

Nutrigenetics, Nutrigenomics, and the Future of Dietary Advice

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ABSTRACT

Our individual metabolic phenotype is the result of the interaction between nutrients and DNA to modify gene expression. This is a combination of epigenetic interactions whereby nutrients modify the structure of DNA to affect gene expression as well as individual genetic variation that alters our response to diet. Our metabolic phenotype is influenced by developmental plasticity, imprinting in early life and interactions with environmental factors over time. Unlike the human genome which is relatively fixed and stable throughout the body, the human metabolic phenotype is far more complex and dynamic, varying over time and among cells and varying greatly from person to person. Dietary recommendations are often generalized and intended to avert chronic illnesses such as diabetes and cardiovascular disease. In a climate where we are striving for personalisation of healthcare maybe we need a simpler approach; one that embraces genetic variation yet focuses on the optimum nutritional benefit of dietary components.

Keywords: Nutrigenomics; Individualised Healthcare; Genome Led Dietary Advice; Epigenetics

1. Nutrigenomic Dietary Advice

In the context of personalized nutrition or dietary advice, nutrigenetics approaches an individual's genetic information from the point of view that such information is, "a mechanism of individual empowerment" [1]. Nutrigenetics can help an individual determine their genetic susceptibilities and, with assistance, choose foods that have medicinal properties and known health benefits, but are genetically appropriate. That is to say, red wine may reduce *your* risk of ischemic heart disease; cocoa may reduce *my* risk of cardiovascular disease, depending on our genetic information [2]. Given the diversity and availability of food products in a developed, Western nation, the potential for genetically tailored dietary advice is vast. The added benefit of nutrigenetic dietary advice, developing within such a dietary composition, is that it may assist in combating the disadvantageous aspects of Western dietary patterns, *i.e.*, excessive intake of high energy, refined foods [3]. Nutrigenomics and nutrigenetics are two fields derived from nutrition science and genetics. Their main goal is to elucidate the influence of interactions between genes and diet on individuals' health. Nutrigenomics looks at the interplay between our

dietary and lifestyle behaviour and how that interacts with our genome in terms of regulating genes that are important in the control of metabolism. Encompassing epigenetics and nutrigenetics, nutrigenomics aims to look at the holistic effect of diet and lifestyle on our genome and hence on our state of health.

In such the same way that components of indigenous diets have been studied to examine their medicinal utilization [4], nutrigenetics and nutrigenomics could afford clinical researchers the opportunity to examine those foods, within the Western diet, that could be considered part of a multidimensional, gastronomic pharmacopoeia. Such an approach may be useful as it encourages clinicians (and health-conscious individuals) to find intra-dietary solutions to health issues born out of a Western dietary composition [5]. For example, type 2 diabetes continues to be one of the major health threats facing Western-European populations [5]. Adjustments to diet that encourages a decreased intake of cereals and dairy products and an increased intake of meat and vegetables, has been shown to improve glycemic control for type 2 diabetes patients [5]. While there may be socio-economic factors restricting access to food products like lean meat and fresh vegetables, the availability and diversity of

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such foods, within the Western diet, makes it an ideal dietary composition for the exploration of food-based dietary advice [6].

The nutritional paradigm inherent to nutrigenomic dietary advice is one that relies fundamentally on an ancestral exemplar. As such, any genetic considerations must bare witness to mankind's historical genetic profile [7]. This is perhaps best illustrated in the highly popular Palaeolithic diet. This diet takes into account the historical migration and consequent rapid change in nutrition of human populations, understanding that this ultimately put mankind at odds with established, genetic dietary patterns [7]. The result was the initiation and progressive development of chronic degenerative diseases. The Palaeolithic diet then, is a clarion call back to the diet of old; one more suited to the protracted nature of mankind's genetic evolution. Through such diets, nutrigenomics helps to remind people that their genes do not work independently of their nutritional environment [7]. Furthermore, it asks that the conceptual framework surrounding nutritional health advice be expanded to include ideas associated with genetic dietary patterns [8].

Arguably, nutrigenetics and nutrigenomics can help unravel the complex relationship between dietary composition, genetic profile, and disease prevention. The genetic profile of an individual may be such that their diet affects (or is affected by) biological mechanisms, that in turn, influences their risk of developing certain cardiovascular diseases [9]. Atherosclerosis has associated risk factors (such as LDL cholesterol) that are greatly influenced by key regulatory genes for cholesterol metabolism [9]. Individualized dietary advice that takes into consideration genetic profile could help to reduce a risk factor like LDL while examining the impact of dietary constituents (MUFAs and PUFAs) on gene expression. Such dietary advice then would be conscious of the fact that certain genes (*CETP*, *LPL*, *APOE*) and their polymorphisms can be affected by dietary intervention and may even modify the onset of (or protection from) diseases like CHD [10].

Genetics has built upon the Hippocratic concept of positive health by helping expound the biological dimension of "man's primary constitution" and how it relates to the nutritional "power" of food [11]. Research that has focused on the interaction between genetic predisposition and Western dietary patterns, has given strong support to the notion that a diet high in intake of refined food products and red meat, can increase the risk of diabetes among individuals who have the established genetic variants for the disease [3].

In light of such findings, a nutrigenetic approach to dietary advice is therefore ideal in taking into consideration an individual's genetic predisposition score (GPS) for disease risk (*i.e.*, type 2 diabetes risk), and adjusting

dietary patterns accordingly [3]. However, for this approach to be effective, it is necessary for those involved in the field to give greater consideration to health promotion around genetic predisposition and encourage people to learn more about their GPS [11]. Nutrigenetic health promotion can also make people aware of other significant attenuating factors, such as physical activity, and how these can be adapted to those who would benefit the most given their genetic predisposition [12]. Recent findings even suggest that regular physical activity can reduce the genetic predisposition to common obesity by 40% [12]. By coupling individualized dietary advice with the promotion of factors that attenuate disease risk, nutrigenetics is arguably a powerful tool in combating nutrition-related disorders.

Research into the relationship between genetic predisposition and athletic performance may also have beneficial implications for nutrigenetics. Studies conducted on the relationship between the *ACTN3* gene and athletic performance have produced findings that suggest *ACTN3* is a factor that can influence an individual's fitness capacity [13]. It could even be considered in the development of gender specific health advice as research has indicated that there is a significant association between *ACTN3* genotype and muscle strength in women [14]. Such findings can be used by nutrigenetics in the recommendation of physical activity as an attenuating factor. A tailored physical activity program could be used in conjunction with individualized dietary advice, to produce a comprehensive, genetics-based approach to disease risk attenuation [13].

2. Genomic Health Promotion

Nutrigenetics may even be able to broaden the framework for health promotion, by drawing together research in historical genetic profile, genetic adaptation, and environmental alteration (in the context of diet), thus helping to form a more cohesive ontological basis for nutritional science [8]. Understanding past, present, and future interactions between genes and diet, within a more unified, paleo-anthropologic framework, may help to reduce the stigma of suspicion that seems to plague genetics based health advice. If this is who we were, who we are, and who we will be—biologically—then it behoves us to consider our health and wellbeing accordingly [5].

Advocation of the paleolithic diet is driven primarily by consideration of the impact of familial factors on disease risk [11]. However, it also finds support in the consideration of unique dietary challenges that arise as a result of environmental factors; factors that have been found to relate to (even influence) predisposition to nutrition-related disease [15]. A dietary challenge, such as

exposure to palatable high-fat foods, is arguably a greater obstacle for an individual who is genetically predisposed to a nutrition-related disease, and has a taste preference for palatable foods. The difficulty is compounded when food selection occurs within a diet that is dominated by palatable high-fat foods (*i.e.* a Western-type diet) [15]. In this instance, the intersection of taste preference and food selection can result in the individual over-eating foods that are likely to promote the onset of disease [16]. By embracing the paleolithic diet, an individual is able select foods from a composition, more in tune with mankind's ancestral genetic dietary patterns [15]. A significant factor for nutrigenetics to consider then is that the diet does not explicitly address the challenge of an individual overcoming taste preference, in order to select foods that contain beneficial dietary constituents [16].

3. Dietary Epigenetic Effects: Link between Genes and Environment

Early life nutrition has importance as a key determinant for disease risk in adult life. Epigenetic control of gene expression by diet and environment in utero determines lifelong health trajectories. Imprinting in early life modulates gene expression during development and maturity and enables phenotypic development in response to environmental cues. An adverse environment during pregnancy or lactation periods has been well documented as having a role in the future development of obesity, suggesting that the mother's nutrition and lifestyle could alter the developmental programming of the foetus [17]. Both research into human health [18] and animal studies show that diets that contain too many or too few calories during pregnancy result in offspring that are at increased risk of obesity and/or metabolic syndrome.

The role of nutrition in adulthood is also emerging as increasingly important in the acute epigenetic plasticity in the control of genes. Bioactive food components have been shown to modulate the activity of enzymes that integrate the epigenetic machinery [19,20]. A wonderful example of phenotypic plasticity is in the honeybee where diet produces different phenotypes from the same DNA genome. The larvae are genetically similar but only the larvae fed royal jelly will develop as queen bees, the others, fed less sophisticated food become worker bees [21]. This phenotypic plasticity also occurs in humans, for example fat cells show altered DNA methylation in response to calorie restriction [22], and dietary folate supplements in men and women are linked to increased global genome methylation, *i.e.* gene suppression. Other factors that have been linked to DNA methylation in adulthood are alcohol, vitamin B6, vitamin A and some minerals [23]. Diallyl disulfide, found in garlic, has been shown to regulate histone acetylation in cultured cancer cells. Pre-

liminary studies suggest that diallylsulfide has a role in down-regulating genes involved in promoting the early stages of cancer development. Similarly, experiments with the isoflavone genistein (found in soybeans, fava beans and coffee, among other sources) have shown that it reverses methylation on tumour suppressor genes. As methylation of tumour suppressor genes silences them, the reversal of methylation effectively "switches" these tumour suppressor genes back on and may help to prevent early cancer development [24,25].

4. Way Forward

Nutrigenetics has tended to focus on the utilization of specific nutrients (often in nutrient mixtures), derived from food substances, when examining gene/nutrient interaction and disease outcome [26]. A dietary approach, that treats the food products themselves—not the nutrients inherent to the foods—as the functional component, may be more apt at dealing with the complexities that can arise from using nutrient mixtures to influence molecular pathways [26]. Nutritional advice, as per a dietary approach, considers any known gene/nutrient interaction that may occur from eating a specific food, while at the same time examining the overall nutritional impact of the food eaten. In this way, the effectiveness of nutrigenetic dietary advice is less likely to be limited by unknown variables, such as; the extent specific nutrients have in contributing to observed gene/nutrient effects [26].

With regards to dietary and nutritional advice, the challenge for genomics is to pursue goals of personalization and individualization that are achievable, given the current level of knowledge about gene/nutrient interaction [27]. Genetic testing for alleles related to specific nutritional diseases tends to focus on one genetic factor only. Such findings are important, but should not be utilized hastily (in personalized dietary advice) when the impact of other contributing genetic factors is still unknown. A broader, perhaps simpler approach is still needed; one that embraces genetic variation yet focuses on the optimum nutritional benefit of a diet. Ideally this would incorporate an understanding of specific genetic profiles for optimising diet and exercise programs alongside a deeper understanding of the epigenetic interaction, both transient and long term, our diet and lifestyle have on our transcriptome and the implications for health.

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