

IMMUNOCOMPETENT CELLS OF THE EPITHELIAL LAYER OF SKIN, CONJUNCTIVA AND ORAL CAVITY IN CONDITIONS OF DAMAGE, TRAUMA AND INJURY

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Annotation. Nowadays, the data on the topography, composition and functions of immunocompetent cells in the epidermis, as well as in the covering stratified epithelial lining of the conjunctiva and oral cavity have not been systematized. The interaction of these cells in the stratified (covering) epithelium during damage, trauma and injury remain poorly understood at immunohistochemical and electron microscopic manifestations. To clarify the role of the noted cells in the pathogenesis and s-nogenesis in damage and injuries of skin, mucosal layer of conjunctiva and oral cavity it is advisable to study comprehensively corresponding samples of these epithelia in humans and in experiments on small laboratory animals with an emphasis on the expression of MIF and its receptor CD74.

Keywords: *immunocompetent cells, stratified epithelium, MIF, damage, trauma, injury.*

Defects in the skin, in the mucosa of conjunctiva and oral cavity in humans often serve as “entry gates” through which various pathogenic factors enter the bloodstream, causing the development of life-threatening complications, or dramatically slow down the repairing of the region damaged after trauma or injury [1].

The stratified epithelium of human possesses till now insufficiently studied immune defense apparatus. Despite the more than 150-year history (1868) of the discovery and regular description of non-epithelial cells in the epidermis, in the epithelium of its derivatives,

also in the conjunctiva and the lining of the oral cavity, there is still no generally accepted systematization of possible types of noted cells, as well as - their functions, genesis, features of regeneration and migration. According to the researchers, the vast majority of these non-epithelial cells belong to the local immunocompetent elements of the stratified epithelium of one or another region. At the same time, data on their pathogenic role, diagnostic and prognostic value in pathologies of the skin, conjunctiva and oral cavity are extremely contradictory [2,3,4].

As regarding the human skin, to today it can be considered firmly established only that in the epidermis and epithelial structures of hair follicles are constantly present the differences of Langerhans cells and lymphocytes. There is almost no data on migrating monocytes and granular leukocytes in the epidermis of healthy skin [2,3,5].

The same applies to the epithelial covering of the conjunctiva, the immunocompetent cells of which remain poorly understood both in normal conditions and in conditions of damage, trauma and injury [4].

The situation is relatively better in relation to the epithelial layer of the oral cavity. So, to date, various leukocytes and Langerhans cells have been found in the covering epithelia of the oral cavity in humans.

It is indicated that in the absence of inflammation, mechanical damage and injury in the epithelium lining of the oral cavity, as well as on its superficial surface are found only a small number of neutrophilic granular leukocytes. It has been proven that neutrophils, possessing high phagocytic activity, are capable of causing the death of microorganisms by intracellular and extracellular mechanisms. Recently, a third antimicrobial mechanism of

neutrophils has also been described. It was found that when interacting with microbes, as well as under stimulation of cytokines, they are able to release the content of their granules and decondensed chromatin into the intercellular space in the form of thin filaments that form networks called NETs (neutrophil extracellular traps).

The mechanisms formation of NETs in humans under normal conditions, experimentally and in various pathological conditions require detailed study, especially from the standpoint of immunohistochemistry and electron microscopy.

Lymphocytes with relative constancy are found in the stratified epithelium, where they are located mainly in its deeper third. Their content in the epithelium of the oral mucosa is higher in areas covered with non-keratinized epithelium and about 40 times higher than in the epidermis [6]. About 40% of the lymphocytes in the epithelial sheath are mobile, but not activated. The behavior of lymphocytes population of the epithelium oral cavity with damage and injuries also requires a more detailed complex immunomorphological analysis.

Dendritic antigen-presenting cells (Langerhans cells) are derived from monocyte-like progenitors. These cells express CD1 α , S100 protein, Human Leukocyte Antigen (HLA / CD45), CD40, CD68, CD80, CD83, CD86, and langerin (CD207). Their precursors migrate into the blood stream from the red bone marrow, are evicted from the vessels of the lamina propria and move into the epithelium of the oral mucosa, conjunctiva and also into the epidermis. In the epithelium, the marked cells are located in the stratum spinosum, acquiring the ability to capture and elaboration exoantigens. It has been shown that Langerhans cells of the oral mucosa stimulate T-lymphocytes more efficiently than analogous cells of skin. Also, the motility and migration of about 70% of Langerhans cells was confirmed [6].

The features of the functioning and pathogenetic significance of Langerhans cells in the epithelial lining of the oral cavity with damage and injuries in humans also require a

comprehensive immunomorphological and electron microscopic study.

Immunocompetent cells of the epithelium of skin, conjunctiva and oral cavity in humans interact with epithelial cells. In particular, epithelial cells produce IL-1, colony-stimulating factors and TNF- α , which attract neutrophils, macrophages and affect the functions of Langerhans cells. In turn, Langerhans cells produce IL-1, which activates IL-2 secreting T lymphocytes. The latter is necessary for the proliferation of T cells capable of responding to antigenic effects [6, p.31-36].

At the same time, remain practically unexplored the features of the interaction of immunocompetent cells of stratified epitheliums of the skin, conjunctiva and oral cavity in humans with damage, injury and various traumas from the standpoint of immunohistochemistry and electron microscopy.

The functional morphology of immunocompetent cells of the epidermis, epithelium of the conjunctiva and oral cavity under the influence of various cytokines (interleukins, lymphokines, factors growth and inhibition) in the pathogenesis and sanogenesis of their damage, traumas and injuries needs a systematic study. Among these cytokines should be emphasized the macrophage migration inhibition factor (MIF).

Initially, MIF was found as a lymphokine involved in delayed hypersensitivity reactions and various functions of macrophages [7]. Recently, MIF has been overestimated as a pro-inflammatory cytokine and a pituitary gland produced hormone, that enhances endotoxemia.

It turned out that this protein is expressed in various organs. As regarding its secretion by the mucous membrane of the conjunctiva and the oral cavity, there are no exact data yet.

Among cytokines, MIF is unique in terms of its abundant expression and deposition in the cytoplasm of producer cells. MIF has anti-glucocorticoid effects [8]. Antibodies against MIF suppress tumor growth and tumor-associated angiogenesis, suggesting that MIF is involved not only in inflammatory and immune responses, but also in the growth of

tumor cells. It has been proven that this cytokine promotes the accumulation of monocytes / macrophages in the inflammation focus [9].

The results of separate researches demonstrate that in the absence of the putative primary MIF receptor - CD74 - this cytokine inhibits the migration of monocytes also through the "CXCR4" receptor. In other words, CXCR4 can mediate MIF signaling also in the absence of CD74. In addition, along with CD74, CXCR4 also serves as a coreceptor for MIF [10].

It was found that MIF and its receptor CD74 may be useful targets for reducing neutrophilic inflammation of the lungs and acute lung injury [11, 12].

As for the biochemical nature of MIF, it is interpreted in different ways. According to some authors, MIF cannot be clearly attributed to either cytokines, hormones or enzymes [13]

MIF is also expressed in the skin. Clinical evidence of increased expression of MIF in inflammatory diseases confirms the potential role of MIF in inflammation of the skin and, possibly, in its damage and injuries [14].

It is believed that MIF overexpression is a negative factor in diseases such as systemic sclerosis, atopic dermatitis, psoriasis, eczema, injuries of the skin and eyes by ultraviolet radiation [15]. However, the significance of the overexpression of MIF, its CD74 and CXCR4 receptors in other skin pathologies, including its damage and injuries at trauma, is currently unclear.

Although the expression of MIF in intact skin has been studied, little is known about the role of MIF in cutaneous homeostasis in general. There is evidence that its local expression is significantly induced upon injury, but the role of such overexpression in the subsequent repair process remains a source of controversy [16].

Conclusion. Thus, from the standpoint of immunohistochemistry and electron microscopy, the immunocompetent cells of the stratified (covering) epithelium of the skin, conjunctiva and oral cavity in humans are poorly understood, as well as in damage, trauma and injuries of these regions. To clarify the possible role of the noted cells in the pathogenesis

and sanogenesis of damage and injuries of skin, conjunctiva and oral cavity are required the complex immunomorphological and electron microscopic studies of samples of these epithelia in humans and in experiments on small laboratory animals.

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ZƏDƏ, TRAVMA VƏ YARALANMA ŞƏRAİTİNDƏ DƏRİNİN, KONYUNKTIVANIN, AĞIZ SELİKLİ QIŞANIN İMMUNOKOMPETENT HÜCEYRƏLƏRİ

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Annotasiya. Hazırda epidermisin, həmçinin konyunktivanın və ağız boşluğu çoxqatlı (örtük) epitelinin immunokompetent hüceyrələrinin topoqrafiyası, tərkibi və funksiyaları haqqında məlumatlar sistemləşdirilməmişdir. Zədələnmələrdə, travmalarda və yaralanmalarda örtük epitelində bu hüceyrələrin qarşılıqlı əlaqələrinin immunhistokimyəvi və elektronmikroskopik təzahürləri səthi araşdırılmışdır. Dərinin, konyunktivanın, ağız selikli qişasının zədələrinin və yaralanmalarının patogenezinə

və sanogenezində qeyd olunan hüceyrələrin rolunu aydınlaşdırmaq üçün insanlarda və üzərində eksperimentlər aparılmış kiçik laborator heyvanlarında müvafiq epitel nümunələrinin, MİF və onun reseptoru CD74 ekspressiyasına xüsusi diqqət yetirməklə, kompleks tədqiqi məqsədəuyğundur.

Açar sözlər: immunokompetent hüceyrələr, çoxqatlı epitel, MIF, zədələnmələr, travmalar, yaralanmalar.

ИММУНОКОМПЕТЕНТНЫЕ КЛЕТКИ ЭПИТЕЛИАЛЬНОГО СЛОЯ КОЖИ, КОНЬЮНКТИВЫ И ПОЛОСТИ РТА В УСЛОВИЯХ ПОВРЕЖДЕНИЯ, ТРАВМЫ И РАНЕНИЯ

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Аннотация. На сегодняшний день не систематизированы данные о топографии, составе и функциях иммунокомпетентных клеток в эпидермисе, эпителиальном покрове конъюнктивы и полости рта. Остаются малоизученными иммуногистохимические и электронно - микроскопические проявления взаимодействия указанных клеток в многослойных (покровных) эпителиях при повреждениях, травмах и ранениях. Для уточнения роли отмеченных клеток в пато-

генезе и саногенезе кожных, конъюнктивальных и оральных повреждений и ранений целесообразны комплексные исследования образцов этих эпителиев у человека и при экспериментах на мелких лабораторных животных с акцентированием внимания на экспрессии MIF и его рецептора CD74.

Ключевые слова: иммунокомпетентные клетки, многослойный эпителий, MIF, повреждения, травмы, ранения.