



Nutrigenomics - An emerging field of science and technology unrevealing inter-relationships between nutrients and human genome using modern tools such as transcriptomics, metabolomics, epigenomics and proteomics

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Abstract

Nutrigenomics is one of the upcoming sciences that have the potential to open up new arenas towards health and disease management. Earlier generalized approach towards health and disease management was employed in the health sector in which human genetics and its respective environment was taken into account, nevertheless in this contemporary approach nutrition and its interaction with human genome holds focal position. With regards to nutrition and human genomics and their interaction two terms as nutrigenetics and nutrigenomics are employed but both of these terms are distant as well as closely related depending upon the context. According to various different research studies conducted on the subject revealed that nutrients have the potential of influencing gene and its expression. Nutrients do serve as qualifying agents that can affect the overall functioning of genes at all levels. In order to uncover the various aspects and to deepen our comprehension on the subject various different approaches-more precisely 'OMICS' sciences are employed. Transcriptomics, Proteomics, Metabolomics and Epigenomics greatly serve the purpose. Nutrigenomics has been anticipated as a revolutionary scientific approach that will provide us with more customized, tailor-made and individual specific approach towards health and disease management.

Keywords: epigenomics, metabolomics, nutrigenomics, proteomics, transcriptomic

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Nutrigenomik - Transkriptomik, metabolomik, epigenomik ve proteomik gibi modern araçları kullanarak besinler ve insan genomu arasındaki ilişkilerin açıklığa kavuşmadığı gelişen bir bilim ve teknoloji alanı

Özet

Nutrigenomik, sağlık ve hastalık yönetimine yönelik yeni alanlar açma potansiyeline sahip olan gelecek bilimlerden birisidir. İnsan genetiğinin ve ilgili ortamın dikkate alındığı sağlık sektöründe sağlık ve hastalık yönetimine daha önce genelleştirilmiş yaklaşım uygulanmış, buna rağmen bu çağdaş yaklaşımda beslenme ve insan genomu ile etkileşimi odak noktasındadır. Beslenme ve insan genomikleri ve bunların etkileşimi ile ilgili olarak, nutrigenetik ve nutrigenomik olmak üzere iki terim kullanılır, ancak bu terimlerin her ikisi de içeriğe bağlı olarak uzak ve yakından ilişkilidir. Konuyla ilgili yapılan çeşitli farklı araştırmalara göre, besin maddelerinin geni ve ekspresyonunu etkileme potansiyeli olduğunu ortaya koymuştur. Besin maddeleri, tüm seviyelerde genlerin genel işleyişini etkileyebilecek nitelikli ajanlar olarak hizmet eder. Çeşitli yönleri ortaya çıkarmak ve konuyla ilgili anlayışımızı derinleştirmek için çeşitli yaklaşımlar - daha kesin olarak 'OMIK' bilimleri kullanılmaktadır. Transkriptomik, Proteomik, Metabolomik ve Epigenomik bu amaca büyük hizmet eder. Nutrigenomik, bize sağlık ve hastalık yönetimine daha özelleştirilmiş, kişiye özel ve kişiye özel yaklaşım sağlayacak devrimci bir bilimsel yaklaşım olarak öngörülmüştür.

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Anahtar kelimeler: epigenomik, metabolomik, nutrigenomik, proteomik, transkriptomik

1. Introduction

With the increase in scientific knowledge and advancement in technology it has been unearthed that nutrition emphatically influences the overall functioning of gene, thus affecting the overall physiological processes occurring in an individual. Nutrigenomics is the study based on human nutrition and its corresponding effects on its genetic makeup. Furthermore it uncovers both the useful and the harmful effects of various different nutrients composing ones' diet and their influence on the usual functioning of the gene and then on health [1]. Any transformation and variation brought about by diet in the genomic organization can potentially affect the transcription and DNA composition [54]. Thus, it is indispensable to understand interaction of nutrition with human genomic organization and its ultimate affect on phenotype. The influence of diet on an individual's genomic organization in context of health and disease management is gaining worldwide scientific recognition. Thus nutrigenomics serves as a sine qua non towards understanding that how diet actually affects ones' genomic organization and subsequently influences the overall performance of an individual in both health and diseased states. Nutrition has a significant contribution towards the maintenance of one's health and increased susceptibility to various known diseases such as cancer, osteoporosis, diabetes and cardiovascular disease. Nutrigenomics studies can be furthered with the help of 'OMICS' technologies. By using the vast array of information available the influence of one's diet on health can be evaluated further. Erratic responses have been observed with regards to particular dietary intervention and are the burning topic amongst the scientific community [1]. Various different factors can influence one's reaction to diet, such as one's age, gender, lifestyle, habits and genetics being the significant in this regard [2].

Amongst the various different factors contributing towards gene health, diet in particular, essentially contributes towards gene health. It is affirmative that a dietary choice is a determining factor towards gene expression. Therefore, it is apt to opine that a diet of an individual underlines the expression of one's genes. Custom-made, scientifically tailored nutritional plan as per ones details can prove beneficial towards achieving the long desired scientific goals of disease prevention and cure. A diverse collection of naturally sourced victuals are found enriched with plant based nutrients such as carotenoids, coumarins, and flavonoids, to name a few in recent times have been found to have been naturally endowed with health promoting and disease preventing attributes. Recently increased scientific interest in this area of research have demonstrated that various diseases can be lessened by up to 50% or even more by making appropriate dietary choices and often by adding recommended supplements to ones' daily routine [3]. It has been reported many a times that same type of dietary plans produces very different responses in different individuals depending upon their genetic backdrop thus inviting the need to personalized dietary plans [4]. This type of individualized and targeted dietary plans successfully helps the dietitian to help resolve the issue of congenital metabolic syndromes caused by single gene mutations and help the sufferer towards normal healthy lifestyle nevertheless continuous monitoring remains indispensable and obvious in order to avoid any disquieting situation [5].

2. Emerging trends of nutrition, nutrigenomics and nutrigenetics

Due to an ever increasing world population it is the need of an hour to work towards disease prevention so that the cost on disease management and cure could be reduced. Nutrigenomics and nutrigenetics are intended to achieve the long standing of goals of health and disease management with the help of diet rather than using external means so that human beings can have an overall improved quality of life, that's why it necessitates the need of diet as per ones requirement based on ones DNA analysis rather than a generalized plan for everyone that can work towards only a limited no. of health issues [6].

In order to achieve this goal, appropriate scientific research in this regard is essential. Genetic alterations and modifications in response to various different dietary plans can be evaluated using nutrigenomics and nutrigenetics. Disease prevention and management cannot be thoroughly established by just relying on the already determined determiners and neglecting the determiner being under discussion [7].

Nutrigenomics and Nutrigenetics are per se different in context and also how these two recent sciences are exploited is also unique and distinguishable, nevertheless the ultimate goal of these sciences is improved human health, disease prevention and disease management by employing the concept of customized, tailor-made and individual specific dietary plans. Nutrigenomics deals with effect of one's diet on ones genome, proteome and metabolome, more precisely at all the levels of one's regulation and composition. Nutrigenomics aids us in both health and disease for example unearthing galactosemia a disease that is attributed to inherited genetic deficiency of any one of the three enzymes that is involved in galactose metabolism comes under the heading of nutrigenomics, while nutrigenetics deals with differences at single point that focuses on single nucleotide polymorphism rather than a complete set of nucleotides composing a gene for example Methylene-tetra-hydro folate reductase gene (MTHFR) impressively explain the pattern of studies conducted under the heading of nutrigenetics as this malady implies to SNP (C677T and A1298C) mutation rather than a gene itself, owing to this type of mutation the conversion of homocysteine to methionine gets hampered,

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while this conversion is essential for the metabolism of folic acid and also for regulating normal amounts of homocysteine in the blood. Those individual that have genetically slow performing MTHFR enzyme fail to maintain the normal amounts of homocysteine in their blood and increased amounts of homocysteine in blood leads towards various different health related issues such as inflammation, cardiovascular diseases, congenital defects, complicated pregnancies, detoxification inabilities to name a few. Nutrient deficit in folate, B6 and B12 are found to be the cause of elevated levels of homocysteine in the blood [8].

Contemporary research supports the idea of personalized nutrition plans based on nutrigenetics and nutrigenomics in order to avoid or at least limit the onset of nutrition related diseases so that we can achieve the age old scientific goals of health and longevity both in general and in particular amongst the masses [9]. Nevertheless understanding the phenotype and genotype of an individual in context of one's personalized attributes and specific physiological state that the individual is going through such as pregnancy etc. require to be deemed essential while devising an individualized nutritional plan [10].

3. Modern approaches and Technologies used in nutrigenomics

Variation in genetic information can be observed at various different regulatory points that can influenced by diet. Advancement in field of 'OMICS' sciences have provided more elaborate insight on the subject and have revealed the fact that how various different bioactive substances influence human health and activities. Bioactive substances that are thought to be endowed with health promoting and disease alleviating abilities can be tested in the laboratory by using scientifically advanced techniques such as cell culture. Additionally the research conducted on animals or humans regarding bioactive compounds duly serve the purpose, nevertheless the various different techniques being employed in this regard have their own merits and demerits, and the conclusion drawn from the varied results need to be based on cautious comprehension. Moreover the nature of experiment should always be considered while working with them as the experiments are either in vitro, clinical or based on epidemiologic studies as the nature of experiment have potential effects on the conclusion being drawn from them. Furthermore other factors around which human life revolves such as nutritional habits, clinical and physiological states, ambiance and the respective habitat need to be taken into account. Moreover recently mico flora of an individual are found to greatly influence one's genome so having been fully aware of its state is the pre-requisite and indispensable for drawing practical conclusions [11]. Bioinformatics can also be employed both in order to generate and process large data sets being obtained as result of these dynamic experiments [12]. It has been reported that physiological processes occurring in an organism have the potential to influence the biological effects of biologically active compounds. Different processes such as absorption, transport and biotransformation are found to influence the effects of biologically active compounds. Additionally the different mechanism both generalized such as storage and excretion and cellular mechanism such as regulation of transcription factors have their own influences, as various types of genes are under their influence and thus these can alter or modify their functional or physiological performance towards different nutritional substances. Thus the nutritional habits and genes together regulate the homeostasis of an organism [13]. Recently food products have been designed considering human genetics so that these can conferring health benefits and are also in line with ethical rulings of society [14]. The notion that nutrients have the potential to alter or modify gene expression at various different levels is in accordance with various different research studies. These alterations or modifications occur during signal transduction, or can also happen as consequence of chromatin structure modification or else can potentially change the function of a protein.

Diet can lead towards epigenetic alterations and thus require scientific attention towards its understanding and then its management [15]. Epidemiological reports garnered from various research studies also depict some serious reservations regarding the inclusion of genetic polymorphism into nutrition studies. For instance the research study conducted on coffee consumption and cardiovascular disease sheds light on nutrigenomics and other unusual dietary aspects [16]. Research studies provide varying results with regards to coffee, as increased risk, no effect or lessened threat can be observed [17]. Nevertheless coffee is a complex compound being composed of several different biologically active constituents, one of them being caffeine which can have a deleterious impact on cardiovascular system. Here in this regard it is important to note that caffeine enriched coffee negatively affects only those individuals who have potentially low rate of caffeine metabolism- slow caffeine metabolizers, per contra individuals who have naturally high paced caffeine metabolism- fast caffeine metabolizers does not involve such risk and are relatively innocuous towards its consumption [16].

Similarly a research conducted by Norwegian Scientists revealed that both coffee drinkers and cigarette smokers are less susceptible to some liver diseases such as rare primary sclerosing cholangitis PSC disease in contrast with those who abstain from them. Surprisingly 20% of those who daily consume coffee and smoke were compared with 43% healthy controls. It was found that PSC sufferers consumed less coffee at that moment as well as in their past compared with the healthy control group. Thus coffee consumption was found to be associated as a preventive measure towards the development of liver cirrhosis and liver cancer. The fact of the matter is that both coffee and cigarettes possess caffeine and nicotine respectively which are sympathomimetic in nature and thus enhance the amounts of

intracellular cyclic adeno-monophosphate. This adeno- monophosphate has the potential to prevent the development of liver cancer or liver cirrhosis [18].

The influence of diet on genetics of an individual is imperative to be considered while analyzing the issues of human health and its associated problems in order to resolve these issues in a holistic context [19].

Recently the significance of nutrigenomics towards cardio metabolic diseases has revealed that nutrigenomics in conjunction with micro biome and interactions of gene with its respective environment can help us towards overall improved disease management [20]. Similar attempt with regards to cancer suggests that cancer is also closely linked with dietary intake and an individual's response towards particular diet can be varied depending upon the various other factors acting at the same time, typical dietary routine and its respective implication on genes is diverse and thus targeted nutrition using nutritional genomics approach can help us in better management of the disease [21].

As far as regulation of these recent prolific scientific facts and their application is concerned, an organized body comprising of world's experts has been established so that systematized evaluation and assessment could be carried out in near future in order to reap the actual benefits of the knowledge being acquired [22].

4. Nutrigenomics in relation to epigenomics

Nutritional Epigenomics is vital while working on the subject of precision nutrition as epigenetic alterations caused by nutrients is found to manipulate intracellular signaling pathways [23]. Obesity is one of the leading causes of various different chronic diseases that human beings suffer from and it is the need of an hour to find the methods towards its prevention and management. It has been proposed that in order to cope up with the predicament of obesity that underlines scores of medical issues in addition to nutrigenomics and nutrigenetics, nutriepigenetics should be taken into account while devising a diet plan- precision nutrition as it is one of the contributing factors like the two discussed erstwhile [24].

The significance of nutrition over the offspring is both overwhelming and stupendous as until recently it has been reported in various different studies that nutritional attitudes of an individual not only casts its influence on somatic cells, but also has an effect on offspring in terms of its action of on the epigenome of germ line cells [25].

5. Nutrigenomics in relation to transcriptomics

Transcriptomics is one of the high throughput technological scientific development that provides us with the information regarding how different genes perform their functions in response to changing ambience and therefore in effect it the study of the expression of genes at the time of transcription more precisely mRNA synthesis [26].

Modern technology and advancement in the field of biological sciences has provided biologists with the extraordinary aptitude to have an insight into the entire set of genes that an individual is composed of, not just at the handful of popular ones as it used to be in the near past. Human genome project and its successful completion is big achievement in this regard. The researchers have gone into the details of even more than the DNA of plant and have successfully explored the messenger RNA generated as consequence of the transcription of various different genes. Understanding both DNA and RNA is essentially required because if DNA has potential of developing a tomato plant than RNA has the set of guidelines to materialize the potential [27].

Transcriptomics studies have been conducted in order to study in detail the effects of different types of nutritional substances being consumed as well as the varying diet patterns on mammalian liver have been taken into consideration and it has provided with much needed details on the matter nevertheless further substantiation has been suggested [28].

Additionally transcriptomics have provided us with the opportunity towards nutritional intervention in the backdrop of enhancing our understanding of gene, its function, its ambience and then its affects on gene function when undergone with some variation [29]. Transcriptomics have been successfully employed to understand the differences in response to dietary challenges in two different clusters respectively [30].

6. Nutrigenomics in relation to proteomics

Proteomics delineates the overall expression of sum total of proteins in an individual [26]. In the present context proteomics can help us in both the identification and quantification of biologically important proteins and peptides and can help us in understanding the potential of them [31]. The effect of nutrition on health has been understood by mankind since the ancient times. Recent research studies conducted also accentuates and opines to have a diet that confers health promoting effects, either by preventing the disease onset or else delaying its onset, and overall better performance Dietary components are actually composed of multitude of constituents with each having varying patterns of bioavailability and bio efficacy, and their inter- relationships, thus it calls for further research using intricate analytical tools in order to understand their mode of action precisely [32]. Proteomics is a challenging science and requires the application of intricate technologies such as mass spectrometry (MS) based proteomic techniques for protein identification and quantification with reference to nutritional intervention and biological efficacy analysis of

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various components employing proteomics. There are nutrients which are found to alter RNA translation to proteins and thus the subsequent events. Such events can be analyzed using proteomic analyses. The proteome analysis can serve us in sorting out various different nutrition linked diseases in human beings for instance obesity, diabetes, cardiovascular disease, melanoma, senile decay, and pregnancy related complications and can even lead us towards devising practical solutions to these medical problems [32]. Additionally the use of nutrigenomics and nutriproteomics based knowledge can help us towards better athletes development employing the concept of personalized nutrition which can help individual to fully develop its potential, so in addition to serving the health goals, it can serve towards betterment in other arenas of life [33].

7. Nutrigenomics in relation to metabolomics

Metabolomics is the most recent amongst all 'OMICS' sciences and it finds its ways in nutrigenomics as one of the incredible opted tool for furthering research that in due course will be serving the purpose of Nutrigenomics. It makes use of several different intricate analytical tools such as mass spectroscopy (MS) and nuclear magnetic resonance (NMR) to gain complete insight on low molecular weight metabolic products, nutrient substances and other substances related to human biological fluids which together constitute a metabolome. Metabolomic tools such as mass spectrometry (MS) and liquid chromatography (LC), GC-MS and NMR are being employed in order to obtain a holistic picture of variations occurring in food composition both as per its nutritional index and quality are concerned. As far as nutritional quality of crop plant is concerned it is fairly based on the metabolite content of the crop plant under study [34]. Metabolomics duly serves us in understanding the process of domestication of a particular crop so that we can devise strategies for target oriented crop improvement endeavors. Identification of apposite molecular markers can help us in further development of need based food products in near future [35]. Lenhard et al. [36] used GC-MS based profiling of both wild and numerous cultivated tomato species in order to comprehend what changes have had occurred during the entire process of domestication. Tools such as nuclear magnetic resonance (NMR) gas chromatography along with the liquid chromatography-mass spectrometry (LC-MS), and desorption ionization-electro spray ionization-mass spectrometry are extensively used in metabolomic analysis. Bioinformatics tools are widely used while analyzing the data obtained by as a result of comparison of different cell conditions. However, metabolomics in spite of being one of the best approaches so far is not yet a standardized approach owing to its limitations, such as it fails to compute and work out the entire metabolome or proteome, identification of external food based metabolic products and internal metabolic products quantification in human samples or to the extent human dietary changes affect the metabolic profiles. Lipid metabolome quantitative analysis provided data exhibited varied outcomes of dietary fats on cardiac and liver phospholipid metabolism [37]. The changes have been mapped in the amounts of lipid metabolites to their biochemical pathways [38]. Similar approach was employed to assess the possible implications of drug rosiglitazone that is in actual insulin- sensitizer on liver, plasma, heart and adipose lipid metabolism in mice model and thus is being employed to generate an extensive data base comprising of human lipid metabolite profile based on concentration. Since various different effects of dietary macromolecules on metabolism of tissue can be revealed in the plasma lipid metabolomics, thus metabolome can provide us with an approximated controlled variations as per the metabolic response to dietary intake amongst different individual is concerned. Metabolomic approach can be successfully employed towards the development of improved crop that could be able to meet the ever increasing demand of food round the world, as through it identification of the key loci becomes possible and thus enabling us to understand the basics of complex interactions that occur during metabolism [39]. Nutritional constituents differently interact and influence the biochemical networks of living organisms and thus these diverse modes of actions and implications of food, needs to be understood in order to unearth the various different issues pertaining to health, disease prevention and management, thus nutrigenomics and nutrigenetics via metabolomic analysis attempts to resolve the human medical issues thus providing quality life to world citizens [40].

8. Biomarkers

Novel biomarkers are required in order to determine association between human health and food consumption as the food being composed of various different nutrient constituents, thus human body in response to them need to maintain the homeostasis and alterations in it appropriately [41]. The extraordinary vitality of biomarkers in the present context can be estimated from the fact that recently it has been said that various determining factors known as risk factors for a disease are not exact and just a clue towards disease onset, progression and exacerbation, rather the precise determining factors to a particular disease which are rampant in our society like cardiovascular or metabolic diseases can be biomarkers which will be more exact and reliable and so we should work on these grounds in order to work on practical terms thus achieving the goal of disease prevention and management [42].

9. Effect of different nutrients on human genome and microbiome in health and disease

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In nutrigenomics the variations which occur in the human genome, and indirectly on the micro-biota that an individual possess are influenced by dietary choices and thus these have very personalized responses in human beings.

There are various different examples which throw light on the fact that different types of element being found in food differently interact with human genome and these interactions subsequently causes different types of alterations and modifications to it for instance a naturally occurring nutrient in the body Coenzyme Q10 (CoQ10) found in human muscles has been reported to influence nearly 12,000 genes [43]. Furthermore an essential vitamin D, that governs the absorption of intestinal calcium and phosphate. Research studies have revealed that Vitamin D3 influences nearly 20,000 genes occurring in human prostate cancer cells [44].

Likewise another research study revealed the potential of Zn to cause an influence on human genome, more precisely Zn was found to have been endowed with inherent potential to either switch on or switch off certain genes depending upon its concentration in the diet. Some of the genes were switched off by diminished amount of zinc in diet nevertheless subsequent experiments revealed that these were responsible in activating diverse group of white blood cells, thus conferring protection to the body against various different types of infections. Nevertheless on increasing the levels of Zn in body those genes were switched on. This provided scientists with a valuable cue and thus with this knowledge they were able to devise treatments for various different immune related disorders. They successfully treated malaria and diarrhea by adjusting the amounts of Zn in accordance with the medical condition [45].

Human micro biome has been considered while employing this concept of customized tailor-made individual specific diet plan as the micro biome these days has been regarded to be the second- genome of an individual [46].

Increased postprandial blood glucose level suggests high risk towards the development of prediabetes and type II diabetes nevertheless the generalized pattern recommended to cope up has not been found efficient to an extent it is needed, thus it calls for personalized approach in order to deal with situation appropriately, currently the personalized approach applied on towards the problem has provided us with promising results and suggests more research on the same line [47]. Furthermore another study using two different types of bread one traditionally prepared sourdough-leavened whole grain bread and white bread was conducted and the results suggested personalized response regardless of bread type [48].

Prebiotic diet comprising of dietary fibers and resistant starches which adds roughage to food have been known to be beneficial for human gut for some time ago, nevertheless until recently are found to maintain the healthy gut micro biota, which then contributes towards healthy life style of an individual. Very recently in context of personalized nutrition, personalized approach towards prebiotic diet has been suggested so that one can move towards better understanding of microbial or host/physiological response that can lead towards better management of problem based on the individual in particular [49].

Human genome and Micro biome both work synergistically towards individual health and well being, nevertheless it has been reported that micro biome is more dependent on individuals living together and having interactions with each other regardless of their genetic ancestry and to some extent also depends on type of diet, medicine and other activities specific to an individual. It has been found that more reliable information regarding diabetes and obesity can be garnered while taking it into account in contrast the data obtained on the basis of mere host genetics and ambience is not that much reliable, therefore while devising any clinical measures, it should always be taken into account as an indispensable unit towards disease management [50].

10. Conclusions

In the past decade researchers have provided public with various different types of food that were developed in order to confer general health benefits to the public. These newly developed foods have nutrients that have the potential to influence human genome thus having effects that are far from being human comprehension and anticipation. Human beings are very complex and even more complex are their habits and desires. Thus these artificially designed foods have raised ethical concerns as well owing to them being totally different from the nature sourced food items. One such popular and controversial development is the development of genetically modified food (GMO). Joint center of bio-ethics (JCB) in collaboration with the university of Guelph philosophy, have been established in order to examine, evaluate and assess the outcomes of nutrigenomics and nutrigenetics based scientific developments. There they analyze the newly developed foods, their nutrient constituents and their respective influence on human genome.

An important and considerable fact about Nutrigenomics is that despite being valuable there is shortage of experts and trained individuals in this field. Primary health care professionals at present do not have expertise in this relatively new area of nutritional science. Similarly there is a lack of geneticists and molecular nutritionists' experts at present. More experts are required in this field in order to reap the practical benefits it [51].

Nutrigenomics services can be divided into three classes: Firstly devising genetic tests based on the scientific knowledge and understanding. Secondly computing the disease susceptibility based on the genetic test results. Thirdly formulating and devising individual specific dietary plan. These three points are imperative to be considered as these are the ones which potentially raise ethical, legal and social concerns in the society.

Direct to consumer referred to as DTC is one of the most ominous potential threat encountered these days as the knowledge pertaining to nutrigenomics is increasing, the common people couldn't care less to wait for the result

that can at least adumbrate the potential outcomes of having dietary supplements and consuming them recklessly that can be even injurious to their health, owing to the grave risk potentials ingrained in any of their constituents [52]. Nevertheless until recently a set of guidelines have been proposed in order to calculate and estimate for such dietary recommendation and consumption, nonetheless the study is just an initial attempt and will be required to be furthered further [53].

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Nutrigenomics - An emerging field of science and technology unveiling inter-relationships between nutrients and human genome using modern tools such as transcriptomics, metabolomics, epigenomics and proteomics

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