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# Nutrigenomics: An Interface of Gene-Diet-Disease Interaction

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## Abstract

Healthy diet and proper nutrition are basic necessity of life and play a key role in preventing diseases. Nutrigenomics (NG) is an emerging approach in nutritional research which deals with the gene-diet interactions. The concept of nutrigenomics is not new and it is commonly associated with “inborn errors of metabolism”, the rare genetic (inherited) disorders in which the body cannot properly turn food into energy. These disorders are related to insufficient availability of metabolic enzymes or cofactors due to alteration of gene. Usually cure of these diseases lies in restricted diet. Presently non communicable diseases (NCDs) like cardiovascular diseases, obesity, diabetes and cancers are outnumbering the other health ailments among the different human populations of world. The main reason behind the occurrence of these NCDs is the abruptly changing life style and food habits after industrial revolution. With the advent of industrial revolution and economical concerns, the life style of people across the world has changed so much so that it resulted in approximately millions of death cases due to these NCDs. Study related to NG is one step forward in nutritional research involving the techniques of nutrition, molecular biology, genomics, bioinformatics, molecular medicine and epidemiology together to understand the role of food as an epigenetic factor which unravel its role in the occurrence of these diseases. Hence, under the prevailing scenario of world health, it has become an urgency to boost NG research to find cure for dreaded diseases caused due to lack of healthy food and improper nutrition. Thus, such type of research findings ensures the effective benefit of genomic revolution for mankind near future.

**Keywords:** nutrigenomics, non communicable diseases, personalized nutrition, human health, genomic study

## 1. Introduction

Life, as a single-cell embryo, which is literally an envelope of the human diploid genome primed for replication. Almost every cell of a multicellular organism contains the same type of genetic material—its genome. Chromosomes, nucleic acid molecules that are the repository of an organism’s genetic information, are the largest molecules in a cell and may contain thousands of genes as well as considerable tracts of intergenic DNA. This genome has to be replicated with high fidelity millions of times during development to a fetal and adult stage and millions of times thereafter simply to replenish dead cells and cells lost as a result of exfoliation. Many cofactors and substrates are required for DNA replication and DNA repair. Any error during proof reading of DNA may lead to faulty

replication, accumulation of such errors may further trigger cell death by apoptosis. Consequently, there is an accumulation of mutations at the base sequence or chromosomal level as a result of genotoxic insults due to endogenous and exogenous factors is now recognized as a fundamental underlying cause of developmental defects and accelerated aging as well as of an increased risk of degenerative conditions such as infertility, immune dysfunction, cancer, and cardiovascular and neurodegenerative diseases [1–5].

Dietary reference values (DRVs) provide us a guide for the appropriate intake of nutrients for prevention of diseases caused by deficiency (e.g., scurvy in the case of vitamin C deficiency) or excess (e.g., iron-overload disease, which may be fatal in excess iron in the cell system) [6]. It is important to determine these extreme conditions associated with nutritional disorders now-a-days and the biggest challenge lies in the prevention of these type of developmental and degenerative disease in populations which are not short of food, fortified food, or supplements but needs intervention through appropriate intake of micronutrients individually or in combination (nutriomes) to optimize cellular and organism performance on both a personal and a genetic subgroup level at different life stages. Optimization of cellular function ultimately depends on the prevention of damage to the nuclear and mitochondrial genome [7–9].

### **1.1 Nutrigenomics**

Nutrigenomics, an globally emerging high-throughput science which depicts the effect of genetic variation in response to diet. The term “nutrigenomics” was first given by Peregrin [10] and after one year it was reviewed by Van Ommen and Stierum, [11]. In a molecular era, Wellen and Hotamisligil, [12], considered nutrients as “signalling molecules” which transmit and translate the dietary signals into the cell and within the cellular system it changes the expression of genes in nucleus leads to changes in protein and metabolite expression. Now the big question arises that what is happening within the cell system when we are having our meals in less or excess amount? So to get the answer of this question we have to study in detail of food-gene interlinking signaling mechanism which is the science behind nutrigenomics.

The sciences of nutrigenetic and nutrigenomic are based on three central factors i.e. firstly, there is a great inherited genomic diversity between the ethnic groups and individuals affected by nutrient bioavailability and its metabolism. Secondly, people may differ greatly in their food habit/nutrient availability and choices depending on cultural, geographical, economical, and taste perception differences. Thirdly, malnutrition (deficiency or excess) itself can affect gene expression and genome stability [13].

The field, nutrigenomics involves multiple disciplines under one umbrella to the study the designing of individual's diet that leads to stability of genomes by minimizing the DNA damage, epigenome alterations (DNA methylation), transcriptomics (i.e. RNA and micro-RNA expression), proteomics (protein expression) and finally metabolomics i.e. controlled metabolite changes. Study of all the field individually and interlinking of all is very important.

Within nutrigenomics, the studies related to nutrient-gene interaction and its potential for both intra- and transgenerational effects is epigenetics [14, 15]. In genetics, epigenetics is the processes which control the expression of certain genes by up/down regulating without altering the DNA sequence, whereas the reversible changes of gene expression in epigenetics is due to DNA methylation, histone modification and chromatin-associated proteins which controls the expression of house-keeping genes and suppress the expression of parasitic DNA such as transposons. However,

epigenomics is the study which deals with the analytical part of complete epigenetic changes takes place on a genome in a cell/entire organism. Epigenetic processes strongly influenced the normal growth and development of an organism. The epigenomic changes can be inherited upto 2 to 3 generation, which is modified by diet.

In a nutshell, the study of nutrigenomics requires a collaborative effort to protect the human population from endangered diseases by maintaining the balance in genetics and the industries of public health, food science and culinary. It's very easy task to make a tasty food by putting some lard or butter in it, and it's going to be tasty and yummy. But the whole population have to accept the challenge that how to prepare good tasty healthy food without using much oil or butter or ghee or any kind of unhealthy food product which is not good for health. By observing the present trend of increasing lifestyle disease, personalised nutrition diet chart should be prescribed based on individuals genomic construction by the nutritionist and this will be the future aspect of nutrigenomics. This chapter has emphasized on the nutrigenomics approach based on gene-diet interaction in relevance to existing advance studies to understand its present and future prospect, and how to protect human population from such non-communicable diseases?

## **2. Dietary signals and nutrient sensors**

Dealing with the complex human genome, nutrigenomics has the ability to decipher variability of genome in terms of wide range of nutrient concentration and a variety of food nutrition by identification of specific dietary signal, signal sensing or perceiving receptors. Ruden et al., [16] did an nutrigenomics research, an experiment with *Drosophila* which is model organism and depicted that each and every nutrient have numerous targets sites with various affinities and specificities. It was found that, *drosophila* has adipose-like tissues and a lipid transport system, which has a similarity with humans in respect to obesity and associated diseases than any other model organisms. In addition, Müller and Kersten [17] recognized specialized cellular-sensing mechanisms and considered nutrients and dietary metabolites as signaling elements. The molecular structure of the nutrients are naturally designed in such a way that it carries the information that how to activate a specific signaling pathways to hit the target site. Minor changes in structure (e.g., saturated vs unsaturated fatty acids or cholesterol vs plant sterols) can have a profound influence on which sensor pathways are activated. Its a great challenge for the scientist to identify the molecular pathways and the up/downstream regulation by each nutrients. Study of nutrigenomics can allow the identification of molecular pathways by genome-wide characterization of nutritional target genes. This type of information can help the researchers to understand the plan of action of individual nutrient and how it is linked with diet which has an important role in good health and diseases. Ultimately, nutrigenomics research will lead to development of evidence-based healthful food and lifestyle advice and dietary interventions for contemporary humans.

For instance, Patsouris et al., [18] revealed that though the role of PPAR $\alpha$  towards obesity is unclear then also there is some clue where PPAR $\alpha$  has some important function in obesity-linked pathophysiology of type 2 diabetes. Recently, it has been demonstrated that PPAR $\alpha$  directly regulates expression of genes involved in hepatic gluconeogenesis and glycerol metabolism [18, 19]. Visceral obesity is linked to increased free fatty acid levels [20], elevated levels of free fatty acids in the cytosol promote the plasma free fatty acids to binds with the PPAR $\alpha$ , and these molecules may be recognized by the liver as “hunger” or “in need of glucose” signals resulting in increased gluconeogenesis in a PPAR $\alpha$ -dependent manner, particularly under conditions of hepatic insulin resistance.

Mandard et al., [19], Kersten et al., [21] reported that fasted PPAR $\alpha$  null mice mutant (lack of functional PPAR $\alpha$ ) suffers from a variety of metabolic defects, include hypothermia, hypoglycemia, hypoketonemia, and elevated plasma-free fatty acid levels.

### **3. Nutrigenomic diseases and biomarkers**

Research regarding nutrigenomics is based on the principal of individuals nutrition-gene-disease interaction and how to protect the mankind from endangered non communicable diseases (NCDs) like cardiovascular diseases, obesity, diabetes, respiratory diseases, metabolic syndrome and cancers globally? Such type of NCDs are mediated by exposure of particular food components chronically, these are basically busy junk food eating lifestyle diseases of cities. These kinds of nutritional disorder are detected by biomarkers. It may be some disturbed lipid profiles to check the levels of cholesterol and/or triglycerides, increased blood pressure, or abnormal sensitivity of insulin as indicator of NCDs, like cardiovascular disease or metabolic syndrome. These biomarkers are mainly single proteins or metabolites or certain body functions that leads to be an detector for proteomics and metabolic changes in individuals body may be a causative agent's of a variety of chronic diseases which depends on the particular individuals genotype. The molecular aspects of individuals DNA damage can be diagnosed by a number of complementary ways are as follows: (i) damage to single bases (e.g. DNA adducts such as the addition of a hydroxyl radical to guanine caused by oxidative stress); (ii) abasic sites in the DNA sequence (measurable by use of the aldehyde-reactive probe); (iii) DNA strand breaks (commonly measured using the Comet assay); (iv) telomere shortening (measured by terminal restriction fragment length analysis, quantitative PCR or flow cytometry); (v) chromosome breakage or loss (usually measured using micronucleus cytochrome assays or metaphase chromosome analysis), and (vi) mitochondrial DNA damage (usually measured as deletions or base damage in the circular mitochondrial DNA sequence). These use of damaged DNAs as a biomarkers were recently validated at various levels based on the nutrient associated evidence (cross-sectional epidemiology and intervention studies) and disease (cross-sectional epidemiology and prospective cohort studies) as reported by Fenech, [8]. The micronucleus assay in cytokinesis-blocked lymphocytes is currently the best validated biomarker for nutritional genomic studies of DNA damage. In addition, a well validated nutrigenomics tool is transcriptomics, it includes the microarray assay to analyze the mRNA copies for all actively transcribed genes. The advantage of this technique is within same time it can analyze the expression level of transcripts, thousands of genes in a single assay. In peripheral blood cells, studies of gene-expression patterns have been shown to be specific for diseased states. Whereas, Martin et al., [22] noted that disease-specific gene-expression patterns in blood cells have been identified for breast tumors and leukemia was revealed by Valk et al., [23], and those patterns now used as biomarkers for the detection of diseases.

### **4. Gene-diet-disease interaction**

SNPs (Single nucleotide polymorphism) or SNVs (single nucleotide variants) are most widely acceptable markers now a days, responsible for genetic variation. Genotypic variations can be detected by SNPs or SNVs, and we can prescribe proper diet plan to avoid non communicable diseases (NCDs) like cardiovascular diseases,

obesity, diabetes and cancers. In this context, Ramos-Lopez et al., [24] revealed the sweet taste receptor (TAS1R2) related to taste perception and Ramos-Lopez et al., [25] depicted cluster of differentiation 36 (CD36), were associated with dyslipidemia in the peoples of Mexico, consume high amounts of carbohydrates and fats respectively. In addition, common variants of genes which regulate homocysteine metabolism, like methylene tetra hydrofolate reductase (MTHFR) and methionine synthase (MTR), are linked with the increased risk for breast cancer among individuals who intakes lower amount of folate, vitamin B6, and vitamin B12 [26]. The status of Vitamin D show polymorphism among the population and have the ability to modulate various metabolism in the organism [27]. Interestingly, the SNPs of the vitamin D receptor (VDR) gene, affect the availability of vitamin D [28, 29], and results osteoporosis in postmenopausal women with low calcium intakes [30]. Moreover, SNPs in genes encoding lipid proteins such as apolipoprotein C3 (APOC3) and apolipoprotein A1 (APOA1) conferred a higher risk of metabolic syndrome in subjects with a Western dietary pattern [31, 32]. Likewise, an increased risk of hypertension and CVD was observed with moderate and heavy coffee drinkers which was associated a genetic variation in the cytochrome P450 family 1 subfamily A member 2 (CYP1A2) gene [33, 34]. Additionally, studies using genetic risk scores (GRS) have been examined the cumulative effect of SNPs on diet interactions and susceptibility of diseases. Macronutrient is having the ability to modify the obesity GRS with greater values of adiposity [35]. Furthermore, obesity GRS interacted with the intake of sugar-sweetened beverages [36], and fried food consumption [37] in relation to BMI and obesity in several cohort studies.

#### **4.1 Nutrigenomics and obesity**

Obesity is a chronic low-grade nutrition related inflammatory disorder and the important factor which is associated with a group of metabolic abnormalities/comorbidities commonly includes insulin resistance and hyperinsulinemia, hypertension, impaired glucose tolerance, noninsulin-dependent diabetes mellitus cardiovascular disease (CVD), type 2 diabetes, and a number of cancers [38, 39]. For the progression of obesity and the associated comorbidities are resultant of abnormal lifestyle leading habits, so here is the perfect place where nutrigenetics and nutrigenomics contribute their work to minimize obesity. Now the question which can be raised that is; whether all the individuals or populations are affected with obesity if obesogenic environment is provided; the answer is no, it is based on genetic variability and interaction with environmental factors according to Nakamura et al., [40], Nettleton et al., [41], Reddon et al., [42]. With reference to this the obesogenic environment comprises dietary nutrients, age, gender, ethnicity, duration of sleep, amount of physical activity, sedentary behavior, stress, smoking, alcohol consumption, use of medication, and depression. So it is a conclusive evidence that environmental factors is the primary cause for obesity vis gene-nutrient-disease interaction. If an individual having a good dietary habit with specific timing throughout the day along with physical exercise of at least 30 min daily, then he/she can avoid such kind of metabolic disorder and its comorbidities. Nutrigenomics explain us the complex interactions of genome and its regulation differences among the obese phenotype that vary both within and across populations [43–46].

However, Hill et al. [47] given a concept positive energy balance which include increased intake of energy, decreased energy output and results deposition of energy. In this concept energy is represented as calories, if the intake of energy from diet is greater than the output then it cause (i) resting metabolic rate, (ii) absorption and metabolism of dietary nutrients, (iii) heat production or thermogenesis, and (iv) physical activity, a state of positive energy balance results to promote

deposition of triacylglycerol within adipose tissue. Likely, in vice-versa condition, a state of negative energy balance results to promote lipolysis of triacylglycerol and mobilization of fatty acids from adipose tissue.

In addition, Stockard [48] described a fact that environment has an immense impact in obesity. 100 years ago he stated that the embryo and fetus develops in mother's womb can show a dramatic variation in the phenotype without changing the genomic constitution of the offspring while providing a moderate environmental constraint during specific periods of time in the development of the embryo. Along with this findings a new concept is explains the science working behind this i.e. epigenetic changes associated with obesity. Goldberg et al., [49] demonstrate the prenatal and early postnatal periods have a critical role in the developmental induction of obesity. Here, the epigenetics performed the lead role, during early nutritional environment of the fetus can increase the susceptibility to develop obesity in later life. Epigenetics can induce a heritable changes in gene expression without altering the gene sequences, it is basically the integral regulating and determining factor of when and where specific genes are expressed. The detail methylation pattern of epigenetics was depicted by Bird, [50], he noted that methylation at the 5' position of cytosine in DNA within a CpG (cytosine and guanine nucleotides linked by phosphate) dinucleotide is very common in mammalian genomes and leave a stable epigenetic mark which is transmitted through DNA replication and cell division. This de novo methylation is catalysed by DNA methyltransferases (Dnmts) 3a and 3b, and maintained through mitosis by gene-specific methylation of hemimethylated DNA by Dnmt1 [51].

Furthermore, different experiments done by various scientist describes versatile experiences related to obesity. Some evidential facts revealed by nutrigenomic scientists that if a new born with lower birth weight means the baby have reduced fat mass. Infants with lower birth weight who undergo early catch-up growth which is characterized by greater accumulation of fat relative to lean body mass have an increased risk of becoming obese in later life compared with those born at higher birth weights [52–54]. Similarly, in another experiment Singhal et al., [55], Singhal, [56] reported that infants born with lower birth weight having an catch-up growth were fed formula milk show increased risk of cardio-vascular disease in later life. A number of studies revealed that there is a greater chance of incidence of obesity in adults who were fed formula milk as compared to breast fed during infancy [57, 58], but exception are also there who were not fitted into this condition [59].

#### **4.2 Nutrigenomics and cardiovascular disease (CVD)**

Cardiovascular disease (CVD), basically a heart disease affecting the heart and blood vessels includes arteries, capillaries, and veins. The CAD disease includes atherosclerotic, coronary and ischemic heart diseases, individuals carrying such diseases having plaques throughout the inner walls of arteries and leads to heart attacks. While age, gender and genomic constitution are an immutable risk factors for the occurrence of CVD, modifiable risk factors play a major role in the causation and progression of the disease. Some of the extra risk factors which is very common now a days due to busy and stressful life schedule like hypertension, hyperlipidemia, obesity, diabetes, atherosclerosis, thrombosis and smoking is a causative agent of CVD. Analyzing the complexity of the etiology of CVD outlined here Juma et al., [60] narrate some dietary recommendation for CVD prevention based on individuals genetic constitutions. In nutrigenomics diet is considered as environmental factors and which has a direct relationship with the development of chronic diseases, the CVD is not aloof of that. It's a well established fact proved by scientists that the personalized diet composition has a strong risk factor for development of CVD [61–64].

Obesity, itself is a curse in human population and is a leading risk factor to develop cardiovascular disease, diabetes mellitus and a number of cancers which is already discussed. In this context, to maintain the energy balance several polymorphic genes are involved to control the development of CVD in certain “favorable” or “unfavorable” condition [65]. Moreover, Lusis, [61] describes the role of atherosclerosis in the pathogenesis of CVD, it constitutes the key element and can be regarded as a complex combination of lipid transport and metabolism disorder with chronic inflammation. The levels of total cholesterol, LDL cholesterol, and triglycerides elevated permanently in the blood plasma which is causative agent for the development of atherosclerotic plaques, whereas increased levels of high density lipoprotein (HDL) i.e. cholesterol showed a protective role [65]. Genes responsible for encoding the apolipoproteins can be regulated by some signaling agents like hormones and enzymes but, it show differential sensitivity in population to develop cardiovascular diseases. In this context, individuals carrying the allele E4 of the apolipoprotein E gene show higher low-density lipoprotein-cholesterol (bad cholesterol) levels with increased intake of dietary fat as compared to those who carrying the E1, E2 and E3 alleles having equivalent amounts of dietary fat [66]. AG to A transition in the promoter of APOA1 gene is associated with increased HDL-cholesterol concentration but the results across studies are not consistent [67]. Whereas, Ordovas et al. [68] found that the allele A was associated with the decreased serum HDL levels. The genetic effect was reversed, however, in women who ate more polyunsaturated fatty acids (PUFA). In men, this type of fat effect was significant when alcohol consumption and tobacco smoking was considered in the analysis. Also specific polymorphism in genes encoding lipid transport proteins, their receptors, and lipid-processing enzymes and inflammation related proteins were shown to be associated with the characteristic changes in blood lipid concentrations [69–73].

To prevent or treat CVD an intense debate/discussion has been taking place for best dietary plan where the composition of macronutrients, the percentage of total fat along with different fatty acids presents are important [74–79]. Likewise, the source or origin of diet's composition is very essential, for e.g., individuals taken monounsaturated fatty acids from olive oils are different from monounsaturated fatty acids intake from meat and other foods of animal origin [79, 80]. Similarly, there is lots of controversy over the best origin and type (omega-6 and omega-3 series) of polyunsaturated fatty acids (PUFA) as reported by Jakobsen et al., [79] and Russo, [81] for prevention or treatment of CVD. In a same platform and same type of case study done by Shai et al., [82] and Sacks et al., [83] for controlling body weight and cardiovascular related risk factors where emphasis is given on to take high carbohydrate, low fat diet in comparison to high fat, low carbohydrate diet. In 1965, Keys et al, [84] in their study stated that it was an individual's “intrinsic characteristics” which controls the effect of diet in plasma concentrations of cholesterol, is an variable factor for person to person. Based on the facts, nutrition related counseling focused on weight reduction and normalization of lipid profiles through diet, exercise, and medication for the prevention of CVD.

### **4.3 Nutrigenomics and Diabetes mellitus**

Diabetes mellitus (DM), a group of metabolic diseases, results from defects in insulin secretion and insulin activity or both which is characterized by hyperglycemia. Georgoulis et al. [85] reported that due to this metabolic disease DM, various organs like blood vessels, heart and kidneys are dysfunction and/or failure, and now a days this disease is considered a global burden [86]. The International Diabetes Federation's recent estimates indicate that 8.3% of adults (382 million



individuals) have diabetes, and the number of individuals with this disease is expected to rise beyond 592 million in less than 25 years [86]. DM fall into two broad etiopathogenetic categories: type 1 and type 2 DM known as T1DM and T2DM, respectively. The epidemic global obesity noted by Prentice [87], he stated that virtually T2DM will be a major health issue in the world create a major drain on health budgets. Individual with obesity increases the risk of developing the disease DM by at least 10 fold as compared to normal one [88, 89]. In developing countries, peoples are shifted their lifestyle from traditional diets system to modernized fast food eating habit which include frequent consumption of red meat, refined carbohydrates and saturated fats is leads to obesity [90]. The insulin hormone, which is an important controller of glucose and fat metabolism is secreted from  $\beta$ -cells of pancreas. Irregular secretion insulin is observed in both the cases i.e. obesity and T2DM. Glucolipotoxicity is the results of high sugar and saturated fatty acid in diet on regular basis as suggested by Prentki et al. [91] and it negatively controls the secretion of insulin of from the  $\beta$ -cells, and results hyperglycemia and hyperlipidemia.

Flavonoids present in the diets include flavones, flavonols, flavanones, isoflavones, and anthocyanins. Various experimental studies suggested the protective role of polyphenols on glucose homeostasis mechanism, along with this some specific molecules like flavanols, luteolin, quercetin and others have a great impact on different steps of intracellular signalling pathways (insulin secretion, insulin signalling and glucose uptake, enhancing mitochondrial status, suppression of inflammatory cytokine production and reactive oxygen species (ROS)/reactive nitrogen). In addition to flavonoids, phenolic acids and tannins also have inhibiting property of the enzyme  $\alpha$ -glucosidase and  $\alpha$ -amylase which is responsible for carbohydrate digestion [92–97]. For instance, Song et al. [98] noted that consumption of apple or tea was associated inversely with T2DM risk. This is in accordance with the Health Professionals Follow-Up Studies also suggested that higher consumption of anthocyanins, particularly from pears, apples and blueberries, were inversely associated with T2DM [99].

Caffeic acid, chlorogenic acid (present in coffee) and ferulic acid (esterified to hemicelluloses in cereals) are the most common phenolic acids [96]. An inverse result with caffeinated, decaffeinated coffee and caffeine intake with T2DM in a dose-response manner (1–6 cups/day), compared with no or rare coffee consumption was observed in different epidemiological studies, which support the hypothesis i.e. habitual coffee consumption is associated with a substantially lower risk of T2DM [100, 101].

Resveratrol (trans-3,5,4'-trihydroxystilbene) is a natural phenol act as an phytoalexins, found in the skin of grapes, blueberries, mulberries, raspberries, peanuts and red wine, helps in reducing the complications of diabetes in many organs and tissues including liver and pancreatic  $\beta$ -cells and in different diabetic animal models [102]. It also improve the glucose homeostasis and give protection to pancreatic  $\beta$ -cells. It has an important role in insulin secretion and amelioration of metabolic disorders [103].

Whereas, Afzal et al., [104] depicted that lower vitamin D levels represent a risk factor for incident of T2DM in humans. However, the levels of hypovitamin D along with increased levels of parathyroid hormone (PTH) is an independent predictor of  $\beta$ -cell dysfunction, insulin receptor and glycemia [105]. Patients with T2DM with established hypovitaminosis improve glycaemia and insulin secretion by Vitamin D replenishment, not only through a direct action on pancreatic  $\beta$ -cell function but also via regulation of plasma calcium levels, which regulate insulin synthesis and secretion [106, 107].

#### 4.4 Nutrigenomics and cancer

Cancer is a multiple stages process in which gene expression, and protein and metabolite function begin to run aberrantly [108]. In today's genomic era, the cellular events which intercede the activation of carcinogenesis upon modulation by dietary factors, has led to flow of significant information which helped in understanding of this disease [109]. Cancer susceptibility may increase due to inherited mutations in genes. Gene diet interaction may increase the risk of developing cancer. Endogenous reactions, such as oxidations or from exogenous agents, sunlight exposure (skin cancer), such as tobacco smoke (lung cancer), aflatoxin (liver cancer), and relatively high doses of ionizing radiations (many types of cancers) [110] induces cancer.

It is mandatory to have communication between nutrition, metabolism, and gene expression for upholding body homeostasis. Human genome and nutrition jointly interacts to do the same. Individual's health condition and susceptibility to disease may get affected due to this [111]. Nutrient regulates transcription factors at the molecular level which then modifies the gene expression (up or down), consequently to adjust the metabolic responses [112].

Diet is a blend of protective, carcinogenic, and mutagenic agents all together and are metabolized by the enzymes of biotransformation process. Risk of developing cancer can be modified through genetic polymorphisms that change protein expression or the function of these enzymes. Foods ingested by humans are proposed to contain more than 25,000 [113]. Role of different bioactive food ingredients in cancer pathogenesis has been studied and found that, among these, more than 500 types of bioactive food ingredients is proved to be possible predisposing agents.

For carcinogens, diet is considered as a source (intrinsic or cooking-generated) present in certain foods or constituents acting in a protective manner (vitamins, antioxidants, detoxifying enzyme-activating substances, etc.) [114]. Carcinogen metabolism affecting polymorphisms may modify probability of contact between carcinogens and target cells, thus acting at the stage of cancer initiation [65].

In hormone dependent tumors such as breast, prostate, ovarian and endometrial cancers, influences of polymorphisms of gene encoding factors involved in hormonal regulation are most strongly manifested. Polymorphisms in sex hormone receptor genes comprising those encoding estrogen receptors, progesterone receptor, and androgen receptor have been shown to be associated with cancer risk modulation [65]. Hormonal regulation can be influenced on interaction with dietary factors. Obesity has strongly impact on hormonal status. Apparently, some food components, such as phytoestrogens are known to be processed by the pathways similar as sex hormones [115].

There are various examples of the effects of diet on cancer risk. High consumption of red meat increase the risk of colorectal cancer [66]. N-Acetyl transferase (NAT) exists in two forms: NAT1 and NAT2, it is a phase II metabolism enzyme. Several polymorphisms exist in NAT1 and NAT2, some of them are capable of slow, intermediate, or fast acetylations. Heterocyclic Aromatic amines found in heated products like cooked red meat get through acetylation by NAT. On cooking of muscle meat at high temperature, some amino acids may react with creatinine to generate heterocyclic aromatic amines (HAA). Acetylation activates HAA to reactive metabolites which bind DNA and cause cancers. This acetylation can only be performed by NAT2 fast acetylators. People who consumed relatively large quantities of red meat with NAT fast acetylator genotype had a higher risk of developing colon cancer in them [66].

Specific dietary irritants, such as salts and preservatives have been suggested as being carcinogens for gastric cancer [116]. C667T polymorphism in MTHFR gene

which reduces enzymatic activity is inversely associated with occurrence of colorectal cancer. Less consumption of folate, vitamin B12, vitamin B6 or methionine in diet are associated with increased risk for cancer in CC or TT phenotype of MTHFR gene [117].

It has also been found that reactive oxygen species (ROS) such as superoxide anions, hydrogen peroxide, and hydroxyl radicals attack DNA bases, resulting in potential mistranscription of DNA sequence [118]. Such disruptions can interfere with DNA replication and thus produce mutations in oncogenes and tumor suppressor genes. ROS can also result in breakage of DNA strand, resulting in mutations or deletions of genetic material [119].

Dietary fibers have a protective effect against bowel cancer [120]. Growth of colonic tumors in both *in vitro* and *in vivo* systems gets inhibited on consumption of fish oil which is rich in omega-3 fatty acids [121–123].

Fruits and vegetables rich in bioactive components can prevent carcinogenesis by several mechanisms such as blocking metabolic activation through increasing detoxification. Detoxification enzymes as flavonoids, phenols, isothiocyanates, allyl sulfur compounds, indoles, and selenium can be modulated on consuming plant foods [124, 125].

Some of these bioactive components which may influence carcinogen metabolism, cell signaling, cell cycle control, apoptosis, hormonal balance and angiogenesis are calcium, zinc, selenium, folate, vitamins C, D and E, carotenoids, flavonoids, indoles, allyl sulfur compounds, conjugated linoleic acid and N-3 fatty acids [126]. Bioactive ingredients which play protective role in the cancer development are lycopene from tomatoes, resveratrol from grapes and berries, cinnamic acid from cinnamons, hesperidin from citrus fruits, carotenoids from red vegetables and fruits, ascorbic acid, coffee acid from coffee, types of soluble fibers, polyunsaturated and fatty acids from marine animals have [127]. Intake of proper diet with sufficient minerals and vitamins which are involved in regulatory and enzymatic processes reduces the risk of cancer. The deficiency of these micronutrients may lead to abnormalities. For example, zinc and folate is involved in DNA repairing process. Further natural compounds from plant source like apigenin (celery, parsley), curcumin (turmeric), epigallocatechin-3-gallate (green tea), resveratrol (red grape, peanuts, and berries), genistein (soybean), and allyl sulfur (garlic) have been reported to affect the cell cycle by different mechanisms. Some of these changes may be associated with the processing of synthesized proteins at the post-translational level like shifts in the phosphorylation process of the main regulatory factors of cell division [128]. Tumor behavior can also be changed by other food ingredients through accelerated cell death and enhanced apoptosis. Apoptosis occur through two known pathways: the intrinsic, mitochondrial-mediated pathway; and the extrinsic, death receptor-mediated pathway [129].

Many of the studies by American Cancer Society [130] have shown the reduced risk of cancer associated with consumption of foods rich in vitamin C, such as fruits and vegetables. On contrary, evidence indicates that vitamin C supplements do not reduce cancer risk. From the above finding it can be said that, activity of fruits and vegetables in preventing cancer is due to consumption of many vitamins and other phytochemicals in a combination, not due to vitamin C alone.

## 5. Conclusion

This chapter deals with the role of nutrigenomics for the prevention of non-communicable diseases. The mother nature has made all humans almost genetically similar but, only 0.1% variation makes one individual unique from others with

respect to their phenotype and individual susceptibility to disease or health and also their differing response to nutrients. Interestingly, same diet can be a risk factor for some individuals whereas in others, it may prove beneficial. Besides, some diets may regulate genes to help in maintenance of health whereas, Some of them act as possible inducer of disease. Thus, based on knowledge of individual nutritional requirements, nutrition status and genotype; personalized nutrition & diet recommendations can be made to maintain the balance between health and disease to offer a healthy life. Major challenge is, in a populous country like ours, where people are still fighting for their basic needs, personalized nutrition system approach is a dream. Now, even the rural India is not spared from this menace of non communicable disease as it has also started embracing city culture, post era of globalization and urbanisation has brought significant changes in eating habits of rural India as well. At this moment, the most pertinent question is how to overcome this public health concern. The nutrigenomics approach is most effective and the only way out but on contrary it is not going to be so cheap to be available for masses. Also it is a very difficult task to handle the huge population with nutritional intervention as it will require adequate qualified professional along with advance lab facilities. For the time being as an alternative, public health awareness programme can play an important role in different way to protect the people from these diseases in broader sense. It shall basically focus on early identification of at-risk individuals and appropriate intervention in the form of weight reduction, changes in dietary habits and increased physical activity to help to prevent, or at least delay the onset of dietary disorders until India build itself capable in all respect to implement fully functional individual nutrigenomics approach.

### **Conflict of interest**

The authors declare no conflict of interest.

### **Notes/thanks/other declarations**


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