Personalized skincare: from molecular basis to clinical and commercial applications

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Abstract: Individual responses of human skin to the environmental stress are determined by differences in the anatomy and physiology that are closely linked to the genetic characteristics such as pigmentation. Ethnic skin phenotypes can be distinguished based on defined genotypic traits, structural organization and compartmentalized sensitivity to distinct extrinsic aging factors. These differences are not only responsible for the variation in skin performance after exposure to damaging conditions, but can also affect the mechanisms of drug absorption, sensitization and other longer term effects. The unique characteristics of the individual skin function and, particularly, of the ethnic skin type are currently considered to shape the future of clinical and pharmacologic interventions as a basis for personalized skincare. Individual approaches to skincare render a novel and actively growing area with a range of biomedical and commercial applications within cosmetics industry. In this review, we summarize the aspects of the molecular and clinical manifestations of the environmental stress on human skin and proposed protective mechanisms that are linked to ethnic differences and pathophysiology of extrinsic skin aging. We subsequently discuss the possible applications and translation of this knowledge into personalized skincare.

Keywords: pigmentation, gene polymorphism, photodamage, environmental stress, cosmetics

Melanogenesis as a protective mechanism against photodamage

Clinical evaluations of the effects of sun exposure and photoprotection on skin damage and the classical signs of aging have been documented in a range of studies involving volunteers from different ethnicities, skin type and age groups using multiple criteria and clusters. The studies identified that ultraviolet (UV) exposure can be responsible for as much as 80% of aging sings in Caucasian and Asian skin, with predominance of the changes in pigmentation occurring independently of age, but are strongly linked to such exposure.\(^1\) Theoretical calculations of the maximal daily exposures to solar UV radiation that could prevent the development of photoaged skin until old age were estimated at 0.14 minimal erythema dose (MED) of average yearly dose 200 MED for unprotected skin, therefore limiting the exposure to 2.54 min/day.\(^2\) Adaptive melanization, known as tanning, protects the skin against UV penetration, and molecular defects in this pathway are associated with epidermal hyperplasia and cancer susceptibility.\(^3\)-\(^7\) UV is also responsible for early signs of photoaging, including pigment irregularities, solar elastosis and telangiectasias.\(^1,8\)

Skin color is defined by the Fitzpatrick system that categorizes the skin into six types (I–VI) based on basal complexion, inflammatory response, tanning and sun
burning susceptibility, with fair skin being more susceptible to this type of damage than darker skin. The color of human skin is largely determined by the amount and type of melanin pigment produced by melanocytes.

Melanins are complex and multifunctional biopolymers represented by several types of pigment that are synthesized within lysosome-related organelles, melanosomes and transferred from melanocytes in the basal layer of epidermis to the surrounding keratinocytes. The amount and type of melanin are the main factors that determine skin complexion and UV sensitivity. Melanin exists in two main isoforms: dark-brown eumelanin that is more efficient at blocking UV photons and light pheomelanin that remains constant between dark- and lightly pigmented skin. Skin complexion and UV sensitivity are, therefore, determined predominantly by the levels of eumelanin in the epidermis.

Melanogenesis is a complex and heterogeneous process that is not organized into simple linear succession, but into multidimensional and overlapping network of biochemical reactions. Central to this process is stimulation of the melanocortin receptor 1 that binds to α-melanocortine stimulating hormone and transmits differentiation signals through activation of adenyl cyclase and generation of cAMP. This leads to increased levels and activity of tyrosinase (TYR), TYR-related protein 1 (TYRP1, dihydroxyindole [DHI] oxidase) and dopachrome tautomerase (DCT) that catalyze the synthesis of melanin. The major biochemical reactions, substrates and enzymes in the biosynthesis of melanins and the transport and maturation of melanosomes involve hydroxylation of phenylalanine, tyrosine hydroxylation (TYR), DOPA oxidation (TYR), dopachrome tautomeration (DCT/TYRP2), DHICA oxidation (TYRP1 or peroxidase), DHI oxidation (TYR or peroxidase), hydrolysis of glutathionyl-dopa (g-glutamyltranspeptidase), oxidation of cysteinyl-dopa (peroxidase), intramolecular cyclization of cysteinyl-dopaquinone (peroxidase), DOPA decarboxylation (AAD), hydroxylation of dopamine (DBH) and methylation of norepinephrine (PNMT).

Epidermal melanocytes are located in the basal layer above the basement membrane in the epidermal melanin unit comprising ~50 neighboring keratinocytes. Initial stages of UV-mediated skin darkening involve actual redistribution of the existing melanin pigment, which is followed by subsequent de novo melanin synthesis that begins several hours or days later. Several studies demonstrated decreased DNA damage in the lower epidermis, redistribution of melanin from the lower to the middle epidermis and increase in UV-induced apoptosis in darkly pigmented skin, suggesting the mechanism of both more efficient UV filtration and removal of the permanently damaged cells.

In addition to direct protection from UV, melanogenesis may play other important physiologic roles in epidermal homeostasis. A study aiming at understanding the responses of differently pigmented skin types to UV measured the distribution of DNA damage and melanin content alongside the expression of melanocyte-specific genes after single MED exposure. Interestingly, while such responses were not accompanied by significant changes in both the density of melanocytes at the dermal–epidermal junctions and the melanin content, expression of melanocyte-specific proteins TYR, TYRP1, DCT as well as MART1 and MITF did change significantly within 1 week after UV exposure. This suggests that the genes involved in the melanin synthesis pathway also demonstrate the expression patterns regulated in response to the environment, which could be independent from the positive selection for skin pigmentation.

Ethnic variations in the pigmented traits and phenotypic differences in extrinsic aging

Genetic polymorphism in constitutive pigmentation across worldwide populations

Human skin pigmentation is an atypical trait primarily determined by the quantity and distribution of melanin, which shows a remarkable, latitude-correlated phenotypic variation among continental populations. Recent genotype/phenotype association studies have uncovered a spatial distribution in the single-nucleotide polymorphisms (SNPs) located within constitutive pigmentation candidate genes alongside gradual increase in skin darkness across worldwide populations from Northern Europe to Southern Europe to Northern Africa, the Middle East and Western Asia geographic regions. Human SNPs represent >9 million DNA sequence variations scattering the entire genome (the National Center for Biotechnology Information dbSNP database) that can alter the response of the individual to environmental exposure. SNPs occur in both gene coding and noncoding regions and can lead to changes in the biologic properties of the encoded protein or affect gene expression levels. Using a combination of systematic approaches, including genome-wide association studies, gene expression databases and genotype–phenotype correlations based on skin melanin index, significant variations in SNP pigmentation genes have been found between European,
East Asian, South West Asian and African large populations in case–control studies. Many of these genes have been uncovered based on naturally occurring mutations that affect the constitutive pigmentation through the melanin or melanogenic precursor levels. In addition, a number of noncoding SNPs involved in transcriptional regulation of pigmentation genes have also been identified. General interpretation of the inter-and intra-ethnic populations’ SNPs could be proposed to affect the genes involved in dark melanocyte pigmentation, vitamin D status and skin tanning response in Caucasian skin, darker and lighter skin reflectance in Oriental and Asian skin, with constitutive levels or activity of certain markers typically higher in African skin. There is also a profound cross-talk between melanogenic and oxidative stress response signaling pathways (Table 1).

Genetic polymorphisms underlying phenotypic variation of pigmentation require further understanding of the effects on target proteins and correlation with the cellular functions. This is achieved by combination of biochemical and cellular approaches including mRNA transcription and stability, protein assays, ligand interactions, enzymatic activity and histochemistry. For example, recording of the association between allelic distribution and melanosome density at different stages of biogenesis could provide further insight into the cellular basis of diversity in skin pigmentation.

**Structural differences and aging properties of ethnic skin types**

It has been suggested previously that environmental changes could have an impact on selected pigmentation genes. One of the major factors that could affect extrinsic aging and, in particular, photoaging is genetically determined skin type with established content and composition of melanin. Susceptibility toward extrinsic skin aging is also recognized to be strongly influenced by other endogenous factors such as antioxidant or DNA repair capacity, which may be determined by individual genetic traits and ethnic differences in skin properties.

It is well established that the number of melanocytes in different skin types remains relatively constant and is defined by the epidermal melanin unit. Darker skin, however, is characterized by the presence of more dispersed, larger and labile melanocytes that contain more melanin consistent with higher tyrosinase activity and slower rate of melanosome degradation in the epidermis. In contrast, lightly pigmented skin presents with more aggregated and smaller melanosomes that contain less melanin due to the rate of synthesis and enhanced degradation. The greater ethnic capacity toward melanogenesis in darker skin that is not exposed to UV could suggest additional contribution to the epidermal structure and barrier permeability and function. In addition to better photoprotection against UV through pigmentation, epidermis in the African skin has, indeed, a thicker stratum corneum, with more cornified cell layers and lipid content compared to Caucasian skin. Consequently, the African skin is suggested to have stronger antimicrobial defenses linked to more acidified outer epidermis and rapid barrier recovery after damage. Consistent with the degree of pigmentation, African skin and Asian skin have thicker and more compact dermis compared to Caucasian skin. African skin contains larger, more frequent and active fibroblasts in parallel orientation as well as more macrophages. Such phenotype is associated with more pronounced structural integrity of collagen in dermis that is preserved during aging and photoaging. In contrast, extrinsically aged Caucasian skin is characterized by profound disorganization of the elastic fibers and decreased expression of collagen in dermis. The atrophic manifestations in dermis are moreover linked to the skin type within the Caucasian population, with multiple telangiectasia (dilated superficial blood vessels) in lightly pigmented skin and solar elastosis (accumulation of abnormal elastin) in darker skin.

In addition to the loss of elasticity and volume, the most common signs of skin aging and, particularly, photoaging are decreased number of melanocytes, dyspigmentation and changes in pigment distribution observed in all skin types. The aging process and sun-induced damage are, however, distinguished by unique structural and functional differences observed between light (types I–II) and dark skin (types III–VI). Darker skin, despite being more resistant to wrinkles, is generally more pronounced to dyspigmentation including both hypopigmentation and hyperpigmentation. The changes in pigment distribution are the principal manifestation of photodamage in Oriental and Asian skin, with the former also characterized by hyperpigmentation and increased melanin index with age. Increased occurrence of pigment spots can be partially associated with higher frequency distribution of SLC45A2 gene variant. Furthermore, population studies of age-related changes reveal that although uneven pigment distribution is more prevalent in Oriental and Asian skin, solar damage and wrinkle onset are significantly delayed compared to Caucasian skin, which could presumably be correlated with the antioxidant levels in fasting blood.

Finally, different skin types have also distinct physiologic responses that are influenced by the environment,
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<td>AHCY</td>
<td>Higher expression levels in the darkly pigmented melanocytes&lt;sup&gt;81&lt;/sup&gt;</td>
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<td>Constitutive levels of protein expression are typically higher in African individuals&lt;sup&gt;32&lt;/sup&gt;</td>
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<td>ASIP</td>
<td>Allelic diversity. Associated with darker skin color&lt;sup&gt;32,81&lt;/sup&gt;</td>
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<td>BNC2</td>
<td>Allelic diversity&lt;sup&gt;81,84&lt;/sup&gt;</td>
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<td>DCT</td>
<td>Allelic diversity&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Intronic polymorphism at high frequency&lt;sup&gt;85,86&lt;/sup&gt;</td>
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<td>DRD2</td>
<td>Allelic diversity, positive selection&lt;sup&gt;85&lt;/sup&gt;</td>
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<td>EDEM2</td>
<td>Higher expression levels in the dark-and moderate-pigmented melanocytes&lt;sup&gt;81&lt;/sup&gt;</td>
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<td>EGFR</td>
<td>Allelic diversity&lt;sup&gt;85&lt;/sup&gt;</td>
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<td>Allelic diversity&lt;sup&gt;85&lt;/sup&gt;</td>
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<td>EXOC2</td>
<td>Correlates with the levels of serum 25(OH) D, impact on vitamin D status and deficiency common in the Caucasian population&lt;sup&gt;88&lt;/sup&gt;</td>
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<td>GGT7</td>
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<td>GSS</td>
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<td>HERC2</td>
<td>Allelic diversity&lt;sup&gt;81&lt;/sup&gt;</td>
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<td>IRF4</td>
<td>SNP strongly associated with skin tanning response in Europeans&lt;sup&gt;89&lt;/sup&gt;</td>
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<td><strong>ITCH</strong></td>
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<td>Allelic diversity, positive selection&lt;sup&gt;85&lt;/sup&gt;</td>
<td>Allelic diversity&lt;sup&gt;85&lt;/sup&gt;</td>
<td>Significant association with higher melanin index in African-American population&lt;sup&gt;32&lt;/sup&gt;</td>
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<td><strong>KITLG</strong></td>
<td>Allelic diversity, positive selection&lt;sup&gt;85&lt;/sup&gt;</td>
<td>Allelic diversity&lt;sup&gt;85&lt;/sup&gt;</td>
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<td><strong>c-KIT receptor</strong></td>
<td>Allelic diversity high. Same effects on pigmentation appear at increased frequency with increasing latitude. Associated with fair skin and freckling&lt;sup&gt;32,93,94&lt;/sup&gt;</td>
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<td><strong>MAP1LC3A</strong></td>
<td>Allelic diversity low&lt;sup&gt;95&lt;/sup&gt;</td>
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<td>Allelic diversity low&lt;sup&gt;94&lt;/sup&gt;</td>
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<td><strong>MC1R</strong></td>
<td>Correlates with the levels of serum 25(OH) D, impact on vitamin D status and deficiency common in the Caucasian population&lt;sup&gt;88&lt;/sup&gt;</td>
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<td><strong>MITF</strong></td>
<td>Allelic diversity, positive selection&lt;sup&gt;81&lt;/sup&gt;</td>
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<td>Hypofunctional alleles with 70% of the function of the wild-type protein. Lighter skin pigmentation&lt;sup&gt;94,97,98&lt;/sup&gt;</td>
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<td><strong>OCA2</strong></td>
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<td>Accounts for lighter skin&lt;sup&gt;93&lt;/sup&gt;</td>
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<td><strong>PROCR</strong></td>
<td>Higher expression levels in the dark- and moderate-pigmented melanocytes&lt;sup&gt;81&lt;/sup&gt;</td>
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<td><strong>RALY</strong></td>
<td>Higher expression levels in the dark- and moderate-pigmented melanocytes&lt;sup&gt;81&lt;/sup&gt;</td>
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<td>Accounts for differences between darkest and lightest skin reflectance. Mutations that impair gene function (OCA4) are highest in Asian populations&lt;sup&gt;32,99&lt;/sup&gt;</td>
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<td><strong>SLC24A4</strong></td>
<td>The key skin pigmentation SNP; strong evidence for selection in Europeans&lt;sup&gt;32&lt;/sup&gt;</td>
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<td>Accounts for differences between darkest and lightest skin reflectance; highly associated with lighter skin color&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Allelic diversity&lt;sup&gt;32&lt;/sup&gt;</td>
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<td><strong>SLC24A5</strong></td>
<td>Allele strongly associated with olive skin&lt;sup&gt;85&lt;/sup&gt;</td>
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<td><strong>SLC45A2 (MATP)</strong></td>
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<td>Accounts for differences between darkest and lightest skin reflectance. Mutations that impair gene function (OCA4) are highest in Asian populations&lt;sup&gt;32,99&lt;/sup&gt;</td>
<td>Allelic diversity&lt;sup&gt;32&lt;/sup&gt;</td>
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<td><strong>TYR</strong></td>
<td>Allelic diversity. Mutations lead to OCA&lt;sup&gt;81&lt;/sup&gt;</td>
<td>Correlates with the levels of serum 25(OH) D, impact on vitamin D status and deficiency common in the Caucasian population&lt;sup&gt;88&lt;/sup&gt;</td>
<td></td>
<td>Largely absent&lt;sup&gt;32&lt;/sup&gt;</td>
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such as skin hydration. Transepidermal water loss (TEWL) is indicative of skin surface moisture and defined as the body loss of water that passes via diffusion and evaporation to the atmosphere through the epidermis, and this parameter is increased in African skin compared to Caucasian skin.\textsuperscript{52} Across all populations, TEWL and skin surface moisture decrease with age, and this is more pronounced in Caucasian skin, coinciding with thinner stratum corneum.\textsuperscript{43,45,53} Changes in the epidermis are also evident in the rate of desquamation or corneocyte variability, which increases with age and accounts for xerosis, which is frequently more pronounced in African skin.\textsuperscript{52,54} The conditions can currently be treated with a range of externally applied moisturizing products to restore the integrity of the stratum corneum through replacement of the natural natural moisturizing factor components. The active ingredients, categorized as emollients, occlusives and humectants, provide a barrier that softens the skin, bind water in the stratum corneum and prevent TEWS.\textsuperscript{55-57}

### Personalized skincare

Transcriptomic data generated from young and old sun-protected and sun-exposed skin provide much information on the gene clusters and hierarchical pathways implicated in intrinsic aging and photoaging. The biomarkers identified in both types of aging are relevant to skin barrier maintenance through lipid biosynthesis and epidermal differentiation as well as oxidative stress and antioxidant defenses. Differences between intrinsically aged and photoaged skin can be detected at the level of extracellular matrix, with reduced expression of collagen genes in intrinsic aging and increased expression of elastic tissue genes in photoaging.\textsuperscript{58}

Much information on skin biology and aging processes obtained through molecular and cell biology-based technologies requires development and applications of advanced statistical and modeling tools. Integrative biology applied to the gene expression data aims at understanding the biological relationships and dynamic processes through the reconstruction of gene regulatory networks. Such networks, representing groups of genes with various functions and the interactions between the groups, have been built using linear and Boolean network models, Bayesian networks and other purpose-built new algorithms. The knowledge gained on the possible gene interactions can be extended further, for instance, to include other parameters such as the transcription–translation feedback or the effect of local environments on the proteins. The outcomes of mathematical modeling are furthermore applicable toward the already established knowledge on gene interactions and the likely overlap between certain genes identified in different independent studies. The need for development of additional computational approaches is also suggested to take into account more subtle changes in gene expression that are specific for single individuals within similar groups.\textsuperscript{59-61}

Genetic variations that contribute to the unique characteristics of each individual are currently considered to shape the future of clinical and pharmacologic interventions. This is consistent with the idea of treating the person rather than the particular problem, which gains increasing recognition as a more effective approach.\textsuperscript{62} Based on this, the concept of “personalized medicine” recognizing underlying forms of genetic variations emerges as an exceptional strategy with unique applications in pharmacogenomics and pharmacoproteomics. This concept can be extended further onto the field of experimental and clinical dermatology and personalized skincare.\textsuperscript{52,63} Recent progress in molecular assays and diagnostic tests facilitates addressing the physiology of

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<td>TYRP1</td>
<td>Allelic diversity; positive selection\textsuperscript{65}</td>
<td>Allelic diversity\textsuperscript{66}</td>
<td>Constitutive levels of protein expression are typically higher in African individuals\textsuperscript{10,100}</td>
<td>Mutations (OCA3) frequently associated with red bronze skin phenotype\textsuperscript{101}</td>
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<td>Tyrosinase-related protein 1</td>
<td>Stabilization of tyrosinase protein levels and melanosome maturation</td>
<td>Increased expression after UV exposure\textsuperscript{100}</td>
<td>Stabilization of tyrosinase</td>
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skin processes and the pathogenic mechanisms of specific problems including inflammatory and autoimmune skin conditions. Understanding the biology of individual skin structure, sensitivity and hormonal balance and identifying the network of representative genes in the context of specific genetic makeup will drive the design of novel pharmaceuticals and mimetics to modulate appropriate biologic processes.

Skin ethnicity strongly manifests in distinct structural and physiologic traits that can be defined for each major population. In general, Caucasian skin is characterized by smaller melanosomes, less melanin, thinner stratum corneum and dermis and decreased TEWL. These factors contribute further to increased photodamage, loss of collagen and decreased elasticity of dermis as the major outcomes of extrinsic aging process. Darkly pigmented skin of African origin is characterized by bigger melanosomes and more melanin as well as thicker stratum corneum and dermis that is proportional to the degree of pigmentation. Both African skin and Asian skin are more resistant to photodamage and demonstrate preserved elasticity that translates into delayed appearance of wrinkles during aging. However, darkly pigmented skin is more prone to age-related changes in pigmentation, which are particularly evident in Oriental and Asian skin. In addition, ethnic differences in skin type may also manifest in regard to relative skin hydration, with dry skin and xerosis frequently more pronounced in African skin in both low relative air humidity and during aging (Figure 1). Differences between skin phenotypes are also evident within the major ethnic groups. For example, degree of pigmentation and dermal elasticity are the individual characteristics determined by both genetic and environmental factors.

Ethnic and individual diversity in skin structure and physiology may be responsible for different reactivity of the tissue to chemical factors, for instance, it could affect the rate and effectiveness of drug penetration, absorption and sensitization, the parameters important for carefully considered skincare. Whereas Caucasian skin demonstrates stronger resistance to water barrier damage, African skin is more resistant to transcutaneous penetration. Caucasian skin and Oriental skin have similar basal TEWL, but Oriental skin is more sensitive to mechanical and chemical stress, presumably because of the weaker barrier and thinner stratum corneum in the epidermis. Compared with other ethnic skin types, Oriental skin also demonstrates higher eccrine gland density and smaller pore size, which reflect the activity of the sebaceous glands. In contrast, African skin frequently shows the most severe damage around facial pores. The differences between ethnic skin types in response to the environmental factors can also manifest in the dermis, with Caucasian skin being more prone to inflammatory lesions and African skin presenting more often with hypertrophic scarring and keloids.

The phenotypic variations and challenges in defining specific genome–drug interactions can also be applicable to the field of dermatology. One important aspect of pharmacogenomics is the assessment of individual response efficiency, appropriate dose and adverse effects of the proposed formulations, which have a direct influence on their development, cost-effectiveness and safety regulation. The approach to development of skin products usually occurs in stages, commencing with in-depth characterization of raw materials, their nature of exposure to the body and a maximum concentration for use, through in vitro safety tests and clinical trials to product marketing and vigilance procedures.

Current strategies for personal protection against air pollution include topical products that improve skin barrier function for reduced air pollutant penetration and antioxidants to reduce reactive oxygen species, such as vitamins C and E, in formulations. In parallel, substantial progress has been made in topical sunscreen formulations that combine skin moisturizers with broad-spectrum UV filters and sunscreens that filter both UVA and UVB in a ratio that mimics the natural exposure for optimal photoprotection. Effectiveness of the sunscreen is based on the measurements of the sun protection factor in the precisely defined parameters such as application layer (mg/cm²), UV irradiation dose and clinically established changes in the skin in the defined time after exposure. For the purpose of personalized skincare, both the skin type and the environment should be taken into account as the skin is exposed to varied levels of air pollutants on a daily basis. On the molecular level, sunscreens with a well-balanced sun protection factor/UVA-PF ratio were demonstrated to prevent UVA-induced expression of the genes associated with oxidative stress response and ECM degradation in the dermis. This type of protection would be particularly suitable for lightly pigmented Caucasian skin that is prone to wrinkles. Darkly pigmented and, particularly, Oriental skin could benefit from the sunscreens that filter shorter wavelength UV that affects epidermis and could exacerbate the hyperpigmented lesions. Development of new personalized products that support skin barrier renewal and enhance NMF to prevent TEWS could be particularly beneficial for African skin.

Frequently, the knowledge on genetic background, gene/environment interactions and the response to the cosmetic ingredients is not always available. One step toward more
complete databases would be gathering the information on the use of personal care products in the studies of consumer use practices, including the amount of the applied product and the frequency of its use. This also provides an exposure assessment of the active ingredients in such products.\(^\text{73,74}\) For instance, the awareness of the UV-induced damage is reflected by greater photoprotective measurers recorded in clinical studies among volunteers with group I/II compared to III/IV skin types.\(^\text{75}\) Randomized trials also provide a useful tool to define long-term effects of the product.\(^\text{76}\)

Relevant studies also describe the construction of new models of population exposure to regulated personal care products based on the recorded usage profiles.\(^\text{77,78}\) Another complementary approach to personalized information is

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**Figure 1** Representative differences within the epidermis and dermis among four ethnic skin types and the age-related changes typical for the traits sensitive to environmental damage.

*Abbreviation:* TEWL, transepidermal water loss.
through visualization techniques based on the Electronic Health Records as a summary of individual’s physical health and guidance to optimal health level. Such a system has been described for several case studies and subsequently translated into a model and information visualization tools recommendations to explore multiple Electronic Health Records. Interestingly, one important parameter to assess the overall health status is the facial complexion of the individual. Such a factor implemented in the construction of the visualized health report might provide an alternative to the conventional, text-based clinical description as part of the personalized health information.  

Conclusion
Molecular and physiologic responses of the skin to the environmental factors that affect pigmentation, dermal elasticity and epidermal moisture are strongly dependent on the skin type. Ethnic skin phenotypes can be distinguished based on defined genotypic traits, most specifically SNP in the genes involved in biosynthesis of melanin and responsible for pigmentation. Melanin production is stimulated by UV radiation and has an important role in protecting the skin against photodamage. Skin types defined as Caucasian, Oriental, Asian and African origin demonstrate significant differences in the organization and compartmentalized sensitivity to distinct extrinsic factors. This translates further into different demands regarding preventive measures and relevant cosmetic product applications focusing on distinct aspects of skin damage and regeneration. Personalized skincare is an actively growing area with the biomedical and commercial applications that could provide new generation of skin products. Individual approach to skin, based on the recorded profiles and the in silico modeling of unique characteristics such as structural and biometric measurements, dermal/epidermal biomarkers, hormonal and stress response, could be an effective and affordable treatment of many skin conditions in the future.

Disclosure
The authors report no conflicts of interest in this work.

References


