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The Role of Personalized Nutrition in Human Physiological Disorders

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ABSTRACT

The nutrients in regular diet are considered as environmental factors which have long-term effect on human genome. Personalized nutrition includes nutrigenetics and nutrigenomics studies that explains how food and genes interact and alters the gene expression. The "omics" studies are important tools to study the food-gene interactions. Most of the foods that are included in food habit of an individual exerts some physiological effects on the cells, organs or the whole body. These foods are referred as functional foods and the branch of science which deals with medicinal properties of nutrients is known as "nutraceuticals". The functional foods may affect the genotype of different individuals in a different way and not all the foods are suitable for all the persons having various pathophysiological conditions. Function foods should be should be recommended based on one's health, physiological condition, age and most importantly, their genetic setup. The concept of personalized nutrition was derived from "personal medicine" and in both cases regulation of gene expression is given priority based on the knowledge genomic studies. Understanding the complete molecular mechanism underlying the food-gene interaction and their effect to prevent the diseases like cancer, diabetes, obesity, thyroid, chronic degenerative diseases, etc, is required to assess the importance of personalized nutrition and functional foods as future tools for maintaining human health.

KEY WORDS: PERSONALIZED NUTRITION, NUTRIGENOMICS, FUNCTIONAL FOODS, PHYSIOLOGICAL DISORDERS, GENE EXPRESSION.

INTRODUCTION

Personalized food refers to genetically tailored diet which acts as therapeutics to treat certain physiological disorders in human beings. The concept of nutraceuticals or functional foods, where food is used as medicine paves the path of personalized diet, which mainly deals answers the question how genetic variations occurs due to the effect of consumed food. For example, a single gene mutation can cause phenylketonuria (PKU) and the affected person should refrain from taking foods like eggs, cheese, chicken, beef, pork, which are rich source of phenylalanine. Another such example is lactose intolerance, where the gene responsible for proper functioning of the enzyme lactase is turned off permanently. Polymorphisms in genes coding for the enzyme 5,10-methylene tetrahydrofolatereductase (MTHFR) affect its catalytic activity, which is directly related with individual'smetabolism and nutrient requirements (Reddy et al., 2018). People with lactose intolerance should avoid dairy products in their diet. The term like nutrigenetics and nutigenomics are closely related with personalized medicine. The ultimate goal for personalized food is to recommend a diet in accordance to one's genetic setup.

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To understand the background of personalized medicine, we have to look back in 1989 when Dr. Stephen De Felice coined the term "nutraceutical", a hybrid word derived from the two words "nutrition" and "pharmaceutical". The use of food as medicine is an age old concept which was gained a proper scientific acknowledgement at that time. In 1990, the famous Human Genome Project (HGP) was started aiming the determination of the actual base pairs present in human DNA as well as to identify and map all the genes of the human genome. After the completion of HGP in April, 2003, influence of foods in diet was studied with respect to the change in genetic expression. Sales et al., 2014 pointed out three important questions regarding food-gene regulation:

1. Can metabolic processes regulate the gene expression at cellular level which in turn can affect human health?
2. Do the genotype and nutrient interaction is responsible for regulation of gene expression by metabolic processes?
3. Studying the underlying mechanism of gene-nutrient interaction and ultimately will give rise to specific diet plan for each individual.
4. Nutrigenomics and nutrigenetics addressed all the above queries and emerged as a new topics of research.

Due to genetic polymorphism, the process of transcription in human is variable and regulated by variable factors among which nutrients is most important (Dauncey, 2013). The expressed mRNAundergoes alternate splicing and translation and gives rise to proteins having variations in function and half-life (Heyd and Lynch, 2011).The knowledge of metabolites and translation products will provide a clear idea about any pathophysiological condition. The end product of any metabolic pathwayexplains the expression of a gene at a given physiological scenario. The qualitative and quantitative analysis of all metabolites in a living system with respect to its gene expression is called metabolomics. Thus, personalized nutrition deals withnutritional research which comes under the broad terminology "nutigenomics" which includes nutrigenetics, transcriptomics, proteomics and metabolomics.Nutrigenomics refers to the ability of nutrients toupregulate or downregulate gene expression, and ultimately altering individual phenotype. On the other hand, nutrigenetics refers to polymorphic and mutant genes that can modify the bioactivity a metabolic pathway and its mediators.The basic concept of nutrient-gene interface can be summarized as (Farhud et al., 2010):

1. Nutrients directly or indirectly can alter gene expression
2. In some individuals under certain physiological conditions, food habit can be a determining factor for the onset of some diseases.
3. Certain diet-regulated genes and their variants are responsible for the onset and progression of some chronic diseases.
4. Depending on one's genetic makeup, the food habit regulates the metabolic pathways in healthy and diseased state of body.
5. Dietary intervention based on one's nutritional needs and genotype can be used to prevent, reduce the risk or cure chronic diseases. This explains the concept of personalized nutrition.

Personalized nutrition can be administered for the management of several diseases, though there are some challenges too. The underlying biological mechanisms at a single gene or protein level to study the nutritional effectsneedsdynamic interaction among diet, genes andphysiological condition rather thanhighlighting the interaction of nutrients on specific gene (Verma et al., 2016).There is an urgent need to build up a proper computational infrastructure that will deal with personalized nutrition. Standardization of data and intervention of improved methods to understand the topic in a detailed manner is the need of the hour. This review focuses on the impact of personalized nutrition to prevent, manage and treat physiological disorders as well as points out certain disadvantages/lack of study.... And the need of personalised diet for decreasing the risk factor of health issues due to the daily hectic schedule and unbalanced diet.

2. Interaction between genes and nutrients: The interaction between genes and nutrients is mediated by three probable mechanisms:
a) Direct interaction, where nutrients acts as transcription factors and bind to DNA to regulate the expression of related genes;
b) Epigenetic interactions, where nutrients modify the structure of DNA resulting in altered genetic expression;
c) Genetic variation: single genetic variations like nucleotide polymorphisms (SNPs) can regulate the functionality or expression of genes.

Direct Interaction: There are evidences which show that gene expression can be regulated by cholesterol, carbohydrate and the metabolites can behave as direct effectors of transcription factors. When there is excess intake of simple carbohydrate in diet, a major portion of carbohydrate is converted to triglycerides in liver, regulating hepatic enzymes. Pyruvate kinase (glycolysis), acetyl CoA carboxylase and malic enzyme (fatty acid biosynthesis), glycerol-3-phosphate acyltransferase (triglyceride synthesis) are induced by carbohydrate diet due enhanced levels of mRNA.

Cell membrane biosynthesis in mammals require cholesterol which may derive from diet or synthesized by cells. Low-density lipoprotein (LDL) receptor mediate the cholesterol uptake in cells. Low cholesterol levels induce production of more LDL receptor to uptake more of the cholesterol and vice versa. Low cholesterol upregulates the synthesis of two rate-limiting enzymes responsible for biosynthesis of cholesterol, namely, HMG-CoA synthase and HMG-CoA reductase. The cell ensures that is receives the required amount of cholesterol from diet and maintains the transcriptional regulation of genes that encode HMG-CoA synthase and HMG-CoA reductase.

This was experimentally demonstrated by Goldstein and Brown, 1990. Moreover, the nutrients andmetabolites can regulate the transcription by a well-established pathway.

The genes of steroid family acts as transcription factors and have receptors for steroid hormones, thyroid hormones, retinoic acid, vitamin D3 thatcan directly enter the cell to exhibit their biological activity (Towle, 1997). However, no ligands were identified for activating these receptors and hence they were termed as "orphan receptors". Later it was found that the intracellular nutrients and metabolites behave as their natural ligands. One of the most common examples of orphan receptors are peroxisome proliferator-activated receptors (PPARs) and the fatty acids were detected as their natural ligands. It was reported that consumption of high fat diet leads to selective induction of fibroblast growth factor1 by PPARγ in adipose tissues which is necessary for remodelling of adipose tissue (Jonker et al., 2012).

Epigenetic Interaction: Nutrients with potential bioactive molecules have the capability to induce protective epigenetic modification. The three-dimensional conformation of chromatin is regulated by environmental factors like pollutants, chemicals and nutrients which directly effects gene expression. Complete understanding of molecular mechanism by which environmental factors (nutrients, pollutants, chemicals) exerts their epigenetic effects will lead to the development of personalized nutrition strategies to prevent many diseases including cancer (Tiffon, 2018). The nutritional status at an early stage of an individual have a long term effect on DNA methylation pattern which in turn is related with chronic degenerative diseases (Lillycrop et al., 2014).

The nutrients modify the epigenetics by inhibiting DNA methyltransferases (DNMTs), histone deacetylases (HDACs) or histone acetyl transferases (HATs); or alters the substrate availability for these enzymes to carry out the enzymatic action. This ultimately leads to regulation of gene expression linked with pathophysiological processes like aging, embryonic development and carcinogenesis (Choi et al., 2010). Personalized nutrition and bioactive nutrient compounds can emerge as epigenetic therapeutical agents to combat with type 2 diabetes mellitus, inflammation, obesity, cancer, neuro degenerative diseases. Though there are a handful of studies regarding the preventive measure and disease management with this approach, nutritional epigenetics warrants better understanding of the molecular mechanisms of the bioactive nutrient components. Some examples of bioactive food components and their roles are as follows (Tiffon, 2018):

- Folic acid, vitamin B12, vitamin B6 play role in methionine synthesis
- Choline acts as methyl donor to S-Adenosyl methionine (SAM)
- Methionine plays role SAM synthesis
- Betaine lyses the toxic byproducts formed during synthesis of SAM
- Resveratrol, a well-known compound against breast-cancer, can remove acetyl group from histone
- Diallyl sulphide, butyrate, sulforaphane, turn on the anti-carcinogenic genes by increasing histone acetylation
- Genistein increases DNA methylation and has anti-cancer activities

2.3 Genetic Variation: The majority of the qualities have differences in small sequences– polymorphisms – that fluctuate among people. Single nucleotide polymorphisms (SNPs) are the most well-known sort of variety (Debusket al., 2005). The single nucleotide polymorphisms consortium is mapping polymorphic areas of the genome that control individual phenotypic contrasts among the human populace. The significance of this hereditary variety to the fluctuating requirements for and physiological reactions to the specific supplements was expressed by Ames (Afman and Müller, 2006). Missense single nucleotide polymorphisms happen around 1 in each 1000 bases in communicated qualities, so one anticipates that there will be a lot more polymorphisms to be found in micronutrient and dietary investigations. Explicit hereditary polymorphisms in human populaces change their metabolic reaction to slim down and impact the hazard examples of infection as SNPs are like varieties in a formula. Every quality is a formula for a particular protein or gathering of proteins that either manage organic capacities or fill in as basic structure hinders for tissues (e.g., collagen). A few SNPs change the formula for the quality so that either an alternate amount of the protein is created or the structure of the protein particle is modified (Schneider et al., 1998)

3. Dietary Habit Affects Gene Expression: These hereditary polymorphisms lead to modification of the reaction to the dietary segments by affecting ingestion and digestion. Epigenetic occasions can incite changes in DNA methylation example and along these lines impacting overall quality articulation that can be altered because of the food segments. Nutrition has played a recognizable and prevalent role in the management of health. Nutrigenetics is the science that recognizes and portrays the gene variations related with the reaction to supplements and relating this variety to variable diseases states particularly cancer, diabetes, obesity and other diseases. Numerous dietary constituents influence post interpretation occasions and numerous record for in any event part of the variety in light of the dietary segments (Ames, 1999).

3.1. Cancer: Various studies has considered that SNPs in a few Se-related qualities may influence weakness to disease. For instance, the Leu allele in the SNP at codon 198 in GPX1 was accounted for to be related with lung, bosom, and bladder malignancy (Villette et al., 2002), despite the fact that this was not affirmed for bosom disease (Ahn, 2005). Strangely, the relationship with bladder malignant growth might be affected by a SNP in the manganese superoxide dismutase (MnSOD) quality (Ichimura et al., 2004), demonstrating the expected significance of investigating different SNPs based on a metabolic pathway.

Basic variations in qualities controlling homocysteine digestion, for example, methylenetetrahydrofolate reductase (MTHFR), and methionine synthase (MTR), have been connected to expanded hazard for bosom malignant growth in people with low admissions of folate, nutrient B6, and nutrient B12 (Hill et al., 2004;Ahnet al., 2010). Likewise, it has been accounted for that notwithstanding daylight, nutrient D status can likewise be impacted by a few polymorphisms in nutrient D pathway qualities (Barry et al.,2014;Desmarchelier et.al., 2016), accordingly tweaking its natural capacities in the creature. Strikingly, SNPs in the nutrient D receptor (VDR) quality, which influence nutrient D accessibility (Heap et al., 2009; Stathopoulou et al.,2011), have been related with osteoporosis inclination in postmenopausal ladies with low calcium admissions (Hosseini-Esfahani et al., 2014).

The 15-kDa selenoprotein quality includes two varieties inside the 3′ UTR, at positions 811 and 112 selenocysteine insertion sequence or SECIS. Most of the findings showed that the two SNPs influence Se insertion, and the 2 polymorphisms were accounted for to influence the harmful effect of cancer. Fundamental information recommend that the T-C variation in the 3′ UTR of glutathione peroxidase-4 (GPX4) influences danger of colon malignant growth (Dumitrescu et.al, 2005). SNP affiliation considers have been completed on moderately little populaces and with single SNPs. Moreover, not many examinations have joined the SNP relationship with point by point investigation of Se status. Future investigations ought to examine bigger, rehash populace accomplices and consolidate genotyping with investigations of healthful admission or status to survey the significance on supplement quality collaborations in deciding defencelessness. A wide scope of SNPs ought to be examined, at first dependent on a pathway approach, to incorporate qualities encoding items engaged with Se consolidation instruments and Se transport.

As per our review is concerned the lipid is the key factor for this disease. The complete lipid based personalised food are found to be harmful for cancer as the cancer cells need more energy as they replicate and differentiate much faster than the normal cells. A personalised diet along with protein, Vitamin D, B12 and also vitamin C to boosting up our immune response and carbohydrate is always been recommended to be more effective than any other diet to stop these gene up regulations in cancer.

3.2. Obesity: Obesity has become one of the worldwide epidemics with over 35% of the total populace (2,100 million individuals) being assessed as either overweight or fat as indicated by weight list (BMI) (Kassebaum et al., 2015). Corpulence is related with an enormous number of medical issues including dyslipidemias, cardiovascular infections (CVD), type 2 diabetes mellitus (T2DM), non-alcoholic greasy liver sickness (NAFLD), and a few sorts of disease, with significant financial and social expenses (Seidell and Halberstadt, 2015). Deliberate investigations have uncovered that weight and overweight caused 3.4 million passing in 2010. The unbalanced eating regimens like, fat, fructose, the high substance of calories, and high omega-6/omega-3 unsaturated fat proportion and obvious combination of the inactivity in daily life, found to add the advancement of obesity and the diseases related to this. Additionally, it is currently perceived that associations of hereditary and epigenetic genes with ecological elements (dietary admission or physical action) assume a significant job in deciding individual phenotypes (Ramos-Lopez et al., 2017). In recent studies has shown after analyses of 240 SNPs, responsible for the genes which are nutrient-sensitive lipid metabolism among the people with obesity and overweigh, there is an interaction between the dietary protein and the LPIN1 rs4315495, which may lead the result of lowering the concentration TAG for minor allele which carriers on the high-protein weight maintenance diet (Braheet al., 2013).

Moreover, it was accounted for that revelation of hereditary data with respect to angiotensin I changing over chemical (ACE) genotype for customized nourishment brought about more notable changes in sodium admission contrasted with all-inclusive community based dietary exhortation (Nielsen and El-Sohemy, 2014). Moreover, people who consumed unsaturated fat desaturase 1 (FADS1) genotype were found progressively upregulation of omega-3, the unsaturated fats (Roke, 2017). These findings showed that the identification of good supplements of dietary products are dependent on hereditary diseases than general dietary is concerned (Nielsen and El-Sohemy, 2012). We have found that the unsaturated fatty acids are the key factor for developing the up regulation of the genes responsible for obesity and recent studies have shown that the most developing disease in the adults for changes in the food behaviour. The personalised food will be a great help for them. This may be designed as per the concerned age, BMI, food habit and the habitant. The personalised food may be composed of only proteins and necessary vitamins needed.

3.3. Thyroid: Thyroid hormone receptor-beta obstruction has been related with metabolic order. THRA quality sequencing of different genes has introduced as observational changes in the thyroid hormone receptor-α (THRA), may identified as a polymorphism (rs12939700) in the critical region of TRα processing . Genome-wide studies consider having the proof of numerous quality variations identified with thyroid and obesity. Another method of distinguishing the upregulation of the genes are found to be the hereditary approaches of different clinical cases. It has been observed that the treatment with higher percentage of l-thyroxine lead to the biochemically hyperthyroid, in this case the person may interface weight loss drastically within 6 months, and also raised thyroid hormones (Jiang et al., 2004).

Sequencing of the THRA locus uncovered a polymorphism in a basic district engaged with the guideline of grafting. In some case studies it has been found that the two polymorphisms of the THRA locus that had an important role with various aspect of body mass index (BMI).

Some of the reviews have mentioned, the polymorphism present in the record case (rs12939700) was related with obesity. Another polymorphism (rs1568400) that has a moderately high recurrence in the populace was likewise connected with BMI as per both cross-sectional (in two free overall communities of Spain and France) and follow-up examinations in the Spanish populace based associate (Fox, 2008; Reinehr, 2010; Fernández-Real et al.,2013).

It can be concluded from some of the findings that the co-operations of variations of the poly [ADP-ribose] polymerase 1 (PARP-1) expression play the key roles in sorting out the different changes that happen during the upregulation of thyroid. It has also been established that there is a connection between the PARP-1 polymorphisms (particularly rs1136410 TC) and the advancement of thyroid. Iodine and the unsaturated fats are found to be responsible for the up regulation of the genes responsible for the thyroid. The personalised diet excluded of unsaturated fat may be a possible way to stop these regulations of the genes.

3.4. Diabetes: In recent studies showed that the carbohydrate diet plays an important role in the pathway regulation of IFN- γ and IL-15 and both IFN-γ and IL-15 are proinflammatory cytokines that play role in advancement oftype 1 diabetes mellitus (T1DM) in non-stout diabetic (NOD) mice, while scurfin or Foxp3 is a transcription factor that coordinates the differentiation of the T cells (Patrick et al, 2013). In some case studies cereal diets has been given to the bio-breeding diabetes-prone (BBDP) rats and maintained a condition of specific pathogen-free, i.e., they have allowed the growth of gut microbes, thus these rats have showed an upregulation of the Lck gene or lymphocyte-specific protein tyrosine kinase (Sildorf et al., 2012).

Lck promotes the tyrosine kinase/p56 which is a lymphocyte-specific protein and plays an important role in the activation of the T cell (Knip et al., 2011). In fact the, BBDP rats has also showed the down regulation of the antimicrobial peptide, cathelicidin antimicrobial peptide (CAMP) gene. CAMP gene which may alter the gut microbes by immunomodulatory host defence factor (Hyppönen et al., 2011). Thus, for type 1 diabetes mellitus it has been found that diet can modify alone or through the changes in the gut microbes by the changes of the expression of genes which are found to be involved in the immune response (Wu et al., 2011).

More than 70 genes have been identified through different studies, which are involved and associated with the type 2 diabetes mellitus (T2DM). Through GWAS arrays, it has been reported that there is an association of 100 SNPs with T2DM. Previously identified 50 novel loci which are directly associated with T2DM, secondly with T2DM related traits there are more than 40 loci have been associated, including insulin and glucose and fasting proinsulin (Fu et al., 2010). However, the HOMA index known as the pancreatic β cell function for T2DM-related traits and studies has found that there is a profound relationship between these traits or the genotype and environment interactions. Some Clinical investigations on the loci have found that the genes of T2DM risk through the function of β cell.

Recent studies have shown that the function of the β cell may improve by the vitamin D by limiting the expression of the chemokinine and normalizing the partial expression of the class I molecules of the major histocompatibility complex (MHC) and decreasing the amount of the MHC I proteins on β cells (Gysemans et al., 2005; Wolden-Kirk et al., 2014). Some of the findings has also showed that the insulin secretion may increase with the help of the biotin (Vitamin B) which up regulates the genes of the islets (Lazo de la Vega-Monroy et al., 2013; Berná et al., 2014). The diet includes carbohydrates and some of the fatty acids are found to be responsible for the gene regulation in diabetes by influencing the β cells. Some of the Vitamins have also found to be involved in these regulations. Personalised food enriched in protein and certain amount of fats and also depending on the body weight, BMI may play a vital role in the management of this disease.

4. Personalised Diet and its relevance: Personalised diet is established in the idea that one size doesn't fit all; distinctions in organic chemistry, digestion, heredity, and microbiology contribute to the individual differences observed in response to nutrient status, nutrition, and timing of eating, dietary patterns, and environmental exposures. Personalised diet has been described in many possible ways, and various terms has also been used to describe such as "individualized nutrition," "precision nutrition," and "nutritional genomics". Biological systems like the immune system and the changes in immune cells due to age can propagate to the thymus to such a degree, that the capacity to react to new insusceptible difficulties is debilitated when an individual ranges midlife (Aspinall& Andrew 2000). But in most other organs like muscle, does not allow the changes due to different heavy training (Frischknecht 1998).

Long-term conditions that expansion in commonness with age can affect dietary needs. A person's portability will affect on vitality needs and poor versatility may add to the expanded pervasiveness of corpulence in individuals matured more than 50 years. Muscle versus fat deposition is a conspicuous and basic phenotypic measure that has significant ramifications for an individual's long-term wellbeing and requires a simple-to-administer test. Muscle to fat ratio synthesis information will feature expanded hazard for metabolic infection on one hand just as expanded hazard for feebleness on the other. While progresses in nourishment science have to a great extent annihilated supplement lack infections in the western populace, there are developing difficulties of stoutness with its comorbidities and of maturing.

Personalised diet, i. e., the daily intake of the energy may be advised to the people dependent on their present age group is one of the easiest nutriphenomic intercessions accessible and is as of now broadly applied

during the management of obesity. It has found that due to deposition of fat in the visceral organs, the risk of human health are being increased day by day (Direk et al., 2013).

CONCLUSION

Personalized nutrition came into limelight fifteen years ago through scientific publications, conferences and nutritional genomic analysis, though the term was first used by Dr. R.O Brennan in the year 1975 (Simopoulos, 2010). The outcome of Human Genome Project and knowledge of functional foods spurred research demonstrating the link between dietary habit, physiological disorders and genotype. Personalized nutrition deals with single nucleotide polymorphisms (SNPs), epigenetic modifications that dictates the diet plan for an individual to maintain optimum health condition. There are approximately ~20,000 genes in human body, having ten million SNPs present in one individual. On an average every five to fifty genes have at least one SNP per gene.

Thus, to analyse nutritional genetic tests, the gene-gene or gene-nutrient interactions have to be studied more extensively. In some cases nutritional genetic test data proved to be psychologically promising, though medical history, family history of genetic disorders, present physiological condition, regular dietary intake, and preference for certain types of foods, etc. had to be taken in account. The research on personalized nutrition needs robust computational approach to analyse individual data based on genetic setup, age, sex, and race and integrate them with "omics" data to actually recommend a personal diet. In the past ten years, no long-term study was carried out on personalized nutrition in a large population. Some investigators consider the change in lifestyle in a population and prefers a universal approach, rather than a targeted one, to lifestyle intervention (Langenberg, 2014) for prevention of diseases.

The progress of personalized nutrition can be facilitated by developing sound theoretical knowledge on the subject to identify the most prominent personal characteristic on the basis of which personal diet will be administered. The efficacy of the recommended diet and cost effectiveness data should be well documented from authentic intervention studies. Moreover, initiatives should be taken by the policy makers to introduce regulatory framework and proper guidelines for health professionals and dieticians to familiarize personal nutrition concept to public. The present state of knowledge regarding personalized nutrition warrants increase in scientific evidences.

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