



## NUTRACEUTICALS MIRACULOUSLY ALTER HUMAN GENOMICS: A REVIEW ON NUTRIGENOMICS

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### ABSTRACT

*Nutrient deficits and health problems are the main focus of nutrition study at the moment. Healthy diet and genetics have a significant impact in the development of chronic illnesses as cancer, osteoporosis, diabetes and cardiovascular disease. To better understand the impact of diet on health, researchers are using high-throughput 'omics' technologies including transcriptomics, proteomic, and metabolomic methods to study the relationship between nutrition and disease. 'Pharmacogenomics' studies how a patient responds to medicine, while 'nutrigenomics' examines the influence of nutrients and dietary components on an individual's health. With the goal of providing a comprehensive summary of the nutrigenomics change from nutraceuticals, this review paper presents current tactics, future possibilities and problems.*

**Keywords:** Genetics, Health, Disease, Nutraceutical, Components

### I. INTRODUCTION

One of the most important outcomes from the Human Genome Project and the detection of SNPs (single nucleotide polymorphisms) in populations has been the development of 'tailored medicine.' It is a recent offshoot of this genetic revolution that includes (1) nutrigenomics: the study of interactions between dietary components and the genome; (2) nutrigenetics: understanding the gene-based differences in response to dietary components, as well as developing nutraceuticals that are most compatible with health for each individual

based on genetic makeup. Genetic polymorphisms have been widely studied in humans, but their translation into medical practise has been delayed due to the time necessary to gather population data on SNP occurrence, comprehend the importance of a specific SNP in illness, and create appropriate diagnostic tools. Nutrition and botanicals may interact with the genome and influence subsequent gene expression, which has created a huge push for nutrigenetic research and nutraceuticals based on nutrigenetics to flourish. A few notable examples for learning

basic nutrigenetics include polymorphisms in the MTHFR (methylene tetrahydrofolate reductase), ApoE and ApoA1 (associated with cardiovascular disease), and the leptin/leptin receptor (associated with obesity) genes. It is explored in the context of 'personalised nutrition' when developing nutraceuticals for women with thrombophilic gene variants to prevent and control their thrombosis risk. "The field of nutrigenetics will become more widely recognised as a critical component of nutrition and dietetics practise as more study into the genetic variations and nutritional needs of individuals is conducted." [Subbiah M. T. 2007].

## II. CONCEPT OF NUTRACEUTICAL

De Felico initially described nutraceuticals as 'foods, food components or dietary supplements that exhibit particular health or medical advantages including the prevention and treatment of illness beyond basic nutritional functions' back in 1989. Later, nutraceuticals evolved as a natural dietary source that may help prevent cancer. Baichwal RS, 1999 [Baichwal RS, 1999]

Nutraceuticals are naturally occurring bioactive chemical substances that have a positive impact on human health. Health-promoting, disease-preventing, or semi-medicinal qualities distinguish nutraceuticals from other types of supplements. There are a variety of sources for nutraceuticals, including food, herbal and dietary supplement industries, as well as the pharmaceutical business and bioengineered microbes, agroproducts, and active biomolecules that have recently appeared. Foods that have been genetically altered and processed into 'custom' foods and goods including cereals, soups, and drinks may be included in this category [Dureja D et al., 2003].

Nutraceuticals can be classified chemically as isoprenoid derivatives (terpenoids, carotenoids, saponins, tocotrienols, tocopherols, terpenes), phenolic compounds (coumarins, tannins, lignins, anthocyanins, isoflavones, flavonones, flavanoids), carbohydrate derivatives (ascorbic

acid, oligosaccharides (Ca, Zn, Cu, K, Se) [Malik A et al., 2008].

### Classification of Nutraceuticals Based on Modes of Action

Nutraceuticals are thought to improve human health and prolong life expectancy by slowing the ageing process and preventing chronic illnesses [Golla, U. 2018]. Numerous studies on the effects of nutraceutical supplements on heart disease, cancer, diabetes, obesity, osteoporosis, and the immune system have revealed promising results. In most cases, nutraceutical modes of action aim to improve health by increasing functional components. Biological actions of nutraceuticals are discussed in this section.

#### *Anti-Cancer Activity*

Nutraceuticals have been examined as chemopreventative drugs, and encouraging findings have been found in terms of their capacity to prevent and cure cancer. Various sources of nutraceuticals have been shown to have anti-cancer properties. Garlic, ginseng, ginger and green tea extract all have a variety of anti-cancer properties. Cancer start, proliferation and metastasis are all inhibited along with autophagy and intrinsic apoptosis, as well as DNA alkylation. Nutraceuticals have also been shown to lessen cancer signalling pathways, which are thought to be involved in cancer development. Studies on the mechanisms of action of nutraceuticals against various types of cancer have been conducted in great numbers, and a wide range of nutraceuticals have been found to express anti-cancer properties against cells from various types of oral and prostate cancers, as well as from the breast, lung, and colons. [Shukla, Y.; George, J. 2011].

#### *Anti-Inflammatory Activity*

Chronic inflammation-related disorders may be prevented and treated using the anti-inflammatory properties of nutraceuticals. It is possible to reduce the dose of anti-inflammatory therapeutic medications by supplementing them with anti-inflammatory nutraceuticals, which has the added advantage of minimising side effects. Chronic inflammation is the primary cause of many

chronic illnesses, including cardiovascular disease, lung disease, diabetes, and cancer, as well as a host of other conditions. [Petiwala et al., 2015].

#### ***Antioxidant Activity***

The buildup of free radicals in the body causes oxidative stress, which may then lead to a variety of chronic illnesses, such as cancer, cardiovascular and autoimmune disease, ischemic disease, atherosclerosis, diabetes mellitus, and hypertension. ROS production and elimination are normally maintained by the cell's redox (reduction/oxidation) balance [Simioni, C. et al, 2018]. ROS buildup and decreased antioxidant capacity due to an imbalance in the redox state may lead to oxidative stress, which is why redox imbalance is so important.

#### ***Anti-Lipid Activity***

Vitamins, minerals, and antioxidants are among the numerous nutraceuticals that are thought to be beneficial in the treatment of hypercholesterolemia in illnesses including hypertension, diabetes, and heart disease. "An excessive amount of low-density lipoproteins in blood is called hypercholesterolemia." [Houston et al., 2007] For patients with increased lipid levels, the effects of nutraceuticals on their lipid profiles have been studied; consequently, this section will focus on the effects of nutraceuticals on a wide range of illnesses. For decreasing total cholesterol (TC) and low-density lipoprotein (LDL) values, the use of nutraceuticals as hypolipidemic medicines has shown tremendous promise. "The mechanism of action of lipid-lowering nutraceuticals may be divided into three categories." LDL excretion and suppression of cholesterol absorption are examples of these processes. [Riccioni et al., 2018].

### **III. ORIGIN AND DEVELOPMENT OF NUTRIGENOMICS**

Diet has long been thought to have an impact on health. It has long been recognised that nutrition may be used to address genetic conditions known as 'inborn errors of metabolism' by changing the food we consume. Phenylketonuria (PKU) is an example of a

genetic disorder that is caused by a single gene mutation. Phenylalanine, an amino acid, must be avoided by those who have phenylketonuria. A further example of lactose intolerance is the fact that the gene producing lactase, the enzyme responsible for breaking down lactose, is generally 'shut off' after weaning in the vast majority of individuals across the globe. However, a single nucleotide variation arose 10,000–12,000 years ago among northern Europeans. Due to the lactase gene's continuous expression in adulthood due to this single nucleotide polymorphism (SNP). With the advent of molecular genetics in the late twentieth century, scientists were able to find additional genes that interacted with dietary components, making it easier for persons with this SNP to consume nutritionally-rich dairy products in places with short growing seasons. The field of nutrigenomics has already begun to be commercialised by the 1980s. Nutrigenomics was given a boost by the Human Genome Project in the 1990s, which sequenced the whole human genome. There was already a slew of connections between genes, diet, and illness discovered by 2007 [Bhatt SN, Sharma AD, 2011]. High-throughput technologies that allow for the worldwide investigation of gene expression in a cell or organism are part of the new approach to nutrition research brought about by nutrigenomics.

The fields of genetics and public health, as well as food science and the culinary arts, would have to work together to develop nutrigenomics. Making tasty cuisine is a piece of cake. Adding some fat or butter to it will make it delicious. The problem is to find ways to reduce fat content while still producing tasty, nutritious meals. For this reason, public health reform is imperative, and nutrigenomics may one day prove to be the magic bullet for combating obesity and other chronic illnesses like type-2 diabetes [Kore KB et al., 2008]. Since the Universal Declaration of Human Rights (1948), when the 'right to food' was first acknowledged as a fundamental component of an acceptable quality of living, the world has achieved significant progress in terms of food

availability. International commerce opened up in the last several decades, allowing food to be available throughout the globe regardless of religion, geography, or resource. In order to improve food safety and nutrition, international organisations such as the Codex Alimentarius Commission (CAC) have set international standards that are relevant and approved worldwide [Ramsingh B. 2012]. It was only in the late 1990s that policymakers began to pay attention to the relevance of 'nutritional food as a right,' after the completion of the human genome project. Food and nutrition were also highlighted during the 1996 World Food Summit, which underlined the connection between the two. Recent years have seen a

considerable influence on people's health and nutritional status due to the ease with which processed meals are available, to rising incomes, and to the availability of diverse food due to the reduction of trade barriers. Lifestyle-related illnesses rose as a result of increasing and diverse food intake (e.g., animal and partly hydrogenated fats consumption) and sedentary lifestyles [Popkin B.M. 2006]. Molecular mechanisms of how diet, nutrition, and genes influence human health have been revolutionised in the post-genomic age. 'Nutritional genomics or Nutrigenomics' was developed as a result of a dramatic change in the therapy of nutrition-related disorders from the use of drugs to the use of food.

**Table 1: Significant milestones in nutrigenomics.**

<b>Year</b>	<b>Milestone (s)</b>
1859	Publication of Charles Darwin's theory on origin of species and their evolution
1865	Gregor Mendel describes that heredity is transmitted in discrete units
1869	Friedrich Miescher was the first to identify DNA as a distinct molecule <i>i.e.</i> 'nuclein'
1879	Walter Flemming observed mitosis and described chromosome behavior
1902	Archibald Garrod observed orderly Inheritance of alkaptonuria disease according to Mendelian rules.
1903	Walter Sutton connect Mendel's laws of heredity and given chromosome theory of heredity
1909	Wilhelm Johannsen coined the word gene to describe the Mendelian units of heredity
1943	Erwin Schrödinger proposed gene as the information carrier
1944	Oswald Avery, Colin MacLeod, and Maclyn McCarty identified DNA as the 'transforming principle' and showed that it can transform the properties of cells
1944	Barbara McClintock observed that genes can 'jump' or be transposed from one position to another on chromosomes and revealed that the genome was much more dynamic
1952	Alfred Hershey and Martha Chase experiments proved that genes are made of DNA
1953	Francis Crick and James Watson described the double helix structure of DNA
1955	Joe Hin Tjio defined 46 as the exact number of human chromosomes
1956	V.M. Ingram discovered that cause of disease (sickle-cell anemia) is a specific chemical alteration in a hemoglobin protein
1966	Marshall Nirenberg, Har Khorana and Severo Ochoa and their colleagues elucidated the genetic code Genetic Code Cracked Khorana and Nirenberg, along with Robert Holley interpretation of the genetic code and its function in protein synthesis
1968	Restriction nucleases enzymes described that revolutionized ability of DNA manipulation.
1983	First genetic disease (Huntington) mapped using DNA polymorphisms
1990	Launch of human genome project by U.S. Department of Energy (DOE), National Institutes of Health (NIH) and international groups
	Ethical, Legal and Social Implications (ELSI) programs founded
1994	DOE initiated microbial genome program
1997	Galileo laboratories became the first Nutrigenomics company
1999	Nancy-Fogg Johnson and Alex Merolli used 'Nutrogenomics' term publically

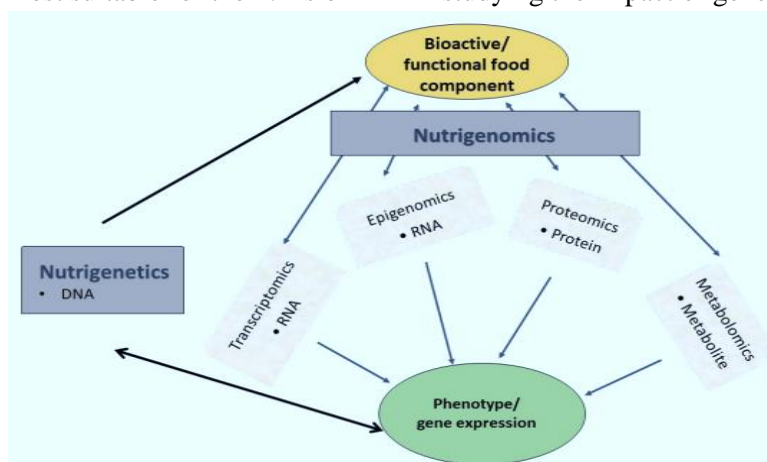
<b>1991</b>	Food and Drug Administration (FDA) approved Gleevec, an oral medication to treat chronic myeloid leukemia (CML)
<b>2003</b>	Establishment of National Centre of Excellence in Nutritional Genomics in US to explore link between diet, genes and diseases Human genome project completed and published
<b>2004</b>	The European Nutrigenomics organization (NuGO) born
<b>2011</b>	Personalised nutrition: An integrated analysis of opportunities and challenges (Food processing)

Nutrigenomics is the application of genomics in nourishment. Transcriptomics, epigenomics, metabolomics, and proteomics are just a few of the cutting-edge methods being used to unravel the intricate web of interactions between nutrition, the human genome, and health [Fenech M et al., 2011]. Dietary bioactive chemicals affect gene expression, our genes' route is regulated by nutrient intake, nutrients affect genes to prevent and cure illness, and nutrients and gene responses have molecular links, according to this new knowledge. For over two decades, researchers have been investigating the fundamental molecular interactions between nutrition and genes, even though the genetic component had been thought in previous times to be a factor controlling differences in dietary response [Ordovas JM, Mooser V. 2004].

Examines how our genes and the stuff we consume interact. A specific focus is on the effects of different diets on individuals with various types of genetic makeups. Using this technology, individuals may be matched with the meals that are most suitable for them. As of

2017, [Murgia C, Adamski MM]. Scientists, politicians, and health experts are working together to produce customised nutrition guidance and functional foods that may be tailored to each person's specific health requirements in this new discipline. What we consume, what our ancestors ate, and how it affects our cells and biological systems all come together. The food's influence on our anatomical development follows a similar pattern to that of our genetic make-up. Using nutrigenomic profiling (Pavlidis C, et al., 2015), we may learn more about the processes that underlie individual differences in dietary requirements and the ability to react to food-related therapies.

Every piece of the jigsaw of personal fitness has genetics at its core. Transcriptomics, metabolomics, epigenomics, and proteomics are just a few of the cutting-edge techniques being used in the growing area of nutrigenomics (Figure 1). 4 Personal variations in nutrition may be explained in part by genetic variation, which has expanded techniques to studying the impact of genetic variation.



**Figure 1** The interrelation of how food intake contributes to phenotype.

#### IV. PUBLIC AWARENESS TOWARDS USE OF NUTRIGENOMICS

Increasing public understanding, confidence, and trust in genetics and nutrition genomics can help eliminate societal concerns. It's important for science and the food business to address public concerns about nutrigenomics. Food crises of the past and present, such as those around genetically modified organisms (GMOs), show how critical it is to address public concerns as quickly as possible and to treat social problems surrounding science with the same gravity as technical ones. Regulation is required to guarantee that research is used in a responsible manner and to reassure the public that goods can be trusted. Regulators and the public must be involved in the process of improving the safety, dependability, and health benefits of manufacturers' goods. Theodore (2006).

##### Awareness Programmes for Public

[Rao, 2001] explains the connection between a nation's shifting dietary habits and the development of effective public education programmes and methods. For the purpose of discussing the importance of genomes in India, Acharya and colleagues (2004) organised a Genomics Policy Executive Course. Participant familiarity with genomics' impact on health in India was a primary objective of the course, as was the development of a multi-sectoral network for sharing views.

Krishnaswamy (2008) discovered that developing and implementing Food Based Dietary Guidelines is vital to overcoming diet-related illnesses and promoting health (FBDG). The genes we inherit cannot be changed in this post-genomic age, but their reaction to the environment (dietary changes) may be tweaked to get the desired effects. FBDG was developed by a multidisciplinary team of nutritionists, agriculturists, technologists, home scientists, and dieticians. FBDGs' ultimate goal is to grow what is needed and conserve what is necessary in order to avoid both malnutrition and overnutrition.

In this article, the future of nutrigenomics foods, as well as its advantages and disadvantages, were discussed. Consumer expectations for nutrigenomics are high, yet there are two key issues. "To begin, it's debatable whether or not the objective of matching diets to certain genotypes in order to promote health can be achieved." Secondly, the introduction of customised nutrigenomics foods to global food markets is dependent on various obstacles being overcome: some of scientific character, some of technological nature, and others connected to consumer, market, or ethical concerns. They all fall under the category of barriers.

Ghosh presented the new paradigms of nutritional genomics in relation to the functional food business (2010). In order to promote human nutrition and health, as well as bring social and economic advantages, he stressed the importance of the product's customer acceptability and market penetration. Ghosh and Gorakshakar (2010) underlined the objective of integrating genetics into public health in India, while Aswini and Varun (2010) also presented a broad understanding about the new gene-based technologies that may be readily exploited by the current healthcare institutions in the country.

#### V. NUTRIGENOMICS: THE NEXT GENERATION NUTRACEUTICALS

A new generation of natural product inventors may take use of the current buzzwords in genomics and biotechnology to produce new goods. It was Christine Houghton's successful career as a nutritionist and practitioner of nutritional medicine that inspired her to launch her own company, "Cell Logic, in 2010. In the field of nutrition genomics, cell logic is a leading supplier." Sydney is where the firm is headquartered. Broccoli and other fruits and vegetables were used by Houghton in the development of nutritious goods. A considerable number of active molecules may be extracted from them by processing in order to have a noticeable effect on the human body.

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Raw fruits and vegetables seldom contain sufficient levels of active chemicals to be immediately beneficial to the body.

Human cells' biomarkers are supposed to be affected by the products she produced. Genes get a signal from the product, which they use to either increase or decrease the activity of a positive or negative action. All of Cell Logic's nutritional products are based on this nutrigenomics approach. She compiled scientific data to back up the claims that these items have therapeutic properties. She then conducted a human experiment. To paraphrase Houghton, these studies demonstrate that nutraceuticals work. In testing using the broccoli product, several negative impacts on the body were discovered. ' This is normal. Molecules are the building blocks of all things, biological or inorganic. A common perception among natural product fans is that these items are free of negative effects, although this is not supported by the facts. However, the negative consequences of Cell Logic's nutrigenomics products should not overshadow the fact that they represent a significant advancement in the field of supplement precision goods. Kaput, J. (2007, January 1).

The field of nutrigenomics might be considered a branch of genomics. When the DNA was fully sequenced in 2003, scientists already knew that human traits were influenced by genes. We were aware that genetics had a role in a plethora of health issues. Soon, it became clear that certain medications were unsuccessful for some people but very beneficial for others. Genes were thought to be responsible for this. By mapping genes and tying them to particular treatment actions, scientists have come up with a better understanding of this phenomena. Precision or customised medicine was born as a result of this.

Biomarkers may now be discovered via the use of diagnostic testing. These are often found inside or on the genes, but they may also be found outside of the DNA molecule.

Biomarker-targeted medication may be able to improve or worsen a health condition. New medication treatments were created as knowledge of biomarkers expanded. Over 140 such tailored medicines have been created by the pharmaceutical sector, according to the 2016 keynote talk at the Personalized Medicine Coalition (PMC). FDA has approved all of these for use in treating a wide range of life-threatening illnesses, including cancer. FDA or any other globally recognised body has not yet authorised nutrigenomic products for use as medicine, unlike pharmaceuticals. As a result, they are still considered to be dietary supplements. Supplemental nutrition is often overlooked by the medical community as a whole. It was suggested by Houghton [Ferguson, L. R. 2009] that physicians' apathy was due to a dearth of nutrigenomics training and understanding.

There are likely analogies that might provide light on the industry's current state of affairs. Tech company founders that become unicorns were not just excellent inventors, but also aggressive businesspeople.' Even a small team with a firm started in a garage would include individuals with a wide range of complimentary and contrasting professional backgrounds. Companies like Cell Logic and others developing new natural product innovations were focused on the person. One must look outside oneself in order to have a commercial effect. There seemed to be a lack of desire to develop institutional processes that would aid in the advancement of an idea.

Until then, raw material and ingredient suppliers from Asia and elsewhere, as well as product distributors, will have sway over science-based product makers. It's time for science-based nutra enterprises to rethink their commercial strategies [El-Sohehy, A. 2007].

## **VI. CURRENT TRENDS AND FUTURE PROSPECTS OF NUTRACEUTICALS**

With greater public knowledge about health concerns and access to information on the

internet, the usage of nutraceuticals has expanded rapidly in recent years [Ortega et al, 2013]. People are increasingly turning to nutraceuticals as a treatment option due to the well-documented side effects and lack of efficacy of current medications. Medicinal use of nutraceuticals is supported on the assumption that they cure deficiency-related illness. Nutraceutical supplementation has been shown to boost health and stave against illness, according to available research. Nutritional supplementation does not need an expert practitioner, and antioxidant-rich nutraceuticals are believed to have a positive impact on the body's overall health, rather than only cure illness symptoms. Nutraceutical users are able to take charge of their health on their own, without the assistance of a doctor. Despite its advantages, self-medication with nutraceuticals on a long-term basis may have financial consequences for consumers and may be more costly than other pharmaceuticals. Nutraceutical promotion and media attention have exaggerated the health advantages of these products. General practitioners, nurses, pharmacists, and nutritionists all know a lot about nutraceuticals and may utilise that knowledge to help their patients and clients get the most out of these products. While long-term usage of nutraceuticals is safe and effective for the prevention of chronic diseases, self-medication for severe illnesses is unacceptable. Carnitine and flaxseed oil are common anti-heart disease nutraceuticals, whereas antioxidants are mostly used to fight cancer. Consumers now feel that nutritional supplements are safer than other synthetic chemicals, however this assumption might be incorrect and a medical diagnostic is necessary for severe illness to prescribe effective traditional medications. This is the case. The use of alternative medicine by diabetes patients has been found to have grown [Brower, 2005]. Nutraceutical producers know exactly how much it costs to make their products and how much money they stand to make. Nutraceutical companies are always introducing new products to the market in order to grow their

business. To prevent and cure chronic illnesses, the use of nutraceuticals has been promoted. When it comes to preventing cancer, green tea and soy products are two examples [Blades, 2000].

It is becoming more and more common for pharmaceutical firms to promote nutraceuticals instead of new medicines because of the high costs and risks involved in developing new medications. The pharmaceutical business 'Novartis' has also introduced functional foods to the market and pharmacies for the benefit of consumers' health. For the first time in 1998, 'Columbus better eggs' from Dean Farms, Tring and Hertfordshire, which were high in fatty acids, were offered in major shops. Allied Bakeries created burgeon bread in September 1997, which is another example of a function food. Naturally occurring plant estrogens in soy and flax seed may be utilised to alleviate menopausal symptoms. Government financing for clinical trials and nutraceutical research has risen at the same time, though. "Regulators supervise the supply of nutraceuticals and the drafting of analytical monographs for routine quality assurance." Consumer groups create product analysis profiles to help consumers choose the finest quality items. Even while there is some evidence that some life-threatening disorders may be treated with nutraceuticals, there isn't enough evidence to support the widespread usage of these products. As a result, government funding is essential if research in these areas is to be improved or strengthened. SNPs, or single nucleotide polymorphisms, have been discovered in the human population, allowing us to make predictions about how different people would respond to different pharmaceuticals. This has given rise to the novel idea of customised medicines. 'Nutrigenomics' has now evolved, which incorporates dietary component interactions with the genomes and resulting in alterations in proteome and metabolic processes. Nutrigenetics, the study of how different people react to the same nutraceutical based on their genetic make-up, has also grown in recent years. Pharmaceutical firms employ



genotyping to predict medication effectiveness, safety, and toxicity during clinical trials, thanks to the widespread availability of genetic data. 'Pharmacogenomics' studies how a patient responds to medicine, while 'nutrigenomics' examines the influence of nutrients and dietary components on an individual's health. Nutraceutical supplementation may be predicted based on an individual's genetic information, which can be used to maintain health or avoid sickness.

## VII. CONCLUSION

In order to understand how nutrients, metabolic intermediates, and the mammalian genome interact, nutritional genomics is necessary. Genetic factors (Nutrigenetic effects) may impact the absorption and metabolism targets or locations of action of bioactive dietary components. Furthermore, DNA methylation and other epigenetic changes influence the response to dietary components. To some extent, the entire reaction may be predicted by looking at how bioactive dietary components alter gene expression patterns (nutrigenomics effects). Final thoughts: Food bioactive ingredients may affect protein synthesis, degradation, and post-translational modifications. For optimum human health and illness prevention, understanding the interrelationships between human genetic diversity, genome function, and dietary components will be necessary.

As we learn more about the gene-nutrient connection, we may be able to use dietary changes and single-nutrient therapies to help prevent cancer, reduce the risk of cardiovascular and other chronic illnesses, and maybe lengthen human life.

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