Alpha2-antiplasmin: A New Target for Fibrotic Diseases

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Abstract

Fibrotic diseases are characterized by excessive scarring due to excessive production, deposition, and contraction of the extracellular matrix (ECM). However, the detailed mechanism underlying the development of fibrosis was unclear. Recently, it has been reported that alpha2-antiplasmin (α2AP), which is serine protease inhibitors (serpins), is associated with the development of fibrosis. This review considers the physiological and pathological roles of α2AP in the development of fibrosis, and proposes that α2AP may be a new target for fibrotic disease.

Introduction

Fibrotic diseases are characterized by excessive scarring due to excessive production, deposition, and contraction of the extracellular matrix (ECM). This process usually occurs over many months and years, and can lead to organ dysfunction or death. The development of fibrosis is generally considered to result from maladaptive repair processes induced by profibrotic factors such as transforming growth factor-beta (TGF-β) and connective tissue growth factor (CTGF). These profibrotic factors stimulate the formation of myofibroblasts via the differentiation from tissue-resident fibroblasts and bone marrow-derived mesenchymal stem cells (MSCs), and epithelial-to-mesenchymal transition (EMT). The accumulated myofibroblasts subsequently synthesize and deposit components of the extracellular matrix (ECM) [1-4]. However, the regulation and mechanism responsible for the development of fibrosis remain poorly understood. This review focuses on the role of alpha2-antiplasmin (α2AP) in the development of fibrosis.

The Expression of α2AP in Fibrotic Disease

α2AP is known to inhibit plasmin activity. Plasmin can directly and indirectly (activation of latent metalloproteinases (MMPs)) degrade some matrix proteins (collagen, fibronecctin, laminin, entactin, tenasin, thrombospondin and perlecan), which is the proteinaceous component of fibrotic tissue [28]. Additionally, plasmin can activate HGF, which contributes to antifibrosis [29, 30], and promote the apoptosis of myofibroblasts [31]. The inhibition of plasmin by α2AP may attenuate ECM degradation and induce myofibroblast deposition, and promote the development of fibrosis.

The Role of α2AP as a Plasmin Inhibitor in the Development of Fibrosis

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Conclusion

α2AP induces the production of TGF-β through ATGL, and is associated with myofibroblast formation, ECM synthesis. Conversely, α2AP inhibits plasmin activity, and then attenuates ECM degradation. It is quite likely that α2AP plays a critical role in the development of...
fibrosis such as myofibroblast accumulation and ECM deposition, and is a potential therapeutic target for fibrotic disease. The inhibition of α2AP-initiated pathways may provide a novel therapeutic approach to fibrotic diseases.

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