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The role of mast cells in accelerating our skin aging

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Abstract

Everyone wishes to appear younger. Actually, women spend a lot of efforts and money to fight aging appearance of skin. In the recent decade, skin aging has become an annoying social and medical problem at the levels of modern societies. Unfortunately, up to now, scientists have not discovered an effective treatment to overcome the appearance of the elderly skin. Although, researchers try hard to discover the main causes and mechanisms of getting skin more aged to earn a youthful look for skin appearance, some researchers suggested that mast cells (MCSs) were scarcely found neither in fetus dermis nor the youth while they are clearly detected in dermis of senile people which proposes the function of these cells in controlling the process of skin caducity. Researchers have taken into consideration the beneficial effect of MCS in controlling skin caducity. Recently, MCS is considered as an effective route in treatment elderly skin. Non-synthetic products can inhibit MCS activation so considered as a good functional ingredient fighting skin aging process as this cell implicated in skin damage and aging; degranulation of papillary dermal MCS might result in inflammation, reconstruction of extracellular matrix and angiogenesis with subsequently induced skin caducity.

This mini review summarizes the crucial role of activated MCS in the dermal aging process.

Keywords: skin; aging; mast cell.

Introduction

Skin aging results from a combined change in both pathological and physiological process along with continuous changes, Hence, it leads to morphological damage as well as dysfunction of skin tissue [1]. Chronic sun exposure and smoking are considered the most two important factors profoundly impacts the epidermis and dermis resulting in the appearance of the signs of skin aging e.g skin wrinkle, sagging, and laxity [2].

Until now, no effective therapy is discovered to prevent or treat skin aging while the predicator study reveals that some skin aging mechanisms still are not discovered [3].

Mast Cells (MCS) are essential components of hematopoietic progenitor cells that are widely distributed throughout the connective tissue in the body [4]. MCs are mainly settled in the tissue which is contacted to the external surrounding such as

gastrointestinal tract, skin and nose [5]. Skin has multiple cutaneous immune cells, which share in evoking an immune response and inflammatory reactions when exposed to any type of forging particle [4].

It is well known that the degranulation of activated mast cells significantly modifies various aspects of physiological and pathological conditions in various settings [6]. With regard to the normal physiological functions, MCSs are reported to regulate vessels vasodilation, vascular homeostasis, innate, and adaptive immune responses [7,8]. On the other hand, mast cells have also been involved in the pathophysiology of various diseases e.g. allergy, asthma, anaphylaxis, gastrointestinal disorders, many types of malignancies, and cardiovascular diseases [4].

Additionally, they able to diffuse in the papillary dermis surrounding the blood vessels, However, they are rarely found in the deep dermis and almost absent in the epidermis [9]. Investigators have been suggested that the importance of mast cell in skin aging [10].

Recently, literatures documented that MCS granules are contributing a great diversity of sever toxic and active mediators [11]. MCs degranulation in papillary dermis leads to extracellular matrix reconstruction, angiogenesis, and inflammation with stimulated skin aging [12].

MCS can respond in several mechanisms: (a) when activated they release stores of pre-formed mediators. (b) they secrete mediators de novo in the absence of degranulation, or (c) a combination of two previous mechanisms can occur [13]. The MCS granules are in the form of MCs-specific and non-specific proteases (tryptase, chymase, cathepsin G), lysosomal enzymes (b-hexosaminidase), biogenic amines (histamine, serotonin, dopamine), cytokines (TNF, interleukin[IL]-4, IL-5), and growth factors (stem cell factor [SCF], basic fibroblast growth factor [bFGF]) [14].

Interestingly, activated MCS could stimulate degranulation of neighboring MCS *via* its paracrine effect e.g tryptase enzyme; released from this cell can induce histamine release from then neighboring in activated mast cells [15].

Origin of mast cells

Mast cells (Mcs) are immune cells derived from the myeloid lineage as progenitor cells then circulate in blood and home to various tissues [15]. Under the influence of various stem cell factors locally secreted by numerous cells in the tissue, these progenitor cells differentiates into Mcs; present only in tissue and are not found in circulation [16].

Mcs are found in loose (areolar) connective tissue throughout the body, mostly every organ. They play an important role in initiating the inflammatory cascade [17]. Innate or adaptive immune mechanisms can stimulate the mast cell to degranulate and release inflammatory mediators into the extracellular compartments [18]. Furthermore, Mcs are related to many pathologies e.g type I hypersensitivity reactions, mastocytosis, mast cell activation syndrome, and urticarial [19].

Mast cells structure

Mcs are considered as mononuclear cells. They characteristically by numerous small secretory granules, ranging from 0.2 to 0.8 um [19]. These granules are usually very dense so obscure the MCs nuclei. The IgE receptors are noticed in their plasma membrane which bind the Fc region of circulating IgE, to induce cell degranulation [20].

Two major types of MCs have been detected and are distinguished by the content of their secretory granules [21]. MCs cells contain mainly tryptase as well as chymase and carboxypeptidase [22]. Most these cells are settled in the submucosa and connective tissue adjacent to the conjunctiva and skin, also often adjacent to blood and lymphatic vessels. it was found that these cells play a potential role in tissue repair [23].

What makes our skin looks older?

Many factors make our skin appear older. Unfortunately, some factor we cannot fight it while others we can influence. The thing that we cannot influence is intrinsic aging, the natural aging sequence. With time, we all get visible wrinkles on our face. It is normal for our face to lose some of its elasticity and youthful fullness, and we notice our skin becoming thinner and drier. Our genes mainly control when these changes occur [24]. In contrast, we can suffer from another type of aging named extrinsic aging; our environment and lifestyle choices can make our skin to age prematurely. By taking some preventive actions, we can slow the hazard of this type of aging [25].

Effect of mast cell on collagen fiber

Histamine produced by mast cell is capable to stimulate keratinocyte cells to synthesis MMP-9, that accelerate migration of immune cell resulted in induce type IV collagen fragmented. Additionally, the remaining scanty dermal collagen fibers could be afforded by synthesis and accumulation of reactive oxygen species; increases with aging (Campa and Baron, 2018) eventually, this result in aggregation of destroyed collagen fibers and prohibition of normal synthesis for collagen fiber [26].

It was documented that the MC tryptase enzyme possessed a potential effect in inducing dermal matrix degradation in which being in agreement with who discovered active enlarged degranulated mast cells in aged dermal skin [12]. The tryptase enzyme is able to stimulate matrix metalloproteinase -9 (MMPs) synthesis [27] which is documented as the main enzymes contributing in degradation of ECM so leads to injury of ECM proteins mostly types I and III collagen; critical components of dermal extracellular matrix [28]. The activated MCS of skin lead to a potential raise in heparin levels as well as skin histamine in the aged group [12].

Interaction between mast and fibroblast cells

Dermal fibroblasts are the main cells managing synthesis, maintenance, and remodeling of the dermal extracellular matrix [29,30]. Found small fibroblast cells having inactive dark nuclei in dermal aged skin [29]. Demonstrated that with aging, fragmented little collagen, decreased fibroblast-ECM binding and mechanical forces, fibroblast shrinkage is resulted aligning with little collagen formation, and dermal histological integrity impairment [12]. Observed in her study the frequent contacts between the MCs and fibroblast cells. This cell to cell contact form is involving secretions of MCS products to the neighboring cells types and it was previously mentioned in MCS co-culture

and fibroblast cells [31,32]. Suggested that MCS enhance MMPs released from fibroblast cells either by direct cell to cell contact or indirectly *via* secretion of soluble mediators that elevate in case of high incidence of the Fc epsilon receptor I on MCS. These interactions has a great effect in triggering tissue remodeling.

Interaction between mast cell and eosinophil cell

It is assumed that MCS mediator likely allow some interaction with eosinophils including IL-5, (a potent survival and growth factor), CCL5 [(RANTES), a chemotactic molecule, chymase (eosinophil, apoptotic suppressor), tumor necrotic factor (chemotaxis and survival) and heparin (stabilize exotoxins) that interact with eosinophil-derived stem cell factor in order to elevate proliferation, differentiation and activation of MCS [33].

Interaction between mast cell and skin appendices

Large sized sebaceous glands were noticed by [12] in aged skin. This result is matching with [34] who explained this size due to the down regulation of cellular turnover [35]. reported that sebaceous gland function could be significantly controlled by histamine secreted from the dermal MCS. Sweat glands were also detected surrounded by active mast cells. This finding goes with [36] who explained it as the sweat glandular cells have proteinase-activated receptors; these receptors response to tryptase enzyme secreted from MCS.

Interaction between mast and macrophage cells

[37] found that, cultures of IgE sensitized, antigen-stimulated MCS mixed with macrophage cells subsequent lead to the secretion of more concentration of pro-inflammatory cytokines than either cell population alone [29]. Suggested that these cytokines released from macrophages decrease the synthesis of collagen fiber from the dermal fibroblast [29].

Interaction between mast cell and adipose cells

Degranulation of MCS near adipose cells was reported by [38] and it was explained as the adipocyte cells have sensory receptors for histamine secreted from the MCS which will result in enhancing lipolysis. It may explain the reduction of aged dermal fat [39].

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