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Articles

NGS-Based Nutrigenomic Biomarkers for Personalized Nutrition: A Review of the Current State of Research

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Abstract

The integration of next-generation sequencing (NGS) technology into the area of personalized nutrition provides a breakthrough approach to studying the intricate relationships between food, genetics, and health consequences. By allowing the discovery of nutrigenomic biomarkers, NGS has allowed the customization of dietary recommendations to fit with an individual's genetic predispositions and metabolic capacity. This innovation promises to enhance the control of dietary responses, optimize nutrient metabolism, and decrease the risk factors linked with nutrition-related chronic illnesses such as obesity, type 2 diabetes, and cardiovascular problems. This review offers a complete examination of the present status of NGS-based biomarker research in personalized nutrition. It investigates the methodology applied in sequencing technology, the finding of gene-diet relationships, and the applicability of such biomarkers in clinical and public health contexts. Particular focus is given to the significance of NGS in identifying genetic variations regulating macronutrient and micronutrient metabolism, gut microbiome composition, and epigenetic changes. Despite the great advances in applying NGS to nutrition research, many hurdles exist. These include the difficulty of data interpretation, the requirement for thorough clinical validation of discovered biomarkers, and the ethical concerns connected to genetic data privacy and fairness in access to customized nutrition services. Furthermore, the integration of multi-omics data, such as transcriptomics, proteomics, and metabolomics, into NGS investigations is critical for a comprehensive understanding of nutrigenomic interactions but remains neglected. Advancing the area of NGS-based customized nutrition will need multidisciplinary cooperation among geneticists, nutritionists, bioinformaticians, and physicians. Additionally, the development of novel approaches, such as machine learning algorithms for data analysis and rigorous clinical trials for biomarker validation, will be vital. As these issues are solved, NGS offers the promise to change nutrition research and enhance public health outcomes by providing extremely accurate and tailored dietary treatments.

Keywords: next-generation sequencing (NGS), personalized nutrition, nutrigenomic biomarkers, gene-diet interactions, macronutrient metabolism, gut microbiota, multi-omics, clinical validation.

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1. Introduction

Personalized nutrition, an emerging field at the intersection of genetics and nutritional science, aims to optimize dietary recommendations by tailoring them to individual characteristics such as genetic makeup, metabolic responses, and gut microbiome composition (Shahzad et al., 2024). Traditional dietary guidelines have largely followed a one-size-fits-all approach, which may not adequately address the complex and individualized relationships between diet and health (Kolodziejczyk et al., 2019). With advancements in understanding genetic diversity in nutrient metabolism and dietary responses, personalized nutrition offers the potential for precision dietary interventions that could improve health outcomes and reduce the risk of chronic diseases (Wang et al., 2024). The development of next-generation sequencing (NGS) technology has been a game-changer in this field, enabling large-scale, high-resolution analysis of the human genome. Unlike traditional sequencing methods, NGS allows for the rapid and cost-effective identification of genetic variants, including single nucleotide polymorphisms (SNPs), copy number variations, and other genetic markers that influence dietary responses and disease risk (Singar et al., 2024). These advancements have paved the way for the development of nutrigenomic biomarkers, which are essential tools for studying gene-diet interactions and their implications for health and disease.

Research using NGS has generated significant insights into how genetic variations affect nutrient absorption, metabolism, and utilization. For example, polymorphisms in genes such as *FTO* and *MC4R* have been linked to obesity and energy metabolism (Resende et al., 2021), while variations in *MTHFR* affect folate metabolism and homocysteine levels, influencing cardiovascular health (Gospodarczyk et al., 2022). Additionally, NGS has facilitated research on the gut microbiome, a key component of personalized nutrition, by identifying microbial genes involved in dietary fiber metabolism, short-chain fatty acid production, and metabolic disorders (Abeltino et al., 2024).

This review explores the current applications of NGS in personalized nutrition, focusing on the discovery and validation of nutrigenomic biomarkers. It provides an overview of key findings in the field, highlights the methodologies used, and discusses the challenges and opportunities in translating NGS findings into clinical practice. Specifically, the review examines the role of NGS in identifying genetic drivers of dietary responses, such as lactose intolerance, gluten sensitivity, and omega-3 fatty acid metabolism. It also explores the integration of multi-omics approaches, including transcriptomics, proteomics, and metabolomics, with NGS to gain a comprehensive understanding of the molecular mechanisms underlying personalized nutrition.

2. Discussion and results

Key Nutrigenomic Biomarkers Identified Using NGS

a. Single Nucleotide Polymorphisms (SNPs)

Single nucleotide polymorphisms (SNPs) are among the most extensively studied genetic variants in nutrigenomics. Using NGS, researchers have identified SNPs in various genes that significantly influence dietary responses, metabolism, and disease risk. These findings have advanced our understanding of the molecular basis of personalized nutrition.

One notable example is the *FTO* gene, where SNPs such as rs9939609 have been associated with increased susceptibility to obesity (Abd Ali et al., 2021). This variant affects energy balance by altering appetite control and energy expenditure (MacLean et al., 2017). Similarly, SNPs in the *MC4R* gene, which also plays a critical role in energy balance, have been linked to obesity and related metabolic disorders (Adamska-Patruno et al., 2021).

The *PPARG* gene, encoding peroxisome proliferator-activated receptor gamma, has also garnered significant attention in nutrigenomics. Variants such as Pro12Ala are associated with improved insulin sensitivity and a reduced risk of type 2 diabetes in response to specific dietary interventions, such as increased intake of polyunsaturated fatty acids (Abaj et al., 2021). These findings underscore the importance of incorporating genetic information into dietary planning for metabolic health.

In the context of lipid metabolism, SNPs in genes such as *APOA5* and *CETP* play crucial roles. Variants in *APOA5* influence triglyceride levels and modulate individual responses to dietary fats. For example, the -1131T>C polymorphism in *APOA5* has been linked to hypertriglyceridemia and variable responses to omega-3 fatty acid supplementation (Wierzbicki et al., 2022). Similarly,

SNPs in *CETP*, such as rs5882, affect HDL cholesterol levels and cardiovascular risk, highlighting the gene's role in tailoring dietary fat recommendations (Asl et al., 2024).

Folate metabolism is another area where SNPs have significant implications. Variants in the *MTHFR* gene, particularly C677T and A1298C polymorphisms, reduce the enzyme's activity, leading to elevated homocysteine levels. This has been associated with an increased risk of cardiovascular diseases, neural tube defects, and other health issues. Personalized interventions, such as folate supplementation, can mitigate these risks, demonstrating the practical benefits of SNP research in dietary management (Di Renzo et al., 2019).

b. Gene Expression Profiles

Gene expression profiling, enabled by RNA sequencing (RNA-seq), has provided critical insights into the dynamic interactions between diet and gene activity. By examining how dietary interventions alter gene expression, researchers can identify biomarkers that predict individual responses to specific nutrients and guide personalized dietary plans. One prominent example is the expression of the *INSR* gene, which encodes the insulin receptor. RNA-seq studies have shown that dietary modifications, such as caloric restriction and low-glycemic diets, influence *INSR* expression in individuals with type 2 diabetes. These findings suggest that monitoring *INSR* expression levels could help tailor dietary recommendations to improve insulin sensitivity and glucose homeostasis (Liu et al., 2024).

The *LEP* gene, which encodes leptin – a hormone critical for appetite regulation and energy balance—is another key player in personalized nutrition (Odriozola et al., 2024). RNA-seq studies have demonstrated that high-fat diets downregulate *LEP* expression in individuals prone to obesity, while dietary interventions rich in fiber and polyphenols restore *LEP* expression. This highlights the potential for gene expression profiles to inform dietary strategies aimed at weight management and metabolic health.

Additionally, research on genes involved in inflammatory pathways, such as *TNF-α* and *IL-6*, has shown how diet influences systemic inflammation (Saghafi-Asl et al., 2021). RNA-seq findings reveal that anti-inflammatory diets, characterized by high omega-3 fatty acid and antioxidant content, downregulate the expression of these genes, reducing inflammation and associated chronic disease risks. These findings emphasize the importance of incorporating gene expression data into dietary planning for inflammatory conditions.

Emerging research has also focused on nutrient-specific gene expression patterns. For example, the expression of genes involved in vitamin D metabolism, such as *CYP24A1* and *VDR*, is influenced by dietary vitamin D intake (Iriani et al., 2024). RNA-seq studies have shown that individuals with reduced vitamin D receptor activity benefit more from increased dietary or supplemental vitamin D, highlighting the need for personalized approaches to nutritional supplementation (Aoun et al., 2024).

c. Epigenetic Modifications

Epigenetics, which refers to heritable changes in gene expression that do not involve alterations in the DNA sequence, has emerged as a critical area of study in personalized nutrition. NGS technologies have enabled high-resolution mapping of epigenetic modifications, such as DNA methylation and histone modifications, which are influenced by dietary factors and have significant implications for health.

One of the most studied epigenetic markers in nutrigenomics is DNA methylation. For example, the methylation status of the *PPARγ* gene has been shown to influence metabolic responses to dietary fat intake (Porcuna et al., 2021). Increased methylation of *PPARγ* is associated with reduced gene expression and altered lipid metabolism, which can be mitigated by personalized dietary interventions, such as the inclusion of monounsaturated fats (Rai, 2024).

Similarly, the *CLOCK* gene, which plays a key role in circadian rhythm regulation, has been found to undergo diet-induced epigenetic changes (Engin, 2024). DNA methylation of the *CLOCK* promoter region is associated with disruptions in circadian rhythms and metabolic health. Studies suggest that diets rich in polyphenols, such as those found in berries and green tea, can reverse these methylation patterns, restoring normal circadian function (Chen et al., 2024).

Histone modifications, another epigenetic mechanism, also play a role in personalized nutrition. Acetylation and methylation of histones can alter chromatin structure, thereby influencing gene expression. For instance, histone acetylation in inflammatory genes such as *NF-κB* has been shown to be regulated by dietary components like resveratrol and curcumin, which

act as natural histone deacetylase inhibitors (Kang, Kim, 2023). These findings highlight the potential of dietary interventions to target epigenetic regulators for managing inflammation and chronic diseases.

Emerging research also points to the role of microRNAs (miRNAs) in diet-gene interactions. MiRNAs are small non-coding RNAs that regulate gene expression post-transcriptionally. NGS-based studies have identified diet-responsive miRNAs, such as miR-33, which is involved in cholesterol metabolism (Zhang et al., 2023). Modulating the levels of such miRNAs through dietary interventions holds promise for personalized approaches to lipid management (Kura et al., 2019). By integrating epigenetic data with genetic and transcriptomic information, NGS technologies provide a comprehensive understanding of how dietary factors influence gene regulation and disease risk. These insights pave the way for the development of precision nutrition plans that account for an individual's epigenetic profile, ultimately promoting better health outcomes.

Applications of NGS-Based Biomarkers in Personalized Nutrition

Next-generation sequencing (NGS) has significantly advanced the discovery and application of biomarkers in personalized nutrition, providing a powerful tool for tailoring dietary interventions to individual genetic, transcriptomic, and epigenomic profiles. These advancements have important implications for managing various health conditions, including obesity, diabetes, cardiovascular diseases, and metabolic syndromes, by offering insights that enable precision nutrition strategies.

a. Tailored Diets for Obesity Management

Obesity is a multifactorial condition influenced by genetics, environmental factors, and lifestyle choices. Traditionally, dietary interventions for obesity have been generalized, often overlooking individual genetic differences that affect dietary responses. However, the use of NGS-based biomarkers allows for more precise and personalized dietary advice, incorporating genetic predispositions that may influence an individual's ability to manage weight effectively (Górczyńska-Kosiorz et al., 2024).

A key genetic factor in obesity is the presence of specific single nucleotide polymorphisms (SNPs) in genes such as *FTO* (fat mass and obesity-associated gene). Studies have shown that individuals with certain *FTO* SNP variants are genetically predisposed to increased appetite, reduced satiety, and inefficient fat metabolism (Abd Ali et al., 2021). These genetic variations can significantly impact an individual's responsiveness to different dietary interventions. NGS enables the identification of these SNPs, allowing healthcare providers to design dietary recommendations that are more likely to be effective based on an individual's genetic profile.

The impact of *FTO* SNPs on dietary responses is particularly evident when considering the macronutrient composition of diets. Research indicates that individuals with *FTO* variants associated with insulin resistance may benefit more from low-carbohydrate diets, which can reduce insulin spikes and improve metabolic health (Xue et al., 2024). Conversely, individuals with *FTO* SNPs linked to impaired lipid oxidation may experience greater benefits from low-fat diets that minimize fat storage (Gkouskou et al., 2024). By integrating NGS-derived genetic profiles into dietary planning, dietitians can provide more effective weight management strategies, leading to improved long-term health outcomes.

NGS also plays a crucial role in studying the gut microbiome, which has been shown to influence obesity (Vallianou et al., 2023). The gut microbiota can be analyzed through metagenomic sequencing or 16S rRNA sequencing, identifying unique microbial patterns that affect metabolic processes. For example, individuals with reduced microbial diversity may benefit from fiber-rich diets that promote the growth of beneficial gut bacteria, thereby improving overall gut health and metabolic function (Ranganathan, Anteyi, 2022). Additionally, probiotic or prebiotic supplements may be recommended to restore microbial balance and reduce metabolic inflammation, further supporting weight management efforts (Van Hul, Cani, 2023).

Furthermore, NGS technologies enable the study of epigenetic modifications, such as DNA methylation and histone acetylation, that influence gene expression in response to environmental factors, including diet. These epigenetic changes can impact obesity-related genes, and targeted dietary interventions can help mitigate these effects (Mehta et al., 2024). For instance, a diet rich in methyl donors like folate and choline can counteract adverse epigenetic changes associated with obesity, improving gene expression patterns related to metabolism and fat storage.

Finally, personalized nutrition based on NGS extends beyond genetics and diet to include lifestyle factors such as physical activity and sleep (Fischer, 2024). These factors, which interact with genetic predispositions, are essential components of a holistic approach to obesity management. By integrating NGS-based biomarkers into personalized nutrition strategies, healthcare providers can develop comprehensive plans that consider not only genetic and epigenetic factors but also individual lifestyle preferences and behaviors, ultimately supporting more sustainable and effective weight management strategies.

b. Cardiovascular Disease Risk Mitigation

Cardiovascular diseases (CVDs), including heart disease and stroke, are leading causes of morbidity and mortality worldwide (Iso, 2021). Genetics play a significant role in the predisposition to CVD, influencing factors such as lipid metabolism, blood pressure regulation, and inflammatory processes. The advent of NGS technology has opened new avenues for tailoring dietary recommendations aimed at reducing CVD risk, particularly through the identification of genetic variants that influence an individual's response to specific nutrients (Strianese et al., 2020).

One of the most extensively studied areas in cardiovascular genetics is the impact of SNPs in genes related to lipid metabolism, such as *APOA5* and *LIPC*. *APOA5* encodes apolipoprotein A-V, which plays a critical role in regulating triglyceride levels in the blood (Alves et al., 2024). Variants in the *APOA5* gene have been shown to significantly affect an individual's lipid profile, particularly their triglyceride levels, which are a known risk factor for cardiovascular disease (Su et al., 2018). For individuals with certain *APOA5* alleles associated with elevated triglycerides, dietary interventions that include omega-3 fatty acids, commonly found in fatty fish, flaxseeds, and walnuts, may help lower triglyceride levels and reduce cardiovascular risk.

Similarly, the *LIPC* gene, which encodes hepatic lipase, is involved in the hydrolysis of lipids, regulating both high-density lipoprotein (HDL) cholesterol levels and triglyceride metabolism (Dijk et al., 2022). Variants in *LIPC* have been linked to altered lipid profiles, and individuals with specific *LIPC* SNPs may benefit from omega-3 supplementation to reduce triglyceride levels and increase HDL cholesterol, which has protective effects against CVD (Kardassis et al., 2022). Omega-3 fatty acids, particularly EPA and DHA, are known to have anti-inflammatory and lipid-lowering properties, making them a critical nutrient in the prevention of hyperlipidemia and cardiovascular diseases, especially for individuals with genetic predispositions to dyslipidemia (Omachi et al., 2024).

The ability to identify individuals at high genetic risk for CVD through NGS-based biomarker analysis offers a precision approach to cardiovascular risk reduction (Papadopoulou et al., 2023). Rather than providing generic dietary recommendations, healthcare professionals can offer personalized guidance based on an individual's genetic profile, focusing on specific foods that are most likely to benefit their lipid metabolism and overall cardiovascular health. In the case of *APOA5* and *LIPC* variants, omega-3 supplementation becomes a targeted intervention that could reduce the need for more invasive treatments, such as pharmacological lipid-lowering therapies, thereby offering a more holistic, preventive approach to managing cardiovascular risk (Wazir et al., 2023).

In addition to omega-3 supplementation, NGS can also identify other genetic markers that influence responsiveness to dietary interventions, such as those related to inflammation and oxidative stress. For example, individuals with specific variants in genes such as *MTHFR* (methylenetetrahydrofolate reductase) may benefit from increased intake of folate or other B vitamins, as these nutrients play a role in homocysteine metabolism, which is linked to cardiovascular health (He, Li, 2023). Ultimately, the integration of NGS-based biomarkers into the dietary management of cardiovascular disease offers a tailored approach that takes into account an individual's genetic predispositions, lifestyle, and specific nutritional needs. This approach allows for more effective interventions, improved preventive measures, and better overall cardiovascular health outcomes.

c. Nutritional Management of Diabetes

Diabetes, particularly Type 2 diabetes (T2D), is a chronic metabolic disorder characterized by impaired insulin sensitivity and glucose metabolism (Lima et al., 2022). The dietary management of diabetes is crucial for maintaining blood sugar levels, managing weight, and reducing the risk of complications. In recent years, the role of genetic markers in guiding nutritional interventions has gained increasing attention, enabling more targeted, personalized approaches to managing the disease.

Next-generation sequencing (NGS) technologies have facilitated the identification of genetic variants associated with glucose metabolism, providing critical insights into the personalized management of diabetes. One such important genetic variant is in the *TCF7L2* gene, which encodes a transcription factor involved in insulin production and glucose homeostasis. Variants in *TCF7L2* have been shown to increase the risk of developing T2D and influence an individual's response to dietary interventions (Verma et al., 2022). For individuals with *TCF7L2* variants, higher intake of dietary fiber, particularly from whole grains, legumes, and vegetables, may be beneficial in improving insulin sensitivity and glycemic control. This is because fiber-rich foods slow glucose absorption, reduce postprandial blood sugar spikes, and promote gut health, all of which are critical factors in managing diabetes.

Other genes involved in glucose regulation also play a significant role in determining an individual's response to various dietary patterns. For example, *PPARG* (peroxisome proliferator-activated receptor gamma) and *KCNJ11* (a gene encoding the potassium channel subunit) have been associated with insulin sensitivity and secretion (Yahaya, Salisu, 2020). For individuals with specific polymorphisms in these genes, low-glycemic index (GI) diets, which focus on foods that cause slower rises in blood glucose, may be more effective in managing blood sugar levels. These diets emphasize foods such as non-starchy vegetables, legumes, and whole grains, which have a moderate impact on blood glucose levels compared to high-GI foods like white bread and sugary snacks.

Additionally, NGS-based approaches allow for the identification of gene-diet interactions that extend beyond macronutrient composition to include micronutrients and bioactive compounds. For instance, individuals with genetic variants affecting vitamin D metabolism may benefit from vitamin D supplementation as part of their diabetes management plan, as vitamin D has been shown to play a role in insulin sensitivity and glucose metabolism (Contreras-Bolívar et al., 2021). Similarly, genetic variations influencing the metabolism of polyphenols in fruits and vegetables could guide recommendations for dietary strategies high in antioxidants to reduce inflammation and improve glycemic control.

Challenges and Future Directions

The integration of next-generation sequencing (NGS) with personalized nutrition holds immense promise for improving healthcare and disease prevention. However, its widespread implementation is not without significant challenges. These challenges include data interpretation, clinical validation, and ethical considerations, all of which need to be addressed to fully realize the benefits of NGS-based personalized nutrition.

a. Data Interpretation

One of the most significant challenges associated with NGS is the interpretation of the vast amounts of data it generates. NGS techniques can produce gigabytes or even terabytes of data in a single sequencing run, encompassing genetic, transcriptomic, and epigenomic information (Satam et al., 2023). While this wealth of data provides a comprehensive picture of an individual's biological makeup, it also presents major challenges in deriving meaningful, actionable insights.

A key issue is distinguishing clinically relevant genetic variants from benign ones. In a typical NGS experiment, hundreds of variants are identified, but not all of them are related to the individual's health (Spielmann, Kircher, 2022). Many of the identified genetic variants may be benign or have minimal impact on the individual's disease risk or treatment response. The process of determining which variants are significant – those that influence health outcomes and should guide clinical decisions – requires advanced bioinformatics tools and algorithms. Moreover, the interpretation of these variants is often context-dependent, influenced by the individual's lifestyle, environment, and other factors.

While bioinformatics tools have made significant progress, there is still a need for more sophisticated and standardized approaches to accurately select and interpret genetic findings. Variants of unknown significance (VUS) remain a common problem, as their role in disease onset or treatment response is not fully understood. The complexity of multi-gene interactions and gene-environment interactions further complicates the ability to predict health outcomes based solely on genetic data (Hequet, 2024).

Additionally, the clinical significance of specific biomarkers may not be universally agreed upon, as there is often variability in how these biomarkers are interpreted across different research studies and clinical settings (Kraus, 2018). As such, a clear and consistent approach to data

interpretation is essential to ensure that NGS results are accurately translated into personalized diet and health recommendations.

b. Clinical Validation

Although numerous biomarkers have been identified using NGS technologies that show promise for personalized nutrition, only a few of them have undergone rigorous clinical validation. Clinical validation refers to the process of evaluating whether a specific biomarker or genetic variant truly leads to predictable, reproducible health outcomes when used in clinical practice (Paver, Morey, 2024). This step is necessary to determine whether a biomarker is truly useful in guiding dietary recommendations or whether it is merely a correlation without practical value.

For example, while certain genetic variants, such as those in the *FTO* gene associated with obesity or *TCF7L2* for diabetes, have been shown to influence health outcomes in large cohort studies, there is still limited evidence on how these variants perform in real-world clinical settings, particularly when used to guide personalized nutrition (Gkouskou et al., 2024). Many studies linking genetic variants to diet-related health outcomes are observational in nature and may suffer from confounding factors, such as environmental influences and lifestyle habits, which make it difficult to attribute observed effects solely to genetic predisposition. Additionally, clinical trials that rigorously test the effectiveness of nutritional interventions based on genetic profiles are often limited in scope and number (Salminen et al., 2021). While there is growing interest in clinical studies aimed at validating genetic markers for nutrition, the process of conducting large-scale, longitudinal trials is time-consuming and costly. As a result, many biomarkers that have shown promise in preclinical research have not yet been tested in the context of personalized dietary interventions (Cuparencu et al., 2024). Without this clinical validation, it is impossible to confirm the reliability and utility of NGS-based dietary recommendations.

c. Ethical Considerations

As with any emerging technology, the use of NGS in personalized nutrition raises several ethical considerations that need to be carefully addressed to ensure fair and responsible use. One of the most fundamental ethical concerns is genetic privacy. Genetic data is inherently sensitive, and improper handling or unauthorized access can lead to privacy breaches and potential misuse (Seaver et al., 2022). In the context of personalized nutrition, genetic information could be used for purposes beyond healthcare, such as insurance discrimination or employment decisions, raising concerns about the potential for genetic profiling and stigmatization. To mitigate these concerns, robust data protection regulations, such as those outlined in the General Data Protection Regulation (GDPR) in the European Union or the Genetic Information Nondiscrimination Act (GINA) in the United States, are essential to ensure that genetic information remains confidential and is not misused. However, even with such safeguards in place, there are uncertainties about the consent process, particularly regarding the long-term use of genetic data. Individuals may not fully understand the implications of sharing their genetic information, and the ability to revoke consent may be limited once genetic data has been collected.

Another ethical challenge is the issue of equitable access to personalized nutrition services. As NGS-based personalized nutrition becomes more widely available, there is a risk that it could exacerbate existing health disparities. The costs associated with NGS technology and genetic testing, as well as the specialized healthcare expertise required to interpret and implement personalized dietary recommendations, may limit access to affluent individuals or those living in developed countries (Strianese et al., 2020). This creates the potential for a two-tier healthcare system, where only a select few benefit from personalized nutrition, while others remain excluded. Ensuring that personalized nutrition is accessible to all individuals, regardless of socioeconomic status, would require significant investment in public health infrastructure, subsidies for genetic testing, and efforts to reduce the cost of sequencing technology.

Furthermore, there are broader societal implications involving the use of genetic information in public health initiatives. For example, public health campaigns promoting personalized nutrition based on genetic testing may inadvertently promote genetic determinism, where individuals are led to believe that their genetic makeup is the sole determinant of their health, overshadowing the importance of environmental and lifestyle factors such as diet, exercise, and social determinants of health (Gong et al., 2024). This could have unintended consequences for how individuals perceive and manage their health, either leading to a reduction in personal responsibility or undermining efforts to address larger systemic health issues.

Future Directions

The future of personalized nutrition, driven by next-generation sequencing (NGS), is poised to become more sophisticated, diverse, and impactful. As the understanding of the complex interactions between genes, diet, environment, and health deepens, integrating NGS data with other omics technologies, such as proteomics and metabolomics, promises a viable path for enhancing personalized nutrition recommendations.

a. Integration of NGS with Other Omics Technologies

While NGS has enabled the deep analysis of genetic predispositions and biomarkers related to nutrition, it is only one piece of a larger, integrated biological system. Proteomics (the large-scale study of proteins) and metabolomics (the analysis of metabolites) are two other omics technologies that provide complementary insights into an individual's health status, nutritional needs, and disease risk. When combined with genetic data from NGS, these technologies can help build more comprehensive and accurate models for personalized nutrition.

Proteomics allows for the identification and quantification of proteins, which are the direct effectors of many biological processes. The patterns of protein expression in an individual's body can be influenced by genetic predispositions, as well as environmental factors such as diet, physical activity, and stress. By integrating proteomic data with NGS, researchers can identify proteins that mediate the effects of genetic variants related to nutrition and disease. For example, proteins involved in metabolic pathways, inflammation, or nutrient absorption could help refine dietary interventions for specific individuals based on both their genetic profile and the actual expression of these proteins (Singh et al., 2023).

Metabolomics, on the other hand, provides insights into the metabolites present in an individual's biological samples, such as blood, urine, or saliva. These metabolites reflect the body's response to both endogenous and exogenous factors, including dietary intake. When combined with NGS, metabolomics can provide real-time, functional information on how an individual's genes are regulating their metabolism in the context of diet. For example, certain genetic variants may predispose individuals to more efficient fat metabolism, while others may require specific dietary adjustments to optimize their metabolic pathways (Qasim et al., 2018). Metabolomics can highlight these differences by analyzing how metabolites such as lipids, amino acids, and carbohydrates change in response to different dietary patterns.

Together, genetics, proteomics, and metabolomics can provide a more holistic understanding of how an individual's body processes and responds to nutrients. This integrated approach – often referred to as "multi-omics" or "systems biology" – can uncover complex gene-environment interactions that influence health outcomes (Noble et al., 2022). By analyzing this data in concert, nutritionists and healthcare providers can develop highly personalized and dynamic nutrition plans that go beyond genetic information alone, providing insights into how dietary interventions affect an individual's health at a molecular level.

b. Large-Scale Longitudinal Studies

In order to move from the theoretical promise of personalized nutrition to its real-world implementation, large-scale longitudinal studies are necessary. While small-scale studies have successfully demonstrated the potential of NGS-based biomarkers in personalized nutrition, the field requires larger and more diverse cohorts to validate these findings and establish the long-term impact of personalized dietary interventions. Longitudinal studies are particularly important because they can track health outcomes over time, providing valuable evidence on the durability and effectiveness of personalized dietary plans (Coman et al., 2024).

Such studies would need to recruit diverse populations to account for genetic variability, lifestyle factors, and environmental influences that could affect an individual's nutritional needs. For example, different ethnic groups may respond to the same diet in varying ways due to genetic differences, such as those regulating nutrient metabolism. By including individuals from diverse backgrounds, researchers can ensure that the biomarkers identified are applicable to a wide range of populations, making personalized nutrition more inclusive and globally relevant. Additionally, large-scale studies that track long-term health outcomes such as disease incidence, weight management, metabolic health, and cardiovascular function are essential to assessing the impact of personalized nutrition on public health (Coman et al., 2024). These studies can help determine whether genetic-based dietary modifications lead to sustained improvements in health or whether the benefits diminish over time. They can also provide insights into the cost-effectiveness of

personalized nutrition, enabling policymakers and healthcare providers to evaluate whether the widespread implementation of these interventions is feasible.

c. Artificial Intelligence and Machine Learning in Personalized Nutrition

Incorporating artificial intelligence (AI) and machine learning (ML) into personalized nutrition is another promising avenue for the future. AI and ML algorithms can analyze vast amounts of multi-omics data, including genomic, proteomic, metabolomic, and lifestyle data, to identify complex patterns and predict the effectiveness of various dietary interventions (Mohr et al., 2024).

The integration of Artificial Intelligence (AI) and Machine Learning (ML) with personalized nutrition represents a transformative approach to health and wellness. Leveraging advanced computational techniques, AI and ML can analyze complex datasets to provide tailored dietary recommendations, optimize health outcomes, and address individual nutritional needs. This field is rapidly evolving, with significant potential to revolutionize our understanding and application of personalized nutrition.

AI and ML are adept at analyzing and interpreting large, multi-dimensional datasets, including genetic, proteomic, metabolomic, and lifestyle information. These tools can identify complex patterns and relationships that are often undetectable by human researchers. For example, AI algorithms can analyze genetic variants to predict how an individual will respond to different foods or dietary changes. This capability is particularly significant in nutrigenomics, which studies the interaction between nutrition and genetics to optimize health outcomes (Topol, 2019).

AI-driven systems can integrate genetic data with metabolomic profiles to identify biomarkers that influence nutrient metabolism. This approach enables the development of personalized dietary plans that align with an individual's unique biological makeup, potentially reducing the risk of chronic diseases such as obesity, diabetes, and cardiovascular disorders (Zeevi et al., 2015).

One of the most promising applications of AI in personalized nutrition is the use of predictive models to prescribe diets tailored to an individual's health status and goals. These models can integrate multiple data sources, including genetic predispositions, gut microbiome composition, and real-time health monitoring data from wearable devices. By analyzing these inputs, AI systems can predict the effectiveness of specific dietary interventions and recommend optimal nutritional strategies (Ordovas et al., 2018). For example, ML algorithms can be trained to predict glycemic responses to different foods, enabling the creation of personalized meal plans for individuals with diabetes. Such models have been demonstrated in studies like the Personalized Nutrition Project, where AI was used to predict postprandial glucose responses based on individual gut microbiota and lifestyle factors (Berry et al., 2020).

A key advantage of AI and ML in personalized nutrition is their ability to adapt and improve over time. As new data from clinical trials, research studies, and individual health monitoring becomes available, AI systems can update their algorithms to provide more accurate and relevant recommendations. This dynamic adaptability ensures that personalized dietary plans remain aligned with the latest scientific findings and individual health changes (Price et al., 2017).

For instance, AI-powered systems can incorporate real-time data from wearable devices, such as continuous glucose monitors or fitness trackers, to adjust dietary recommendations based on an individual's current physiological state. This continuous feedback loop enhances the accuracy and effectiveness of personalized dietary interventions (Dunn et al., 2018).

AI can also play a significant role in interpreting gene-environment interactions, which are crucial to understanding how diet affects health. By analyzing large datasets, AI can identify clinically meaningful biomarkers and understand the complex interplay between genetic factors and environmental influences, such as diet and lifestyle. This knowledge can inform the development of personalized dietary interventions that address specific health risks (Corella, Ordovas, 2014).

For example, AI has been used to identify genetic variants associated with nutrient deficiencies or intolerances, such as lactose intolerance or vitamin D metabolism disorders. These findings enable the design of personalized dietary plans that mitigate these risks and promote optimal health (Ferguson et al., 2016).

3. Conclusion

The integration of next-generation sequencing (NGS) with personalized nutrition represents a transformative approach to healthcare, offering the potential to tailor dietary interventions to

individual genetic, transcriptomic, and epigenomic profiles. By leveraging NGS technologies, researchers and healthcare providers can identify key biomarkers that influence dietary responses, metabolism, and disease risk, enabling precision nutrition strategies that improve health outcomes and reduce the burden of chronic diseases.

However, the widespread implementation of NGS-based personalized nutrition faces significant challenges, including data interpretation, clinical validation, and ethical considerations. Addressing these challenges will require continued advancements in bioinformatics, large-scale longitudinal studies, and robust ethical frameworks to ensure equitable access and responsible use of genetic information.

Looking ahead, the integration of NGS with other omics technologies, such as proteomics and metabolomics, promises to provide a more comprehensive understanding of the complex interactions between diet, genes, and health. Additionally, the application of artificial intelligence and machine learning offers exciting opportunities to enhance the precision and adaptability of personalized nutrition recommendations.

As the field of personalized nutrition continues to evolve, it holds the potential to revolutionize healthcare by moving beyond a one-size-fits-all approach to diet and embracing a more individualized, data-driven model of nutrition that empowers individuals to achieve optimal health and well-being.

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