Mini Review

Is the Aging Code Genetically Determined at Birth or can we Control the Process by Epigenetic Factors such as Sun Exposure and Nutrition?

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Abstract

Aging shows first on our skin and depends on a variety of factors: Heredity, diet, lifestyle, personal habits, and exposure to the sun. Recent research showed that using data generated by the Human Genome Project-the international effort to decode human DNA-researchers have found 1,500 separate genes that govern how long people stay free from wrinkles. Out of the 20,000-25,000 known human genes, they found about 1,500 that play a key role in aging skin. Skin ages in eight different ways, each controlled by its own group of genes.

Environmental or epigenetic factors, such as sun exposure and diet, have a major impact on the aging process in general, and on skin aging in particular. The balance between the gene code for aging and the environmental/epigenetic factors that we are exposed to during our life can determine how we eventually age. This brief review covers the genetic, environmental, and dietary factors that impact skin aging.

ABBREVIATIONS

ROS: Reactive Oxygen Species; UVR: Solar Irradiation also known as Ultraviolet Radiation; MMP: Matrix Metallo Proteinase; ECM: Extra Cellular Matrix

INTRODUCTION

Genomics of skin aging

Scientific advances over the last two decades on the human genome [1], along with innovations for understanding the skin aging process by using genomics technology, has provided insights into the molecular events that trigger skin aging [2-4]. In fact, out of the 20,000-25,000 known human genes, skin scientists have reported that 1,500 different genes play key roles in skin aging [5]. Ties man NY Daily News 2009 see reference section.

It is thought that skin aging is related to in eight different factors, each controlled by groups of genes that maintain dermal health. These factors are: 1) chronological aging; 2) photo aging or exposure to the sun; 3) collagen, elastin, and other extracellular proteins; 4) inflammation;5) skin growth, repair, and/or rejuvenation; 6) antioxidants; 7) hydration; and 8) protection against various insults, such as Reactive Oxygen Species (ROS). In this regard, the identification of genes promoting youthful skin has been reported [6,7].

Pertaining to natural compounds especially found in dietary sources that can influence human-skin gene expression via antioxidants and other mechanisms, only a few polyphenolic molecules have been examined. For instance, resveratrol and equol are polyphenolic molecules found in plants and food products that have been shown to positively impact human-skin gene expression [8,9].

UVR induces oxidative stress, leading to skin aging

Repeated exposure to solar irradiation (UVR) is among the principal environmental factors contributing to the aging process of the skin, accompanied by the progressive impairment of epidermal stem-cell function [10]. Ultraviolet A (UVA) and ultraviolet B (UVB), known as mutagens, and long-term exposure to sunlight are associated with photo aging and the formation of skin cancers [11]. Photo aging is mediated through the direct and indirect toxicity of UVR to the DNA [12]. Photo aging is expressed in increased skin pigmentation, loss of skin elasticity, and the appearance of wrinkles.

The direct effect of UV irradiation occurs when DNA absorbs photons from UVB. This results in structural rearrangement of nucleotides that then leads to defects in the DNA strand.
UVR induces ROS (Reactive Oxygen Species) production, leading to DNA damage and skin aging. ROS production can also be a by-product of cell exposure to environmental factors, such as ionizing radiation, pollutants, cigarette smoke, alcohol, heavy or transition metals, and certain drugs [13-15]. ROS include not only free radicals, such as superoxide anion radical ($O_2^-$) and hydroxyl radical (OH•), but also non radicals, such as singlet oxygen ($O_2^*$) and hydrogen peroxide (H$_2$O$_2$). ROS play a dual role as both harmful and useful molecules in the cell; as such, an appropriate level of ROS is needed for the normal physiological function of mammalian cells and, therefore, it is essential for life.

**ROS induce wrinkles**

UVR causes ROS production that breaks down the collagen and elastin fibers in the dermal skin layer. These fibers form the skin's connective tissue. They are located under the surface of the skin (under the epidermis), and they support the skin. Breaking down this layer causes the skin to become weaker and less flexible. The skin then starts to droop, and wrinkles appear.

ROS induce skin fibroblasts to secrete high levels of matrix metalloproteinases (MMPs), which cause extracellular matrix (ECM) remodeling in dermal layers [16-19], and accelerate the formation of wrinkles and the loss of skin elasticity.

In addition, long-term UVR exposure can cause restructuring of the extracellular matrix. Proteins in extracellular-matrix components contain UV-absorbing chromophores that are vulnerable to UV-induced structural changes [20]. UV-induced changes in ECM are well characterized. UVR exposure not only up regulates the expression of MMP-1, MMP-2, MMP-3, MMP-7, MMP-9, and MMP-12 [21], but also promotes a pro-oxidative environment in human skin, by which the structure of the skin will be further damaged.

**Prevention of wrinkle formation by natural antioxidants**

Photo aging can be prevented and treated by strengthening the antioxidant defense of skin cells. Our body has non-enzymatic and enzymatic antioxidant systems that work in a complex network to maintain the optimal level of ROS in the cells or a redox balance by several mechanisms. These mechanisms work to neutralize oxidants, inhibit oxidative damage, and regulate transcription factors involved in redox and scavenging reactions [22]. The proliferation and differentiation of human cells underlie a delicate control of several signaling pathways [23]. The balance of redox homeostasis and the regulation of ROS-mediated signaling are part of the central regulation involved in self-renewal, proliferation, and the differentiation of normal stem and progenitor cells in human tissues, including the skin [24].

The endogenous antioxidants function as a crucial defense system to preserve redox balance required for regulation of epidermal homeostasis and to prevent ROS-induced skin damage [25]. Important endogenous antioxidants include enzymatic antioxidants, such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase, and thioredoxinreductase, and nonenzymatic antioxidants or low molecular-weight antioxidants, such as ascorbate or vitamin C, glutathione (GSH), and α-tocopherol or vitamin E [25]. SOD is an important antioxidant enzyme that converts $O_2^-$ into H$_2$O$_2$, which is finally degraded into water by CAT and GPx.

Excess of ROS generated by UVR, smoking, pollution, illness, or other processes can promote oxidative stress that can damage cellular structures and biomolecules, including lipids, proteins, and DNA, and can also interfere with normal signaling cascades, and collagen and elastin degradation.

One of the new approaches for dealing with a lack of endogenous antioxidants and the potential excess of ROS is to provide an external supplement of natural antioxidants. An external supplement of powerful antioxidants of all kinds can indeed change the aging code determined by our genes. Some of these natural and novel antioxidants belong to a family of compounds called flavonoids, also known as vitamin P.

The new generations of antioxidants are chemically stable and not sensitive to changes in temperature or exposure to oxygen and, thus, they maintain their long-lasting activity and are able to scavenge ROS and prevent skin aging. One of the mechanisms related to flavonoids is the inhibition of matrix metalloproteinases (MMPs), which are responsible for elastin degradation and the appearance of skin wrinkles [21].

Some flavonoids can be consumed in food and some can be added as food supplements.

Over 6,000 flavonoids have been identified, many of which occur in fruits, vegetables, and beverages (tea, coffee, beer, wine, and fruit drinks). Flavonoids have aroused considerable interest recently because of their potential effects on human health: they have been reported to exhibit anti-viral, anti-allergic, anti-platelet, anti-inflammatory, anti-tumor, antipatelet, and antioxidant activities. Flavonoids are also further divided into flavones, flavonols, isoflavones, and flavanones, each with a slightly different chemical structure [26,27].

Almost all fruits, vegetables, and herbs contain certain amounts of flavonoids. They can also be found in other food sources, including dry beans, grains, red wine, and green and black teas. The general rule is that the more colorful a food item is, the richer it will be in flavonoids. Oranges, however, are an exception to the rule because the flavonoids they contain are mainly found in the white and pulp interior of the fruit skin.

The best way to ensure a good intake of flavonoids is to consume plenty of fresh fruit and vegetables on a daily basis. Experts advise eating five servings of vegetables and four of fruit. Regarding the intake of red wine, men are advised not to drink more than two glasses per day and women should not drink more than one glass per day. Flavonoid supplements are also available, but an excess intake might be harmful.

Frequently researched antioxidants, such as carotenoids, tocopherols and flavonoids, as well as vitamins (A, C, D, and E), essential omega-3 fatty acids, some proteins, and lactobacilli, have been mentioned as agents capable of promoting skin health and beauty [28-30].

**CONCLUSION**

We can enhance skin protection against oxidative stress and skin aging if we support the endogenous antioxidant system by...
Vitamin P (flavonoids) is the most popular antioxidant in most consuming food rich in antioxidants such as fruits and vegetables. A regular consumption of it can help prevent the chronological aging determined by our gene code.

REFERENCES


