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 foraging 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]. MCSs 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 MCSs 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 MCSs have been detected and are distinguished by the content of their secretory granules [21]. MCSs 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 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 MCSs 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.
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References


[22] Mohajer M, Kovanen PT, Bianconi V, Pirro M, Cicero AF, Saheb


