



AYURNUTRIGENOMICS – A STEP TOWARDS PERSONALIZED NUTRITION

Dr Shifa K*	MD Scholar Department of Swasthavritta, Vaidyaratnam PS Varier Ayurveda College, Kottakkal, Kerala. *Corresponding Author
Dr MC Shobhana	Professor and HOD Department of Swasthavritta VPSV Ayurveda College, Kottakkal.
Dr Litty V Raju	MD Scholar Department of Swasthavritta VPSV Ayurveda College, Kottakkal.

ABSTRACT Ahara is one of the three pillars of life according to Ayurveda. Along with medicine, food plays a role in the prevention and mitigation of diseases. Compared to any drug, food is consumed in large quantity. Hence, research on its effect and interaction with the genome is highly relevant towards understanding diseases and their management. The epistemic perspective on health and nutrition in Ayurveda is different from that of biomedicine and modern nutrition. However, contemporary knowledge is reinventing and advancing several of these concepts in an era of systems biology and personalized medicine. Ayurgenomics presents a personalized approach in the predictive, preventive, and curative aspects of medicine. It is the study of interindividual variability due to genetic variability in humans for assessing diagnosis and prognosis of diseases, mainly based on the Prakriti (constitution type of person). In the emerging field of Ayurnutrigenomics, based on the clinical assessment of an individual's Prakriti the selection of suitable ahara, oushadha, and vihara are made. This Ayurveda-inspired concept of personalized nutrition is an innovative perception of nutrigenomic research for developing personalized functional foods and nutraceuticals suitable for one's genetic makeup with the help of Ayurveda. Trans-disciplinary research could be important for pushing the boundaries of food and health sciences and also for providing practical solutions for contemporary health conditions. Hence this novel concept of Ayurnutrigenomics and its emerging areas of research, may unfold future possibilities towards smart yet safe therapeutics.

KEYWORDS : Ayurgenomics, Ayurnutrigenomics, Personalized nutrition

INTRODUCTION

Nutritional Genomics emphasizes on the interaction between bioactive food components and the genome, which includes Nutrigenetics and Nutrigenomics.¹ Nutrigenomics is the study of the interaction between dietary components and the genome, and the regulating changes in proteins and other metabolism and Nutrigenetics that identify the response to dietary components with respect to genetic differences.¹ Nutrigenomics is an emerging science that explores a certain area of nutrition that uses molecular tools to search, access, and understand the several responses obtained through a certain diet applied between individual and population groups.²

Nutrition has a major role on both healthy and disease conditions, and also have importance in the prevention and treatment of multifactorial chronic diseases. Nutrigenomic research may recognize new biological mechanisms governing host response to food.³ Modern medicine incorporates highly reductionist system to define the fundamental basis of our physiology and health by using terms like genome, gene expression, and epigenetics whereas Ayurveda practices a different holistic system, which includes terms such as dosha and Prakriti.⁴

Ayurgenomics provides a new link between Ayurveda and modern medicine by providing a scientific understanding of basic concepts along with incorporating the practical preventative approaches of Ayurveda into modern medicine.⁵ Ayurveda and genomics can contribute to each other. Modern science can help Ayurveda as an evidence-based system of medicine, and Ayurveda can help modern medicine, particularly through its preventive approaches.⁴

In the emerging field of Ayurnutrigenomics, based on the clinical assessment of an individual's Prakriti the selection of suitable ahara, oushadha, and vihara are made.³ This Ayurveda-inspired concept of personalized nutrition is an innovative perception of nutrigenomic research for developing personalized functional foods and nutraceuticals suitable for one's genetic makeup with the help of Ayurveda.³ It is a systematized integration of nutritional practices according to Ayurveda in relation to the Prakriti of an individual, along with the information from genomics, proteomics, and metabolomics projected to provide a strong evidence for the development of personalized nutrition.³

MATERIALS AND METHODS

MEDLINE (www.pubmed.com) or the PubMed database was screened using keywords like *Nutrigenomics Personalized medicine, Nutrigenomics Ayurveda, Nutrigenomics Chronic disease, Nutrigenomics Noncommunicable disease, Nutrigenomics Prakriti,*

Genomics Ayurveda, Ayurgenomics, Ayurnutrigenomics Personalized medicine with their corresponding mesh terms in combination like OR, AND. The inclusion of articles in this review was done by the following process and eligibility criteria: The search was limited to only English literature. Articles published from 1999 to 2021 were included. This search resulted in a total of 110 articles from the PubMed source and 15 articles from other sources such as Google Scholar, MEDSCAPE, and Science Direct. After removing all the duplicates 60 articles were selected. From these 60 articles 26 articles were included as the other 34 articles were unrelated to the topic concerned. This search was undertaken in October 2020.

Applications of Nutrigenomics

Based on the genetic makeup of the person Nutrigenomics determines the individual nutritional requirements. It helps to understand the association between diet and chronic diseases and to understand the etiologic aspects of chronic diseases. Nutrigenomics helps to identify the genes involved in physiological responses to diet and the genes in which small changes, called polymorphisms, may have significant nutritional consequences and the influence of environmental factors on gene expression.⁵

An unhealthy diet is one of the major risk factors for a range of chronic diseases, including diabetes, cancer, cardiovascular diseases, and obesity. Dietary chemicals will alter genetic expression which in turn depends upon specific genetic characteristics or individual genetic makeup. The genes which are regulated by the nutrients play a major role in the severity of diet-related chronic diseases such as lifestyle diseases.

Single nucleotide polymorphism

Single nucleotide polymorphisms are the most important and basic form of variation in the genome and may occur every 100 to 300 bases. Genes comprising one or more SNPs can give rise to two or more allelic forms of mRNAs. These mRNA variants may have different biological functions as a result of differences in primary or higher-order structures that interact with other cellular components. They are responsible for genetic effects that produce a predisposition to most autoimmune diseases.⁶

The standard gene mapping was formulated from the human genome project so the gene sequence of any person can be compared with it and can identify the possible risky genes in the genotype of individuals and can modify it by giving proper diet. The progress of detailed single nucleotide polymorphism (SNP) maps of the human genome along with high-throughput genotyping technologies may allow us to untie complex genetic traits, such as multifactorial disease.⁷

How does diet affect our gene expression?

The macro and micronutrients and active ingredients of the food act on the gene. It may enhance individual genetic potential or may suppress gene activity. Gene expresses themselves through proteins. Enzymes are special proteins designed for metabolism. Our gene instructs ribosomes to produce the enzyme for metabolism. During the transcription process, one strand of DNA is copied into mRNA. The molecule of mRNA then leaves the nucleus and moves to a ribosome in the cytoplasm where translation occurs. During translation, the genetic code in mRNA is read and used to make a protein.⁸

Gene diet-disease interaction

Phenylketonuria is a monogenic disease caused by the change in the gene that is related to phenylalanine metabolism. Affected individuals must avoid food containing the amino acid phenylalanine. Foods such as cauliflower, broccoli, and Brussels sprout are an example of food rich in amino acid phenylalanine. So intake of these foods leads to an excess of amino acid in the body due to altered activity of the gene related to the metabolism. So following a diet that limits phenylalanine could improve symptoms in children with phenylketonuria. Fortunately, newborns are now routinely screened for phenylketonuria and are prescribed a special phenylketonuria diet before symptoms even appear.⁹

Galactosemia is an inherited disorder of galactose metabolism caused by deficient activity of the GALT enzyme. GALT is responsible for galactose metabolism. The single nucleotide polymorphism in the GALT enzyme-producing gene leads to the improper metabolism of galactose. Milk and dairy products are the main dietary source of galactose. The currently available therapeutic strategy is dietary galactose restriction.¹⁰

Red meat consumption has been shown to produce high levels of aromatic hydrocarbons and aromatic amines. These are potentially very harmful carcinogenic agents. Cytochrome P450 is a highly polymorphic gene, that is it tends to show different sequences. Biological harmful action of these compounds is seen more in people exhibiting polymorphism of the cytochrome P450 gene. Three main polymorphism is observed among which, this sequence ATGCGT is most vividly seen. So we have to advise the person in whom such sequence is found to avoid red meat which is a possible reason for colorectal cancer.¹¹

Nutrigenomics, lifestyle diseases, and non-communicable disease

Lifestyle-associated diseases are a group of diseases resulting from exposure of humankind over a longer period to unhealthy diet, lifestyle, and living environment. These diseases share almost similar risk factors, owing to, slow progression, non-infectious and non-transmissible e.g. cardiovascular, nutrition-induced cancers, diabetes, chronic bronchitis, renal failure, hypertension, etc.

Obesity

Obesity is the consequence of higher dietary energy intake and lowers energy expenditure. It is influenced by Environmental, Behavioral, Hormonal, Metabolic, and Genetic predisposition. The Genetic factors accounts for 45 to 75% of the inter-individual variations in BMI. Through genome-wide association studies of common diseases, the "common variant" hypothesis was generated. It means a heritable disease is common in the population, then the specific variation in the genetic code will also be common in the population. If 1% to 5% of the population show a particular genetic variant to a disease then it can be considered as a common variant for the disease. Common variants identified in these 3 genes can cause obesity in future

- INSIG2 (insulin-induced gene-2)
- FTO - an obesity susceptibility locus
- MC4R (melanocortin-4 receptor gene)¹²

Diet in genetic variations of Obesity

There should be an obesogenic environment along with genetic variants for the precipitation of obesity. As dietary nutrient intake is an important environmental factor, it plays a key role in the development of obesity. With the same dietary intake, some may get obese, some may not what makes the difference, the answer is a difference in genetic variation. Therefore nutrigenomics may shift towards the effective management of obesity through personalized nutrition.

Diabetes

Genomic studies identified more than 40 independent T1DM

associated single nucleotide polymorphism. Individuals with type 1 diabetes have a genetic predisposition, although dietary components also contribute to type 1 diabetes. It is well known that the diet has a profound effect on the gut microbiota. Gut microbiota responds differently to dietary components. Long-term dietary habits related to the abundance of certain microbial genera. These microbial genera affect gut immunity. Alteration in the gut immunity may promote autoimmune responses in individuals predisposed to the conditions. Genomic studies show that there are 65 loci associated with Type 2 DM. But this can explain only 10-30% of estimated type 2 diabetes heritability. The remaining percentage is associated with genetic and environmental interaction.¹³ Among the diabetes related gene variants, TCF7L2 gene variant is mostly seen. Studies show that restriction of polyunsaturated fatty acid intake can modulate the polymorphism of this gene. Here comes the role of nutrigenomics. That is by advising the person with TCF7L2 gene variant to avoid PUFA compounds, can reduce the risk for type 2 diabetes.¹⁴

Cardiovascular disease

The gene-diet interaction have a definite role in the biochemical changes as well as symptomatic changes of CVD Gene diet interaction and biochemical changes

The Apolipoprotein gene is related to fat metabolism. Individuals with polymorphism in the apolipoprotein E gene show higher LDL levels compared with other individuals having normal genetic sequences. People with apoprotein A1 gene polymorphism, despite consumption of polyunsaturated fatty acid, show an increase in the protective HDL level. People with polymorphism in the hepatic lipase gene show an increase in the protective HDL level with the intake of polyunsaturated fatty acid. This shows the difference in the disease manifestation despite consuming polyunsaturated fatty acid in people with different genotype Gene diet interaction and the manifestation of CVD

Consumption of alcohol in people with ADH3 polymorphism shows an increased risk for the development of myocardial infarction. Consumption of diet containing arachidonic acid (which is a polyunsaturated fatty acid) in people with polymorphism in 5 lipo oxygenase gene also shows a high risk for the development of MI. Isothiocyanate in the cruciferous vegetable has a protective effect for MI in people with polymorphism in the GST gene (glutathione S transferase gene). So people with this genetic variation in their genome should make alterations in their dietary pattern based on their genetic make up.¹⁵

Cancer

One of the pathologies involved in the development of cancer is abnormal cell multiplication. Thus introducing an arrest in the cell cycle or inducing apoptosis by dietary bioactive compounds will help in the prevention of cancer. Dietary components like isothiocyanate can regulate the expression of the P21 gene which helps to inhibit cell proliferation and can induce apoptosis.¹⁶ Another pathology involved in the development of cancer is enzymatic biotransformation and metabolic activation. A bioactive component present in fruits and vegetables like flavonoids, phenols, etc block metabolic activation through increasing detoxification and thus helps in the prevention of cancer.¹⁷ Reactive oxygen species are also included in the pathology of cancer. These reactive oxygen species attacks DNA sequence and thus produce mutations in oncogenes and tumor suppressor genes. Many dietary components such as flavonoids, Vit E, Vit C that scavenge reactive oxygen species stimulate the repair of oxidative DNA damage. For eg dietary supplementation of carrots has been shown to increase the repair of oxidative DNA damage in white blood cells.¹⁸

Gene disease interaction to some specific nutrients

Turmeric

Cyclooxygenase 2 enzyme is related to the production of inflammatory prostaglandin. This increased prostaglandin production increases the chance of inflammatory disease. Curcumin in the turmeric helps in the suppression of gene which produces the enzyme COX-2 which in turn help the reduction of prostaglandin thereby having anti-inflammatory action.¹⁹

Green Tea

Green tea contains a chemical compound called EGCG, under normal circumstances, it helps cancer prevention. But the major drawback of the compound is that it is unstable under physiologic pH and also inactivated by the process-methylation. If this compound can be made

stable it will be helpful in the prevention of cancer. People having polymorphism in the gene-producing COMT enzyme enhances the biological availability of the compound EGCG which will help in cancer prevention. So green tea will have a protective effect only in those people who have a polymorphism in the gene-producing COMT enzyme.²⁰

Ayurnutrigenomics

Nutrigenomics establishes the influence of nutrients and other bioactive food components on gene expression and gene regulation. The recent availability of human genome sequence and the cataloging of human genetic variation can identify specific polymorphisms linked to altered risk of disease or sensitivity to diet. Information on the genetic order of polymorphic markers will provide powerful molecular tools to decipher the role of nutrition in human health and disease and help to define optimal diets. Nutrigenomics provides specific dietary recommendations based on the genotype of individuals.²¹

Ayurnutrigenomics is the systematic integration of nutritional practices according to Prakriti of an individual. Prakriti represents the basic principles of Ayurveda having a great impact on predictive medicine and it is the corollary of the comparative proportion of tridoshas. In Ayurveda, selection of suitable dietary, therapeutic, and lifestyle regimes is made based on an assessment of Prakriti. Prakriti is not only genetically determined (Shukra sonita) but also influenced by environmental factors (maha bhuta vikara) like maternal diet and lifestyle (mathura ahara vihara) and age of the parents (kala garbhasaya).²²

Prakriti and genome

The identification of genomic link to the theory of Prakriti led to a search for a possible classification of people on their Prakriti based on their genetic makeup. A significant correlation between various alleles of HLA genotype and Prakriti provides preliminary experimental support for the concept of association between HLA polymorphism and individual Prakriti types.²³ Association between Prakriti and gene-related to drug metabolism such as CYP2C19 have been drowned out, where the genotype related to extensive metabolizer genotype was associated with pitta Prakriti, while the poor metabolizer genotype was highest in Kapha prakriti.²⁴ Assessment of Prakriti through genotype mapping is a method of objective assessment of Prakriti. On searching for links of Prakriti and genotypes is the need of the hour to bridge the gap between Ayurveda and current sciences with the development of common vocabulary

Prakriti and Personalized nutrition

Prakriti can be considered as phenotypes that have a distinct link with a particular genotype. Through Prakriti genome correlation studies possibility of identifying specific genotype linked to a particular Prakriti (objective method for assessment of Prakriti) is approaching. Thus it can be predicted shortly that genotype ascertainment in newborns itself can be used as a predictive marker for prakriti.²⁵

Detection of Prakriti at the time of birth has far-reaching implications. Knowing the Prakriti of newborns can lead to the adoption of suitable dietary practices from early childhood onwards which will result in the prevention of diet-related chronic disease.²⁶ This is how a Prakriti-based diet plays its action. If a specific genotype is identified related to a particular type of Prakriti, the concept of a gene-specific diet can be taken to authenticate diet according to Prakriti.

CONCLUSION

The concept of nutrigenomics is already merged in Ayurveda, further studies are needed in this field to establish the relationship between Prakriti and genotype for developing personalized functional foods and nutraceuticals suitable to one's genetic makeup. Genetic expression are altered by environmental factors, unhealthy lifestyle and diet. The Ayurveda dietetic principles have a major role in maintaining this genetic expression. Hence a relook into the basics of Ayurveda dietetics and therapeutic approaches could enable researchers and practitioners to have fresh insights in the prevention and management of lifestyle disorders caused by gene alteration. In this regard streams of genomics like epigenomics, proteomics and metabolomics may help in better understanding of Ayurveda dietetic principles and Ayurnutrigenomics. Hence this novel concept of Ayurnutrigenomics and its emerging area of research which aims at prevention than cure, may unfold future possibilities towards smart yet safe therapeutics.

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