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Dermatonutrigenomics: Past, Present, and Future

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The impact of diet on skin health is receiving growing interest. The global beauty supplements market is expected to reach over USD 13, 845 million by 2025, expanding at a compounded annual growth rate of 9.5% from 2017 to 2025. Of this total, 30% of dollars spent will go toward skin care supplements – the highest of any subcategory [1]. Despite interest from media, patients, and the dermatological community, the role of diet in dermatologic conditions has historically been difficult to elucidate. One of the key reasons is nutrigenomics, the impact of inherited traits on an individual's response to a dietary pattern, functional food or supplement. This theory suggests that dietary factors and associated health outcomes are highly personalized. In 2005, the term "nutrigenomics" first appeared in the dermatological literature in an article on psoriasis patients in *Archives of Dermatology* [2]. In 2010, Subbiah [3] coined "dermagenetics," which involves testing for select genetic mutations related to skin health and recommending the use of nutraceuticals or cosmeceuticals based on the individual results. Despite many exciting advances, nutrigenomics and dermatonutrigenomics are still in the early stages of development, and barriers to research include (i) the chemical complexity of food, (ii) genetic heterogeneity of humans, and (iii) the complexity of physiological responses to nutrient intakes in health and disease [4]. To address these challenges, a transition to personalized nutrition guidance and FDA oversight will be crucial in the coming years.

Herein, we highlight the concept of nutrigenomics in dermatology, by reviewing past and present applications of nutrigenomics, and shed light on the future of nutrigenomics in dermatology.

What Is Nutrigenomics?

Nutrigenomics is a subfield within genomics that focuses on the influence of nutrients on gene expression and, ultimately, cellular function. It has been proposed that nutrients act as ligands for transcription factor receptors, serve as signaling molecules, and are metabolized to alter concentrations of substrates or intermediates eventuating in an altered phenotype. The fundamental concept centers on the progression from a healthy to a chronic disease phenotype, which dietary compounds directly or indirectly regulate via expression of genomic information and enzymatic activities [4]. Notably, nutrigenomics is conversely related to "nutrigenetics," which studies the influence of genetics on an individual's ability to process and respond to nutrients.

Past

The notion of nutrigenomics arose at the dawn of the genome sequencing era. In 1999, a prolific study by Lee et al. [5] published in *Science* suggested that gene expression profiles can be used as mechanistic tools to better understand the effects of environmental factors and nutritional interventions (e.g., caloric restriction) on health. Completion of the Human Genome Project in 2001 provided a framework for documenting single-nucleotide polymorphisms (SNPs) in candidate genes and exploring metabolic imbalances, sparking numerous research studies across all organ systems [3]. By that time, individual genetic differences in response to dietary components had been evident for years (e.g., lactose intolerance).

In 2005, the term "nutrigenomics" first appeared in the dermatologic literature in an article on psoriasis patients in *Archives of Dermatology*. Treloar [2] described the role of the SNP C677T in the gene for methylene tetrahydrofolate reductase (MTHFR), an enzyme critical in the activation and regeneration of folate. Psoriasis patients have significantly elevated homocysteine levels and lower folate levels compared with matched controls, which correlated with an increased risk of atherosclerotic disease [2]. This study sparked interest in the role of dietary modulation and supplementations of folate, cyanocobalamin, and/or pyridoxine for cardioprotection.

In 2010, Subbiah [3] coined "dermagenetics," which involves testing for select genetic mutations related to skin health and recommending the use of nutraceuticals or cosmeceuticals based on the individual results. The common mutations examined are related to the enzymes involved in: (a) collagen breakdown, (b) photoaging and free oxygen radical elimination, (c) degradation of environmental pollutants, and (d) generation of proinflammatory molecules [3]. The benefit of such cosmeceuticals is currently heavily under debate given our lack of understanding of their formulation methods, the integrity of the active ingredients, release from carrier vehicles, and limited FDA regulation (Fig. 1).

Present

The central role of diet in determining genome stability and related health outcome diseases is now well established. A Pubmed search of "diet and skin" reveals over 2,900 articles published on this topic in the last decade, and 25% of these have been over the last 2 years. GoogleTrends reports that the search terms "food and skin," "diet and skin," and "skin supplement" have become more popular over the last decade. Elimination diets are widely adopted treatments in genetically predisposed individuals with specific food allergies, celiac disease, Hartnup's disease, phenylketonuria, and acne. A recent review on nutrition in inflammatory dermato-

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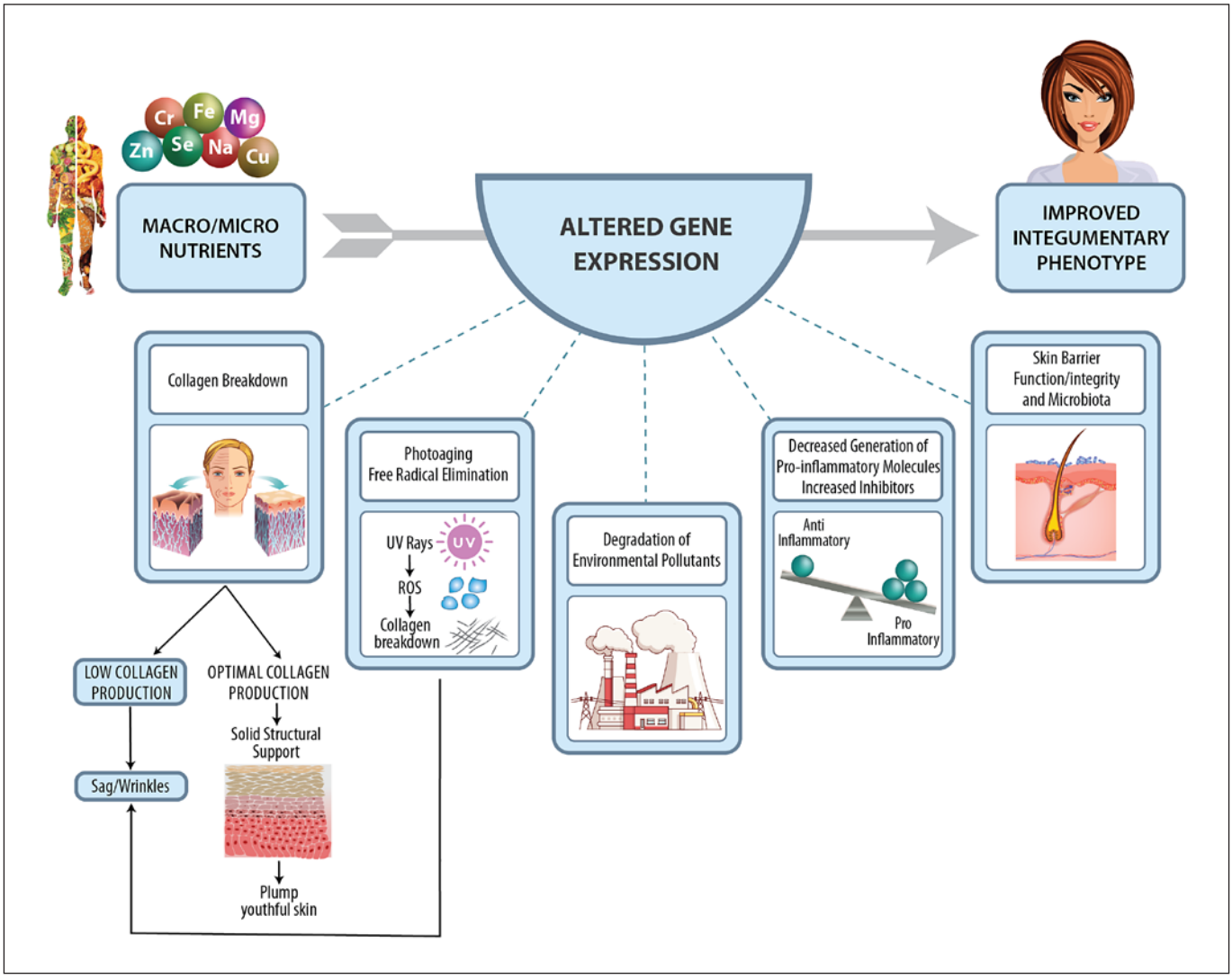

Fig. 1. Potential targets of nutrigenomics in dermatology. A figure showing the potential effects of macro- and micronutrients on gene expression and subsequent downstream effects on skin health and pathology.

ses concludes that imbalanced nutrigenomics induced by the Western diet exaggerates insulin/IGF-1 signaling and contributes to acne pathogenesis [6]. Exacerbation of atopic dermatitis by true food allergies is established by robust and validated testing. "Dermatonutrigenomics" now refers to the study of genes and nutrition and their interrelationships, in order to identify their combined influence on skin health.

Future

Despite many exciting advances, nutrigenomics and dermatonutrigenomics are still in the early stages of development. Barriers to nutrigenomics research exist, and innovative solutions to these well-described challenges are needed. Isolating the responsible gene-nutrient interaction in clinical trials is known to be complicated by (i) the chemical complexity of food, (ii) genetic heterogeneity of humans, and (iii) the complexity of physiological responses to nutrient intakes in health and disease [4]. An example of this is the marked differences in blood glucose responses to the same quantity of carbohydrates consumed [7]. Confounding factors also present a notable research challenge, as does the fact that many health effects may take months to years to manifest, making valid controlled dietary trials extremely challenging. Additional challenges include the variable nature of the epigenome over time, the variability of consumer behavior, and the lack of clear guidelines for applying genetic information to nutritional plans.

To address these challenges, population-based nutrition guidance that transitions into personalized nutrition guidance can be considered. This will likely include technology-based tools that deliver genotype-based dietary recommendations directly to consumers. Clinical trials of such genotype-driven nutrition recommendations delivered to mobile and computer devices are already under way. Start-up companies are already working towards ap-

plying these technologies on the market. Finally, further studies elucidating the interplay of nutrigenomics and nutrigenetics may provide further insight into these multifactorial processes.

The emerging role of nutrition in dermatological practice is evidenced by consumer and research trends. While the role of personalized nutrition in dermatology will likely be limited by cost and time constraints, increasing consumer health awareness coupled with easy availability of products will continue driving growth of nutrigenomics. Direct-to-consumer genetic testing and the associated medical-legal implications are another emerging regulatory issue. FDA oversight for standardization of clinical testing, manufacturing, and product labeling is evolving and crucial in the coming years.

Key Message

We discuss the past and present applications of nutrigenomics and shed light on its future in dermatology.

Disclosure Statement

Dr. Vivian Shi holds stocks in the company Dermveda. Dr. Rajani Katta is the author of a book for the general public on the topic of diet in dermatology. The authors do not have any other financial interests (stocks, patents, employment, honoraria, or royalties) or nonfinancial relationships (political, personal, or professional) to disclose.

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