International Journal of Science and Healthcare Research
Vol.4; Issue: 3; July-Sept. 2019
Website: www.ijshr.com
Review Article *ISSN: 2455-7587*

Interplay With Dietary Components - Diet Therapy to Treat the Metabolic Disorders

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ABSTRACT

Our daily life interactions between genetic and environmental factors including over nutrition have promoted the pathogenesis of polygenic diet related diseases. These complex interactions between genetics and nutrition are investigated by nutrigenetics which is relevant to metabolic health and disease. Diet including dietary chemicals can be a serious risk factor for a number of diseases, affect health by altering gene structure and expression. This alteration causes metabolic disorders (MDs) from which round the world 20-25% population is suffering. The Indian scenario includes detection and cure for certain MDs based on the diet modification. Pure MDs like obesity, insulin resistance etc. are generally arise because of poor nutritional habits, thus creating a harmful environment in body due to the diseases. Sometimes, MDs can also lead to genetic basis e.g. hyperlipidemias in which children and apparently healthy adults are also predisposed to coronary artery diseases. In some cases, genetic factors (like unique HLA haplotype) can predispose to either Type 1 diabetes or Celiac disease. At the extreme end of the spectrum, there are inherited MDs which themselves lead to disease. In phenylketonuria (PKU)-restricting amino acids (AA) with dietary protein supplements, Maple syrup urine disease (MSUD)- thiamine with reduced branched AA, tyrosinemia 2- reduced phenylalanine and tyrosine, homocystinuria- reduced methionine but high cystine, galactosemia-reduced milk and milk products are recommended. The above conditions need specific dietary modifications based on the genetic factors involved as well as the knowledge of nutritional requirements and nutritional status. Thus, personalized nutrition based on the genetic makeup is essential to create wonders in both prevention and treatment of metabolic disorders.

Keywords: metabolic disorders, impact of nutrients, nutrition, genetic makeup, polygenic diet, nutrigenetics

INTRODUCTION

Diet related lifestyle, particularly over nutrition and sedentary behavior has drastically promoted today's talk of the town of what is known as Polygenic Diet-Related Diseases.[1] These diseases are caused due to some genes that determine our responses to the food we eat, the supplements we take and how these foods interact with our genes to affect our health. Common variations found throughout the human genome explain individual differences in response to the dietary intake.

Nutrigenomics and Nutrigenetics

Nutrigenomics, the integration of genomic science with nutrition, is the study of the effects of food and food constituents on gene expression.[2] It is a research focusing on identifying and understanding molecular level interaction between nutrients and other dietary bio-actives with genome. Nutrigenomics aims to enhance rational means to optimize nutrition with respect to the subject's genotype. It is associated with the idea of personalized nutrition based on one's genetic profile. It studies the effect of nutrients on genome, proteome, metabolome and explains the relationship between the specific nutrients and nutrient-regimes (diet) on the human health.[2,3] Nutrigenomics is highly personalized because it looks at the

biomarkers within each individual. Researchers suggest that current technology can be used to build an ideal diet/intake of certain nutrients or a 'nutriome' that ensures proper functioning of all pathways involved in genome maintenance.[2]

Nutrigenetics, on the other hand, researches into the effect of a single gene or single food compound relationships. With the modern genetic data, we now know that dietary bio-actives affect health by altering gene expression and structure and also, that dietary practices can be more closely personalized to individual genetic profiles. Nutrigenetics aims to identify how genetic variation affects the response to nutrients. This knowledge can be applied to optimize the health and prevent/ treat diseases. The ultimate aim is to offer people, the personalized nutrition based on their genetic makeup.

Both of these branches require an understanding of nutrition, genetics, biochemistry and range of 'omic' technologies to investigate the complex interaction between genetic and environmental factors relevant to metabolic health and disease.[1]

How do metabolic disorders occur?

It is an old fact that "diet affects health". Nutrients and foods usually interact with genes in a benign manner but sometimes, this interaction can have fatal outcomes. There is an increasing recognition that nutrients have the capacity to directly regulate the metabolic processes, via impacting the expression of enzymes, receptors, hormones and other proteins. For example- different nutrients and food bio-actives have an effect on neurotransmitters like dopamine and serotonin; both influence the mood and behavior.

The food that we eat consists of carbohydrates, proteins and fats that undergo a chemical process to transform it into the fuel that keeps one alive. This chemical process is called metabolism. If this breakdown of nutrients does not occur or metabolism process fails, the metabolic disorder would occur that causes the body to have either too much or too little of the essential substances needed to stay healthy. Metabolic disorders can occur in different conditions[4] i.e.

- Missing enzyme or vitamin that is necessary to complete metabolic cycle.
- Abnormal chemical reactions that hinder metabolic processes.
- External or foreign substances that cause a disease in the liver, pancreas, endocrine glands or other organs involved in metabolism.
- Nutritional deficiencies

Thousands of these metabolic disorders are caused due to single gene mutations e.g. Sickle cell anemia, cystic fibrosis, maple syrup urine disease (MSUD), Gaucher disease, hemochromatosis etc. Around the world, 20-25% population is suffering from metabolic disorders. Among this, metabolic disorders affect 40% of the people over the age of 60 years.[5] The Indian scenario includes the detection and cure for certain metabolic disorders based on the diet modifications.

Effect of nutrients on the body

Common dietary chemicals act on human genome directly/indirectly alter gene expression.[6] Some naturally occurring chemicals in food are ligands for transcription and directly alter the gene expression (Figure 1). Cell signaling is an important component of regulation of gene expression and metabolism, banking on both internal as well as external signals to ensure the maintenance of homeostasis.[2] Individual nutrients can each be considered as signals, which regulate the transcription factors that modify the gene expression. Due to naturally occurring mutations in human genome, humans differ in their DNAs. These mutations are called variations/ polymorphisms of DNA. The most common polymorphisms are "Single Nucleotide Polymorphisms" or SNPs. These SNPs influence the way, individuals absorb, transport, store or metabolize the nutrients.[6] If there is an intake of some

nutrients that are not in accordance to one's genetic profile, it will affect the genes as well as DNA and simultaneous change in the transcription process will be there. As a result, undesired proteins will be formed that would ultimately, lead to the production of altered metabolites. Those would not be accepted by the body, would cause gene alteration and thus, the disease.

Other dietary chemicals alter signal transduction pathway and chromatin structure to indirectly, affect gene expression.[7] Ligands (dietary chemicals-nutrients) are the first messengers that, by binding in a receptor, give rise to changes that ultimately, lead to "signaling cascade". Series of biochemical reactions, that are initiated by stimulus acting on a receptor that is transduced to the cell interior via messengers and ultimately to effector molecules, resulting in a cell response to the initial stimulus (Figure 2). At molecular level, such responses include changes in the transcription/ translation of genes and post-translational and conformational changes in protein, as well as in their location. These molecular events are the basic mechanisms controlling cell growth, proliferation and ultimately lead to "Metabolism".

It is reported that gene, protein and metabolite signatures are linked with specific nutrient or dietary protocols that are systematically organized to serve as molecular biomarkers for the early detection of diseases in response to the nutrient induced changes in the body.[8,9] The effort is to identify these 'dietary signatures' or pattern of effects ranging from effects at the cellular level to the entire body systems. The desired outcome from this research is to place the genetic factors for the chronic diseases and conditions, whether it is a certain gene itself or an epigenetic marker and how foods influence it.[2]

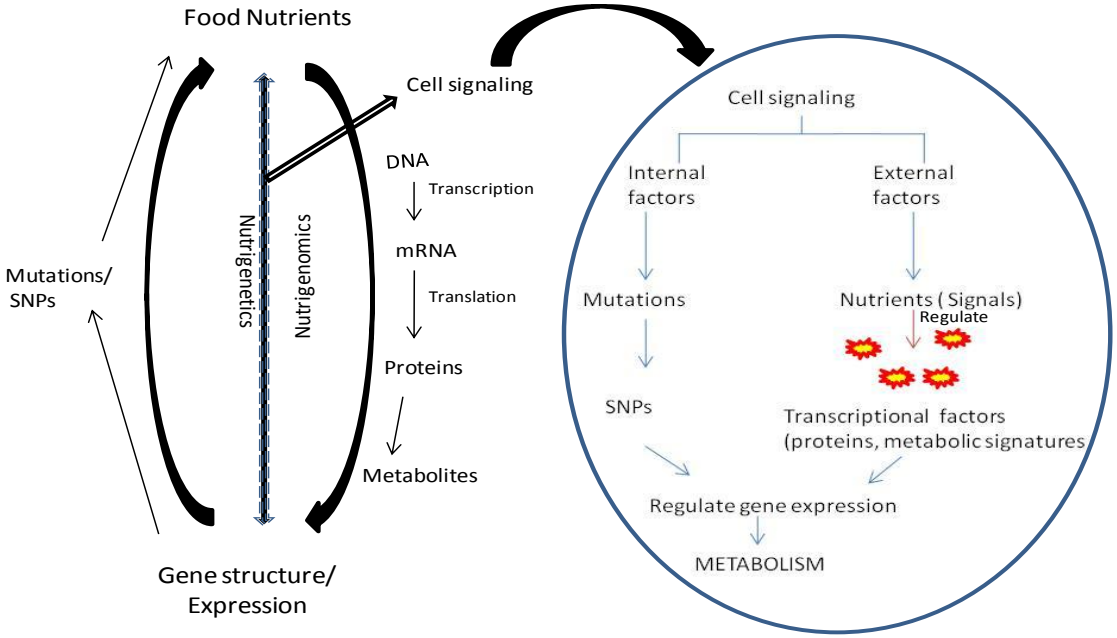

Figure1. Cyclic representation of direct impact of nutrients on genome

Nutritional Therapy

Common variations are found throughout the human genome, explain the individual differences in response to the dietary intake.[10] Some individuals respond differently than others to exactly the same nutrients. This is because of the genes that determine one's metabolic responses to the food supplements he/she takes. That is why; some people who consume high fat diet, have no cholesterol problems; while others, even on taking a small amount of fat, show their cholesterol level at the peak. People drink coffee but for some, it becomes lethal.

CYP1A2 is a gene that breaks caffeine in the liver. Some people's system breaks it faster and gets rid of the caffeine, preserves healthy antioxidants and protects heart. But other's system breaks it at a slower rate, thereby, increasing the risk of heart attack. Therefore, when people grow up with some metabolic disorders, nutritional therapy/ dietary modification is the first option to cure them. Diet can be a risk factor as well as treating weapon for a number of metabolic disorders. (Table 1)

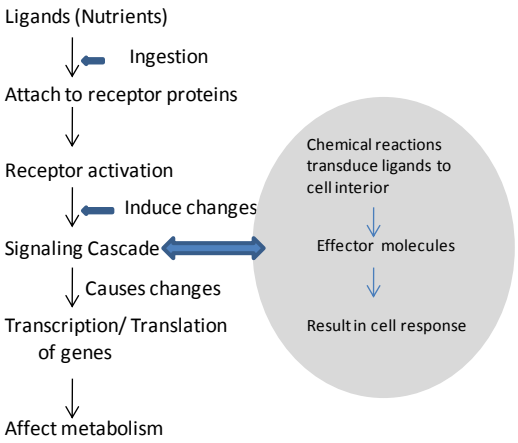

Figure 2. Flow chart to show the signal transduction pathway in response to nutrients

Table 1: Diseases, their cause and dietary plan to cure them

DISEASE	CAUSE	DIETARY GUIDELINES
Phenylketonuria	Phenylalanine hydroxylase is responsible for breakdown of Phenylalanine. Deficiency of this enzyme does not convert phenylalanine to tyrosine.	Limiting the supplementation of amino acids but dietary protein supplements should be given.
Maple Syrup Urine Disorder (MSUD)	Body's inability to use 3 branched chain amino acids (BCAAs) - Leucine, Isoleucine and Valine. BCAAs and their by-products (ketoacids) level increases and causes brain damage and alteration in mental state.	Thiamine should be given with limiting the supplementation of BCAAs. Fruits & vegetables are mostly permitted without measurements except in few diseases like classical MSUD.
Type 2 Tyrosinemia	Deficiency of the enzyme tyrosine amino transferase (TAT) which is required for the multi-step process of breaking down of 'tyrosine' occurs due to the mutations in TAT gene.	Diet with reduced phenylalanine and tyrosine content should be given.
Galactosemia	Deficiency of enzyme galactose-1-phosphate uridyl transferase that enables to metabolise galactose	Exclude galactose/lactose from the diet with the substitution of casein hydrolysate containing formula or infant soy formulas
Gaucher Disease	Inability of the body to breakdown a particular kind of fat that accumulates in liver, spleen & bone marrow	No such dietary guidelines. Only enzyme replacement therapy (ERT) is available.
Glucose/ Galactose mal-absorption	Defect in the transportation of glucose and galactose across the stomach lining which leads to severe diarrhoea and dehydration	Remove lactose, sucrose and glucose from the diet
Hyperthyroidism	Increased secretion of thyroid gland hormone with a consequent increase in metabolic rate	High calorie (4000-5000 kcal), high protein (100-125g) diet including snacks in between meals, multi-vitamin mineral supplements, avoid caffeine rich foods
Hypothyroidism	Condition of decreased production of thyroid hormone called MYXEDEMA. This condition is characterized by a decreased rate of energy metabolism 30-40% below normal	High dietary fiber should be given to prevent constipation, a calorie restricted diet is prescribed
Homocystinuria	Mutations occur in the gene cystathionine beta-synthase (CBS gene). This gene holds instructions for making an enzyme that uses vitamin B-6 to metabolize the amino acids (homocystine and serine). Due to these mutations in the gene, building up of homocystine & other toxins in the blood that damage the nervous system.	Increased cystine with lowered methionine diet is preferred.

METHODS FOR ANALYSIS

Analysis of blood or a cheek swab DNA is done to study the necessary genotype.

1. A common way to assess the genetic data is called 'Candidate Gene Approach'. This study focuses on association between genetic variation with pre-specified genes of interest and phenotypes/ disease states.
   Candidate genes are often selected for study based on 'priori' knowledge of gene's biological functional impact on trait/ disease, i.e. focusing on allelic variation in specific biologically relevant regions of the genome as certain mutations will directly impact the functions of the genes and lead to phenotype/ disease state being investigated.[11]
   When examining functionality between genes in pathways, the gene product are described in 3 different ways (biological

processes, cellular components and molecular functions). Using this information, can further a priori knowledge of a pathway and thus, helps to choose the most likely candidate gene involved. By engineering and modifying these candidate genes, it is able to confirm the ways in which gene is linked to a changes phenotype.

Consequently, the scientists establish positive or negative correlation between candidate-gene expression and nutritional aspects [2] by examining gene-nutrient interactions and further modifying the role of nutrient consumption, as they relate to nutrient status and disease risk in humans.

2. Genome-wide Association Study (GWAS) is used to identify the relevant gene variants by scanning the entire genome. It focuses on associations between SNPs and traits like major human diseases.[2,11] When applied to human data, GWAS compares the DNA of participants having varying phenotypes for a particular trait. These participants

-may be people with traits (cases),

-similar people without disease (controls)

people with different phenotypes for a particular trait.

This approach is 'phenotype –first' in which the participants are classified first by their clinical manifestations rather than genotype- first. By this, we examine the results of various gene-nutrition interaction studies, the association of genetic polymorphisms with disease expression and identification of nutritional factors that modify gene-dependent disease phenotype.

Possible findings

Nutrigenetics analysis is based on the effect of nutritional components on the genome, proteome, metabolome and transcriptome.[1] Via the above two methods of analysis, information about various gene-nutrition interactions can be obtained. By understanding this genetic variability for particular trait, it is possible to explain the inconsistencies that link nutrients, supplements and other bio-actives to a number of health outcomes as well as what food supplements should be taken based on our genetic profiles for healthy outcome.

Nutritional recommendations solely based on genetic background represent a straight- forward approach to the concept of personalized nutrition.[12] It pursuits to develop more comprehensive and dynamic nutritional recommendations based on shifting, interacting parameters in a person's internal and external environment throughout life. It also explains the inter-individual variability of the metabolic response to specific diets.

Treatment approaches for metabolic disorders include:

- Modifying the diet to limit the amount of precursor that is not metabolized properly.
- Using cofactors/vitamins to enhance the residual activity of defective enzyme system.

There are 4 principles to dietary therapy-

- ❖ Diet is considered to be a critical predisposing factor to many diseases in some individuals under particular conditions.
- ❖ Diet ingredients change the gene structure & expression and accordingly, the human genome.
- ❖ The variation of genotype between individuals can explain the equilibrium between health & disease.
- ❖ Genes whose regulation is dependent on dietary factors may have a role in the commencement, extent, advancement and progression of chronic diseases.

Hence, depending upon the individual's genetic profile, certain nutrient regimes are recommended, of what is called 'Personalised Nutrition'. It can be designed according to one's bodily expression towards the food and how that person

absorbs, assimilates, stores and metabolize the dietary components.

Nutrigenetics has a great potential in the diet-related disease prevention and therapy.[10] In future, a personalized nutrition approach may be advocated, wherein patients with a particular genetic profile may determine responsiveness to specific dietary interventions.

CONCLUSION

Hippocrates advised physicians in 400 BC, *"Leave your drugs in chemist's pot if you can heal your patient with food"*.[3]

Personalized nutrition tailors dietary advice to be given to the individuals based primarily not only on their genetic factors but also including other personal information, such as current diet and phenotype. There are 3 levels of personalization that are considered i.e. personalized dietary analysis, personalized phenotype analysis and personalized genotype analysis. This personalized nutritional therapy is the most promising new generational approach that encompasses a challenge to protect the genome from damage by the nutritional factors. The acquisition of personalized nutrition for treatment is likely to have significant societal repercussions on the patients with metabolic disorders.

ACKNOWLEDGEMENT

We would like to thank Dr. Sunita Bijarnia- Mahay, a senior metabolic medicine consultant for Clinical suggestions and discussion regarding modified diet.

Conflict of interest: None declared

REFERENCES

1. Catherine M. Phillips. Nutrigenetics & Metabolic Disorders: Current status & Implications for personalized nutrition. Nutrients.2013, Vol-5:32-57 doi:10.3390/nu 5010032
2. http://nutritionwiki.blogspot.com/2017/12/nutrigenomics.html
3. V.S. Neeha & Priyamvadahn Kinth. Nutrigenomics research: a review J Food Sci Technol. 2013 Jun; 50(3): 415-428 doi:10.1007/s 13197-012-0775-z
4. Sandy Calhoun Rice (2017) Nutrition & Metabolic disorders. https://www.healthline.com/health/nutrition-metabolism-disorders
5. Josh Axe (2016). Metabolic Syndrome: Proven Diet & Natural Treatment Plan. https://draxe.com/metabolic-syndrome
6. M. Nathaniel Mead, Nutrigenomics: The Genome–Food Interface. Environ Health Perspect. 2007 Dec; 115(12): A582–A589. PMCID: PMC2137135
7. http://en-wikipedia.org/wiki/signal _transduction
8. Paraskevi Mentzelopoulos. Nutritional genetics & personalised medicine: the future of prevention & treatment. www.gamedicalcollege.gr/wp-content/.../MENTZELOPOULOU-nutrigenomics-talk.pdf.
9. Ali M. Ardekani & Sepideh Jabbari. Nutrigenomics and Cancer. Avicenna J Med Biotechnol.2009 Apr-Jun;1(1): 9-17
10. John Berardi. Nutrigenomics, www.precisionnutrition.com/nutrigenomics-research
11. John W. R. Zinck & Amanda J. MacFarlane. Approaches for the identification of genetic modifiers of nutrient dependent phenotypes: examples from folate. Frontiers in Nutrition, 1. 14 July 2014, doi: 10.3389/fnut.2014.00008.
12. Juan de Toro-Martin, Benoit J. Arsenault, Jean-Pierre Despres & Marie-Claude Vohl. Precision Nutrition: A review of personalized nutritional approaches for the prevention and management of metabolic syndrome. Nutrients 2017, 9, 913; doi: 10.3390 /nu9080913 www.mdpi.com/journal/nutrients.

How to cite this article: Verma D, Verma J. Interplay with dietary components - diet therapy to treat the metabolic disorders. International Journal of Science & Healthcare Research. 2019; 4(3): 114-119.

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