Nutrigenomics: Exploring the Connection Between Diet and Genetics

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Nutritional science has evolved from identifying essential vitamins and minerals to addressing contemporary health issues such as overnutrition, obesity, and type-2 diabetes. The focus has shifted to understanding how nutrition can optimize cellular and systemic homeostasis and prevent various disorders by studying molecular interactions between nutrients and genes, proteins, and metabolic pathways, thus giving rise to the field of nutrigenomics. Nutrigenomics explores how diet influences gene expression, while nutrigenetics examines genetic variations affecting individual responses to nutrients. This manuscript reviews the historical development of nutrigenomics, highlights key concepts, and discusses the roles of diet and genetics in health and disease. It explores how bioactive food components influence gene expression, the impact of genetic diversity on nutrient metabolism, and the mechanisms through which dietary factors modify genetic processes. The paper also examines the effects of micronutrients on genome stability and their implications for non-communicable diseases such as cancer, obesity, and cardiovascular diseases. By integrating bioinformatics, molecular biology, genomics, and epidemiology, nutrigenomics offers promising strategies for personalized nutrition and disease prevention, aiming to enhance health outcomes through tailored dietary interventions based on genetic profiles.

Introduction

Nutritional science spent most of the 20th century trying to identify vitamins and minerals, define their uses, and prevent deficiency diseases that they cause. The focus of contemporary medicine and nutritional science shifted as the developed world's nutrition-related health issues transitioned to overnutrition, obesity, and type-2 diabetes (Mozaffarian et al., 2018). Nutrition study involves understanding how nutrition can maintain and optimize homeostasis in the body's cells, tissues, organs, and overall body to prevent the onset of various disorders. This requires an understanding of how nutrients act at the molecular level, which, in turn, involves numerous nutrient-related interactions at the gene, protein, and metabolic levels. As a result, nutrition research shifted from Epidemiology and Physiology to Molecular Biology and Genetics, giving rise to nutrigenomics. The two primary elements influencing a person's health or disease are their diet and environment (Cena and Calder 2020). Nutrigenomics is the branch of nutrition that uses molecular methods to investigate, access, and understand the many effects of a specific diet on individuals or population groups (Garg et al., 2014). Nutrigenomics explores how dietary components, such as bioactive compounds, impact gene expression, either enhancing or inhibiting it, based on how genes alter their activity. This field aims to understand genetic predispositions and identify genes affecting the risk of diet-related disorders on a genome-wide scale. The core concept is that dietary chemicals control genomic expression, with changes in gene expression or protein and enzyme activity driving the transition from a healthy to a chronic disease phenotype. Nutrigenomics combines bioinformatics, nutrition, molecular biology, genomics, epidemiology, and molecular medicine to reveal the effects of diet on gene expression. As lifestyle changes increase vulnerability to diet-related issues, advancing research in this area is essential.

Nutrigenetics and Nutrigenomics

Nutritional Genomics is the study of how bioactive food components interact with the genome, encompassing both Nutrigenetics and Nutrigenomics. Nutrigenetics focuses on how genetic variations, such as single-nucleotide polymorphisms (SNPs), influence individual responses to dietary intake, affecting nutrient absorption, metabolism, and action (Meiliana., and Wijaya., 2020) . This field, rooted in classical genetics, provides insights into personalized nutrition by tailoring diets to genetic profiles, In contrast, Nutrigenomics explores how diet influences gene expression, employing epigenomic, transcriptomic, proteomic, and metabolomic analyses to understand the impact of nutrients on health and disease (Hag et al., 2020). Emerging from the Human Genome Project and advanced omics technologies, Nutrigenomics aims to identify how dietary components modulate gene expression, metabolic pathways, and homeostasis (Lucini et al., 2020).

While Nutrigenetics and Nutrigenomics differ in their approaches—Nutrigenetics personalizes diet based on genetic variations, whereas Nutrigenomics seeks to optimize diet through gene expression modulation—they share a common goal: to enhance health and prevent disease through a deeper understanding of diet-gene interactions. Integrating both fields is essential for advancing personalized nutrition and achieving long-term health outcomes.

History Of Nutrigenomics

The concept that diet influences health is an ancient one. Hippocrates gave medical professionals the following advice around 400 B.C.: "Leave your drugs in the chemist's pot if you can heal your patient with food" (Kleisiaris et al., 2014). Marcum, J.A. (2024). Similarly, the understanding that different people have different nutritional needs has been long-established. The "Analytical Chemistry Era" began around the year 1700. During this period, Lavoisier made groundbreaking discoveries about how the body digested food to produce energy, carbon dioxide, and water (Vasconcelos, 2010). In the 19th century, lipids, proteins, carbohydrates, and other macronutrients that release heat were identified. Between the 18th and 20th centuries, in the "Chemical and Analytical Era of Nutrition," Antoine Lavoisier made significant findings about the relationship between food metabolism and energy production, especially its importance in breathing and oxidation (Frayn, 2022). Subsequently, studies on metabolism and chemistry were conducted in the so-called "Biological Era" of the 19th century, and these studies contributed to the understanding of the role of nutrition in the emergence and prevention of chronic illnesses, including cancer, cardiovascular diseases, neurological disorders, and bone metabolism issues.

The "Post-Genomic Era" is now in effect, incorporating scientific advancements in nutritional pathophysiology and metabolism into three disciplines: biological, social, and environmental integration (Goyal et al., 2023). The launch of the Human Genome Project in the 1990s and the subsequent mapping of human DNA sequencing ushered in the "era of big science," marking the birth of the modern discipline of Nutrigenomics (Birla et al., 2022). In 1902, Archibald E. Garrod's report on alkaptonuria in The Lancet identified its genetic basis, highlighting the impact of Mendelian inheritance in humans (Ranganath et al., 2020). In the 1940s, Edward Tatum's work revealed the relationship between gene mutations and nutrient requirements, laying the foundation for understanding gene control in nutrition (Campbell, 2021). The completion of the Human Genome Project in 2000 marked a turning point in genomics research, holding the promise of revolutionizing disease diagnosis and prevention. The term "nutrigenomics," coined by Peregrin in 2001, became central to the study of gene- nutrition interactions (Jabeen et al., 2023). In the early 21st century, major initiatives such as the European Nutrigenomics Organisations propelled nutrigenomics, benefiting from interdisciplinary tools and knowledge (Araujo et al., 2019).

Mechanisms of Diet Components and Gene Expression Interaction

Bioactive diet components influence gene expression through changes in chromatin structure (including DNA methylation and histone modification), non-coding RNA, activation of transcription factors via signaling cascades, or direct ligand binding to nuclear receptors. Nutrients present in food and the diet can affect gene expression in several ways. They may directly act as ligands for transcription factors and alter gene expression (Marcello et al., 2021). Nutrients may be metabolized by different pathways, thereby modifying the concentration of substrates or intermediates that affect gene expression. Alternatively, the substrates or intermediates may act on or alter cell signaling pathways involved in gene expression. Moreover, nutrients may directly alter signal transduction pathways responsible for changes in gene expression. Finally, modifications in the signaling pathways, caused by nutrients, may modulate the metabolism of nutrients affecting gene expression (Candelli et al., 2021).

Principles Of Nutrigenomics

There are four principles of nutritional genomics (Otero, and Bernolo 2023).

(1) Diet is considered to be a critical predisposing factor for many diseases in some individuals under particular conditions.
(2) Diet ingredients change the gene structure and/or gene expression, and consequently, the human genome.
(3) The variation of genotype between individuals can explain the equilibrium between health and disease.
(4) Genes that are dependent on dietary factors in their regulation may have a role in the commencement, extent, advancement, and progression of chronic diseases.

Table 1 Dietary impact on gene activity

Gene	Protein	Functions	Related Foods
NFE2L2/NRF2	Nuclear Factor Erythroid 2 Like2	Regulator of the expression of antioxidant protein.	Curcumin, through epigenetic demethylation, activates the NFE2L2/NRF2 gene, reducing oxidative stress in various cells and offering the potential for diabetes prevention and treatment. (Parsamanesh et al., 2018).
FTO	Alpha-ketoglutarate dependent dioxygenase	It forms a nuclear protein involved in insulin signaling ROS production and adipose tissue development	The Mediterranean diet affects the FTO gene and its link to type 2 diabetes, potentially mitigating genetic predisposition (Renzo et al., 2018)
NFKB1, NFKB2	Nuclear factor kappa B subunit 1, Nuclear factor kappa B subunit 2	Transcription factors are involved in anti-inflammatory pathways	Flavonoids like fisetin, apigenin, and quercetin exhibit anti-inflammatory, antioxidant, and anti-apoptotic effects. They inhibit NF-κB, reducing protein phosphorylation and enhancing vascularization, potentially lowering hypertension risk in diabetics. (Jembrek et al., 2021)
SLC2A1 SLC2A4	Solute carrier family 2, facilitated glucose transporter member 1, and solute carrier family 2-member 4	They encode Glucose transporters (GLUT 1 and GLUT 4)	A variety of polyphenols, such as catechins, flavonoids, phenolic acids, and among others, are related to the increase in glucose transporters in animals and human cells. (Hanhineva et. al., 2010)
FFAR1	Free fatty acid receptor1	Metabolic regulation of insulin secretion and hepatic glucose uptake	Human cells reveal that anthocyanins in purple corn may activate the FFAR1 gene, offering the potential for type 2 diabetes and its complications. Other polyphenols, including anthocyanin, also show promise in FFAR1gene activation in pancreatic Beta cells, suggesting antidiabetic applications (Papuc et al., 2020).

Personalized Nutrition and Nutrigenomics

The advent of genomics is revolutionizing food science and healthcare by enabling personalized nutrition. Nutrigenomics explores how genetic variations affect nutritional needs and responses, emphasizing that dietary requirements are as unique as fingerprints. Studies have demonstrated significant variability in individual responses to identical diets (Maruvada et al., 2020), highlighting the need for personalized approaches. Precision nutrition, which tailors' dietary interventions based on genetic makeup and health status, aims to enhance population health (Lagoumintzis & Patrinos, 2023). The Food4Me study found that personalized nutrition improved dietary patterns more effectively than standard advice (Livingstone et al., 2021), and a systematic review confirmed greater dietary improvements with personalized recommendations (Jinnette et al., 2021). For instance, individuals with the FTO risk allele achieved better weight loss outcomes with personalized interventions (Malcomson & Mathers, 2023).

Mobile apps offering personalized health recommendations based on genetic and metabolic data have also shown promise in cancer prevention and behavioral improvements (Berry et al., 2020). This integration of genomics into nutrition science holds potential for creating tailored dietary strategies that align with individual genetic profiles, improving overall health outcomes.

Conclusions And Future Direction

Personalized or precision nutrition aims to enhance dietary strategies to prevent metabolic deterioration, challenging traditional nutrition paradigms. While significant progress is needed to develop forecasting tools and address ethical issues, the potential benefits for managing obesity and its comorbidities are substantial. The field is expanding with advances in nutrigenomics, proteomics, and biomarker discovery, although facilities are limited, particularly in countries like India. Public awareness and ethical frameworks are essential for advancing this research. Despite challenges related to cost, accessibility, and the need for validated biomarkers, nutrigenomics promises to revolutionize personalized nutrition and healthcare by tailoring recommendations to individual genetic profiles, ultimately improving health outcomes and quality of life.

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