SANITAS MAGISTERIUM

Received: 05.05.2019
Published: 17.07.2019
https://dergipark.org.tr/ijhadec
June 2019 •

IN THE LIGHT OF NUTRI-OMIC SCIENCES "ARE WE REALLY WHAT WE EAT?"

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Abstract

Using high quality genomic tools and bioinformatics techniques has increased after the Human Genome Project (HGP) is completed. As a result of this great step taken to carry out comprehensive analyzes of biological systems, the word –omik was added to the end of the already known sciences names and new techniques with a holistic approach began to be used. These techniques called "omik" includes determination and definition of whether of molecules in a particular biological sample is derived from cells, tissue samples, an organ, or an entire organism. The main purpose of omic studies that have been increasing in recent years is to identify genes (genomics), messenger RNA (transcriptomics), proteins (proteomics) and metabolites (metabolomics) in a sample.

Apart from these technologies, nutri-genomic also known as nutritional - omic techniques, nutri-transcriptomic, nutri-proteomic, nutri-metabolomic subunits are the methods that aim to reveal the relationship between genes and diet more clearly and studies are progressing rapidly. In particular, nutrigenomic research includes high throughput analysis using all sub-sciences of system biology to optimize health through personalization of the diet, clarify the complex relationship between nutrients and genetic polymorphisms.

In this review, both understanding the molecular mechanism of the interaction between the human body and nutrition at all regulation levels (genes, gene expression, proteins, metabolites) in addition to the superiority of nutri - omic techniques over traditional approaches and intending the ability of human health to be optimized by food intervention, evaluation of prevention and treatment potential of diseases with nutrition is aimed.

Keywords:

Nutrigenomic, nutrigenetic, metabolomic, nutrition-gene interaction

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INTRODUCTION

In the last quarter century, nutrition research has undergone a significant development, focusing on molecular biology and genetics as well as epidemiology and physiology. It is not possible to understand the relationship between nutrition and health without clearly determining the effect of nutrients at the molecular level. There are some factors that cause this to be noticed [1]. The first is the important evidence about personalized nutrition that genetic variation analyzes performed after the conclusion of the human genome project and the results of studies linking gene variation with disease markers or other phenotypic changes [2, 3]. Second, there are serious diagnoses that micro- and macro-nutrients can be powerful dietary signals that affect cell metabolic programming and play an important role in the control of homeostasis [4]. At the same time, nutritional researchers have begun to accept that genetic predisposition may be associated with diet, such as cardiovascular disease, type II diabetes and cancer [5]. Nutrigenomics (gene - nutrient interaction) studies have gained speed in order to understand both nutrients and genes or their interaction due to the idea that different individuals cannot give exactly the same response to similar diets. Nutrigenomics called nutritional genomics promises to optimize human health and to prevent the disease by determining the most relevant personal nutrition [3, 6].

Genomic science, which is the fundamental omics technique that directs the researches, investigates in an in-depth and holistic approach the structural and functional properties of the DNA where genetic information is stored. These sciences, led by genomics, later formed nutrigenomics and nutrigenetics together with transcriptomic (examines transcriptomes), proteomics (examines proteomes), metabolomics (examines metabolomes) and epigenetics [7]. Even though these two notions are closely related, they show a different approach to understanding the relationship between genes and diet [8]. Nutrigenomics investigate the effects of nutrients on gene expression, while nutrigenetics study the effect of genetic variations caused by nutrients. Unlike nutrigenomics, nutrigenetics deals with how an individual's genetic structure influences the response to diet and thus explores in detail the underlying causes of genetic polymorphisms [9].

Every food taken into the body is converted into many new substances with different biological effects after being metabolized. It is known that environmental factors such as diet type and frequency and quality of diet have the ability to change gene expression [3, 10, 11]. Even in individuals living in the same geography, exposed to the same environmental conditions and belonging to the same culture, the difference in the response to diet is due to genetic variation [12, 13]. Investigating the potential of food intake to alter gene expression is essential to elucidate the effects of nutrition on health.

Biomic techniques provide the basis for the equipment and methods required for nutrigenomic studies used to explain nutrition-gene interactions. Today, it is possible to come across many studies in which system biology subunits (genomic, transcriptomic, proteomic, and metabolomics) and bioinformatics technologies are used effectively for this purpose [14]. In these studies, unlike traditional methods, biomic instruments used in high volume and efficiency at one time: microarrays, PCR, electrophoretic techniques, chromatographic methods, advanced devices such as mass spectroscopy and

higher statistical methods used to perform data analysis. In this study, after the general information about nutri-omic techniques is mentioned, it is aimed to reveal the relationship between nutrition and health through current studies.

2. TERMS

2.1. Genomics

Genomics is a DNA analysis technique that focuses on the cause of genome diversity among individuals. Small changes such as translocation and inversion during the synthesis of DNA do not lead to phenotypic changes that can lead to gene diversity, and cannot yet be analyzed at the genome level. Changes in expression at the nucleotide level (deletions, insertions, duplications) that are important factors that cause polymorphism can directly create variants [15].

Genomics is divided into two groups as structural and functional genomics. Structural genomics provides access to hereditary information by analyzing DNA expressions. Functional genomics, also known as transcriptomic, is the simultaneous examination of messenger RNAs (mRNAs) obtained by transcription from the cell genome. So, intended that to examine the expression of genes at the genome level in terms of form, quantity and time, as well as to learn the functions of the genes and to understand the importance for the organism [16]. Thus, by examining the changes in the nucleotide sequences, it becomes clear how genetic information is affected by nutrition. As a result, the idea of genetically appropriate individual nutrition recommendations is further approached. At the same time, gene expressions of microorganisms carrying the potential health risk for a food can be identified and stored in the database.

2.2. Proteomics

Proteomic studies focus on proteomes and protein-protein interactions. The most important handicap in these studies is the high dynamics of the potential proteins that can be revealed at the amino acid level. The analysis of many different proteins at proteome level with very different chemical character is quite difficult. However, these difficulties have been minimized largely with the techniques used today. Proteomic analysis process is the separation, visualization and separation of proteins as in the traditional methods. Some of the techniques used are advanced techniques such as two-dimensional gel electrophoresis and advanced mass spectroscopy [15, 17, 18].

2.3. Metabolomics

By defining the genes, the unknowns caused by the genetic differences of organisms have not been completely resolved and transcriptomic and proteomic studies have been carried out to clarify. However, the results of these studies were not sufficient to elucidate the phenotypes. The place where the phenotype information is stored in the cell is metabolites, and all metabolites present in a tissue or physiological fluids at a given moment are called metabolome [19]. Metabolomics technology is based on extensive analysis of metabolites and includes quantitative analysis of chemical molecules obtained by biological processes other than substances such as DNA, RNA or protein in the sample [15, 20]. Nuclear magnetic resonance (NMR) and mass spectrometers are the best equipment used today for metabolomics research [15].

3. USE OF OMIC TECHNIQUES IN NUTRITIONAL SCIENCES

In the science of nutrition, the use of omic techniques such as transcriptomic and proteomics has been increased in determining the mechanisms of action of dietary factors and metabolites. These techniques are used to understand both the positive and negative effects of dietary elements on human health and molecular incidents in nutritional diseases such as obesity, diabetes, cardiovascular diseases and colon cancer [11].

To analyze complex and crowded data sets obtained from nutri-omic studies bioinformatics techniques are used. For instance, there is potential interaction of a particular food with 30000 genes or 100000 different proteins in the human genome. The integration of statistics and bioinformatics with biology is essential for analyzing and interpreting the data from these interactions.

In a study, butyrate treatment of colorectal cancer cells was found to cause cell deaths and it was found that growth was inhibited within 48 hours after application. In order to elucidate this mechanism, gene expression sequences were determined by using HT29 colorectal cancer cells as a model and proteomic techniques were applied. As a result of proteomic applications (2D-DIGE electrophoresis and mass spectroscopy), 1347 proteins (including all isoforms and modifications) were detected and 139 of these butyrate treatments were found to play a role in cancer cell death [21, 22]. In the gene expression part of the study, microarray was performed to HT29 cells. As a result of statistical analysis, it was determined that 2550 genes of human genome were changed by butyrate. These genes have been found to be involved in biological events such as DNA repair and transcription, as well as cell metabolism. However, the correlation between gene expression modulation and protein expression has been reported to be poor [21, 24].

Fenech et al. (2011) mentioned how to use omics techniques to better understand the potential effects of nutrition on gene and protein expression. For this purpose reviewed the changes in the gene and protein expression of colon colorectal cancer cells by butyrate, a metabolite produced by bacterial fermentation of dietary fiber or resistant starch in the colon [22]. Dietary fibrous foods and resistant starch are known to promote intestinal health and protect against colorectal cancer [23]. Butyrate, a metabolite formed by the use of resistant starch by microorganisms in the intestine, has been reported to improve intestinal health [24].

The results of studies on nutrition-gene interaction in the literature should be able to guide the consumer and should be practically applicable in the field of dietetics. Cahill et al. concluded that adequate doses of vitamin C are mandatory in individuals with GSTM1 or GSTT1 (glutathione S-transferase) genotype, as inadequate vitamin C induction causes ascorbic acid deficiency in these individuals [25]. In a case-control study conducted by the Singapore Chinese Health Study Cohort on women, a significant correlation was found between the level of green tea drinking and the activity of angiotensin converting enzyme (ACE). According to this result, the risk of breast cancer due to ACE gene polymorphism decreases with consumption of green tea [26].

One of the most important genes associated with obesity is the FTO gene located on chromosome 16 is associated with fat mass. Duicu et al. (2016) in a study, analyzed FTO gene variants (rs9939609 and rs17817449) and some metabolic biomarkers (fasting blood sugar, total cholesterol, HDL and LDL cholesterol, triglycerides) and leptin levels in a 357 Roman obese children group and their

relationship. FTO rs9939609 SNP (single nucleotide polymorphism) carriers have been found to be more than twice the risk of obesity. Carriers of FTO rs17817449 SNP were found to have higher weight, BMI (body mass index), waist and hip circumference, total cholesterol, triglyceride, fasting blood sugar and adiponectin values [27]. Another important gene associated with obesity is the INSIG2 (insulin-induced gene 2) gene on the chromosome 2. In a study, three INSIG2 polymorphisms (rs12464355, rs17047757, rs7566605) related to dyslipidemia were found in 1058 students who had 85% higher BMI (overweight). The relationship between INSIG2 rs12464355 SNP and high LDL-cholesterol, rs17047757 SNP and excess weight, and rs7566605 SNP and high lipid levels were found to be significant [28].

Estruch et al. (2013) carried out their studies with the prediction of "primary prevention of cardiovascular diseases by the Mediterranean diet". They found that when they enriched the diet with especially in extra virgin olive oil, they reduced the incidence of some chronic diseases in subjects at high cardiovascular risk [29]. The same team presented a more comprehensive result of their work in 2018 (the 2013 study is an interim report). This study was conducted with 7447 participants, 57% of whom were women at the age of 55-80 years, who were at risk of cardiovascular disease (but without any disease at the beginning of the study). Three randomly selected groups were assigned one of three diets: the Mediterranean Diet group enriched with extra virgin olive oil, the Mediterranean Diet group enriched with mixed nuts, and the control group in which it was recommended to reduce the amount of fat in the diet. At the end of the 4.8-year tracing period; on extra virgin olive oil and nuts supplemented diet groups, cardiovascular diseases were found to be lower than the control group. The findings of the study support the beneficial effect of the Mediterranean diet on the prevention of cardiovascular diseases [30].

Kashani et al. (2019) investigated whether the microRNAs of the plants constituting an important part of the diet match the human genes that have potential regulatory function. As a result, they found that 4 common plant microRNAs provide excellent matching with 22 human transcripts (CCNC - cell cycle, GIPR - digestion, MYLK - muscle contraction), which exhibit a wide range of body functions from muscle contraction to suppression of tumor formation. According to these findings, regularly consumed foods have great potential to affect our genome and alter body functions [31].

Konstantinidou et al. (2010), in their study examined the in vivo nutrigenomic effects of extra virgin olive oil consumption within the framework of the Mediterranean Diet. In the study conducted with 90 healthy volunteers aged 20 to 50 years, volunteers were randomly divided into 3 groups, and oil source is extra virgin olive oil in the diet of the first intervention group, washed (removed polyphenols) olive oil in the diet of the second intervention group, while the diet of the control group was not intervened. According to the findings; expression of genes related to inflammatory processes (IFN, ARHGAP15 and IL7R), oxidative stress (ADRB2) and DNA damage (POLK) in peripheral blood mononuclear cells decreased. The reduction in expression of genes related to inflammatory processes showed the protective effect of Mediterranean diet and olive oil phenolic compounds on inflammation. The anti-inflammatory and antioxidant effects of important phenolic compounds (tyrosol and hydroxytyrosol) in olive oil have been proven. Additionally, the data obtained provide further evidence that the Mediterranean diet and rich polyphenol-containing olive oils, such as extra virgin olive oil, can be recommended as a useful tool for the prevention of atherosclerosis [32].

4. CONCLUSION

Nutritional genomics is a powerful tool that can be used to provide individual-specific nutrition. Nutri - omics serve to studies which using of advanced technology tools that investigate the relationship between nutrition - gene from basic biology to clinical practice. The human genome's response to nutrition is a science that will help us understand how defective genes are affected by nutrition. There are many studies suggesting that we can optimize nutrition by defining the genotype of an individual. Though it is not possible to change our genetics, in the near future, we will be able to improve the effects of hereditary defects through nutrition, and select the right foods to support our genetic predisposition. However, researches on nutrition - omics applications, which have a history of about twenty years, is still insufficient to be reflected in practice today. Disease-specific biomarkers should continue to be identified. Thus, it will be possible to improve the quality of life through individual-specific nutrition by moving away from the “one size fits all” approach.

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