

Is a Deep Dive into the Pathogenesis of Aging Could be a Missing Key to Personalized Skin Care?

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Received: 10 Apr 2023

Accepted: 02 May 2023

Published: 10 May 2023

J Short Name: AJSCCR

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Keywords:

Dermatology; Skin; Aging; Genetics; Personalized medicine

Citation:

Sepetiene R. Is a Deep Dive into the Pathogenesis of Aging Could be a Missing Key to Personalized Skin Care?. *Ame J Surg Clin Case Rep.* 2023; 6(11): 1-6

1. Abstract

1.1. Background: Scientists are looking to discover the basic components which could allow slowing the natural aging progress, focusing on fundamental findings following new treatment technologies. Overview of established external and internal factors, underlying definitions of genetics background, working on various skin properties, new capacities of diagnostics and treatment worldwide.

1.2. Methods: The review identifies full text articles in English on NCBI database with keywords: skin aging, skin genetics, clinical treatment of skin conditions, personalized skin care. The period filtered up to 10 years. 46 articles have been found and 32 publications were chosen for final evaluation and references.

1.3. Results: Recently published investigations support the finding that up to 60% of skin aging is caused by genetic factors, while the remaining 40% is due to other, environmental factors. Dermatologists and other skin care specialists suggest searching for optimal diagnostics methods focusing on each individual skin singularity approaching the best result to slow down the visible signs of aging process.

1.4. Conclusions: Performed individual testing followed by personalized care or treatment could work for better results on personalized medicine, allowing the possibility of genetical signature implementation with subsequent skin investigation in full.

2. Introduction

Our skin is the largest and most visible tissue in the body. A composition of the epidermis, with its five layers of epithelial tissue, and the derma (cutis), consisting of connective tissue. Under the derma, one more layer of subcutaneous tissue - the hypoderma (Figure 1). The deep understanding of the pathogenetic mechanisms involved within skin functionality based on the structural components and their localization give us a full picture. The skin performs various vital functions such as protection, thermoregulation, immune response. A unique design of each person's skin with different look which we assume as level of beauty. Such qualities as elasticity, plasticity, hydration, capability to form wrinkles with different formulation of architectonic view on the basis of variable shades of colors create a specific look which is defined as beautiful and healthy skin or formulate an opposite definition. All the time scientists are looking to discover the basic components or background which could allow to stop or to slow down the natural aging progress. We single out a biological and social age of an individual. More often we can conclude that the differences between these two categories varied from few to dozens of years to one or opposite side of the own nature. Recently published investigations support the finding that up to 60% of the skin aging can be determined to genetic factors, while the remaining 40% is due to other, environmental, non-genetic factors [1].

Biological or chronological skin aging is an inevitable physiolog-

ical process that depends on the own genetic outcomes plus environmental modulators working on epigenetics. During chronological aging physiological functions of the organism which work for metabolism and organ, or tissue remodeling are getting slower. This biological skin aging depends on time, which determines

changes in human appearance and functions, which definitely are seen on our skin [2].

This review focuses on research topics with value to determine the main reasons and outcomes for skin aging personalized definition with possible clue for innovative approach.

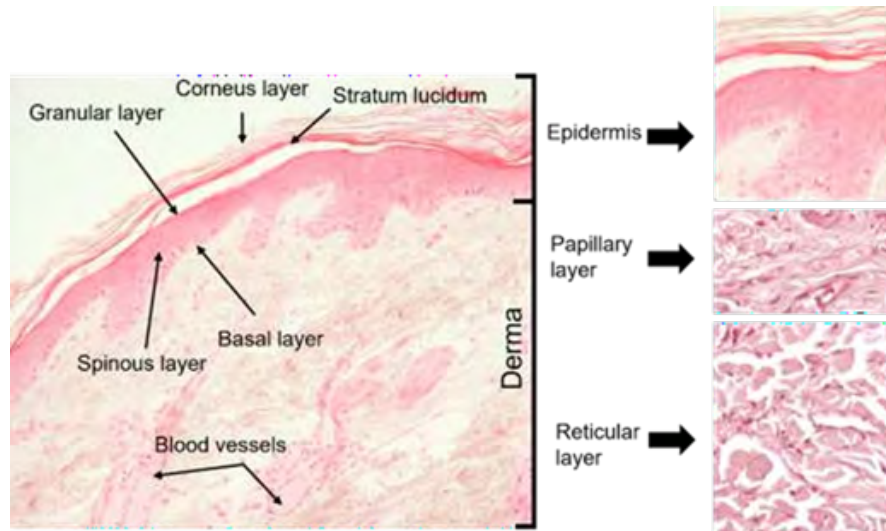


Figure 1: Histological view of skin (H&E staining).

2.1. External or falling inward factors influencing our skin look

Conditions around us definitely have vast and variable impact to the skin and some of them are known long time ago and only recently their pathogenesis has been cleared enough. External factors accelerate the biological processes of skin aging [3]. The main known external factors that cause skin aging are ultraviolet rays of the sun, smoking, polluted environment, lifestyle features, gravity, poor skin care [4].

Ultraviolet light is very dangerous affecting all three layers of the skin: the epidermis, derma and hypoderm (Figure 1). UV rays cause different changes such as skin hyperpigmentation, carcinoma, accelerate loss of skin moisture and wrinkles formation. UV rays affect the skin's regeneration processes, destroying the structure of collagen and elastin, slowing healing or inflammation processes (Figure 2). UV rays with high concentration may cause local dilatation of the blood vessels or even burn affected area with subsequent hyperpigmentation or discoloration and formation of wrinkles and scars [2]. Known molecular mechanisms of reactive oxygen species (ROS) effect for skin through the cascade of different players starting from mitochondrial electron transport chain following subsequent enzymes and receptors activation and/or inhibition with final decrease and suppression of collagen structures [5].

Other external factors that have a significant effect on skin health

and look are lifestyle features – inappropriate nutrition, smoking habits, alcohol, stress, improper skin care. The skin mostly visibly reflects the general state of human health. A healthy, balanced diet improves skin condition [4]. Known value for skin of various vitamins and microelements. Vitamin C is involved in melanin synthesis, A - in keratin production; A, E, D activate metabolism of proteins in the epidermis, vitamin PP reduces the skin's sensitivity to UV light. Water soluble vitamins C, B, B2, B7 and others deficiency adversely affects the general condition of the skin. Also, deficiency of vitamins is changing pigmentation, peeling of the skin, graying, loss of elasticity [6].

One of the important factors affecting skin look is the influence of psychological stress. The response of modern human to stress elucidates the molecular mechanisms of external skin aging but does not fully address human resistance to stress or its consequences. Gene expression, cell identification, and mechanisms of their functionality are responsible for the adaptive response to stressful events an eventually age-related comorbidities to the epigenetic modifications [7].

No doubt, that intake of antioxidants, retinoids or application of other 'modern' stem cell therapies [8], separated own blood components, combining them locally and penetrating 'per os' or injected by various methodologies into a body, help to maintain good skin health.

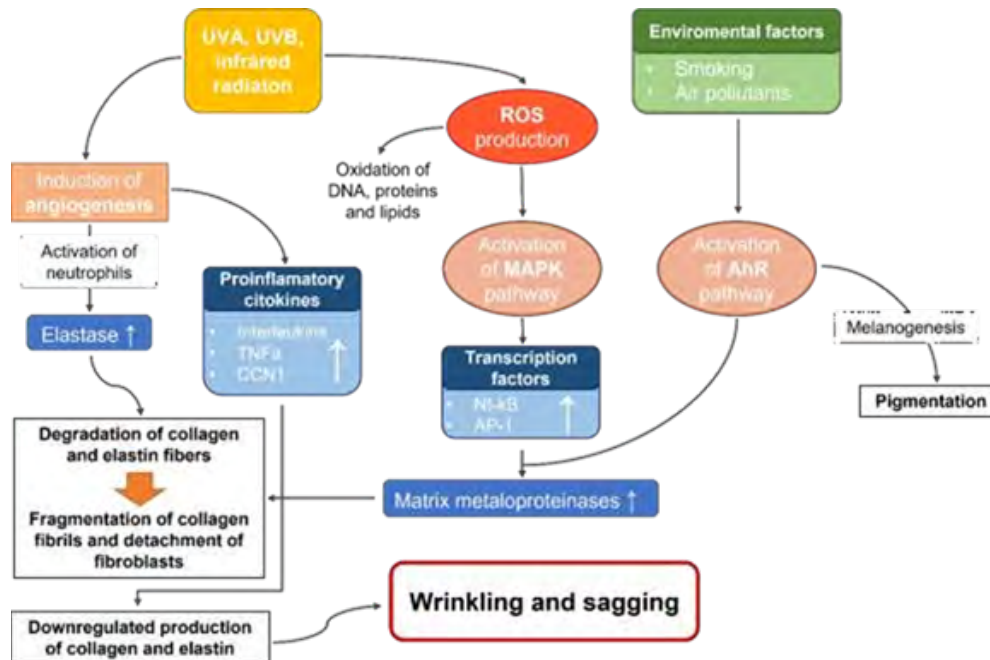


Figure 2: Schematic overview of skin aging mechanisms. Adapted from Kim, M. & Park, H. J., 2016 9.

2.2. Supportive skin properties: structured proteins

Collagen, located in the intercellular matrix, plays an important role in determining the physiology of the skin, maintaining the structure of the skin, and being directly involved in many of its functions. It is an important protein that enhances the appearance of the skin and is responsible for the firm look of the skin as the intercellular matrix retains water and maintains a smooth, firm and strong skin. The structure of collagen consists of three chains that wrap around each other and form a strong collagen spiral. In this way, the spirals merge into even larger and stronger fibers with high and tensile strength [10]. In terms of dermatological examination skin hydration, elasticity, roughness and density use to be assessed evaluating collagen functionality. Dr Bolke with colleagues performed the randomized clinical trial measuring the qualities by cytometry, craniometry and concluded that skin aging could be affected with administration of collagen peptides intake. The study participants also referred that their skin look has been significantly improved [10].

Elastin is another protein found in various connective tissues and its special quality to work for skin elasticity. Elastogenesis taking place in the superficial dermis. From the synthesis of tropoelastin

monomer on the endoplasmic reticulum with subsequent help of elastin binding proteins and establishing the structures with stable and structural functionality within the skin [11]. Elastin plays a crucial role in photoaging after its interaction with UV radiation. There is known skin condition called solar elastosis with dystrophic elastin fibers accumulation after UV exposure [12].

Other molecular components known to collagen and elastin (Figure 3) physiological pathway play an important role supporting each individual's physiological elasticity not only of skin. Fibrillin, fibrinogen, fibronectin, fibulin, thrombospondin, laminin and tenascin are found in several connective tissues and their complexity of functioning is widely investigate by scientists [13,14]. For instance, Fibrillin is important for elastic fibers construction. Known Fibrillin-1 mutations cause weakness and fragility of vessels with subsequent aneurysms and dissections of aorta also this genetical defect is closely related with Marfan syndrome manifestation [15]. The main functionality of these molecular components getting together is based on extracellular matrix role with formation of elastic fibers and participation within cell migration, adhesion and other functions formulating the stability and robustness of skin [14].

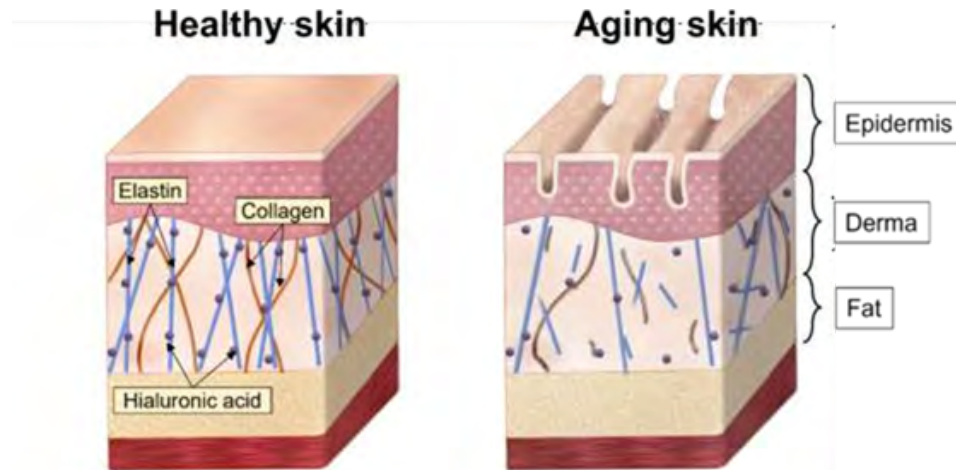


Figure 3: Collagen and elastin role in skin aging. Fragmentation of collagen fibrils and decreased production of both, collagen, and elastin lead to alterations of skin properties, such as wrinkling or sagging. Atrophied collagen fibers and decrease in hyaluronic acid are identified as two major determinants in skin aesthetics during aging.

2.3. Genetics as a background of “looking good”

In recent studies scientists are focused for genetical investigations developing new strategies how to detect the genes directly responsible for skin aging and how to find innovative methods to treat aging skin condition. Already known two main categories of people with clear impact on skin: the gender specific and population specific subjects [16]. Especially in recent years many discussions and possibilities about the perceived and chronological age take place in popular media. Dermatologists and the scientists must be at least few steps ahead to fulfill the expectations of the populations not to be healthy only but also to be beautiful. This perception works to deep dive into physiology of skin structure finding out an updated understanding and innovations for treatment.

The published studies on genetic background and skin aging open new possibilities. Starting from genetic signatures on described actual frequency of genetic polymorphisms and their distribution [1], following other findings which work for DNA damage, telomere shorting, miRNA regulation, accumulation of advanced glycation end products [8].

The end of the first decade of this century was rich of investigations with telomeres and their impact for aging. The fact that telomeres becoming shorter with each cell division resulting cellular senescence [17] was confirmed with telomerase deficient mice [18] and subsequent findings of alterations by UV radiation [19] concluded the telomeres role. Another mechanism with miRNA dysregulation with target on hyaluronan synthase 2 (HAS2) showed increased miR-23a-3p expression affecting hyaluronan synthesis directly involving response of fibroblasts decreased with age [20]. Worth to mention non-enzymatic glycation involved in intrinsic and extrinsic aging. Dermal proteins become stiff and reduce the elasticity under their responsiveness to glycation [21]. Known resistance of glycated collagen to MMP degradation works the same direction with exposure and aging [8].

On another hand mutations caused progeroid syndromes, some of them are well known under Down [22], Werner [23], Hutchinson-Gilford [24] names manifesting with rapid appearance of aging beginning until the adolescent period or even in the early childhood or cachectic children diagnosed with Cockayne syndrome with prematurely aged face [25] or Rothmund-Thomson syndrome also called genodermathosis as rare condition that affects whole body with damage of skin [26] - help us to formulate another hypothesis of genetic skin complexity and applicability to common vitality processes.

2.4. Combined investigations for personalized skin care

Trying to summarize known methods of skin care main dilemma always exists- is it works to everyone depending on individually visible features of different degrees for dry, greasy, elastic or wrinkle body. There are modern and comprehensive technologies defining skin properties status nowadays. From diascopy office based technics to developing an artificial intelligence based tool for skin condition diagnosis in tele dermatology [27].

More often we hear the necessity to employ an evidence based skin care methodologies and subsequent therapies [28] for dermatological patients. The research from cosmetic industry run randomized trials to identify and compare clinical evidence of benefits from simple routine to advanced skin care procedures [29] concluding that personal daily procedures work for short time but performing persistent habits may prevent skin aging. The dermatologists and skin care specialists widely agree that our skin needs individual synergistic and combined services with united cosmetic dermatologists and surgeons' team especially for getting older people [30].

Any evaluation of individual's skin features, capacity for outstanding to external or internal damaging factors lies on overall medicine technologies and deep understanding of total picture from diagnostics to care or treatment. In the light of personalized and individual medicine the combined investigation starting from de-

tecting gens 1, biochemistry, immunology findings and subsequent professional help with confirmed agents for treatment may start a new era fighting with skin aging [31]

3. Conclusions

Regarding of individual properties and signs of skin aging the comprehensive understanding of combined processes pathogenesis 4 should be an outcome to start developing personalized dermatological approach with a team of genetics, dieticians, biochemists, plastic surgeons and, of course, cosmetologists to be involved.

Blood test results, defining biochemistry, hematology, immunology parameters might correlate with skin look and aging 32. Moreover, combining different findings from genetic background with routine blood test results plus multivariable environment factors affecting not only health understanding in general, but determination of healthy look might be valuable algorithm to determine and predict personalized skin outcomes.

4. Acknowledgements

We would like to sincerely thank Lithuanian University of Health Sciences, Department of Histology and Embryology for providing histology images of the skin.

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