Importance of nutrigenomics and nutrigenetics in food Science

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Abstract

Nutrigenomics and nutrigenetics are bidirectional terms that are interrelated as two sides of a coin. Nutritional genomics is the latest scientific discipline that uses modern genomics technology to study the relationship between genes, nutrition, and health. It explores the effects of nutrients on the entire genetic makeup (genome), proteome, and metabolome. Simply, nutrigenomic defines how the diet acts on genes and changes gene expression which is commonly prominent in cancer like non-communicable diseases. Nutrigenetics explains how the genes affect the diet which is generally notable in illnesses like phenylketonuria and lactose intolerance. Nutritional genetics combines the study of nutrition and genetics to discover the different ways people respond to food based on their genetic makeup. Even though humans are similar in genetics, we all have slight differences in our genetic blueprints due to single nucleotide polymorphisms (SNPs) that make us unique from each other. These tiny variations determine both the effect nutrients have on our bodies and how we metabolize the food that we eat. Personalized nutrition connects this two-way relationship between nutrients and genes. This mini-review discusses the applications, advantages, and disadvantages, Sri Lankan context, and future trends of these emerging technologies. Furthermore, this review emphasizes how the consumed nutrients can affect our gene expressions as well as how our genes can influence response to these nutrients. This emerging field could be improved to enhance personalized diet consumption trends depending on individual genetic makeup and to develop innovative functional foods based on genetic patterns. Finally, the production of biomarkers could be applied in the future to predict early disease recognition and to mitigate disease risk.

Keywords: nutrigenomics, nutrigenetics, genome, gene-diet, non-communicable diseases, SNPs

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Abbreviations: SNPs, single nucleotide polymorphisms; PKU, phenylketonuria; PA, phenylalanine; NCD, non communicable diseaes; GMOs, genetically modified organisms; GALT, galactose-1-phosphate uridyltransferase

Introduction

Nutrigenomics is the application of genomics in nutrition.[1,2] This became an apparent field of science unrevealing interrelationships linking nutrients and the human genome and health employing the newest tools such as transcriptomics, epigenomics, metabolomics and proteomics.[2–4] This emerging science reveals,

a. effect of the dietary bioactive compounds on gene expression,
b. the pathway of our genes act influenced by nutrient intake,
c. how nutrients influence on genes to prevent and treat diseases, and
d. molecular relationships between nutrients and gene responses.[5]

Even though the genetic component had assumed in earlier times as a factor that is in control of variations in dietary response, researchers have initiated to investigate these nutrient-gene synergies at the basic molecular level nearly over the recent two decades.[3]

Nutrigenomics

Studies the interaction between our genes and the foods we eat.[2,5,6] Specifically, it studies how people with different genetic makeups are affected by different foods. This technology aims to match people to the foods that suit them best.[7,8] This emerging field brings together scientists, policymakers, and health professionals in pursuit of the goal of one day implementing personalized nutrition advice, and developing functional foods that will optimize health as claimed by individual needs. It converges the way we eat, what our parents ate, and how it influences the growth route of our cells and biological systems. Further, it resembles how the food will govern our anatomical development in distinctive paths based on our genetic makeup. Nutrigenomic profiling will assist to detect the mechanisms that carry individual variations in dietary necessities as well as in the potential to respond to food-related interventions.[9]

Nutrigenetics

Studies at the way that individual's genetic makeup influences their physical response to the ingested nutrients. Also, peoples are considered to be gene variants. As an example, slight changes among people's genetic makeup resulted in different responses to particular nutrients. Depending on the food intake, certain interactions can lead to the incipience of specific disease conditions.[1,9] Genetics is the study of genes; inherited molecules that transferred from generation to generation. Genes manage to make the proteins in our bodies and it decides differences among each other.[6] The aforementioned differences include both visible biological features such as the color of the eye and shape of the nose, as well as hidden attributes like blood group and susceptibility to illness. Humans sustain around 20,000 to 25,000 genes.[7] In the year 1990, scientists had initiated to identify and sequence those genes in which known as the human genome project.[10] In the year 2000, they had outlined the first comprehensive map of human genetic makeup.

Nutrigenetics enables us to realize how our genes affect the method we react to foods, beverages, and supplements. This analyses how genetic makeup or variations of individuals affect their response to diet. It has long been visible that certain people react differently from others to particular foods. For instance, people with lactose intolerance undergo gastrointestinal uneasiness after ingestion certain dairy products, while other people can consume dairy without difficulties. The individuals who cannot digest the natural sugars present in milk products are called lactose intolerance patients.[8,9] The gene which is responsible for making lactase is switched off in lactose intolerance individuals.[9] As a result, abdominal pain, bloating, diarrhea, and nausea-like conditions can occur.[9] The individuals who suffer from Phenylketonuria (PKU) do not have phenylalanine hydroxylase for breaking down phenylalanine (PA) which is present in food products.[10,11] PA is usually converted to tyrosine in a healthy person's body. But in PKU individuals, it is metabolized into phenyl pyruvic acid.[10] If high level of this acid is accumulated up in the body, it can commence to disordered brain functions and in severe cases in mental retardation and seizure.[11]

The ultimate goal of nutrigenetics is to provide nutritional recommendations for individuals according to their genetic makeup.[8] There are important factors to be considered regarding nutritional genomics. The first is to recognize diet as a significant risk factor for certain diseases in some individuals.[2] Additionally, ordinary dietary nutrients can act on the human genome, either directly or indirectly to change gene expression or structure.[1,4,9] Nevertheless, the extent to which diet affects the balance between healthy and disease circumstances may depend on an individual's genetic makeup. Further, most diet governed genes are expected to perform a task in the onset, progression, and acuteness of chronic diseases. Therefore "personalized nutrition" can be used to prevent, mitigate or cure chronic diseases.

The concepts of nutrigenomics and nutrigenetics

Genetics is a critical concern of every individual fitness puzzle. Nutrigenomics is an emerging science and technology field that reveals interrelationships (Figure 1) linked to nutrients and the human genome based on modern tools such as transcriptomics, metabolomics, epigenomics, and proteomics.[4] The genome information has advanced approaches in analyzing the role of genetic variation to explain personal differences related to nutrition, underlying in part the sensitivity for nutrition-related disorders.[1,8] As shown in the Figure 1, the basic analytical tools of the "omics" revolution in nutrition science are genomics, transcriptomics, proteomics, and metabolomics.[4,9] The Greek suffix "ome" defines "complete" or "all" and it has been used with general terms of genes, proteins, etc.[10] Therefore comprehensive analysis of DNA structure and function is done by genomics while, transcriptomics determines patterns of gene expressions. The study of protein synthesis, structures, and patterns of protein expression is covered by proteomics while the analysis of the metabolite profile and function is explained by metabolomics.

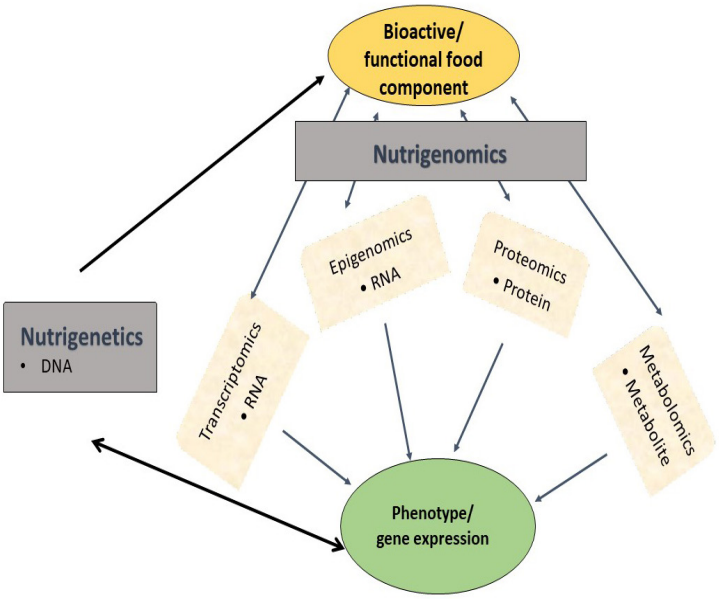

Figure 1 The interrelation of how food intake contributes to phenotype.

Interaction of nutrients and gene expression-Nutrigenomics

Nutrients can act on our genes and can change the genetic expression/phenotype by following pathways as shown in the diagram (Figure 2). As shown in path A, nutrients act as a ligand for transcription factor receptors and affect normal cell growth. Also, diet can influence gene expression by metabolism as depicted in pathway B. These influences can be done either primary or secondary pathways by altering concentrations of substrates or intermediates.[9] Further, normal cell growth can be altered by diet consumption proceeded in signal transduction pathways C as shown in Figure 2.

Researchers have revealed the interrelation of live cells response to varying environments with modified gene expressions. And also they have studied how nutrition can affect the proliferation and differentiation of cells.[1,10–13] Beside metabolome and proteome studies, the transcriptome or genome analysis is becoming more required. Therefore nutrigenomic studies on basic and applied nutrition in food research furnishes new insights into the influences

to food ingredients such as carbohydrates, proteins, fats, carotenoids, vitamins, minerals, flavonoids, and edible phytochemicals at the molecular level.[11,12] Further nutrigenomic applied areas include food safety, food authenticity, researches in genetically modified organisms (GMOs), and personal food planning.[13]

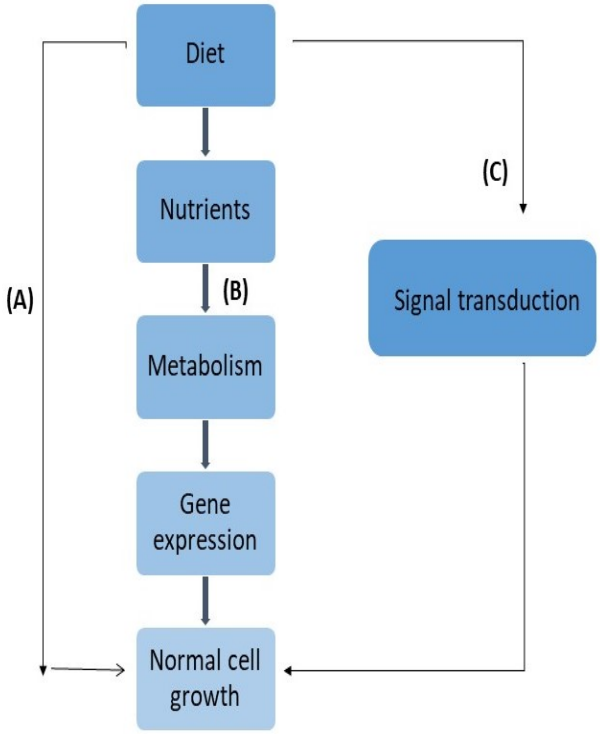

Figure 2 Different pathways of how nutrients act on gene expression in normal cells.

Table 1 shows how certain nutrients can regulate the gene and influence our genetic expression in order to prevent or suppress NCDs like cancers, obesity etc. In diseases like cancers, DNA methilation process is take place which have strong impact on the genetic expression. Pufulete and others have found that DNA hypo methylation can be reversed by intakes of folic acid.[13–20] Aiming delayed or inhibited apoptosis is a huge advance in cancer medication and an extremely emerging area of experimentation. Flavonoids have obtained attention as cancer-preventing agents and have conferred high capability as cell toxic anti-cancer drugs supporting apoptosis in carcinoma cells. Also, studies have found that kaempferol, which falls under flavonoids can induce DNA fragmentation and upregulation of p53 expression and phosphorylation commences to disrupting cell proliferative signaling in breast cancer cells.[21,22] Theaflavins are the major bioactive polyphenols in tea.[21–24] Rheumatoid arthritis is an inflammatory joint dysfunction, whose change leads to the destruction of cartilage and bone. Researches have revealed that Theaflavins as a potential ingredient for the prevention of cartilage degeneration. Also the Mediterranean diet has investigated as a cardio protective diet which is rich in monounsaturated and omega-3 polyunsaturated fats, vegetables, fruits, grains and nuts.[25]

Nutrients works as gene switches

Researchers have experimented the effect on nutrient intake due to prevalence gene expression and disease using rat models and cell culture studies.[26,27] Certain diseases rising in regularity are connected with altered DNA methylation. DNA methylation is achieved by conversion of foods that are rich in methyl donors (folate, vitamin B12, methionine, betaine and choline available foods such as garlic, beets, and onions) into energy.[28] Mice carry a gene named agouti (gene made them yellow instead of brown) cause them to be hungrier and obese. The presence of this gene made them susceptive to complications such as diabetes and cancer etc.[29,30]

Table 1 The relationship of how nutrients impact on the genes and diseases

Nutrient	Gene impact	Related disease	Reference
Folic acid	DNA methylation	Cancer	13,14
Fatty acids	Bind to transcription factors	Obesity	15
Vitamin D	mRNA stability	Kidney disease	16–18
Vitamin E	Radiation mimic (DNA oxidation)	Cancer, heart disease, immune dysfunction	19,20
Theaflavins	Decrease mRNA syntheesis	Arthritis	21,22
Flavones	Increase mRNA synthesis induce DNA fragmentation	Cancer	23,24
Niacin	Disables DNA repair (poly ADP ribose)	Neurological symptoms (memory loss)	19,20

Agouti mice are genetically identical. Scientists have proven that the differences result from variations in the expression of the agouti gene and coat color appearance can be controlled by changing the mother's diet (food supplements rich in methyl donors) before, during, and after pregnancy.[29,31] The nutrient substances (chemical) connected to the agouti genes in the developing baby agouti mice can act as a chemical switch toward the genes (Figure 3). The genes and DNA coding were yet there, but gene expression has turned off. The baby mice were born brown had normal appetites and lived long disease-free survivals.[29,32]

Genetic variation and personalized diets- Nutrigenetics

Nutrigenetics studies how the way individuals' genetic makeup influences their physiological response to the nutrients they consume. It considered that people are gene variants. As proof, the differences between people's genetic makeup cause various reactions to particular nutrients and these interactions can encounter specific disease states.[33] As mentioned in the introduction section PKU, lactose intolerance and galactosemia are common consequences of nutrigenetics.[34,35] PKU is a limited inborn syndrome caused by a mutation in a particular

gene that encodes for the enzyme phenylalanine hydroxylase.[8,10] Galactosemia is resulted from a limited recessive attribute in galactose-1-phosphate uridyltransferase (GALT), commencing to the collection of galactose in the blood and raising the risk of mental retardation.[10,36] Phenylalanine-restricted and galactose-free, tyrosine supplemented diets are recommended to consume later mentioned monogenic diseases, respectively.[10,37] Therefore, nutrigenetics is an important analyses of how the genetic variations in individuals could affect their response to diet.

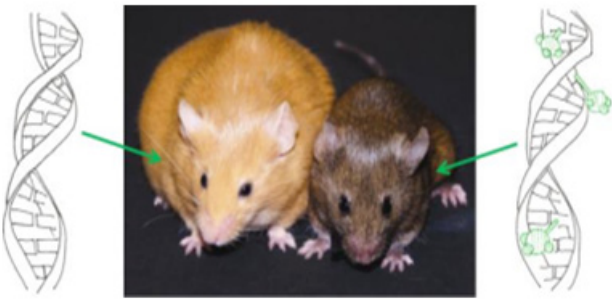

Figure 3 The mouse on the left's mother had fed with a normal mouse diet and the mouse on the right's mother had fed a food diet rich in methyl donors. The left mouse became yellow and obese, while the right moue became brown and healthy.

Genetic variations among population

All humans are 99.9% identical at gene sequence level. But common polymorphisms can determine the dietary requirement of each individual. Generally, 0.1% variations in sequence produce differences in phenotype.[8] This variations manipulate individuals respond differently even with food consumption. Most common type of polymorphisms is single nucleotide polymorphism which is called as SNP.[38,39] A SNP is sequence variation occurred in a DNA by replacing a single nucleotide (adenine (A) or thymine (T) or cytosine (C) or guanine (G)) in the genome among members of a species or paired chromosomes in an individual (Figure 4). SNPs change at single base makes 90% of all variations and about 3 million SNPs are identified in humans. These differ SNPs in an individual can lead unique response to same diet among group of people.[40,41] Other than above variations, structural variations (deletions, inversions, insertions, duplications, and copy-number variations) in chromosome and clines can be observed rarely in organisms that can influences nutrient metabolism pathways.[39,42,43]

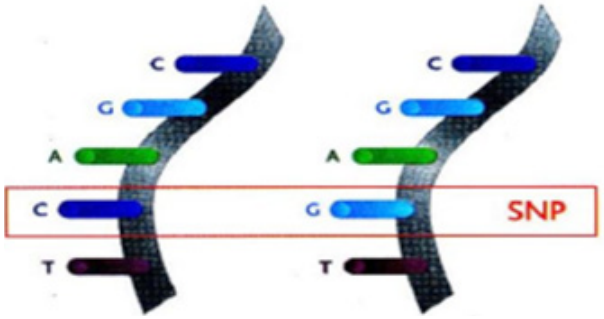

Figure 4 Structural diagram of a Single nucleotide polymorphism. The nucleotide C has been replaced with a nucleotide G.

Applications

It is growing more apparent that nutrigenetics and nutrigenomics are becoming an emerging stage in the researches especially in nutrition and health field. The repercussions of unsuitable nutrient intakes can be assessed comprehensively by the above technologies. Some of these technologies are still in their initial stage whilst others are advanced and accordingly differ in their research-level concerning health issues.

Chronic diseases and various cancer types can be prevented or at least limited by the ingestion of balance and sensible nutrition.[44,45] The awareness gained from examining the diet or gene synergies in distinctive populations may provide knowledge that is demanded to approach the significant global issues like malnutrition. Also genetic diversity is associated to influence absorption, metabolism, consumption, utilization and elimination of nutrients and food bioactive, which ultimately affects several metabolic pathways.[46] Therefore providing personalized nutrition advice that will optimize health according to individual requirments are in demand.[8,47] Further these technologies and findings could be implimented to improve the performance of athletes designing personalied nutition plans.[48]

Also gluten free diets for celiac diseases and pro-biotics for lactose intolerance individuals have been developed in the food industry as a result of nutrigenetics.[49] Further, phenylalanine-restricted and galactose-free, tyrosine supplemented diets are innovated to PKU patients and galactosemia patients respectively. Accordingly, these emerging nutrigenetic and nutrigenomic technologies are applied in novel food technology product developments. Specially research studies are carried out in the functional and medical food applications[42,46,50,51] to develop nutraceuticals and pharmaceuticals. Additionally new researches are carried on to study the complex metabolic pathways which are involved in multiple SNPs. Moreover, genomic medicine strives to develop the shared pharmaceutical decision-making process and to intellectualize drug formula and biomarker production in pharmaceutical industries for the benefit of both the patient and the national healthcare system, by making use of an individual's unique genomic sketch.[52,53]

Another application of nutrigenomics is dermagenetics (testing for selected genetic mutations related to skin health resulted in skin creams or cosmetic innovations) which is directing to commercialization of cosmetic products by aiming the society.[54] As an example, researchers have investigated that the bioactive compounds in the Acmella plant (spilanthol) can reduce the expression of inducible nitric oxide synthase mRNA and protein.[26] This mechanism can inhibit the activation of several transcription factors that sensitize cells to downregulation of Smad (structurally similar proteins that are the major signal transducers). Finally, these alterations lead to anti-inflammatory actions in curing illnesses such as dermatitis and pancreatitis.[26,55]

Furthermore, NuGO is an european funded network of linking human genome, nutrition and health research. Strategically, this network is planning a virtual-center of superiority to unite and promote genomic technologies for the advantage of European nutritional science. NuGO intended to restructure and extend European scientific and technological expertise in nutrigenomics by the implementation and combination of new post-genomic technologies.[56]

Advantages and disadvantages

The intention of both of these technologies are to achieve more effective individual dietary intervention strategies aimed at limiting disease, enhancing the quality of life and managing healthy aging.[6,27] Main advantages of these technologies include improvement of health and preventing diseases through tailored diet and lifestyle prescriptions and effectively controle chronic diseases.

The complex nature of food and polygenic diseases (eg:- diabetes, cancer and etc) make difficult to find out solutions to emerging issues. The high cost involved in these technologies leads restriction for the developing countries. Especially, the requirment of sofisticated research studies limits the appication of these needy technologies in developing countries.

Applications in Sri Lanka

Nutrigenetics is rather applicable all over the world including countries like Sri Lanka as in functional foods applications (eg. lactose-free dairy products), pharmaceutical industries, and cosmetic industries. Even though functional foods have become a reasonably well-established notion, personalized nutrition is still considered with skepticism by many. The general public would have recognized this with their different nutrient requirements depending on their perceptions of food.

Due to the lack of knowledgeable specialists and lack of sophisticated research equipment, nutrigenomic is tough in implementing in developing countries like Sri Lanka. If those technologies are available, people would have a chance to recognize their genetic makeup and get personalized diets which will help to reduce non-communicable diseases. Hence, health conditions can be uplifted through implementing these types of technologies in developing countries. The developing epidemic of obesity, as well as linked diagnostics, such as diabetes, high blood pressure, and cardiovascular disease, indicates a mismatch within the modern diet, lifestyle, and our thrifty human genome. At the climax of the millennium, the utilization of sophisticated technologies connected with genomics to nutritional sciences catalyzed the evolution of nutritional genomics, an advanced research field that directs on characterizing the bidirectional interactions linking genes and nutrition. Further, nutrigenomics uses the omics technologies to determine and identify dietary indications that may reveal the actions of nutrients on the structure and expression of the total human genome. Additionally, nutrigenomics reveals the final impact on human health.

Future challenges and trends

The nutrigenomic applications will lead both short-term and long-term advantages to human health by exposing novel nutrient-gene interactions, promoting new diagnostic tests for unfavorable responses to diets and distinguishing and managing populations with specific nutrient requirements. In future nutrigenomics is expected to deliver biomarkers for the well-being of society, deliver early biomarkers for disease predisposition, distinguish dietary responders from non-responders, and discover bioactive food components. Further, to achieve expected advantages of these bidirectional technologies, a strong network should be build up within both developing and developed countries to share scientific and technological expertise in nutrigenomics by the execution and integration of new post-genomic technologies.

Conclusion

Nutritional genomics is a science that helps us to tailor our diet according to our genes. This field is still developing and recently it will lead us to take the foods which our DNA likes. Nutritional genomics has immense potential to improve the fate of dietary guidelines. Nutrigenetics will furnish the basis for personalized dietary suggestions based on the individual's genetic arrangement. This method has been applied for over the past twenty years for specific monogenic diseases. Nevertheless, the challenge is to achieve a similar opinion for common multifactorial disorders and to generate tools to distinguish genetic options and to anticipate general disorders decades before their indication. The basic issues involving gene-diet interactions for cardiovascular diseases and cancer are assuring but mostly unresolved. The expansion of this field will demand the combination of diverse methods and researches on large population studies to investigate gene-environment interactions in a sufficient manner. Besides the current challenges, the above evidence strongly indicates that these technologies should accomplish and that we will be capable to make use of these information contained in our genomes to achieve healthy life by altering behavioral changes. Finally, as a world, to achieve benefits from these bidirectional technologies, special attention should be given to the dissemination of knowledge both for developing and undeveloped nations.

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Conflicts of interest

The authors declare that they have no conflict of interests.

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