FM Dermatological Applications: Anti-Aging

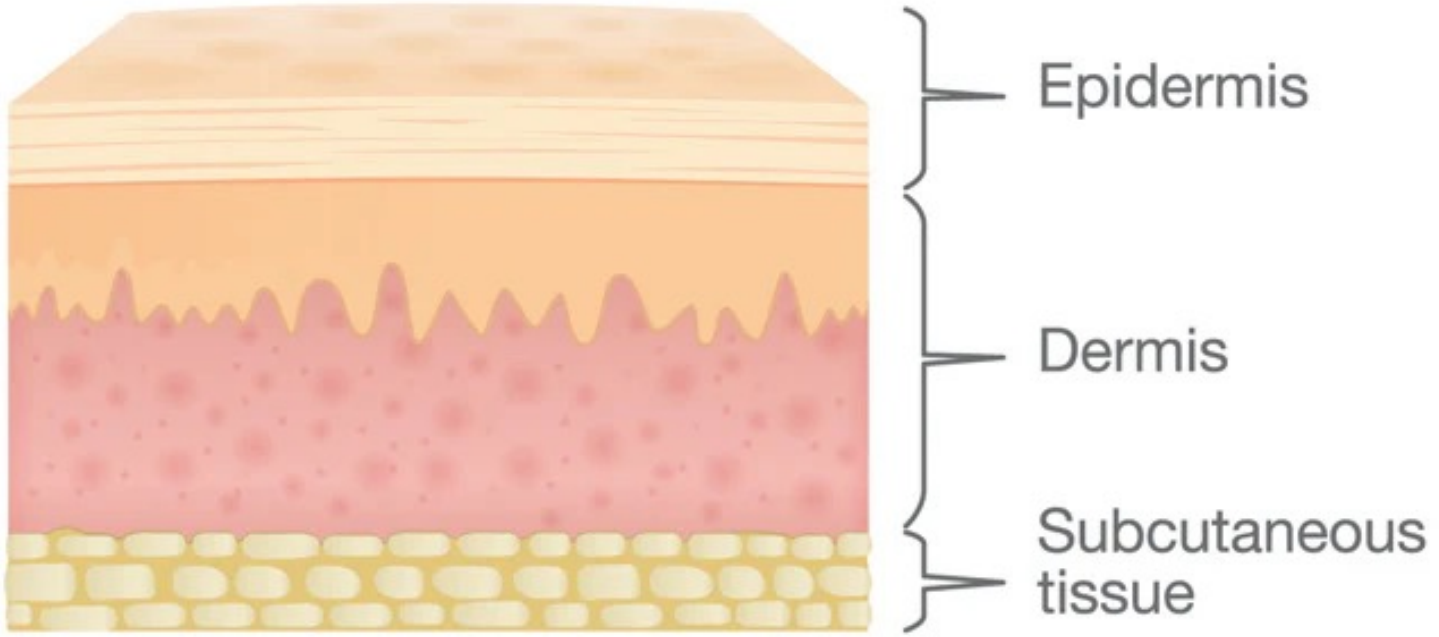
A Biogenetix Clinical Presentation

BIOGENETIX.COM

Disclaimer

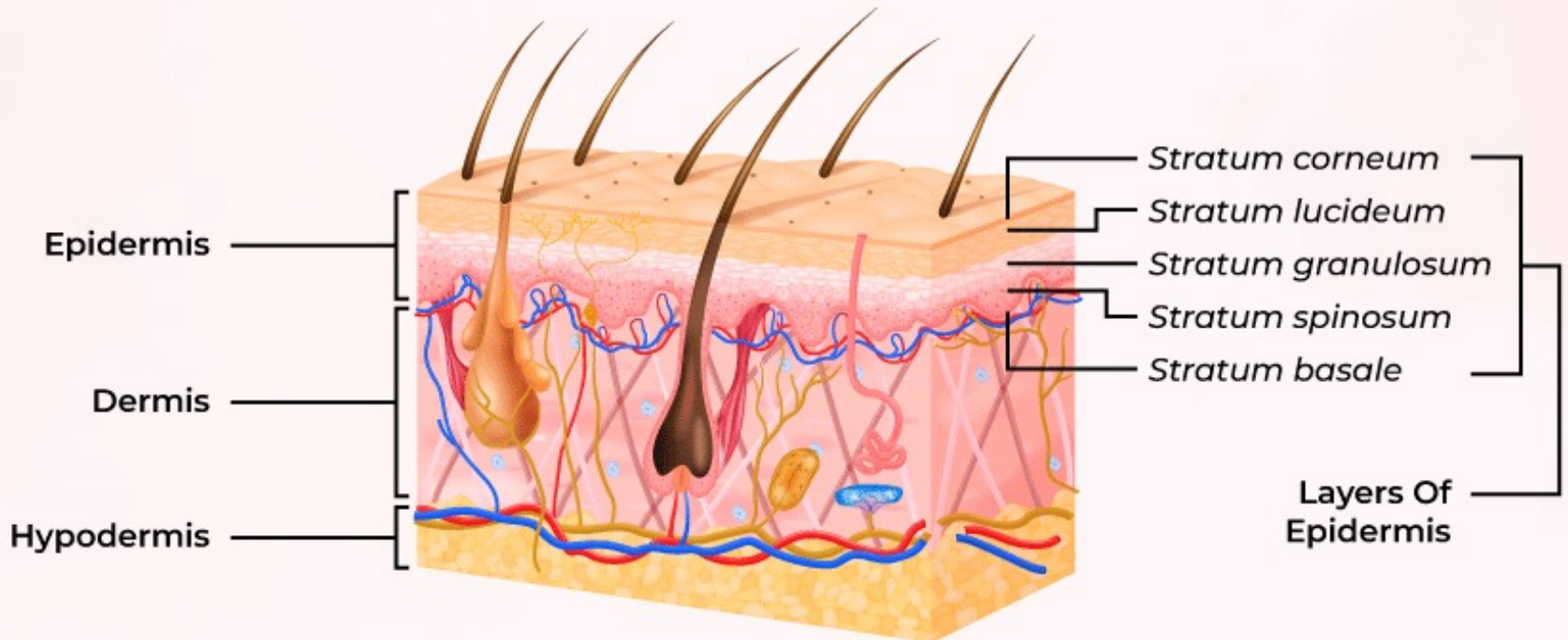
- *Information in this presentation is not intended to diagnose, treat, reverse, cure, or prevent any disease. While this presentation is based on medical literature, findings, and text, The following statements have not been evaluated by the FDA.*
- *The information provided in this presentation is for your consideration only as a practicing health care provider. Ultimately you are responsible for exercising professional judgment in the care of your own patients.*

The Layers of Skin



https://skinkraft.com/cdn/shop/articles/Layers-Of-Skin_1024x1024.jpg?v=1582612390

Layers of the Skin



https://media.geeksforgeeks.org/wp-content/uploads/20230316174511/Layers-of-Skin.png

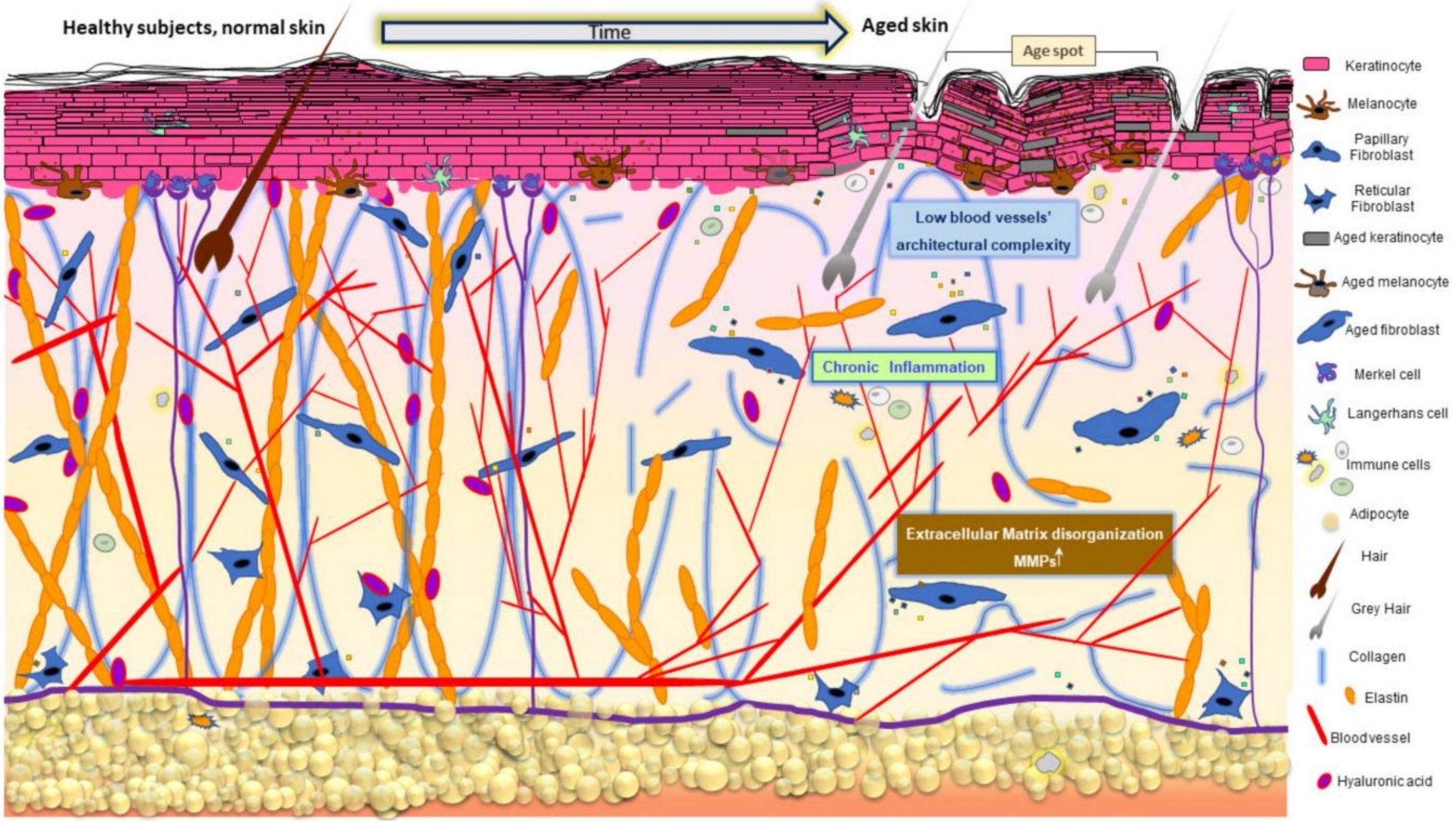
COLLAGEN:
The main structural protein found in skin and other connective tissues.

FIBROBLAST:
A fibroblast is a type of cell that contributes to the formation of connective tissue, a fibrous cellular material that supports and connects other tissues or organs in the body. Fibroblasts secrete collagen proteins that help maintain the structural framework of tissues.

ELASTIN:
A protein forming the main structure of elastic connective tissue, found especially in the dermis of the skin.

MELANOCYTE:
Cell responsible for melanin production.

MERKEL CELLS:
A type of skin cell located at the base of the epidermis, or top layer of skin, and are close to nerve endings that sense touch.



Progressive decline of physiologic functionality.

Antioxidants (Basel). 2022 Jun; 11(6): 1121.
Published online 2022 Jun 6. doi: 10.3390/antiox11061121
PMCID: PMC9220264
PMID: 35740018

Focus on the Contribution of Oxidative Stress in Skin Aging

Federica Papaccio, Andrea D'Arino, Silvia Caputo, and Barbara Bellei*

Stanley Omaye, Academic Editor

Skin aging is one of the most evident signs of human aging. Modification of the skin during the life span is characterized by fine lines and wrinkling, loss of elasticity and volume, laxity, rough-textured appearance, and pallor. In contrast, photoaged skin is associated with uneven pigmentation (age spot) and is markedly wrinkled. At the cellular and molecular level, it consists of multiple interconnected processes based on biochemical reactions, genetic programs, and occurrence of external stimulation. The principal cellular perturbation in the skin driving senescence is the alteration of oxidative balance. In chronological aging, reactive oxygen species (ROS) are produced mainly through cellular oxidative metabolism during adenosine triphosphate (ATP) generation from glucose and mitochondrial dysfunction, whereas in extrinsic aging, loss of redox equilibrium is caused by environmental factors, such as ultraviolet radiation, pollution, cigarette smoking, and inadequate nutrition. During the aging process, oxidative stress is attributed to both augmented ROS production and reduced levels of enzymatic and non-enzymatic protectors. Apart from the evident appearance of structural change, throughout aging, the skin gradually loses its natural functional characteristics and regenerative potential. With aging, the skin immune system also undergoes functional senescence manifested as a reduced ability to counteract infections and augmented frequency of autoimmune and neoplastic diseases. This review proposes an update on the role of oxidative stress in the appearance of the clinical manifestation of skin aging, as well as of the molecular mechanisms that underline this natural phenomenon sometimes accelerated by external factors.

Antioxidants (Basel). 2022 Jun; 11(6): 1121.
Published online 2022 Jun 6. doi: 10.3390/antiox11061121
PMCID: PMC9220264
PMID: 35740018

Focus on the Contribution of Oxidative Stress in Skin Aging

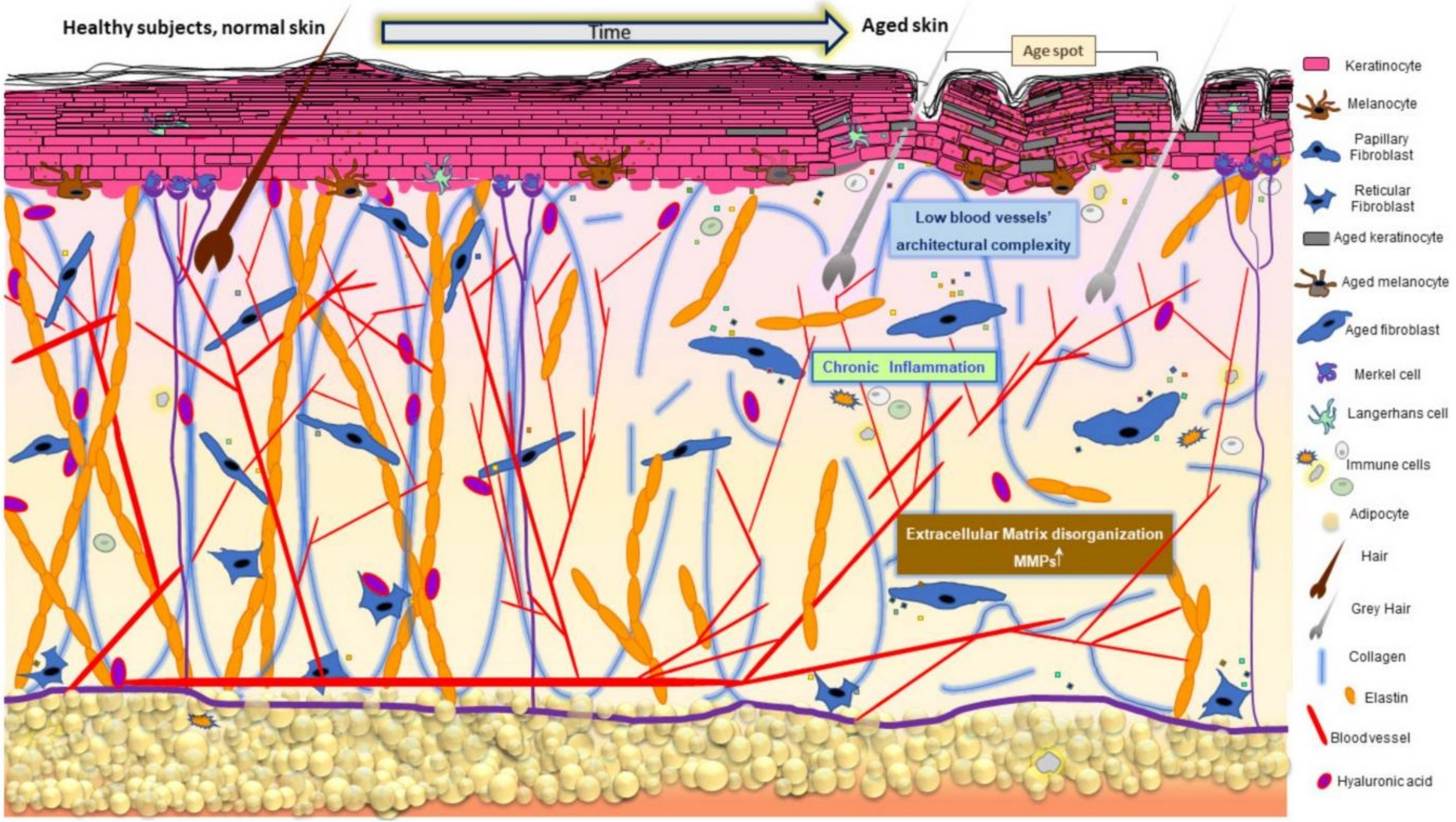
Federica Papaccio, Andrea D'Arino, Silvia Caputo, and Barbara Bellei*

Stanley Omaye, Academic Editor

To scavenge reactive oxygen species (ROS), cutaneous cells utilize a conspicuous apparatus of small antioxidant molecules and endogenous enzymes. Ubiquinol (coenzyme Q10) is a lipid-soluble intracellular and extracellular radical scavenger that protects mitochondria and key cutaneous proteins. CoQ10 also inhibits the expression of some metalloproteinases (MMPs), such as collagenase, preserving the collagen content of the skin [26]. Vitamin E is implicated in membrane stabilization, preventing lipid peroxidation and oxidation of unsaturated fatty acids [27,28]. In the skin, vitamin E level is strongly sensitive to UV-induced depletion [29], and levels of vitamin E also decrease with age [30], suggesting that impairment in its detoxification activity might be involved in both natural and photo-accelerated aging. Vitamin C acts by removing free radicals and repairing oxidized vitamin E [31]. Moreover, in the skin, vitamin C is implicated in procollagen synthesis and collagen cross-linking [32,33,34]. The function of superoxide dismutase (SOD) is to catalyze the breakdown of superoxide radical anion (O_2) into hydrogen peroxide (H_2O_2) [35]. In mammals, three different isoforms of SOD exert non-overlapping functions. The isoform that utilizes Cu/Zn as cofactors (SOD1) localizes in the cytoplasm and the nucleus [36], the isoform that binds Mn (SOD2) localizes in mitochondria, and SOD3, which also binds Cu/Zn, has been detected mainly in the extracellular space [37]. In vivo studies in mice evidenced that all three SODs impact skin aging

Antioxidants (Basel). 2022 Jun; 11(6): 1121.
Published online 2022 Jun 6. doi: 10.3390/antiox11061121
PMCID: PMC9220264
PMID: 35740018

activity has been observed in the epidermis [46]. Another supporter of the antioxidant capability of the cell is the tripeptide glutathione (GSH). The GSH acts as a scavenger because of its thiol functional group. During the reaction, GSH is oxidized by reactive oxygen radicals and makes a dimer with another GSH (GSSG). GSH can be retaken in a reducing enzymatic reaction by the glutathione reductase consuming NADPH [47]. The mouse model demonstrated that not only the absolute amount of the oxidized GSSG but also the GSSG:GSH increases in the dermis during aging [48]. In addition to its role as an antioxidant, GSH is also a cofactor for many metabolic processes. In humans, all eight glutathione peroxidases (GPXs) are known to reduce hydrogen peroxide in water and stop lipid peroxidation [45]. Overall, the endogenous antioxidant capacity (enzymatic and non-enzymatic) of the skin is lowered with age, and the aged skin is more vulnerable to external factors, especially UV radiation, pollution, and microorganisms [49]. Since the epidermis is more exposed to external stimuli than the dermis, the ROS load is higher in the epidermis compared to the dermis [50]. Correspondingly, defensive enzymes and non-enzymatic antioxidants are present in higher concentrations in the epidermis than in the dermis [51]. Particularly, small antioxidants such as vitamins C and E, glutathione, and ubiquinol, and defensive enzymes such as Cat and SODs are concentrated in deeper layers of the stratum corneum [29,52,53]. From the biological point of view, this might correspond to more accurate protection of epidermal stem cells that mostly reside at the dermal–epidermal junction. On the other hand, the production of ROS in the epidermis occurs in the deepest layers, especially at the basal layer, since in the final phase of the differentiation process, keratinocytes of the stratum corneum lose their nuclei and organelles [54]. Moreover, the promelanogenic effect of solar radiation promotes the formation of free radicals related to the melanin biosynthetic pathway at the dermal–epidermal junction [55]. Particularly, in fair-skinned individuals, pheomelanin is responsible for free radical generation in melanocytes even in absence of UV [56,57]. Likewise, carriers of melanocortin 1 receptor



Progressive decline of physiologic functionality.

Antioxidants (Basel). 2022 Jun; 11(6): 1121.
Published online 2022 Jun 6. doi: 10.3390/antiox11061121
PMCID: PMC9220264
PMID: 35740018

Focus on the Contribution of Oxidative Stress in Skin Aging

Federica Papaccio, Andrea D'Arino, Silvia Caputo, and Barbara Bellei*

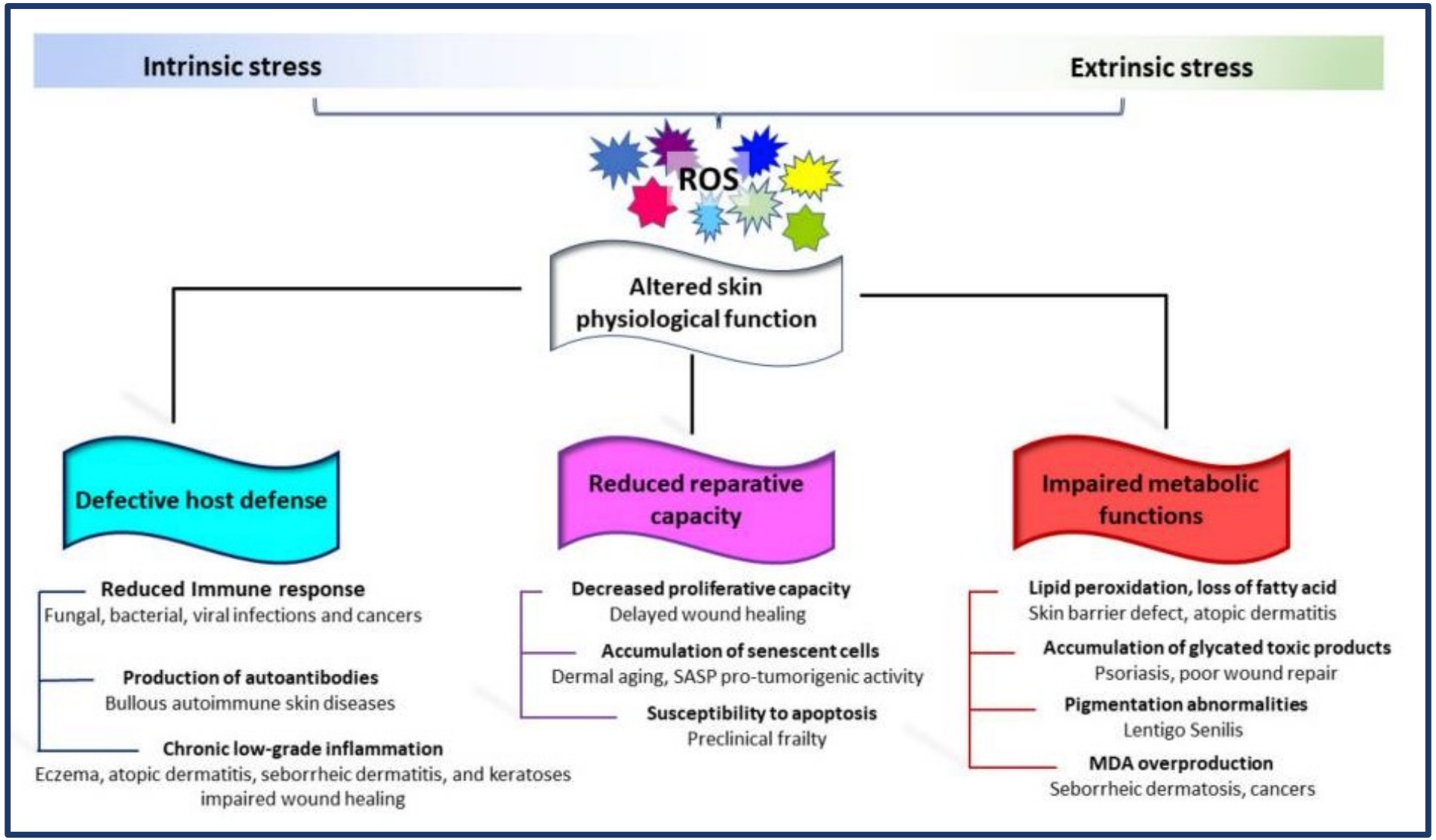
Stanley Omaye, Academic Editor

Fine wrinkles, tissue atrophy with minor elasticity, and remarkable dryness often accompanied by pruritus are the most common phenotypic changes in aging observed in all skin areas [59]. However, they diversify among different anatomical regions and within diverse ethnical groups [60,61]. The subcutaneous adipose tissue is decreased in some body areas, especially the face, shins, hands, and feet, explaining the visible volume reduction, while in other body areas, peculiarly the abdomen in males and the thighs in females, it is augmented. Anatomical differences emerged by the comparative analysis of facial and abdominal adipocyte gene expression profiles, suggesting a possible implication in the diverse modification of subcutaneous tissue of these body areas during aging [62]. Sebaceous glands progressively increase in size, but their secretory output is attenuated in aged individuals [63]. There is a progressive decline in the density of hair follicles, and the hair shaft diameter is frequently smaller [64]. At the cellular level, aging is characterized by the accumulation of senescent cells in both the epidermis and the dermis and by a significant depletion of stem/progenitor cells [65]. Since MSCs do not escape the deleterious effects of natural aging, their propensity to senesce is firstly determined by intrinsic factors [66]. Aging affects MSCs from a quantitative (stem cells exhaustion) and a qualitative point of view, since advanced age subcutaneous MSCs lose their osteogenic potential and in turn augment the adipogenic potential [67]. In line with this idea, Orciani and collaborators demonstrated that MSCs isolated from the skin do not have an efficient antioxidant defense system, but their integrity is preserved by the surrounding microenvironment of the niche [68]. Increased intracellular ROS and lower SOD activity characterizes aged MSCs in both undifferentiated and differentiated conditions. Diabetic subcutaneous MSCs displayed lower proliferation

Antioxidants (Basel). 2022 Jun; 11(6): 1121.
Published online 2022 Jun 6. doi: 10.3390/antiox11061121
PMCID: PMC9220264
PMID: 35740018

Focus on the Contribution of Oxidative Stress in Skin Aging

In addition to the physiological mechanism of aging, exposure to UV light and environmental pollutants accelerate the acquisition of the aged phenotype. UV light is the major extrinsic agent responsible for skin aging. Premature photoaged skin typically presents with increased thickness of the epidermis, irregular pigmentation, and dermal connective tissue damage including the typical solar elastosis, laxity, dullness, roughness, and alteration of the vascular system [220]. The primary modification of the dermis during photo-accelerated aging regards structural components: collagen, elastin, and glycosaminoglycans. In older skin, the collagen network looks disorganized, and the ratio of collagen type III (Col-III) to I has been shown to increase due to less Col-I production [221]. Dissimilar to chronologic skin aging, MMP-induced collagen degradation and elastin degeneration are key mechanisms in photoaging [222]. In addition, the reduction in fibrillin structures and Col-VII involved in the bond between epidermis and dermis contribute to wrinkling formation [223]. Photoaging occurs principally due to UVA and UVB irradiation, which based on their distinct physical properties, induces different partially overlapping biological responses including abnormal ROS accumulation and/or DNA damage in both the epidermal and dermal compartment [224]. The fact that photoaging is largely due to oxidative disequilibrium is confirmed by the efficacy of topical antioxidants in UV-induced damage prevention [53,225]. Overall, depending on the cell type and the intensity of the stress, cells can either transiently block the cell cycle and repair the damage before restarting cell proliferation or enter apoptosis if the sensed damage is too serious. Therefore, sub-cytotoxic acute or chronic stress can induce premature senescence. Several pieces of evidence revealed that under the same conditions, human fibroblasts predominantly respond via senescence, while epithelial cells prefer to exert apoptosis [185,226]. Together with the cell-specific turnover rate, this partially explains the preferential detection of the senescent markers in the dermal compartment compared to the epidermal one.


Intrinsic stress
Extrinsic stress
ROS
Altered skin physiological function
Defective host defense
Reduced reparative capacity
Impaired metabolic functions
Reduced Immune response
Fungal, bacterial, viral infections and cancers
Production of autoantibodies
Bullous autoimmune skin diseases
Chronic low-grade inflammation
Eczema, atopic dermatitis, seborrheic dermatitis, and keratoses impaired wound healing
Decreased proliferative capacity
Delayed wound healing
Accumulation of senescent cells
Dermal aging, SASP pro-tumorigenic activity
Susceptibility to apoptosis
Preclinical frailty
Lipid peroxidation, loss of fatty acid
Skin barrier defect, atopic dermatitis
Accumulation of glycated toxic products
Psoriasis, poor wound repair
Pigmentation abnormalities
Lentigo Senilis
MDA overproduction
Seborrheic dermatosis, cancers

Skin Res Technol. 2023 Jul; 29(7): e13391.
Published online 2023 Jun 30. doi: 10.1111/srt.13391
PMCID: PMC10311288
PMID: 37522497

Reverse skin aging signs by red light photobiomodulation

Virginie Couturaud,[1] Marie Le Fur,[1] Michele Pelletier,[2] and Frederic Granotier[3]

Author information · Article notes · Copyright and License information PMC Disclaimer

The study of skin aging allows us to identify the key mechanisms of skin functions and structure. It is possible to measure the evolution of these mechanisms according to genetic factors (chronological age) but also environmental factors (nutrition, lifestyle, sport, UV exposure) allowing to define a biological age of the skin. This evolution translates into the appearance of visible clinical signs on the face, responsible for the increase in the perceived age of an individual. The main signs of age are the appearance of wrinkles and fine lines, the decrease in firmness, the loss of density.

In order to reverse the visible signs of skin aging, the use of Low-Level Laser Therapy (LLLT) is becoming more and more common and numerous clinical studies demonstrate its effectiveness. This type of nonablative therapy is based on the principle of photobiomodulation, a cascade of cellular responses induced by low-energy lasers or light emitting diodes (LEDs) in a specific wavelength (400-1100 nm).[1]

Photobiomodulation will act through different mechanisms on the skin such as nonvisual opsins, direct activation of Transforming Growth factor β1[2] but also activation of cytochrome C oxidase. Indeed, it has been shown that, in the skin, one of the pathways of aging[3] was mitochondrial dysfunction and that photobiomodulation by red light, activates cytochrome c oxidase,[4] which increases mitochondrial production of ATP, which in turn enhances the metabolic activity of the cell.[5,6] Simultaneously, regulation of the reduction/oxidation (redox) state of the intracellular environment promotes the expression of genes associated with tissue regeneration and repair.[7]

Skin Res Technol. 2023 Jul; 29(7): e13391.
Published online 2023 Jun 30. doi: 10.1111/srt.13391
PMCID: PMC10311288
PMID: 37522497

Reverse skin aging signs by red light photobiomodulation

Virginie Couturaud,[1] Marie Le Fur,[1] Michele Pelletier,[2] and Frederic Granotier[3]

The satisfaction questionnaire after 2 and 3 months of use reflects this effectiveness: 100% of the volunteers find that the mask significantly improves the overall condition of their skin and 85% of the volunteers felt good after a session.

The analysis of the results obtained separately on the men/women panel follows the same trend. Indeed, despite the small number of men included in the test (five men), the results all point in the same direction after 3 months of using the mask:

- 16.7% decrease in the sagging of the oval of the face,
- 31.3% decrease in the R0 value, indicating an increase in skin firmness,
- 62.1% increase in dermal density,
- 28.1% decrease in pore diameter,
- 62.6% decrease in the amount of sebum.

Measurements taken 14 and 28 days after stopping the use of the Skin Light Dior × Lucibel mask confirm that the reversal of the signs of aging is long-lasting and profound. Indeed, the results on crow's feet wrinkles, the sagging of the oval of the face, the firmness, the density, the roughness of the skin, the diameter of the pores, the homogeneity of the complexion, the rate of sebum, and the quantity of porphyrin remain at the same level as those obtained after 3 months of use of the mask (with no significant difference), demonstrating the remanence of effectiveness.

Lasers Med Sci. 2024; 39(1): 104.
Published online 2024 Apr 17. doi: 10.1007/s10103-024-04044-9
PMCID: PMC11024053
PMID: 38630175

Enhancement of skin rejuvenation and hair growth through novel near-infrared light emitting diode (nNIR) lighting: in vitro and in vivo study

Keonwoo Choi,[#1,2,3] Hongbin Kim,[#1,2,3] Sun-young Nam,[1,3] and Chan Yeong Heo[✉1,2,3,4]

also in vivo, comparing it with White or 2chip LED. The results demonstrated that nNIR led to increased ATP synthesis and collagen synthesis, as well as decreased ROS levels. In a UV-induced photoaging mouse model, nNIR treatment resulted in increased ATP synthesis, decreased skin thickness, increased collagen synthesis, and reduced collagenase expression. Moreover, both NIR LED and White promoted hair growth, increased skin thickness, and stimulated follicle proliferation compared to the control group. Notably, the nNIR showed higher efficacy in improving ATP activity, enhancing collagen synthesis, suppressing collagenase expression, and promoting hair growth in vivo compared to conventional White. These findings suggest that the superior ATP synthesis activity of the NIR LED compared to White illumination contributes to these effects. Based on these results, we propose that the broader spectrum emitted by the near-infrared (nNIR) LED, in comparison to White and the conventional 2chip LED, induces more positive biological responses and ATP activity. This suggests that the observed effects can be attributed to the NIR LED's ability to stimulate a wider range of biological processes. This research provides valuable insights for the future development of light-based therapies for skin rejuvenation and hair growth.

J Clin Med. 2023 Mar; 12(5): 1710.
Published online 2023 Feb 21. doi: 10.3390/jcm12051710
PMCID: PMC10003066
PMID: 36902498

The Effects of a Fasting Mimicking Diet on Skin Hydration, Skin Texture, and Skin Assessment: A Randomized Controlled Trial

Jessica Maloh, Formal analysis, Writing – original draft,[1,*] Min Wei, Conceptualization, Methodology, Formal analysis, Writing – review & editing, Supervision, Project administration, Funding acquisition,[2] William C. Hsu, Conceptualization, Methodology, Formal analysis, Writing – review & editing, Supervision, Project administration, Funding acquisition,[2] Sara Caputo, Writing – review & editing,[2] Najiba Afzal, Writing – review & editing,[1,3] and Raja K. Sivamani, Formal analysis, Writing – review & editing[1,4,5,6]

humans [25]. Studies have also suggested that caloric restriction may improve the appearance of wrinkles and decrease the presence of oxidative stress [26,27].

The potential mechanisms by which FMD may exert its effects on the skin are multifaceted. Fasting has been shown to initiate comprehensive cellular and systemic reprogramming in organisms in response to starvation conditions. Biogerontological research in the past 30 years has linked prolonged nutrient deprivation with the downregulation of pro-growth signaling and activation of cellular protection mechanisms, which may have implications for the amelioration of disease-associated factors and the delay of aging [8,28]. The FMD was specifically designed to mimic the effects of water-only fasting and had been shown to induce anti-oxidative stress in cells [29,30], dampen the mTOR-S6K signaling pathway, activate autophagy [31,32,33], promote stem cell-based regenerations in multiple tissues [12,14,34], augment the gut microbiome [12], and reduce risk factors associated with age-related diseases [11]. Further research on the use of period fasting interventions such as FMD may reveal it to be a cost-effective and feasible component of an integrative approach to skin health.

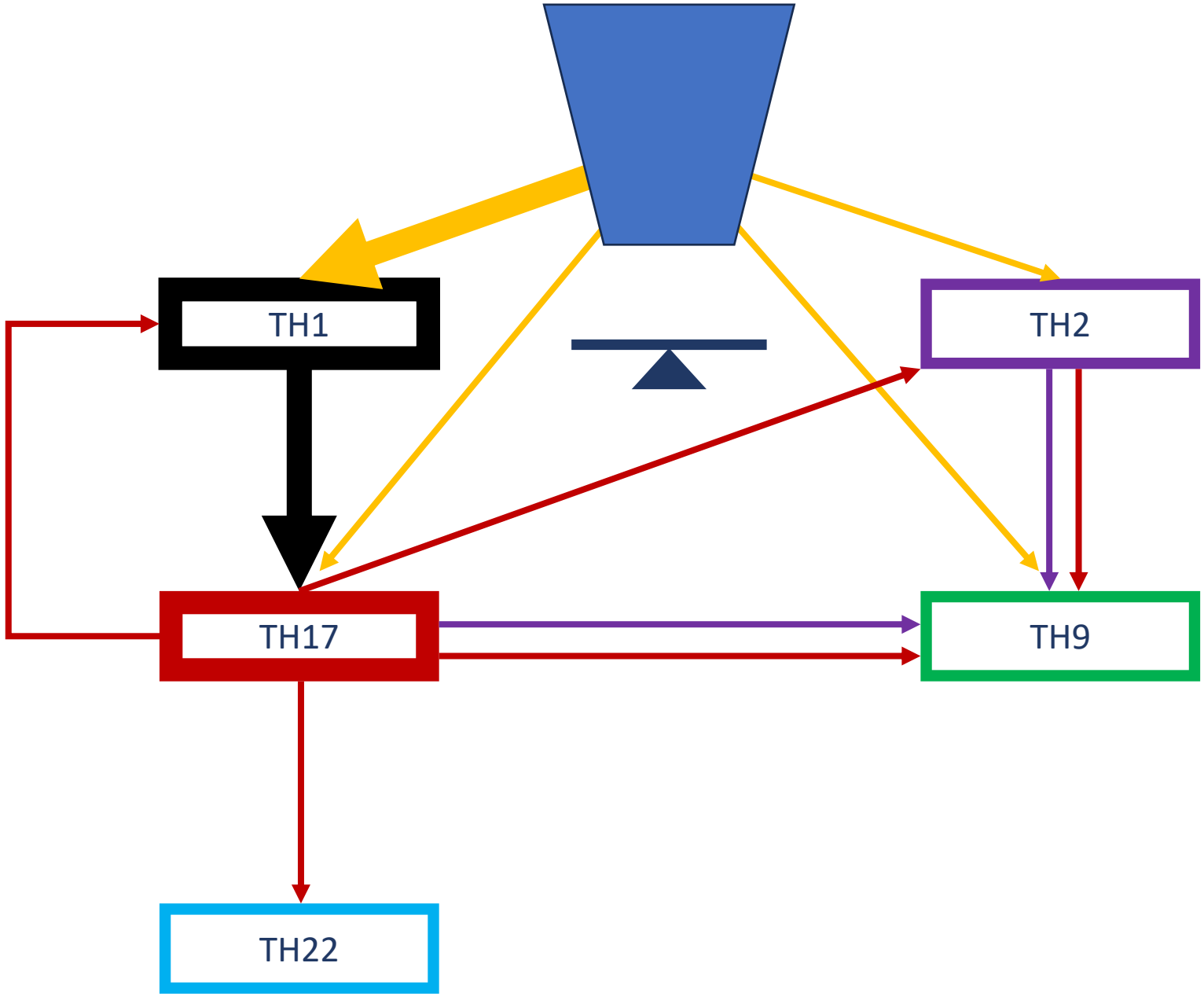
J Clin Med. 2023 Mar; 12(5): 1710.
Published online 2023 Feb 21. doi: 10.3390/jcm12051710
PMCID: PMC10003066
PMID: 36902498

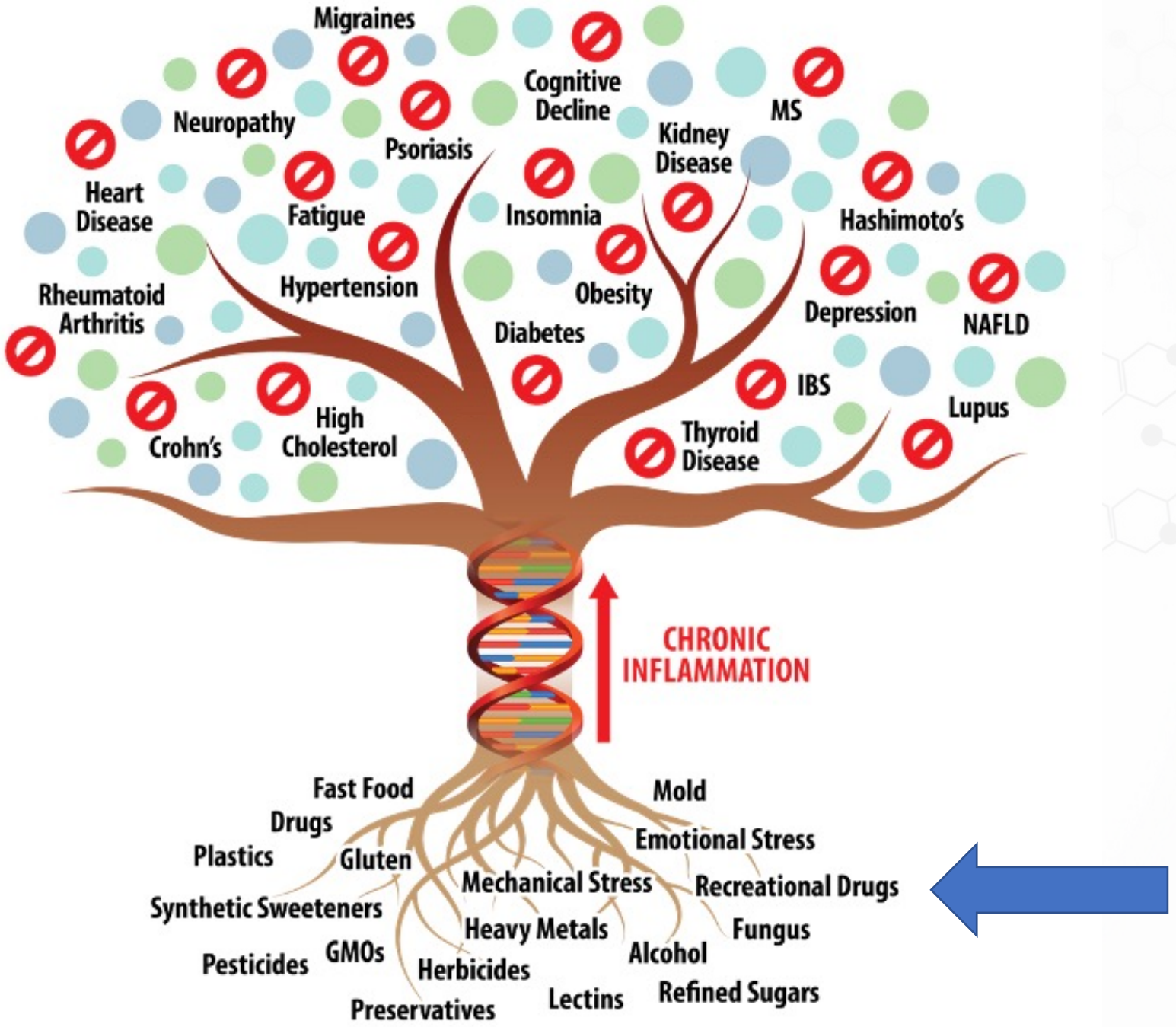
The Effects of a Fasting Mimicking Diet on Skin Hydration, Skin Texture, and Skin Assessment: A Randomized Controlled Trial

Jessica Maloh, Formal analysis, Writing – original draft,[1,*] Min Wei, Conceptualization, Methodology, Formal analysis, Writing – review & editing, Supervision, Project administration, Funding acquisition,[2] William C. Hsu, Conceptualization, Methodology, Formal analysis, Writing – review & editing, Supervision, Project administration, Funding acquisition,[2] Sara Caputo, Writing – review & editing,[2] Najiba Afzal, Writing – review & editing,[1,3] and Raja K. Sivamani, Formal analysis, Writing – review & editing[1,4,5,6]

Vito Di Lernia, Academic Editor

Another potential mechanism by which FMD may impact skin health is through the gut-skin axis. Research suggests that subsequent cycles of FMD may reduce intestinal inflammation and stimulate protective members of the gut microbiome, such as *Lactobacillaceae* and *Bifidobacteriacea* [12]. These specific members of the gut microbiota have been found to be relevant to skin health. For example, children with eczema have been found to have less gut colonization by *Bifidobacterium* and *Lactobacillus* strains relative to healthy control [35,36]. Furthermore, in an animal study, oral supplementation with *Bifidobacterium breve* B-3, a member of the *Bifidobacteriacea* family, has been found to protect against UV-induced changes in transepidermal water loss and changes in skin hydration [37]. However, additional research will be needed to better understand the relationship between fasting-mediated shifts in the gut microbiome and changes in skin outcomes.


TH1
TH2
TH17
TH9
TH22
(Dermatologic)


Migraines
Neuropathy
Psoriasis
Cognitive Decline
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Hashimoto's
Hypertension
Obesity
Depression
NAFLD
Rheumatoid Arthritis
Diabetes
IBS
Lupus
Crohn's
High Cholesterol
Thyroid Disease
CHRONIC INFLAMMATION
Fast Food
Mold
Drugs
Emotional Stress
Plastics
Gluten
Mechanical Stress
Recreational Drugs
Synthetic Sweeteners
Heavy Metals
Fungus
Pesticides
GMOs
Alcohol
Herbicides
Refined Sugars
Lectins
Preservatives