Matrix metalloproteinases and their role in psoriasis

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Cite https://doi.org/10.1016/j.gene.2014.01.068Get rights and content

Abstract

This review summarizes the contribution of matrix metalloproteinases to the pathogenesis of psoriasis. In psoriasis, matrix metalloproteinases are involved in the structural changes of the epidermis *via* the modification of intracellular contacts and the composition of the extracellular matrix, promoting angiogenesis in the dermal blood vessels and the infiltration of immune cells. Moreover, some matrix metalloproteinases become differentially expressed during the disease eruption and their expression correlates with the clinical score. A separate section of the review is dedicated to the pharmacological approaches that are used to control matrix metalloproteinases, such as oral metalloproteinase inhibitors, such as azasugars and phosphonamides.
The aim of this manuscript is to assess the role of matrix metalloproteinases in the physiological processes that accompany the disease. Moreover, it is especially important to evaluate progress in this field and characterize recently appeared medicines. Because any experimental drugs that target matrix metalloproteinases are involved in active clinical trials, this manuscript also reviews the latest experimental data regarding distribution and expression of matrix metalloproteinases in healthy skin and lesional skin. Therefore, the performed analysis highlights potential problems associated with the use of metalloproteinase inhibitors in clinical studies and suggests simple and easy understandable criteria that future innovative metalloproteinase inhibitors shall satisfy.

Introduction

Psoriasis is a chronic skin condition driven by the activated immune system. The manifestation of psoriasis includes essential histopathological changes in the skin (Fig. 1), such as a thickening of the prickle cell layer (acanthosis) with inward growing of rete ridges (epithelial buttressing) and an enlargement of the corny layer (hyperkeratosis). The internal tissue remodeling within psoriatic plaques includes the abruption or disappearance of the granular layer (hypogranulosis), excessive cell division in the extended suprabasal layer (hyperproliferation) and parakeratosis, i.e., the presence of nucleated cells in the corny layer. The eruption of the disease leads to dilation of papillary blood vessels in the derma and an infiltration of the epidermis by immune cells, such as leukocytes, neutrophils and macrophages. These cells trigger the “cytokine storm”, which is a massive secretion of proinflammatory cytokines and chemokines. In turn, the keratinocytes promote a new capillary growth *via* the production of VEGF. Moreover, psoriasis greatly accelerates cell turnover, it alters the terminal differentiation of keratinocytes, and impairs the degradation of desmosomes. This condition results in a compromising of the skin's barrier and creates opportunities for toxins and infectious agents to enter the body. This effect represents a potential health risk to the entire organism.
Matrix metalloproteinases (MMPs) are important for the stability of the extracellular matrix (ECM). They are crucial for both tissue homeostasis and the functioning of the skin in extreme and pathological conditions. Remodeling of ECM requires the cooperation between different groups of exo- and endopeptidases, because the preferential degradation of certain ECM proteins significantly changes the properties of one. In this review, we describe the role of matrix metalloproteinases in the pathogenesis of psoriasis.

Section snippets

Collagenases

Three mammalian collagenases (MMP1, MMP8, and MMP13) cleave fibrillar collagen types I, II, III, V, and IX, which are their principle substrates, as well as several other matrix and non-matrix proteins, including growth factors (Table 1). Collagenases cleave substrates at a specific glycine–isoleucine or glycine–leucine bond. This cleavage produces triple helical fragments that are degradable to gelatin. Although several sites can exist within a given substrate, cleavage typically occurs at

Role of MMPs in pathogenesis of psoriasis

Pathogenesis of psoriasis involves all of the major physiological processes in which MMPs actively participate (Fig. 2). MMPs have the ability to degrade all of the components of both the extracellular matrix (ECM) and the basal membrane (BM). Therefore, MMPs play an important role in tissue remodeling, cell migration, angiogenesis and epithelial apoptosis. During the remodeling, MMPs are required for the structural and compositional modifications of ECM and BM. With respect to angiogenesis and

Pharmacological control of psoriasis and metalloproteinase activity

Presently, a choice is available between several traditional options for the systemic treatment of psoriasis. Topical corticosteroids, (*e.g.*, clobetasol and betamethasone) are popular treatments for localized psoriasis. Corticosteroids have anti-inflammatory and anti-proliferative effects, and their action leads to vasoconstriction of the treated area. Although these medications are considered to be safe, using corticosteroids can cause certain adverse effects, such as skin atrophy, irritation,

Concluding remarks

The recent results of clinical trials suggest widening the spectrum of available anti-psoriatic drugs and a growth of potential interest to new medicines especially to the medicines that selectively target one or few genes and/or blocking a certain signaling pathway with a proven role in the pathogenesis of the disease. Although MMPIs have participated in clinical trials for psoriasis for a long time, a commercial interest to development of new MMPIs has declined. The main concerns regarding

Conflict of interest

The authors have no conflicts of interest.

Acknowledgments

This work was supported by a grant 16.512.11.2056 from the Ministry of Science and Technologies of the Russian Federation, and grant RFBR #14-04-01207 from the Russian Academy of Sciences ("Fundamental Sciences to Medicine" program).

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