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Guide and Position of the International Society of Nutrigenetics/Nutrigenomics on Personalised Nutrition: Part 1 – Fields of Precision Nutrition

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Key Words
Precision nutrition · Omics · Genetic tests · Nutrigenetics · Nutrigenomics · Health and disease

Abstract
Diversity in the genetic profile between individuals and specific ethnic groups affects nutrient requirements, metabolism and response to nutritional and dietary interventions. Indeed, individuals respond differently to lifestyle interventions (diet, physical activity, smoking, etc.). The sequencing of the human genome and subsequent increased knowledge regarding human genetic variation is contributing to the emergence of personalized nutrition. These advances in genetic science are raising numerous questions regarding the mode that precision nutrition can contribute solutions to emerging problems in public health, by reducing the risk and prevalence of nutrition-related diseases. Current views on personalized nutrition encompass omics technologies (nutrigenomics, transcriptomics, epigenomics, foodomics, metabolomics, metagenomics, etc.), functional food development and challenges related to legal and ethical aspects, application in clinical practice, and population scope, in terms of guidelines and epidemiological factors. In this context, precision nutrition can be considered as occurring at three levels: (1) conventional nutrition based on general guidelines for population groups by age, gender and social determinants; (2) individualized nutrition that adds phenotypic information about the person's current nutritional status (e.g. anthropometry, biochemical and metabolic analysis, physical activity, among others), and (3) genotype-directed nutrition based on rare or common gene variation. Research and appropriate translation into medical practice and dietary recommendations must be based on a solid foundation of knowledge derived from studies on nutrigenetics and nutrigenomics. A scientific society, such as the International Society of Nutrigenetics/Nutrigenomics (ISNN), internationally devoted to the study of nutrigenetics/nutrigenomics, can indeed serve the commendable roles of (1) promoting science and favoring scientific communication and (2) permanently working as a 'clearing house' to prevent disqualifying logical jumps, correct or stop unwarranted claims, and prevent the creation of unwarranted expectations in patients and in the general public. In this statement, we are focusing on the scientific aspects of disciplines covering nutrigenetics and nutrigenomics issues. Genetic screening and the ethical, legal, social and economic aspects will be dealt with in subsequent statements of the Society.

Introduction

The purpose of the International Society of Nutrigenetics/Nutrigenomics (ISNN) is to increase through research the understanding of the role of genetic variation and dietary response and the role of nutrients in gene expression among both professionals and the general public [1].

The Society is educational in its mission to serve as a focus for communicating among interested scientists working in nutrition, genetics, cellular and molecular biology, physiology, pathology, biochemistry, clinical medicine, epidemiology, and public health, who are studying the role of genetic variation and dietary response and the role of nutrients in gene expression. It is believed that improved communication across these different branches of medical and biological sciences will stimulate new research and increase the knowledge of gene-nutrient interactions and genetic variation and dietary response. The ISNN will assist in interpreting the new facts into sound nutritional advice for the public as well. As needed, the

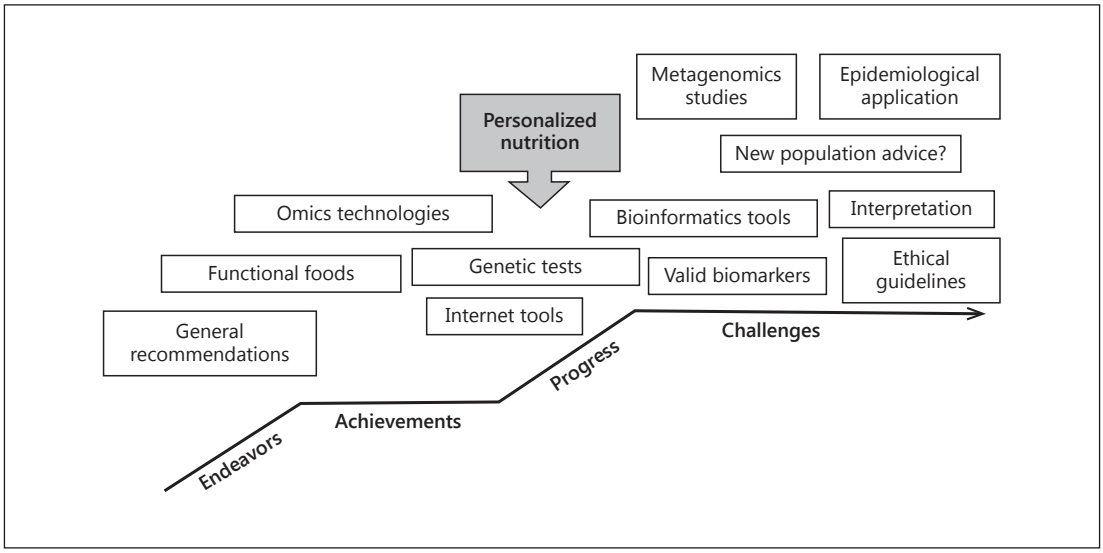

Fig. 1. Endeavors and achievements already made, plus progress and challenges in current and future scenarios with regard to personalized nutrition.

Society will establish committees to handle scientific and educational aspects and develop statements to be approved by the Board.

A first such statement has been developed on the state of the art of the field of nutrigenetics/nutrigenomics, focusing on personalized nutrition and biotechnological advances. Subsequent statements will be on the ISNN position on genetic testing, ethical, social and legal aspects. Some of the statements may be developed in collaboration with other institutes and national societies.

Personalized Nutrition

Individuals respond differently to lifestyle interventions, especially those modulating diet, because of genetic variants that influence how dietary components are absorbed, metabolized and utilized [2, 3]. Therefore, dietary advice that is specific to individuals with a particular genotype should be more effective at preventing chronic diseases than general recommendations about diet [4]. Some consumer genetic testing companies are beginning to provide information as to how diet should be modified, based on the genotype, to prevent disease or improve health, i.e. personalized nutrition (fig. 1).

The sequencing of the human genome and consequent increased knowledge regarding human genetic variation is contributing to the emergence of personalized nutrition [2]. Recognition of diverse individual nutritional needs and responses to diet are changing standards of nutritional care, creating new possibilities for this field.

Dietary reference intake values such as recommended dietary allowance and safe upper limits established by the Food and Nutrition Board of the National Academy of Medicine are based on recommendations for populations rather than for specific individuals or groups of individuals [5]. Some countries emphasize the food guide pyramid of the United States Department of Agriculture (USDA) [6], or the USDA dietary guidelines [7]. Promotion of dietary patterns believed to be beneficial, such as the Mediterranean diet, is another way to

express healthy nutrition [8]. Most dietary recommendations are stratified according to gender and age, but these are not the only factors that should be considered when giving advice on nutrient intake. Diversity in the genetic profile between individuals and specific ethnic groups affects nutrient requirements, metabolism and response to nutritional and dietary interventions [9, 10].

Environmental, cultural and economic factors also play a crucial role in individual food choices and accessibility [10]. Malnutrition in the form of undernutrition or obesity can also modify gene expression and genome stability, resulting in changes in phenotype, and hence it is difficult to choose one population as a reference [11]. New statistical approaches are urgently needed for estimating reference values in different population groups [12]. Features such as age, gender, physical activity, physiological state, social status and special conditions such as pregnancy and risk of disease [13] can inform dietary advice that more closely meets individual needs [14].

Improved health care can be achieved if nutritional recommendations are personalized according to individual genetic profile, phenotype, health status, food preferences and environmental characteristics [10]. Personalized nutrition is an important part of personalized medicine and may assist in establishing guidelines for specific subgroups based on phenotype and genotype.

The suffix 'omics' means 'global' and is used as a modifier for a wide range of endeavors such as the comprehensive analysis of genes (genomics), DNA modifications (epigenomics), messenger RNA (mRNA) or transcripts (transcriptomics), proteins (proteomics), metabolites (metabolomics), lipids (lipidomics), food (foodomics) and microbiota (microbiomics, metagenomics). All these techniques can be applied separately or in an integrated manner for a better understanding of health metabolism and disease progression [10].

As mentioned already, some 'omics' technologies could be used to develop optimal, customized diets to promote health maintenance and disease prevention for each individual, thus expanding into effective public health strategies on diet therapy [15, 16]. With this perspective, the omics tools most immediately relevant to personalized nutrition include nutrigenetics, nutrigenomics and nutriepigenetics. Nutrigenetics investigates the influence of the genotype (variants of the DNA sequence) on the response to nutritional change and on the risk of nutrition-related disease. Nutrigenomic studies investigate the effect of nutrition on gene expression and, consequently, on the proteome and the metabolome [17]. Nutriepigenetic studies explore the chromatin structure and DNA modifications that do not alter the underlying DNA sequence, but affect gene expression [18].

These advances in genetic science are raising numerous questions regarding how personalized nutrition can contribute solutions to emerging problems in public health, by reducing the risk and prevalence of nutrition-related disease. The availability of genetic information also raises questions from health-care professionals as to how to apply such knowledge, and from individuals regarding how to use such information. Furthermore, commercialization of genetic information raises ethical and moral issues. Hence, the interpretation and inclusion of genetic components into nutrition recommendations and products may generate ethical and financial difficulties while simultaneously promoting a revolution in nutrition.

Genome-wide association studies (GWAS) have identified a large number of genetic variants associated with complex diseases and traits [19], but have failed to explain a large part of their heritability [20]. GWAS usually measure the impact of genes on disease using correlations rather than studying interactions between genes and environmental factors such as diet or exercise. These interactions cause genotypic effects to be more pronounced under particular environmental conditions. Therefore, failing to control for such variations means that GWAS data provide only a partial picture of genetic variation contributing to disease development, particularly with regard to heritability [21].

GWAS should be considered as only a first step in the understanding of the molecular basis of complex diseases. The advances in nutrigenetics, nutrigenomics and nutriepigenetics will help to identify the variability in interactions not controlled for in GWAS. This situation means that new bioinformatics and biostatistics tools will be necessary to make this new information useful for health-care professionals [22].

Current views on personalized nutrition encompass omics technologies, functional foods, existing products, future challenges – particularly those relating to legal and ethical aspects, application in clinical practice, and population scope, in terms of guidelines and epidemiological factors (fig. 1). In this statement, we are focusing on the scientific aspects of disciplines covering nutrigenetics and nutrigenomics issues. Genetic screening and the ethical, legal, social and economic aspects will be dealt with in subsequent statements of the Society.

Omics Technologies in Personalized Nutrition

Application of information regarding genes and molecular pathways related to the use and metabolism of nutrients is a key approach for personalized nutrition [23], the knowledge of which is facilitated by the emergence of 'omics' technologies.

Nutrigenetics

A major contribution of the Human Genome Project was to lay the foundation that led to the discovery of millions of differences in the nucleotide sequence of genes. The variants occurring in at least 1% of any distinct population are called polymorphic variants or polymorphisms [23]. A particularly common type of polymorphism is defined by the replacement of one nucleotide base with another, and therefore called 'single nucleotide polymorphism' (SNP). Some SNPs may affect the synthesis and function of proteins, and may therefore alter nutritional requirements and nutrient metabolism [24, 25], as well as playing important roles in an individual's risk of developing disease [26].

A further way in which genetic variations occur is through structural DNA changes that include insertions/deletions, translocations and copy number variations (CNVs). CNVs explain about 1% of the genetic variation between two individuals [27]. Some of them appear to play an important role in human health [28, 29] through association with the risk of disease development and progression [30].

The discovery of diseases associated with genetic variants has provided a better understanding of nutrient/diet effects on human health and disease [10], and has helped individuals to achieve customized nutritional treatments. One example of this is phenylketonuria (PKU), an inborn error of metabolism caused by mutations in the gene that encodes the hepatic enzyme phenylalanine hydroxylase [31]. Individuals with PKU need to avoid foods rich in the amino acid phenylalanine. Another example is lactase persistence, which evolved a few thousand years ago in response to the development of dairy farming. Carriers of variants associated with lactase persistence have their lactase gene permanently 'turned on' after weaning and can digest lactose even as adults. Lactose (milk sugar) is a disaccharide, made from glucose and galactose. Therefore, the 70% of the global population, who do not have such genetic variants, are better off limiting consumption of milk and other dairy products rich in lactose [31].

Recent studies investigating genetic variants associated with obesity risk or with resistance to weight loss in human populations [32, 33] have helped clarify molecular mechanisms involved in obesity [34]. One such example is the fat mass and obesity-associated (FTO) gene. The minority (16%) of individuals with two copies of the common FTO variant (rs9939609) weigh around 3 kg more than noncarriers and have a 1.67-fold increased risk

of obesity [35]. Variants in numerous other obesity candidate genes, such as peroxisome proliferator-activated receptor, uncoupling proteins (UCP1 and UCP3), leptin receptor and melanocortin 4 receptor, can also affect weight gain or loss in genetically predisposed subjects [32, 36].

Variants in genes necessary for lipid metabolism, such as those encoding cholesteryl ester transfer protein, lipoprotein lipase, low-density lipoprotein receptor and apolipoprotein E, may increase the risk of coronary artery disease [37–40]. Further variants are associated with the development of diabetes, cancer and other diseases. Dietary advice specifically tailored to some of these variants may reduce the elevated disease risk better than genetic counselling without knowledge of the genetic information [41].

Many other metabolic pathways and biological functions have similarly identifiable genetic vulnerabilities that are amenable to tailoring of dietary intakes. For example, the combination of low folate intake, a low-activity variant of the 5,10-methylene tetrahydrofolate reductase gene (MTHFR), increases susceptibility to disease, while either of them on their own will not [42, 43]. Technologies such as next-generation sequencing (NGS) platforms (arrays, bead chips and sequencing approaches) provide a rapid scan of known genetic variants to define genetic differences between individuals [44, 45].

Assessing the role of single gene variants in complex traits influenced by many genes [e.g., diabetes, cancer and cardiovascular disease (CVD)] is difficult for many reasons, but not least due to gene-gene interactions. Therefore, simultaneous examination of multiple variants is necessary, given the fact that several of them may affect the function of a particular gene and that multiple genes may contribute to disease development and progression. This approach assists with defining biological response to food components and food patterns, thereby advancing strategies to identify, treat and prevent disease [45]. In particular, the analysis of groups of gene variants (haplotypes) that are related or physically close to each other on the same DNA strand can promote our understanding of biological events and conditions [46].

Telomere length (TL) has also been linked to the risk of several diseases, such as cancer and CVD [47]. Telomeres are tandem TTAGGG repeats of DNA that, together with associated protein factors, protect the ends of chromosomes and become shorter with each round of DNA replication [48]. TL is a biomarker of cumulative oxidative stress, biological age, and an independent predictor of survival and therapeutic treatment requirements. Thus, leukocyte TL has been proposed as a biomarker of biological age [47]. Studies have shown that dietary patterns can protect or damage telomeres. For example, high consumption of fruits and vegetables and a higher intake of omega-3 fatty acids or fiber were associated with longer telomeres [49, 50], whereas higher intake of saturated fatty acids and higher consumption of processed meats were both associated with telomere shortening [51]. Furthermore, recent studies have shown that total dietary antioxidant capacity was associated with longer telomeres, while higher white bread consumption was associated with telomere shortening in a population of Spanish children and adolescents [52].

Nutrigenomics

Nutrients and food components can affect and regulate gene activity both directly and indirectly, including acting as ligands of transcription factors and playing a regulatory role in intermediate metabolites of signaling pathways, with positive or negative effects [53]. Hence, nutrigenomics seeks to show how dietary factors influence gene expression and subsequently impact protein and metabolite levels [54, 55]. A common approach is the examination of individual mRNA levels relative to intake of certain food components. Nutrigenomic strategies thus include analysis of gene expression and biochemical profiles. Early examples of such research strategies include the finding that dietary cholesterol inhibits transcription of the

3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) gene [56], and that long-chain omega-3 polyunsaturated fatty acids reduce gene transcription of platelet-derived growth factor and interleukin-1β [57, 58].

Transcriptomics

The study of the transcriptome (the complete set of RNA transcripts) [23], provides a tool for observing such changes in gene expression in response to different factors including dietary changes [59]. Diet, physical activity, alcohol and smoking habits all modify gene expression and consequently affect the risk of pathological outcome [36, 60]. Dietary components, such as macronutrients and micronutrients influence gene expression, thereby altering metabolism and the development of disease [23]. Transcriptome analysis can evaluate the expression of thousands of genes before and after dietary intervention, showing the difference between healthy and unhealthy individuals and helping to establish new biomarkers for disease diagnosis [23].

Transcriptomics requires the study of cells in which genes are expressed, because gene expression is often tissue specific. It is difficult to access the most relevant human tissues, meaning that samples are usually available only from the more accessible tissues such as subcutaneous adipose tissue, blood mononuclear cells and skeletal muscle [61]. Polymerase chain reaction has been used to measure gene expression in the interaction of the genome and diet [31]. Newer microarray technologies can identify most changes in gene expression and in metabolic pathways after nutritional intervention.

Epigenetics/Epigenomics

Epigenetic processes bring about reversible modifications in chromatin structure and DNA modification without altering the underlying sequence. Epigenetic changes include DNA methylation and histone modification [33, 62, 63]. Different classes of small noncoding RNAs (such as microRNAs) or long noncoding RNAs have been proposed as key regulators of gene expression, chromatin remodeling and epigenetic changes through multiple mechanism, showing a potential as biomarkers of human diseases [64, 65]. Additionally, external effects (including diet) on the epigenome alter the expression of genes, providing a link between environment, nutrition and disease [66].

DNA methylation is the most widely studied form of epigenetic modification. One of numerous specific methyltransferases adds a methyl group to the cytosine in the carbon 5′ position of a CpG dinucleotide (cytosine followed by a guanine). The added methyl group often silences the gene by blocking the binding of transcription factors [61, 67]. In recent years, development of new technologies such as NGS has allowed the detection of site-specific methylation patterns with great accuracy and led to the discovery of new types of epigenetic modifications [68–70].

Histone modifications, consisting of acetylation, methylation, phosphorylation and ubiquitination, affect transcription through compacting DNA. This process can activate or repress gene expression by controlling accessibility of genes to transcriptional regulators [71, 72].

Epigenetics depends on the presence of enzymes and dietary nutrients, and can occur in a gene-specific or in a global manner [73]. S-adenosylmethionine (SAM) is the universal methyl donor for all methyltransferases that methylate DNA and histones. The availability of SAM can be diminished under some circumstances by insufficient availability of folic acid, vitamin B_{12}, vitamin B_6, vitamin B_2, choline, betaine and methionine, both due to low intake and individual genetic vulnerabilities [74, 75].

Some studies have shown a relationship between nutritional intake during pregnancy and changes in methylation patterns in rats [76, 77]. Nutritional interventions in pregnancy and lactation such as energy restriction and excessive dietary fat can alter epigenetic modifi-

cations [78]. Other studies have shown that epigenetic modifications change the risk of inflammation, obesity and chronic diseases [79]. A study of obese men on a hypocaloric diet to lose weight found distinct differences in DNA methylation patterns between individuals with high weight loss compared to those with little weight loss [80]. Studies in diabetic individuals found associations between the secretion of insulin and the DNA methylation pattern in the promoter region of the PCG-1A gene of pancreatic β-cells [81].

New NGS and microarray technologies have enabled the study of DNA methylation at high resolution across the genome, helping to characterize epigenetic outcomes though epigenome-wide association studies [82].

Proteomics

Transcriptomics does not show the number of expressed proteins. Thus, one transcript can be translated into numerous proteins, just as many factors can stop or modify the translation process or cause posttranslational modifications [6]. Proteomics analyzes protein expressed over a given time, and is the most precise method for identifying the effect of nutrients and food components on the genome [6, 23].

Each cell will have a corresponding proteome, depending on the cell's type and function [83]. Proteins are commonly analyzed in blood samples [84], but there is not a single platform capable of evaluating the full spectrum of proteins in blood or tissue samples [85].

Lipidomics

Lipids play an important role in nutrition and metabolism [86]. Lipidomics produces a global profile of lipids found in cells, tissues and fluids [87], studying the interactions between genes, diet, nutrients and human metabolism [86, 88]. It is an emerging tool for identifying individual variability in response to nutritional interventions, and can be used in diet counseling and to optimize food processing [86]. Lipidomic studies are possible due to advances in mass spectrometry technologies [89]. Use of lipidomics in clinical practice is still in its infancy, because the knowledge of lipid metabolism pathways is incomplete and needed tools continue to evolve [90].

Metabolomics

Metabolomics studies metabolites in human systems [83], focusing on changes in the biochemical profile of biological fluids, blood, urine, saliva, cells and tissues [91]. Some authors have proposed a new term, 'nutrimetabolomics', meaning the application of metabolomics in nutrition and health [91, 92].

Metabolomic studies can evaluate groups of metabolites related to a specific metabolic pathway or compare modifications in patterns of metabolites in response to environmental stimuli [93] following targeted or untargeted approaches. Thus, metabolomics is considered the end point of human molecular analysis [94] and can assess the body's response to a diet. Many studies have used metabolic profiling to identify food biomarkers and to define dietary patterns. Other applications of metabolomics include monitoring of food consumption and assessment of food quality [95]. Hence, metabolomics can answer questions such as how a high-saturated fat diet can affect lipid profile, or how the intake of fiber affects glycemia. Recent dietary intervention studies using metabolic profiles have evaluated the consequences of consuming cocoa [96], coffee [97] and fiber [98], and of different dietary patterns [99].

Study of metabolites is only possible with advances in techniques that separate and identify small molecules [100]. However, there is not yet a methodology capable of detecting, identifying and quantifying all human metabolites. Combining techniques such as system-based mass spectrometry, nuclear magnetic resonance, gas chromatography and liquid chro-

matography may be a better approach for global metabolite identification [93]. As with GWAS, many chemicals and metabolites can be tested for and associated with diet and disease [16] through metabolome-wide studies.

Foodomics

Foodomics refers to a new science that evaluates food components using new technologies, with the aim of improving human health through improving human nutrition [101, 102]. In recent years, food scientists have developed new products, packaging and sensory characteristics to better reach target markets [101]. Study of the molecular composition of foods enables such breakthroughs.

Foods originate from living things (animals, plants or fungi) and are affected by agricultural and production technologies. Food composition depends on many factors such as season, maturation and temperatures of storage and cooking. Foodomics can help solve problems related to food safety, food quality, new foods, transgenic foods and functional foods [103, 104], improving dietary constituents and thereby better enabling disease prevention through diet.

Foodomics evaluates the effects of food components at the level of genome, transcriptome, proteome and metabolome, thus providing additional studies of bioactive compounds in food at the molecular level [85]. However, variability and differing concentrations of nutrients and bioactive food compounds create limitations in foodomics studies [93].

Examples of foodomics strategies include the study of oligosaccharides, phytochemicals, antioxidants, bioactive compounds, biotoxins and other factors [105]. Mass spectrometry-based techniques, new separation methods and multidimensional chromatographic techniques have been used in food composition analysis [105].

One complete, multidimensional definition of foodomics is that of a science that studies the role of biomarkers, food components, diets and lifestyle in reaching and maintaining health and wellness [106].

Metagenomics

Metagenomics refers to studies of the global microbial communities, and their genes present in the gut and other body parts [107, 108]. Microbiota are able to alter gene expression, affecting the proteome and the health of an individual. Thus, they can be viewed as further functional, genomic units which regulate metabolic processes [107, 109]. Many food constituents, such as polyphenols, fiber and fat, affect the microbiota in the gut and thereby can have microbiome-mediated effects.

Products of microbial fermentation such as short-chain fatty acids may have a direct effect on cellular metabolism [110]. Dysbiosis can result in inflammation in the luminal gut, contributing to risk and development of diseases [111] including obesity [111–113], diabetes and atherosclerosis [114, 115], Crohn's disease [116], gastritis and gastrointestinal cancer [117] and food allergies [118]. Recent studies have associated nutrition during gestation and childhood with effects on the microbiota, and subsequent effects on immune function and immunocompetence to the onset of obesity and other chronic diseases [119].

Different dietary components have distinct roles in microbial growth and may modulate functions of the intestinal microbiome [120]; for example, the ingestion of phenolic compounds may modulate the microbiota, promoting the growth of beneficial bacteria [121]. The effect of diet on the microbiome depends on the age and environment of the individual [122], and on the genetic characteristics of the host [123, 124]. Microbial exposure during pregnancy and the composition of gut microbiota during the first months of life influence immune function and predisposition to allergy [125].

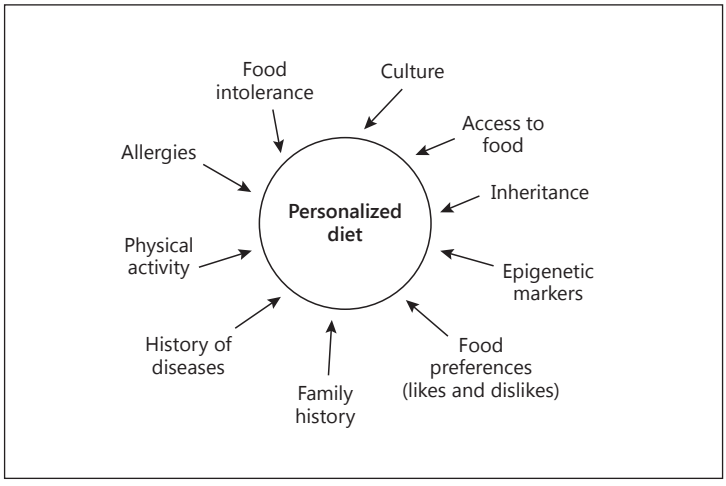

Fig. 2. The interplay between genetic background, biological, cultural and environmental variations on personalized nutrition.

The gut microbiome can also be associated with the progression of CVD, acting in the conversion of choline and L-carnitine present in the diet to trimethylamine and trimethylamine-N-oxide compounds [126]. CVD risk is associated with inflammation, risk of obesity and diabetes; thus, novel strategies of gut microbiome manipulation could lead to improvements in the treatment of CVD and obesity [126].

The gut microbiota are unique to each individual; consequently, the microbiome is emerging as a tool for personalized nutrition [127]. These new findings promote an alternative approach to regulation of gene expression through diet and food components. New technologies for analyzing the gut microbiome are needed, however, before metagenomics can usefully contribute to personalized nutrition [127].

Precision Nutrition

The response of an individual to nutrient intake results from the interaction of metabolic, environmental, social and genetic factors (fig. 2). Analysis of an individual's genome can distinguish responders from nonresponders to dietary interventions and treatments. Personalized nutrition depends on the genetic background plus biological and cultural variations, including food intolerances, preferences and allergies [33], where knowledge and integration will allow precision nutrition.

The traditional concept of personalized nutrition is to adapt the diet according to individual needs and preferences [128]. With the evolution of high-throughput technologies, precision nutrition can finally contribute to the reduction and prevention of disease by using genetic information to predict whether someone is going to respond to specific nutritional patterns or not [129]. Personalized nutrition is based on the principle that particular foods or nutrient quantities may alter disease risk more or less, depending on the individual's DNA sequence [130].

Precision nutrition can be considered as occurring at three levels: (1) conventional nutrition based on general guidelines for population groups by age, gender and social determinants; (2) individualized nutrition that adds phenotypic information about the person's current nutritional status (e.g. anthropometry, biochemical and metabolic analysis, physical activity, among others), and (3) genotype-directed nutrition based on rare or common gene variation [131]. The ultimate goal is to integrate such sources of information to ensure that

Table 1. Major challenges of personalized nutrition

1. Strengthening the science
a Creation of risk map
b Creation of a reliable 'bank' of polymorphisms
c Tests of epigenetic assessment
d Identification of valid biomarkers
e Microbiome and lipidomics studies
f Implementation into public health policies
g Metagenomics view
h Development of new technologies (bioinformatics) for analyzing data
i Applicability to clinical practice
j Tools for evaluating diet in nutrigenomic studies
k Regulation of ethical and legal aspects
l Cost reduction
2. Training personnel and improving knowledge delivery
a Increasing availability of trained allied health professionals capable of interpreting genetic data
b Greater involvement of dietetic professionals in dietary recommendations
c Promoting introduction of nutrigenomic education into the curricula of allied health professionals
d Promoting introduction of nutrigenomic education into medical curricula
3. Public education
a Communication with and involvement of science writers
b Dissemination of 'lay' information via mainstream media in the form of print, screen and social media

health-care professionals, including dietitians, physicians, pharmacists and genetic counselors, know sufficient concepts about nutrigenetics and nutrigenomics to decide on the most appropriate level of care to achieve a precision nutrition which integrates phenotypical and genotypical issues as well as social, environmental and metabolic factors [132–134].

Conclusions

The use of new technologies is paving the way for solid individual nutritional recommendations with important challenges concerning strengthening the science, training personnel and improving knowledge delivery and public education (table 1). It is important that future studies utilize outcome research, not only considering the effects of a nutritional intervention on surrogate parameters in different genetic groups, but also looking at effects on disease development, survival and quality of life. This recognizes that recommendations based on the analysis of intermediate end points can be highly biased and potentially counteracted by opposite effects on some other intermediate end point that was not directly estimated in the investigation. The road ahead for the discipline must involve the integration of several different fields of study in order to formulate solid individualized nutritional recommendations.

Like drugs, nutrients have the ability to interact and modulate molecular mechanisms underlying an organism's physiological functions. Awareness of the different effects of nutrients according to our genetic constitution (nutrigenetics) and how nutrients may affect gene expression (nutrigenomics) is prompting a revolution in the field of nutrition. Nutri-

tional sciences have traditionally studied the effects of nutrients in terms of 'average' responses, largely without considering interindividual variability and the underlying causes. Advances in nutrigenetics and nutrigenomics, with distinct approaches to elucidate the interaction between diet and genes, but with the common ultimate goal of optimizing health through personalized diet, provide powerful approaches to unravel the complex relationships between nutritional molecules, genetic variants and the biological system. Translated as the simple concept of 'personalized nutrition', the promise of nutrigenetics/nutrigenomics is a major step forward in the understanding of individual responses to a component nutrient or to our changing environment for precision nutrition.

A scientific society, such as the ISNN, internationally devoted to the study of nutrigenetics and nutrigenomics can indeed serve the commendable roles of (1) promoting science and favoring scientific communication, and (2) permanently working as a 'clearing house' to prevent disqualifying logical jumps, correct or stop unwarranted claims, and prevent the creation of unwarranted expectations in patients and in the general public. Research and appropriate translation into medical practice and dietary recommendations must be based on a solid foundation of knowledge derived from studies on nutrigenetics and nutrigenomics.

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