirology, vol. 20, no. 6, pp. 904–911, 2015.

Y. Z. Zhang and Y. Y. Li, “Inflammatory bowel disease: pathogenesis,” World Journal of Gastroenterology, vol. 1, no. 20, pp. 91–99, 2014.

G. Cafaro, C. Croia, O. D. Argypoulou et al., “One year in review 2019: Sjogren’s syndrome,” Clinical and Experimental Rheumatology, vol. 37, Supplement 118, pp. 3–15, 2019.

M. N. Manoussakis and E. K. Kapsogeorgou, “The role of intrinsic epithelial activation in the pathogenesis of Sjogren's syndrome,” Journal of Autoimmunity, vol. 3, no. 35, pp. 219–224, 2010.

E. Pontarini, D. Lucchesi, and M. Bombardieri, “Current views on the pathogenesis of Sjögren’s syndrome,” Current Opinion in Rheumatology, vol. 30, no. 2, pp. 215–221, 2018.

M. Ramos-Casals, P. Brito-Zerón, S. Bombardieri et al., “EULAR recommendations for the management of Sjögren’s syndrome with topical and systemic therapies,” Annals of the Rheumatic Diseases, vol. 79, no. 1, pp. 3–18, 2020.

S. Yamachika, J. Brayer, G. E. Oxford, A. B. Peck, and M. G. Humphreys-Beher, “Aberrant proteolytic digestion of biglycan and decorin by saliva and exocrine gland lysates from the NOD mouse model for autoimmune exocrinopathy,” Clinical and Experimental Rheumatology, vol. 2, no. 18, pp. 233–240, 2000.

J. Kiriłowski, R. A. Romano, E. M. Kasperk, G. Yu, and J. M. Kramer, “Activation of Myd88-dependent TLRs mediates
local and systemic inflammation in a mouse model of primary Sjögren's syndrome,” *Frontiers in Immunology*, vol. 10, p. 2963, 2019.

[79] J. Kiripolsky, E. M. Kasperek, C. Zhu et al., “Immune-intrinsic Myd88 directs the production of antibodies with specificity for extracellular matrix components in primary Sjögren’s syndrome,” *Frontiers in Immunology*, vol. 12, article 692216, 2021.

[80] K. F. Rabe and H. Watz, “Chronic obstructive pulmonary disease,” *Lancet*, vol. 10082, no. 389, pp. 1931–1940, 2017.

[81] B. W. van der Strate, D. S. Postma, C. A. Brandsma et al., “Cigarette smoke-induced emphysema,” *American Journal of Respiratory and Critical Care Medicine*, vol. 173, no. 7, pp. 751–758, 2006.

[82] C. A. Feghali-Bostwick, A. S. Gadgil, L. E. Otterbein et al., “Autoantibodies in patients with chronic obstructive pulmonary disease,” *American Journal of Respiratory and Critical Care Medicine*, vol. 177, no. 2, pp. 156–163, 2008.

[83] M. Karayama, N. Inui, T. Suda, Y. Nakamura, H. Nakamura, and K. Chida, “Antiendothelial cell antibodies in patients with COPD,” *Chest*, vol. 6, no. 138, pp. 1303–1308, 2010.

[84] P. Leidinger, A. Keller, S. Heisel et al., “Novel autoantigens immunogenic in COPD patients,” *Respiratory Research*, vol. 10, no. 1, p. 20, 2009.

[85] C. A. Brandsma, H. A. Kerstjens, W. H. van Geffen et al., “Differential switching to IgG and IgA in active smoking COPD patients and healthy controls,” *The European Respiratory Journal*, vol. 40, no. 2, pp. 313–321, 2012.

[86] D. Kruk, M. Wisman, H. G. Bruin et al., “Abnormalities in reparative function of lung-derived mesenchymal stromal cells in emphysema,” *American Journal of Physiology. Lung Cellular and Molecular Physiology*, vol. 320, no. 5, pp. L832–L844, 2021.

[87] C. A. Brandsma, W. Timens, M. Geerlings et al., “Induction of autoantibodies against lung matrix proteins and smoke-induced inflammation in mice,” *BMC Pulmonary Medicine*, vol. 10, no. 1, p. 64, 2010.

[88] J. D. Keene, S. Jacobson, K. Kechris et al., “Biomarkers predictive of exacerbations in the SPIROMICS and COPDGene cohorts,” *American Journal of Respiratory and Critical Care Medicine*, vol. 195, no. 4, pp. 473–481, 2017.

[89] J. C. Rodrigues, M. Haas, and H. N. Reich, “IgA nephropathy,” *Clinical Journal of the American Society of Nephrology*, vol. 12, no. 4, pp. 677–686, 2017.

[90] M. V. Nastase, A. Janicova, H. Roedig, L. T. Hsieh, M. Wygrecka, and L. Schaefer, “Small leucine-rich proteoglycans in renal inflammation: two sides of the coin,” *The Journal of Histochemistry and Cytochemistry*, vol. 4, no. 66, pp. 261–272, 2018.

[91] L. Schaefer, “Small leucine-rich proteoglycans in kidney disease,” *Journal of the American Society of Nephrology*, vol. 7, no. 22, pp. 1200–1207, 2011.

[92] X. Mao, Z. Xu, X. Xu et al., “TGF-beta1 inhibits the autophagy of podocytes by activating mTORC1 in IgA nephropathy,” *Experimental Cell Research*, vol. 1, no. 385, article 116170, 2019.

[93] J. S. Smolen, D. Aletaha, and I. B. McInnes, *Rheumatoid arthritis*, *Lancet*, vol. 10055, no. 388, pp. 2023–2038, 2016.

[94] L. Antonioli, M. Fornai, C. Pellegrini, S. Masi, I. Puxeddu, and C. Blandizzi, “Ectopic lymphoid organs and immune-mediated diseases: molecular basis for pharmacological approaches,” *Trends in Molecular Medicine*, vol. 11, no. 26, pp. 1021–1033, 2020.

[95] T. W. Groeneveld, M. Oroszlán, R. T. Owens et al., “Interactions of the extracellular matrix proteoglycans decorin and biglycan with C1q and collectins,” *Journal of Immunology*, vol. 7, no. 175, pp. 4715–4723, 2005.

[96] A. Polgar, A. Falus, E. Koo et al., “Elevated levels of synovial fluid antibodies reactive with the small proteoglycans biglycan and decorin in patients with rheumatoid arthritis or other joint diseases,” *Rheumatology (Oxford)*, vol. 42, no. 4, pp. 522–527, 2003.

[97] M. Dougados and D. Baeten, “Spondyloarthritis,” *Lancet*, vol. 9783, no. 377, pp. 2127–2137, 2011.

[98] J. Martel-Pelletier, A. J. Barr, F. M. Ciccitini et al., “Osteoarthritis,” *Nature Reviews. Disease Primers*, vol. 2, no. 1, p. 16072, 2016.

[99] K. Ozler, “Relationship between increased serum & synovial fluid decorin levels & knee osteoarthritis,” *The Indian Journal of Medical Research*, vol. 153, no. 4, pp. 453–458, 2021.

[100] Q. Li, B. Han, C. Wang et al., “Mediation of cartilage matrix degeneration and fibrillation by decorin in post-traumatic osteoarthritis,” *Arthritis & Rheumatology*, vol. 8, no. 72, pp. 1266–1277, 2020.

[101] T. Gronau, K. Krüger, C. Prein et al., “ Forced exercise-induced osteoarthritis is attenuated in mice lacking the small leucine-rich proteoglycan decorin,” *Annals of the Rheumatic Diseases*, vol. 76, no. 2, pp. 442–449, 2017.

[102] D. Keene, S. Jacobson, K. Kechris et al., “Mediation of cartilage matrix degeneration and fibrillation by decorin in post-traumatic osteoarthritis,” *Arthritis & Rheumatology*, vol. 8, no. 72, pp. 1266–1277, 2020.

[103] J. Luo, P. P. Ho, M. S. Buckwalter et al., “Glia-dependent TGF-beta signaling, acting independently of the TH17 pathway, is critical for initiation of murine autoimmune encephalomyelitis,” *The Journal of Clinical Investigation*, vol. 11, no. 117, pp. 3306–3315, 2007.

[104] H. Mohan, M. Krumholz, R. Sharma et al., “ Extracellular matrix in multiple sclerosis lesions: fibrillar collagens, biglycan and decorin are upregulated and associated with infiltrating immune cells,” *Brain Pathology*, vol. 5, no. 20, pp. 966–975, 2010.

[105] V. Haist, R. Ulrich, A. Kalkuhl, U. Deschl, and W. Baumgartner, “Distinct spatio-temporal extracellular matrix accumulation within demyelinated spinal cord lesions in Theiler’s murine encephalomyelitis,” *Brain Pathology*, vol. 22, no. 2, pp. 188–204, 2012.

[106] F. E. Lundberg, M. Fujimoto, J. Vencovsky et al., “Idiopathic inflammatory myopathies,” *Nature Reviews. Disease Primers*, vol. 7, no. 1, p. 86, 2021.

[107] Y. Kishioka, M. Thomas, J. Wakamatsu et al., “Decorin enhances the proliferation and differentiation of myogenic cells through suppressing myostatin activity,” *Journal of Cellular Physiology*, vol. 215, no. 3, pp. 856–867, 2008.

[108] K. P. Goetsch and C. U. Niesler, “The extracellular matrix regulates the effect of decorin and transforming growth factor beta-2 (TGF-beta2) on myoblast migration,” *Biochemical and Biophysical Research Communications*, vol. 479, no. 2, pp. 351–357, 2016.

[109] K. Fukushima, N. Badlani, A. Usas, F. Riano, F. Fu, and J. Huard, “The use of an antifibrosis agent to improve muscle recovery after laceration,” *The American Journal of Sports Medicine*, vol. 29, no. 4, pp. 394–402, 2001.
V. Mageriu, E. Manole, A. E. Bastian, and F. Staniceanu, “Role of Myokines in myositis pathogenesis and their potential to be new therapeutic targets in idiopathic inflammatory myopathies,” *Journal of Immunology Research*, vol. 2020, Article ID 9079083, 14 pages, 2020.

C. P. Denton and D. Khanna, “Systemic sclerosis,” *Lancet*, vol. 10103, no. 390, pp. 1685–1699, 2017.

T. Yamamoto, B. Eckes, and T. Krieg, “Bleomycin increases steady-state levels of type I collagen, fibronectin and decorin mRNAs in human skin fibroblasts,” *Archives of Dermatological Research*, vol. 292, no. 11, pp. 556–561, 2000.