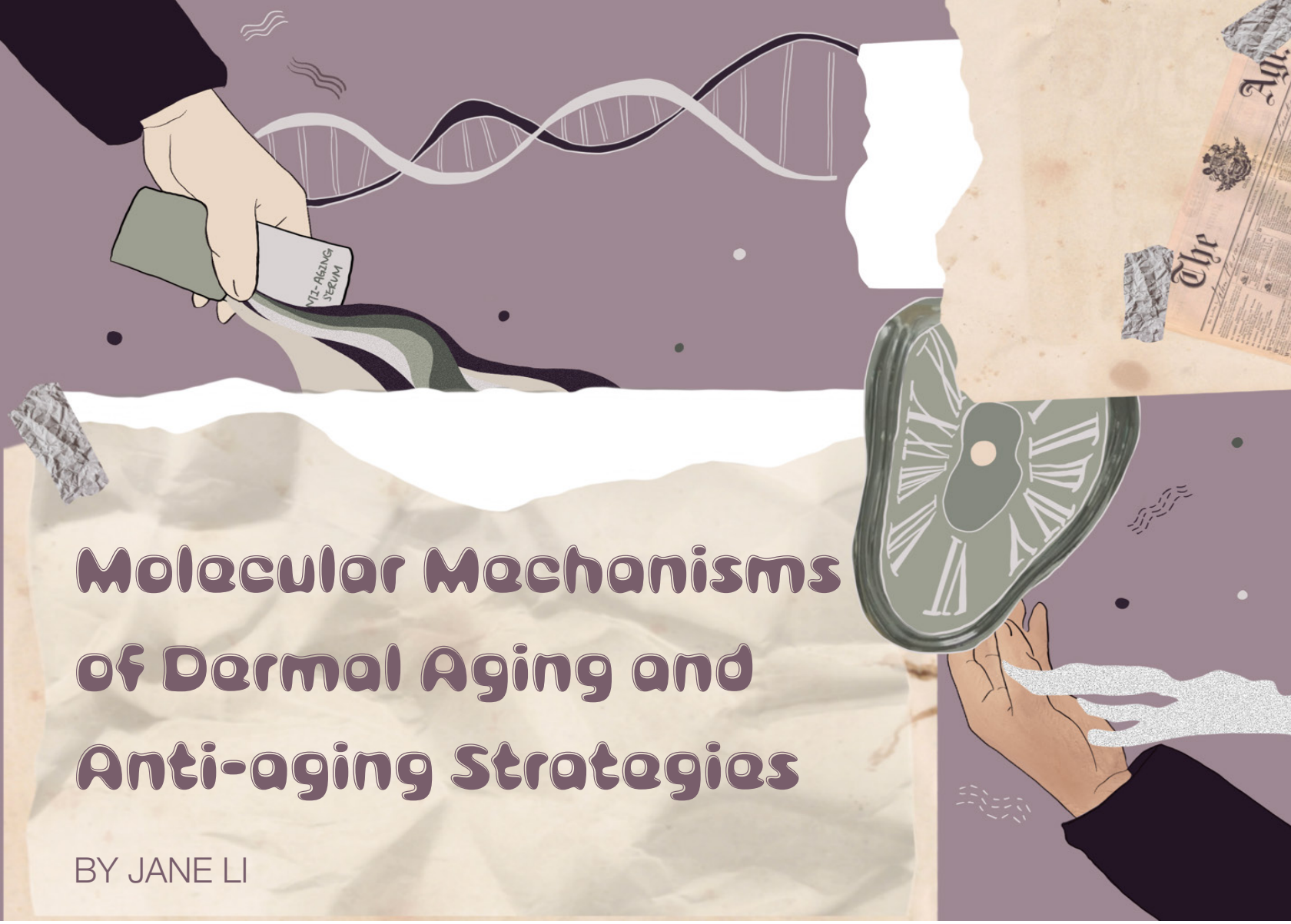


Molecular Mechanisms of Dermal Aging and Anti-aging Strategies

BY JANE LI

The tragedy of old age is not that one is old, but that one is young. —Oscar Wilde, *The Picture of Dorian Gray*

"Time flies" is a phrase we hear often, and the most intuitive evidence of time ticking is the universal process known as aging. For decades, scientists have been actively investigating the mechanisms of aging and researching ways to combat this natural process and its associated diseases. Extensive research has been dedicated to prolonging the lifespan; however, an increased lifespan does not necessarily imply an improved quality of life for those additional years. As an approach to improving life satisfaction, people have been focusing on aging more healthily while combating the most prominent and visible aspect of biological aging—dermal aging. Advertisements of products that claim to reverse wrinkling have generated waves of consumption, market competition, and substantial social anxiety in society. Age discrimination and appearance anxiety have also intensified for professional or social occasions, predominately for women. As dermal aging gains more public attention, it would be beneficial for individuals to comprehend the science behind aging to better understand current anti-aging strategies and face their own aging more rationally.

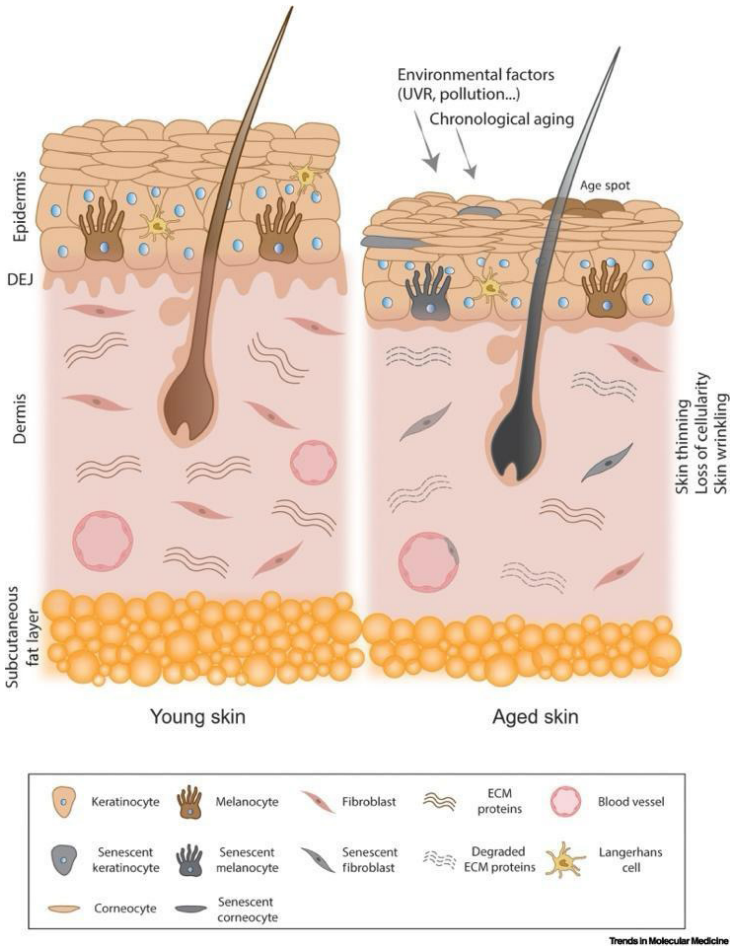
THE HUMAN SKIN

Before discussing theories of dermal aging, it is necessary to introduce the skin—our body's largest organ.

Human skin consists of three main layers: the epidermis, dermis, and subcutaneous fat layer.[1,2] The epidermis, the outermost layer, primarily contains keratinocytes that synthesize keratin and melanocytes that synthesize melanin. Keratin forms a protective layer outside the skin, while melanin is the pigmentation cell responsible for skin color.[3] The dermis is a connective tissue layer that consists of mainly fibroblasts and an acellular component known as the extracellular matrix (ECM). Collagen fibers and elastin are the primary components of ECM, contributing to the skin's elasticity.[4]

DERMAL AGING: THE IMBALANCE OF SKIN HOMEOSTASIS

Skin cells regenerate and turnover rapidly—new skin cells replace the keratinocytes that are lost due to normal cell division or injuries.[5] These new skin cells arise from stem cells and are defined by their ability to self-renew and give rise to specific cell types in mature adult tissues. This process of skin regeneration is called homeostasis, the dy-



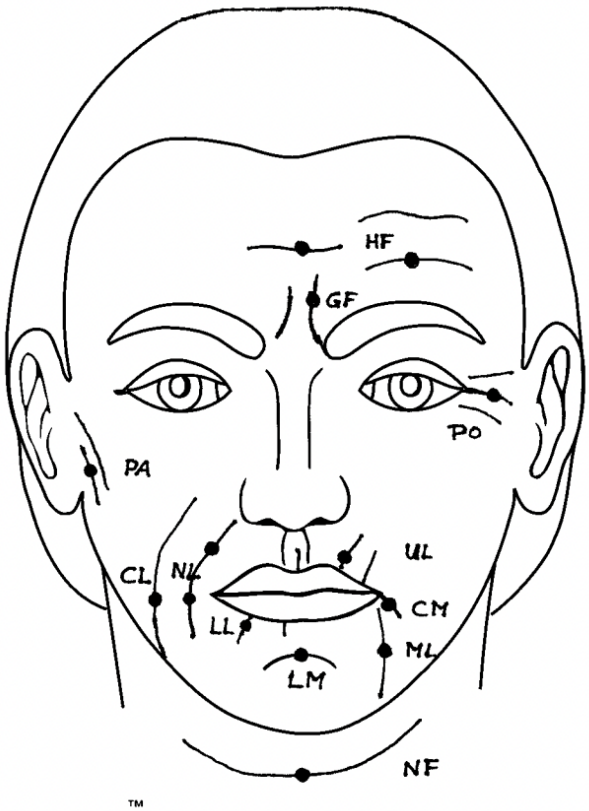


Figure 1 a (left) and b (right): *1a presents the structural difference between young and aged skin. 1b illustrates anatomic reference points for different types of wrinkles. HF, horizontal forehead lines; GF, glabellar frown lines; PO, periorbital lines; PA, preauricular lines; CL, cheek lines; NL, nasolabial folds; UL, upper radial lip lines; LL, lower radial lip lines; CM, corner of the mouth lines; ML, marionette lines; LM, labiomental crease; NF, horizontal neck folds.*

namically balanced state within the body in response to change that allows it to function properly. Aging is characterized by slower skin cell regeneration and results from imbalanced dermal homeostasis.

Dermal aging is a multifactorial process that results from intrinsic aging and extrinsic aging. Intrinsic aging is genetically determined and age-related. On the other hand, extrinsic aging results from environmental factors such as UV exposure, smoking, pollution, and diet. Aging affects the skin structure, leading to a thinner epidermal layer that results from keratinocyte atrophy, or cell death, inducing dryness and fine lines.[6,7] Collagen and elastin in the dermis significantly decreases and fragments, resulting in wrinkling at various locations on the facial skin, as shown in *Figure 1*. The amount of fatty tissue also decreases, affecting the skin's immunity characteristics that render the elderly more susceptible to skin injuries.[7]

Although intrinsic aging happens continuously in the body, it is prolonged by skin cell regeneration and homeostatic balance. Extrinsic factors, on the other side, disrupt this delicate balance and have been shown to accelerate skin aging.[8]

THEORIES OF DERMAL AGING

Considering that aging is multifaceted, there are many theories attempting to explain the molecular processes behind the scenes. In 1990, over 300 aging theories were proposed, and this number only continues to increase.[9] Among these theories, the mechanisms of oxidative stress, cellular senescence, and glycation will be discussed in more detail as they are the pathways that popular dermal anti-aging products target.

Oxidative stress and photoaging

Aging research has focused on a central finding that dates back to 1956 when Denham Harman proposed that reactive oxygen species (ROS) accumulate over time and contribute to aging. ROS result from an unpaired electron in O_2 which forms an unstable radical (*Figure 2*).[10] In the human body, ROS are mainly produced by the mitochondria, peroxisomes, and the endoplasmic reticulum,[11] which are the organelles in cells involved in metabolism and energy production. As the largest and most exposed organ of the human body, the skin contains a high ROS load originating from both internal stimuli produced by organelles in cells and external stimuli (mainly UV light). While the ozone layer mostly blocks UVC rays, UVA and UVB rays reach Earth's surface and penetrate the skin, causing oxidative stress and ROS formation in

molecules in the ECM, plays a critical role in intrinsic dermal aging.[19] All in all, dermal aging induces significant biochemical and structural changes in the skin, and all these mechanisms are highly connected and signal to each other.

ANTI-AGING PRODUCTS AND STRATEGIES

As the role of ROS and AGEs in skin aging has been widely understood, products that target related pathways have arisen and garnered ample attention in the cosmeceutical market. Since aging is a long process that does not occur overnight, these products also require a long-term appliance to the skin to show minimal effects on reversing morphological changes of aging.

One group of products that inhibit damage from ROS formation are antioxidants. Vitamin C, vitamin E, coenzyme Q10, and polyphenols are the main ingredients of many anti-aging products. These ingredients combat wrinkling and collagen degradation by targeting the MAPK pathway.[8] Retinoids are compounds derived from Vitamin A that promote keratinocyte proliferation, strengthen the protective function of the epidermis, restrain water loss, and protect collagen against degradation.[20]

Although many anti-aging ingredients have gained popularity in the cosmetic market, diet and lifestyle changes are the easiest way to combat dermal aging. Researchers have shown that a dietary restriction cutting AGE intake decreases levels of AGEs in rat and mouse skin collagen.[9] So, consuming fewer foods that are high in AGEs—such as certain cheeses/creams, high-sugar foods, and highly processed products—would decrease AGE accumulation in our bodies. Avoiding cooking methods that drive AGE formation—such as grilling and frying (high-temperature processes)—can also be a beneficial anti-aging strategy. Furthermore, we can consume a healthier diet by intaking antioxidants. Polyphenols are the most abundant antioxidants in our diets.[21] High levels of polyphenols reside in foods such as coffee, berries, chocolate, soy products, beans, vegetables, red wine, and nuts.

Finally, lifestyle changes could play an important role in anti-aging, as one of the main theories of aging is known as photoaging. Less UV exposure will substantially decrease ROS levels in our bodies and thus cause less dermal aging. One of the best strategies to prevent photoaging is by avoiding direct exposure to the sun, which could be accomplished by wearing sunscreen or layers of clothing that block UVA and UVB radiation.

CONCLUSION

Entropy, or disorder, always wins, indicating that all organisms will reach a point when deterioration prevails over synthesis and slowly age. While it is a natural and inevitable process, many people still choose to combat the most prominent feature of aging—dermal aging. Most anti-aging products in the market target pathways that lead to ROS and AGE formation. Backed by scientific evidence, these products quickly attract consumers' interests and facilitate the growth of the "anti-aging" movement. Consuming these products over a long period could benefit individuals but act more as a psychological relief from appearance anxiety. However, more and more voices suggest people combat aging via lifestyle and diet changes. While different attitudes arise in society, it is an individual's choice to take—or not take action against dermal aging. As further research investigates dermal aging, people can hopefully gain more insight into the science behind it and use it to help them make more informed decisions.

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IMAGE REFERENCES

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