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Journal of the American College of Nutrition

ISSN: 0731-5724 (Print) 1541-1087 (Online) Journal homepage: https://www.tandfonline.com/loi/uacn20

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To cite this article: Okezie I Aruoma, Sharon Hausman-Cohen, Jessica Pizano, Michael A. Schmidt, Deanna M. Minich, Yael Joffe, Sebastian Brandhorst, Simon J. Evans & David M. Brady (2019) Personalized Nutrition: Translating the Science of NutriGenomics Into Practice: Proceedings From the 2018 American College of Nutrition Meeting, Journal of the American College of Nutrition, 38:4, 287-301, DOI: 10.1080/07315724.2019.1582980

To link to this article: https://doi.org/10.1080/07315724.2019.1582980

JOURNAL OF THE AMERICAN COLLEGE OF NUTRITION
2019, VOL. 38, NO. 4, 287–301
https://doi.org/10.1080/07315724.2019.1582980

Personalized Nutrition: Translating the Science of NutriGenomics Into Practice: Proceedings From the 2018 American College of Nutrition Meeting

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ABSTRACT

Adverse reactions to foods and adverse drug reactions are inherent in product defects, medication errors, and differences in individual drug exposure. Pharmacogenetics is the study of genetic causes of individual variations in drug response and pharmacogenomics more broadly involves genome-wide analysis of the genetic determinants of drug efficacy and toxicity. The similarity of nutritional genomics and pharmacogenomics stems from the innate goal to identify genetic variants associated with metabolism and disease. Thus, nutrigenomics can be thought of as encompassing gene–diet interactions involving diverse compounds that are present in even the simplest foods. The advances in the knowledge base of the complex interactions among genotype, diet, lifestyle, and environment is the cornerstone that continues to elicit changes in current medical practice to ultimately yield personalized nutrition recommendations for health and risk assessment. This information could be used to understand how foods and dietary supplements uniquely affect the health of individuals and, hence, wellness. The individual's gut microbiota is not only paramount but pivotal in embracing the multiple-functional relationships with complex metabolic mechanisms involved in maintaining cellular homeostasis. The genetic revolution has ushered in an exciting era, one in which many new opportunities are expected for nutrition professionals with expertise in nutritional genomics. The American College of Nutrition's conference focused on "Personalized Nutrition: Translating the Science of NutriGenomics Into Practice" was designed to help to provide the education needed for the professional engagement of providers in the personalized medicine era.

KEYWORDS

Personalized nutrition; nutritional genomics; pharmacogenomics; single nucleotide polymorphism; next generation sequencing; gene–diet interactions; metabolic diseases; wellness and genomics; Alzheimer's disease and cognitive decline; autoimmune diseases; overt inflammation and chronic diseases; gut microbiome

Introduction

Nutritional genomics is the study of the effects of foods and food constituents on gene expression. Nutritional genomics aims to develop a rational means to optimize nutrition through the identification of the person's genotype and this defines the relationship between nutrients and human health. Individuals cannot change their genetics, but they can eat the right foods to support genetic predispositions, take the right supplements to support gene variations, and promote normal cell function and structure. Indeed, poor diet can be a risk factor of disease. Given that dietary components can alter gene expression and that the degree to which diet influences health and disease depend upon an individuals genetic make up, the use of pharmacogenomics technologies should be well defined in order to fully embrace their potential application for diagnostic and prognostic purposes. There are many inroads ahead in this realization.

Single nucleotide polymorphisms are now recognized as the main cause of human genetic variability and are already a valuable resource for mapping complex genetic traits. The identification and validation of accurate biomarkers of individual responses to drug or biologic treatment remain prerequisite conditions ascribed to the development of personalized medicine and other evolving therapeutic strategies. The sequence variations in the genes for proteins involved in drug disposition can alter the pharmacokinetics of a drug, while sequence variations in drug target genes can change the pharmacodynamics of the drug (Figure 1). That pharmacogenomics connects genotype to patient-specific treatment intrinsically implies that individuals have variations in the composition of their genetic characteristics (factored on strategies that embrace testing for candidate-genes and genome-wide association) that will affect the availability of functional proteins, which ultimately impacts functional homeostasis and the outcome of drug therapy. Primary candidate genes include those encoding for drug receptors, metabolizing enzymes, and transporters. However, selection of optimal drug therapy may

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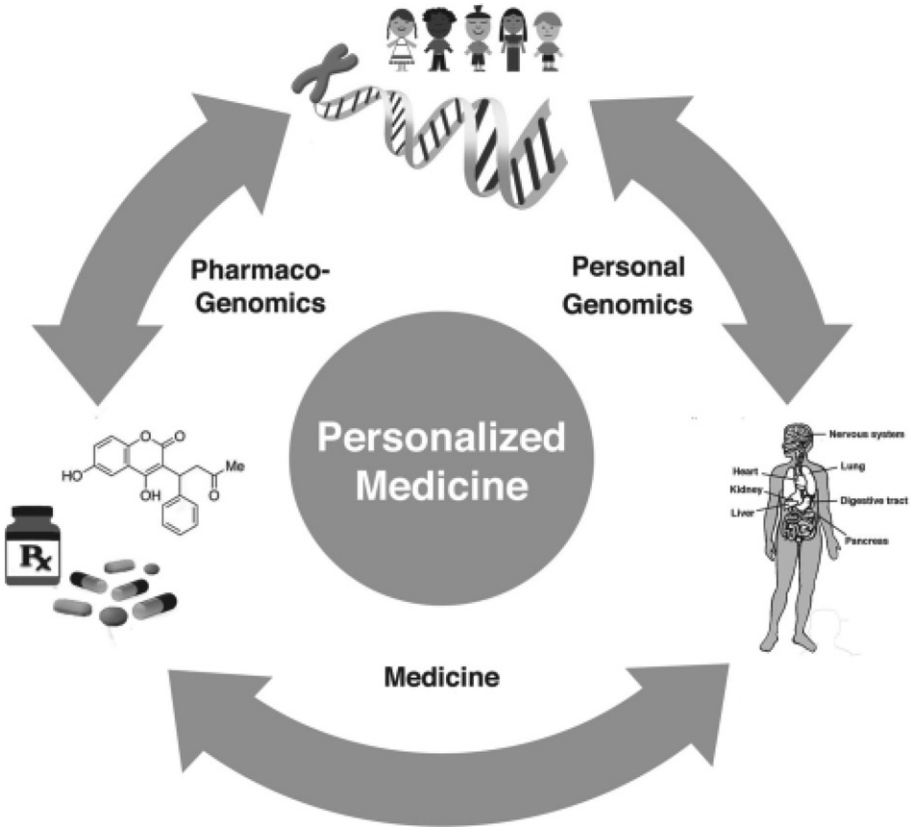

Figure 1. Personal genomics connect genotype to phenotype and provide insight into disease. Pharmacogenomics has helped understand some of the factors responsible for adverse drug reactions (ADRs) caused by high exposures and factors associated with the mechanism of action of the drug and examples continue to emerge where genetic markers identified patients at risk for serious, often life-threatening ADRs before administration of drugs. (The reader is referred to Fernald et al. (1) and to the U.S. FDA website: http://www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics.)

also involve disease susceptibility genes indirectly affecting drug response (Figure 1) (1). This meeting report presents a range of the subject matter covered at the conference depicting the key essence of nutrigenomics and its translation to personalized nutrition benefits and health. The context of the report is limited to the areas of expertise of the presenters/authors and each section included is reflective of the individual presenter/author's presentation at the conference and is not a reflection of a position by the American College of Nutrition (ACN). For additional information on ACN programs and meetings, visit www.americancollegeofnutrition.org.

Understanding genomics

The conference was prefaced with a session entitled "NutriGenomics Primer: Foundational Concepts for Clinical Practice," which emphasized the understanding genomics with a focus on nutrigenomics and clinical assessment and genomic validation (Figure 1). The molecular basis of disease provides the means for personalizing therapy with the expectation of increased therapeutic efficacy as the outcome. Because genetics is integrated into health care, medical, pharmacologic, and nutritional therapies will become more oriented toward the genotype of each person. Nutrition assessment and intervention will be the keys to preventing or mitigating the expression of diseases to which an individual is susceptible; essentially visualizing the potential interactions of the components of foods (Figure 2) can interact with the genetic material to produce biomolecules that work to maintain cellular homeostasis.

Understanding the difference between genomics and genetics, how various single nucleotide polymorphisms (SNPs) work to convey risk or benefit to an individual not just alone but also in combination and how methylation and other factors contribute to the expression of DNA are imperative concepts for the practitioner wanting to use genomics as part of their arsenal of tools. With regard to SNPs, it is important for clinicians to understand that every individual has about 3 million SNPs among their 3 billion base pairs found in the DNA and that these SNPs are what makes each of us unique. SNPs are not innately bad or good, but some SNPs, particularly some of those found in promotor regions or other key regions such as those effecting methylation sites, can have a profound effect on gene transcription. Each of these genes can then contribute to having more or less of key enzymes, receptors, vitamins, inflammatory mediators, neurotransmitters, and more. Most of the health issues facing modern society (obesity, heart disease, osteoporosis, diabetes, Alzheimer's disease, and macular degeneration) are due to complicated polygenic causes. Expanded knowledge of genomics can facilitate a better understanding of the pathophysiology of an individual's various health risks and better modulate these risks with customized personalized prevention and intervention strategies. For example, individuals with multiple SNPs in the signal transducer and activators of transcription 3 (STAT3) pathway will tend to store fat around their waist line when exposed to

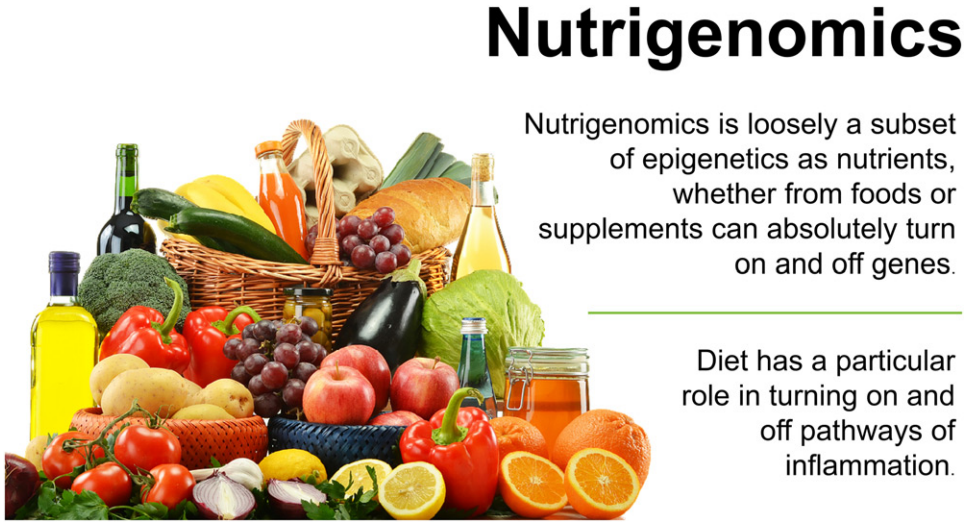

Figure 2. Nutrigenomics and diet. Nutritional genomics offers insight into ways to tailor the diets of individuals and populations. Personalized nutrition, like its parallel in medicine, presents a new way of dealing with individual nutritive health, using a "personalized" approached sustained by high throughput technologies including pharmacogenetics, pharmacogenomics, and epigenetics interlinked with genomic medicine (slide from the presentation of Dr Hausman-Cohen).

saturated fat but not to other forms of fat. Individuals with variants in the cyclin-dependent kinase inhibitor 2A/B (CDKN2A/2B) pathway will be prone to having excessive deposition of calcium in the coronary arteries. The knowledge base of these sort of genomic risk factors allows for personalized prevention in terms of dietary recommendations (very low saturated fat diet in the case of STAT3) and supplementation (vitamin K2 at doses of 35 µcg or more has been shown to decrease calcification of the arteries and decrease cardiac and overall mortality and may particularly benefit individuals with CDKN2A/2B SNPs) (2–4). For others with obesity or cardiac risk with different genomic risk factors avoiding snacking and early morning eating may be the best recommendations, or taking aspirin or addressing inflammatory pathways via diet or supplementation may be highly beneficial. While genomics is still in its infancy and must be used in combination with patient and family history, laboratory testing, and physical exams, personalized medicine allows for counseling to be specific to each patient. Although genomics can help guide personalization of prevention and treatment strategies, many challenges need to be addressed to make personalized medicine a reality (Figure 1). A patient's genetics are consulted only for a few diagnoses and treatment plans and only in certain medical centers. Even if doctors had access to their patients' genomes today and only a small percentage of the genome could even be used (5–8).

Nutrigenomics and clinical assessment and genomic validation

When looking at nutrigenomics we can measure whether an SNP is active by examining the metabolome. This includes laboratory evaluations such as organic acid and amino acid testing. Organic acid testing determines abnormal concentrations of organic acids which serve as markers for metabolism and show us the metabolic effects of genetic SNPs, which may result in insufficient enzyme or co-factor availability. Amino acids play a crucial role in the metabolome as they are the building blocks of proteins and therefore are crucial for the creation of enzymes and serve as substrates and products in various metabolic pathways. One may argue that elementary knowledge of nutrigenomics should focus on three regulatory pathways: one-carbon (1C) metabolism, methylation, and transsulfuration. Not only do these pathways help regulate DNA expression, they intersect with countless other pathways including monoamine synthesis and catabolism, the gamma glutamyl pathway, and the urea cycle. Folate metabolism, which supports a broader set of transformations known as 1C metabolism, is a metabolic process that serves to activate and transfer 1C units for biosynthetic processes including purine and thymidine synthesis and homocysteine re-methylation. 1C transfer reactions (Figure 3) are mediated by numerous enzymes that require nutritional coenzymes such as the B vitamin (folate) that serves as a 1C carrier/donor and vitamins B12, B6, and B2 and methionine. Disruptions in 1C metabolism due to deficiency of the nutrients or genetic polymorphisms of the enzymes involved have been linked to cancer etiology through insufficient DNA synthesis/repair and aberrant gene expression. Animals, unlike bacteria, yeast, and plants, cannot synthesize folate and therefore require dietary folate intake. In adults, insufficient dietary folate leads to anemia. In developing fetuses, it creates a disposition to birth defects known as neural tube defects, which involve failure of neural tube closure early in pregnancy (9–12). The reader is referred to the article by Lim et al. (12) that reported the investigation of genetic susceptibility of selected 1C metabolism enzymes and their interaction with diet using a comprehensive assessment of the metabolic pathways and its association with the etiology of lymphomagenesis. 1C metabolism is essential for the creation of a methyl donor. This pathway centers on the vitamin folate and begins with the enzyme dihydrofolate reductase (DHFR) which requires the niacin-derived co-factor NADPH. This enzyme is used in the conversion of dihydrofolate into tetrahydrofolate (THF; see

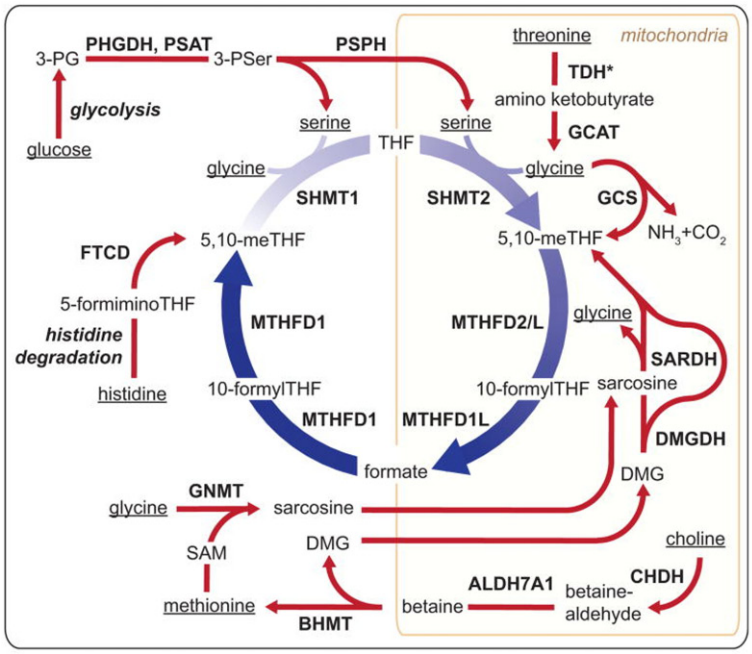

Figure 3. Products and compartmentalization of folate-mediated one-carbon (1C) metabolism. Through an interlinked set of mitochondrial and cytosolic reactions, folate metabolism supports 1C anabolic reactions. All abbreviations are standard gene names. Certain descriptions utilize the common protein name for clarity. SHMT1/2, serine hydroxymethyl transferase, cytosolic(1)/mitochondrial (2); MTHFD1, methylenetetrahydrofolate dehydrogenase, cyclohydrolase, and formyltetrahydrofolate synthetase 1; MTHFD2/L, methylenetetrahydrofolate dehydrogenase 2/2-like; MTHFD1L, monofunctional tetrahydrofolate synthase, mitochondrial; MTFMT, mitochondrial methionyl-tRNA formyltransferase; TYMS, thymidylate synthetase; MTHFR, methylenetetrahydrofolate reductase; MTR, methionine synthase; DHFR, dihydrofolate reductase; GART, phosphoribosylglycinamide formyltransferase; ATIC, 5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase; ALDH1L1/2, cytosolic (1)/mitochondrial (2) 10-formyltetrahydrofolate dehydrogenase (11).

Figure 3) and is both the precursor to 1C metabolism and essential for neurotransmitter synthesis through the formation of tetrahydrobiopterin (BH4).

Through an interlinked set of mitochondrial and cytosolic reactions, folate metabolism supports 1C anabolic reactions. All abbreviations are standard gene names. Certain descriptions utilize the common protein name for clarity. SHMT1/2, serine hydroxymethyl transferase, cytosolic(1)/mitochondrial (2); MTHFD1, methylenetetrahydrofolate dehydrogenase, cyclohydrolase, and formyltetrahydrofolate synthetase 1; MTHFD2/L, methylenetetrahydrofolate dehydrogenase 2/2-like; MTHFD1L, monofunctional tetrahydrofolate synthase, mitochondrial; MTFMT, mitochondrial methionyl-tRNA formyltransferase; TYMS, thymidylate synthetase; MTHFR, methylenetetrahydrofolate reductase; MTR, methionine synthase; DHFR, dihydrofolate reductase; GART, phosphoribosylglycinamide formyltransferase; ATIC, 5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase; and ALDH1L1/2, cytosolic (1)/mitochondrial (2) 10-formyltetrahydrofolate dehydrogenase (11).

DHFR is greatly inhibited by the synthetic folic acid, which has similar effects to the anticancer drug methotrexate which inhibits DHFR to stave off growth and proliferation of cancer cells via decreasing thymine production by rapidly dividing cancer cells (13). When polymorphisms to DHFR are found this SNP may be bypassed by folinic acid. The prescription folinic acid, Leucovorin, "does not require reduction by DHFR to participate in reactions in which folates are used as a source of 1-carbon moieties" (14). Validation of DHFR SNP activity is accomplished by assessing formiminoglutamate (FIGLU), which increases when THF is insufficient. While there are several other enzymes in 1C metabolism, none are as well studied as methylene tetrahydrofolate reductase (MTHFR). This enzyme has two genetic variants, C677T and A1298C, of which the former increases homocysteine and the latter does not. This enzyme requires as its co-factors the riboflavin-derived FAD, NADH, and ATP. Polymorphisms to MTHFR are associated with increased risk for neural tube defects, miscarriage, dementia, mood disorders, peripheral artery disease, colon cancer, and leukemia (15). This enzyme is used to convert 5, 10-methylene THF to L-methylfolate. This newly generated methyl donor is then donated to the methylation cycle where, via methionine synthase (MTR) and methionine synthase reductase (MTRR), it is used to methylate vitamin B12 and ultimately contributes to the formation of the universal methyl donor S-adenosylmethyionine.

Since MTHFR requires FAD as a co-factor, the organic acid glutaric acid which increases with riboflavin insufficiency may be used to validate. Chronically high levels of glutaric acid are suggested to associated with at least three inborn errors of metabolism, including glutaric aciduria type I, malonyl-CoA decarboxylase deficiency, and glutaric aciduria type III. Glutaric aciduria type I (glutaric acidemia type I, glutaryl-CoA dehydrogenase deficiency, GA1, or GAT1) is an inherited disorder in which the body is unable to completely break down the amino acids lysine, hydroxylysine, and tryptophan due to a deficiency of mitochondrial glutaryl-CoA dehydrogenase. Excessive levels of their intermediate breakdown products (including glutaric acid, glutaryl-CoA, 3-hydroxyglutaric acid, and glutaconic acid) may accumulate and can cause damage to the brain (and also other organs; https://pubchem.ncbi.nlm.nih.gov/compound/glutaric_acid).

The methylation pathway centers around two amino acids, methionine and homocysteine. In fact, methionine is simply methylated homocysteine. The recycling and catabolism of homocysteine may go through three routes. Half of homocysteine catabolism involves MTR/MTRR which convert homocysteine back to methionine using vitamin B12 as its co-factor. These enzymes also serve to recycle methyl donors. Methylmalonic acid (MMA), which elevates when there is a cellular vitamin B12 insufficiency, may therefore be used to validate MTR/MTRR activity. The other half of homocysteine catabolism is accounted for by cystathionine beta synthase (CBS), the only eliminating route. This enzyme requires vitamin B6 as its co-factor and the organic acid xanthurenate (when elevated) can validate SNP activity. Less than 1% of homocysteine catabolism may also occur via betaine homocysteine methyltransferase (BHMT) using trimethylglycine and zinc as co-factors. One essential element of the regulation of 1C metabolism and methylation is that there must be enough vitamin B12 present to receive the methyl donor from 1C metabolism. Without enough vitamin B12, folate gets trapped as L-methylfolate and may not be recycled back to THF. Further, this will greatly impair regulation of DNA expression. For someone who is folate trapping, this will result in an elevation of MMA and FIGLU. It also typically increases homocysteine and serum folate. CBS is the bridge between methylation and transsulfuration. It converts homocysteine to cystathione (vitamin B6–dependent). Cystathionine may then be converted to cysteine via cysteine gamma lyase (CTH), which is also vitamin B6–dependent. Ultimately, this leads to the formation of glutathione, sulfate, and taurine. SNPs to CBS may either be downregulated or upregulated, causing an increase or decrease in homocysteine, respectively. Upregulation may be associated with sulfur intolerance and causes increased taurine and sulfate and decreased production of glutathione. It is also associated with increased ammonia production and will increase ammonia-related organic acid test markers including orotate, citrate, and isocitrate.

Given that nutrigenetics and nutrigenomics conceptualizes the research into the relationship between genes and nutrients from basic biology to clinical practice, by understanding how genes alter the body's response to nutrition or how nutrition alters the body's response to defective genes, scientists are unlocking the codes to health and longevity. Profiling of genetic nutritional responses can help in the determination of which specific foods give the best biological response, based on an individual's DNA. The genomic disposition of the individual has a direct bearing in the control of metabolism, which is nicely illustrated here. Nutritional genomics offers insight into ways to tailor the diets of individuals and populations. Personalized nutrition, like its parallel in medicine approach, presents a new way of dealing with individual nutritive health, using a "personalized" approached sustained by high throughput technologies (1,16–18).

Multi-scale omics enables precision medicine: From space flight to clinical practice

The context of omics research was extended to discuss the role of nutritional genomics to help protect humans on a potential space mission (19, 20). Depending upon specific mission parameters, a mission to Mars would result in radiation exposures ranging from 1,000 to 1,600 mSv (millisieverts) (21, 22). Nutritional genomics is being explored as one means to protect molecular networks in astronauts entering spaceflight radiation environments and base countermeasures on a precision understanding of genotype and molecular phenotype (19, 20). While conventional measures of the genome will be important (SNPs, structural variants, such as insertion/deletion (INDEL) and copy number variation (CNV) polymorphisms, etc.), attention to genome stability and relevant nutritional modulators also warrants consideration, potentially from the standpoint of (1) disordered 1C metabolism (nutrients and genetic variants) that can increase uracil substitution for thymine into the genome, representing a mutational event (23, 24); (2) magnesium influences all DNA repair processes, either through direct roles in DNA repair enzymes or indirectly through Mg/ATP complexes (25); (3) NAD (nicotinamide) status can influence DNA stability by virtue of radiation-induced PARP (poly ADP-ribosyl polymerase) activation, where up to 200 molecules of NAD may be consumed in the formation of a single PARP polymer (26); and (4) elevated iron burden and associated genetic variants (H63D, C282Y, S65C) can favor the formation of oxidation products of DNA and RNA (27). Addressing the convergence of individual genotype, the molecular phenotype (nutritional metabotype), clinical phenotype, and the environment represents one means by which health, safety, and performance can be optimized in humans exploring harsh environments, such as space.

The study of cohorts such as astronauts in the NASA Twins study necessarily involves small subject numbers. Small subject numbers are also the rule in our precision medicine work with military Special Forces, professional racing, NFL, NBA, U.S. Olympic teams, high altitude ascent, Mars analog missions, commercial spaceflight, and various clinical settings, where individualized therapeutics (countermeasures) are the rule. Interpreting multi-scale untargeted omics data in small N studies presents inherent challenges of overfitting and the possible generation of false discoveries, due to low subject (sample) numbers and high variable (analyte) numbers. These studies are also highly sensitive to the introduction of experimental variance. For instance, batch effects are problematic in multi-scale omics studies and, unless accounted for, may result in modeling the specific time (and conditions) at which analytical batches are run (28, 29). *Untargeted* work with small subject numbers should control for or annotate as many contributors to experimental variance as is reasonably possible embracing patients, physicians, and the laboratories conducting the analysis. Targeted work in nutritional genomics is less sensitive to generating false discoveries, with targeted assessment being the rule in the clinical application of nutritional genomics and precision medicine. Coupling nutritional genomics with metabolite profiling can provide additional details about the real-time intersection of genotype, diet, environment, and lifestyle. This includes monogenic gene–metabolite pairs (30). For instance, determination of genetic

variants in the FADS1 (fatty acid desaturase 1) gene can be coupled with assessment of EPA, DHA, and AA in red blood cells to better understand the association between the gene and its related metabolites. Polygenic scores can also be coupled with downstream molecular measures. For instance, polygenic scores for low-density lipoprotein (LDL) cholesterol are often constructed based on effect sizes (31). When polygenic scores are coupled with real-time serum measures of LDL cholesterol (including particle number and particle phenotype), a more in-depth understanding can be developed of the convergence of genetics with diet and lifestyle. Polygenic scores can also be coupled with a molecular phenotype consisting of a cluster of associated molecular markers. By example, a polygenic score for glucose dysregulation can minimally be coupled with the molecular phenotype consisting of serum glucose, insulin, hemoglobin A1c (HbA1c), and the homeostatic model assessment of insulin resistance (HOMAR-IR).

Translating the research discipline of nutritional genomics into clinical practice is among our more daunting challenges. The field would benefit from a measured and carefully considered introduction, which would ideally be rooted in a growing consensus within the discipline. However, the current commercial environment faces us with a unique challenge. The availability of genetic testing to consumers ensures that they will present clinicians with personal genetic data for interpretation and recommendations in advance of such consensus. This dynamic compels the field to accelerate the rate at which we provide clinicians with enough rigor and training in the clinical practice setting. Presently, there are few nutrition-related professional organizations that have formally embraced the subject or provided guidelines for its implementation (32). As the field of nutritional genomics advances, it would benefit from the insight gained in the study and management of inborn errors of metabolism, with the integration of data regarding genotype, molecular phenotype (clinical chemistry), and clinical phenotype, existing on a continuum that most reliably informs clinical decisions.

Metabolic adaptability of genetic and nutritional responses

Profiling of genetic nutritional responses can help in the determination of which specific foods give the best biological response, based on an individual's DNA. Of interest, fatty acids in dietary triacylglycerols are transported from the intestines to the rest of the body by large lipoprotein particles called chylomicrons. Hormone signaling releases fatty acids from adipose tissue that bind to an abundant transport protein in serum called albumin. The fatty acids that are synthesized in the liver are carried through the body as triacylglycerols by very-low-density lipoprotein particles. Fat is stored in fat cells (adipocytes). Obesity, especially childhood obesity, can be due to both, that is, more fat storage per cell and a larger number of adipocytes. In contrast, in normal healthy adults, the onset of old age and reduced metabolic rates leads to weight gain resulting primarily from storing more fat per cell (although adults can also add more fat cells if they become obese). The thematic review of Saini-Chohan et al. (33) on fatty acid metabolism is worth perusing by the reader for an illustration of the potential genomic disposition of the individual impacting the control of metabolism.

Full-spectrum approach to healthy metabolism

Assessment and treatment of dysmetabolic conditions requires a "full-spectrum approach," indicating that only one aspect, such as genetic variants (referring to SNPs) and/or the application of nutrigenomics, will be useful, yet perhaps not comprehensive enough to address the multifaceted etiology underlying the dysregulation of the glucose–insulin–adipocyte nexus. Limited research indicates that nutrigenetically tailored diets may be helpful for encouraging better outcomes (34); however, other features, like the composition of the gut microbiome, need deeper clinical evaluation (35). Other areas for exploration include the impact of epigenetics (especially methylation) and evaluating the response of a dietary pattern in the context of one's exposome (36). An exposome may encompass one's total lived experience and relates to socioeconomic disadvantage, lifestyle factors, daily behaviors, choices, and stress response, to name a few. It has been suggested that not every individual has the same exposome, by which a fair comparison of responses to a meal can be analyzed. A meal may be metabolically processed differentially based on the culmination of one's exposome. Some individuals may be at a greater disadvantage than others due to any number of variables. Six emerging concepts in the scientific literature that are part of this greater spectrum of therapeutic options include: (1) the role of tailoring one's ancestral DNA to their dietary pattern, such as the Japan diet, Nordic diet, Mediterranean diet, and even the recently-proposed MedÉire diet; (2) the influence of toxin load (e.g., heavy metals such as arsenic, or even plasticizers like bisphenol A) on obesity and diabetes, and strategies to mitigate risk, from avoidance to tailoring nutrients to facilitate optimized function of endogenous enzymes responsible for metabolic detoxification; (3) the puzzling piece of dietary diversity and whether it helps or negatively effects body weight; (4) the pleiotropic pathways of plants and how they can have multiple actions at the level of cell signaling and protein kinase modulation to induce, sensitize, or decrease dysfunctional metabolic signals; (5) how seasonality (circadian rhythm, shift work) impacts one's eating pattern and propensity toward obesity and metabolic syndrome; and (6) the relationship between food and mood, specifically noting that obesity increases the incidence of anxiety and mood disorders (37) and that, conversely, eating a healthy, whole, plant-based diet, such as the Mediterranean Diet, may help with reducing depression and encourage well-being and satisfaction (38).

Translating the science of nutrigenomics into practice

A great deal has changed in the nutrigenetic testing environment since the first nutrigenetic tests appeared in the early

2000s. The past two decades have seen exponential growth in the number of genetic testing companies in the marketplace. Direct-to-consumer companies such as 23andMe, Ancestry.com, and Helix personify how the consumer market has been captured with low-cost tests and high-technology, consumer-friendly user interfaces. What is missing from this conversation is the use of practitioner-based nutrigenetic tests and the role of the health professional in their execution. Only a small percentage of genetic tests are being sold through health practitioners, yet countless publications have identified the health professional as key to the delivery and translation of nutrigenetic tests. The possible reasons that health professionals have not taken ownership of the growth, translation, and utilization of nutrigenetic tests may reside on the following: (1) the methodology driving nutrigenetic test development (nutrigenetics vs nutrigenomics, associations, interactions and nutritional biochemistry, scientific and clinical validity); (2) the professional development of health practitioners as nutrigenomics experts (professional associations, accreditation and certification); (3) a scarcity in credible nutrigenomic education opportunities (inclusion in undergraduate curricula, postgraduate diplomas and degrees, and continuing education); (4) a network and community of practice to support and connect practitioners across all disciplines; and (5) a mentorship program to support practitioners through the experience of the clinical translation. Until such time as a comprehensive nutrigenomic solution is made available to health professionals, direct-to-consumer companies will continue to monopolize the market. Health professionals need to be able to evaluate the credibility of genetic tests being offered providing explanation of the genetic results based on their knowledge derived from evidence-based learning, and application of clinical translation. These skills are necessary to ensure that the best value is extracted from nutrigenetic tests in an ethical and responsible manner.

Metabolic adaptability of genetic and nutritional responses: Personalizing longevity

As the science of genomics continues to develop and unravel the nuances in chemistry and biology that underpin the etiology of diseases, clinicians and health care providers need to not only understand but articulate this emerging science and understand its value at the point of clinical care in order to create effective and personalized treatment strategies. There is a need to understand too the foundational concepts of epigenomics, the reversible modifications on a cell's RNA, DNA or histones, in order to develop a personalized approach for the assessment and treatment of conditions with epigenetic etiologies, especially regarding cellular aging and inheritance. This positions nutrition and gene interaction to benchmark longevity and chronic disease/condition progression. Aging is a natural process that involves a decline in many physiological functions and eventually results in death. Extensive research is being performed in order to elucidate the biology of aging, which emphasizes that lifestyle and genetic factors play an important role in human longevity by protecting against age-related chronic diseases such as cancer, cardiovascular disease, and dementia. Evolutionary conserved nutrient-sensing pathways mediate the effects of dietary composition, genes, the risk for chronic disease development, and longevity (39). Quantity and quality of dietary intake, sedentary lifestyle, and genetic susceptibility all contribute to an increased risk of comorbidities for the overweight and obese. Obesity contributes to pathogenesis for a variety of diseases and conditions, including cardiovascular diseases, type 2 diabetes, and certain types of cancer (40), together representing the most prevalent age-related diseases. When food intake is reduced (by dietary restriction or fasting), organisms live longer than when fed a normal diet (41).

A similar effect is seen when the activity of nutrient-sensing pathways is reduced by mutations that reduce the incidence of age-related loss of function and disease, including tumors and neurodegeneration, and increase life-span in model organisms of aging (42). Tumors and diabetes are also uncommon in humans with mutations in the growth hormone receptor (43), and natural genetic variants in nutrient-sensing pathways are associated with increased human life-span (44). Data from centenarians indicates a progressive delay in the age at onset of physical and cognitive function impairment, age-related diseases, and overall morbidity with increasing age, and the relative period of time spent with disease was lower with increasing age in centenarians (45). Genetic variations associated with improved nutrient metabolism may explain some of the health benefits observed in centenarians, while people with exceptional longevity are not distinct in terms of lifestyle factors from the general population, suggesting that people with exceptional longevity may interact with environmental factors differently than others (46). Data from Blue Zones (longevity "hotspots" around the globe), including the Seventh Day Adventists in Loma Linda, California, further emphasize the role of nutrition in modulating health span. Commonly observed combinations of diet and other lifestyle choices (exercise, body mass index, smoking status, etc.) account for increases in life expectancy of up to 10 years (47). Despite their geographical differences, all Blue Zones have diets in common that are (1) mostly plant-based, including fish and high intake of nuts, (2) low in animal-based protein and saturated trans fats, and (3) high in complex carbohydrates derived from plant-based sources (48). These findings identify a dietary pattern, often referred to as "Mediterranean diet," consistently associated with the lowest death rates and the greatest survival rates (49–51). Prospective and randomized clinical trials demonstrate that diets with low protein content enhance metabolic health, promote lean physical appearance, lower blood glucose, and decrease the risk of diabetes in humans (39, 52). A study population from the National Institutes of Health–AARP (American Association of Retired Persons) Diet and Health Study cohort of half a million people aged 50 to 71 years at baseline further supports these findings (53): Men and women in the highest vs lowest quintile of red and processed meat intakes (estimated based on a food frequency questionnaire administered at baseline) had elevated risks for overall mortality, cardiovascular disease, and cancer mortality.

The "fasting-mimicking diet" (FMD), a periodic, short-term, low-calorie, and low-protein dietary intervention, is a nutrition-based program focused on health and longevity (54–58). The FMD promotes cellular protection, regeneration, and rejuvenation of multiple organs and systems in old mice, thereby reducing chronic disease incidence and extending health span. In a randomized crossover-style clinical trial that included 100 generally healthy participants, the FMD reduced body weight and trunk and total body fat, lowered blood pressure, and decreased insulin-like growth factor (IGF-1) in all subjects who completed the trial. A post hoc analysis demonstrated that biomarkers associated with cardiovascular disease risk such as body mass index, blood pressure, fasting glucose, triglycerides, total and LDL cholesterol, and C-reactive protein were more beneficially affected in participants at risk for disease than in subjects who were not at risk (58). In the main, biogerontology research links nutrition, genes, chronic disease, and longevity and thereby provides the foundation for nutrition-based approaches to prolong healthy aging.

Neurocognition personalized: Alzheimer's disease and neurocognition genomics

The limitations to care for clinicians that have access to their patients' genomes resides on the context that only a small percentage of the genome could be used because such data come from association studies, which tend to identify variants with small effect sizes and have limited applications for health care. Individuals have variations in the composition of their genetic characteristics (factored on strategies that embrace testing for candidate-genes and genome-wide association) that will affect the availability of functional proteins, which ultimately impacts functional homeostasis and the outcome of drug therapy. The brain reflex-receptor mechanism in signaling for biomarkers and availability of enzymes for metabolism is of critical importance here. Biomarkers can be generically defined as *unique characteristics that can be objectively measured as indicators of a biological or pathological process or pharmacological response to a therapeutic intervention*, which then qualifies them to be potentially used across the whole translational medical research process. Biomarkers are therefore touted as the next frontier in the realm of modern medicine as they would represent the essentials in guiding treatment decisions that could enable complementary matching of specific drugs with individual patients, effective patient therapeutic dose, and management of drug-related risks (16, 18, 59). Neurocognition is of great interest given the fundamental role that the brain reflex receptor mechanism plays in controlling dynamic equilibrium. Developments in the foundational concepts of nutrigenomics and pharmacogenomics would empower and foster an effective personalized approach for the assessment and treatment of neurocognitive conditions including Alzheimer's disease, autism spectrum disorders, and mood disorders. Neural, endocrine, and metabolic mechanisms are also critical mediators of the microbiome-CNS signaling, which are more involved in neuropsychiatric disorders such as autism, depression, anxiety, and stress. The integrity of the microbiome in CNS disorders will remain a cornerstone for developing novel prognostic and therapeutic avenues for CNS disorders.

Alzheimer's disease and neurocognition genomics

Dementia globally is a leading cause of death, more prevalent than breast cancer, and has a spiraling yearly cost of over US$800 billion to society. However, recent observational studies have shown that mild cognitive impairment and early dementia can be reversed using a variety of modalities including diet, lifestyle interventions, and supplementation that address many of the known underlying contributing factors to Alzheimer's disease. While globally addressing potential risk factors based on laboratory data such as homocysteine levels, vitamin B12 and vitamin D levels, free T3 levels, and hormone levels has proven beneficial, genomics allows for not only better understanding of the pathophysiology of cognitive impairment but also personalization of a protocol for the reversal of cognitive impairment utilizing diet, exercise, hormone replacement when appropriate, and supplementation Apolipoprotein Eε4 (ApoEε4) is the most well recognized genomic risk factor for Alzheimer's disease. Looking at how ApoEε4 contributes to and interacts with inflammation, clearance of amyloid beta, phosphorylation of Tau, elevations of TNF-α and many other pathways can help facilitate better understanding of the pathophysiology of Alzheimer's disease. At present, looking at known genomic risk factors with published odds ratios showing combinatorial or independent Alzheimer's disease risk allows for personalization of a prevention and intervention strategy. As a combination of a highly disciplined nutritional approach (generally mild ketosis using mostly plant-based sources of fat) along with targeted supplementation and lifestyle interventions are applied, Alzheimer's disease progression can be prevented and often reversed with measurable improvements in cognition and function (60, 61).

In addressing the genomics of Alzheimer's disease, it is important to understand how genes interact. In addition to risk SNPs, the importance of benefit SNPs that have been shown to decrease risk by helping to increase heat shock proteins and other amyloid-clearing pathways as well as SNPs that decrease inflammation in the brain should not be overlooked. The role of non-inflammatory pathways such as brain-derived neurotrophic factor (BDNF) have also been made clear via genomics studies, and addressing these "non-classic" genomics risk factors such as BDNF and nutrient levels (zinc, choline, and magnesium) can further contribute to positive outcomes for affected individuals. In addition to understanding the science behind the genomics and nutrigenomics of Alzheimer's disease in this disease state, understanding the current laws surrounding genomics privacy is of particular import. Individuals are theoretically protected against health care discrimination based on genomics due to GINA (The Genetics Information Non-discrimination Act of 2008), but there are some caveats to this legislation. GINA only prohibits insurance companies and employers with >

15 employees from acquiring results of genetic tests. There is no law protecting genomic information from being used for discrimination when it comes to long-term care or life insurance policies. Knowledge of genomics law is important so that patients can be properly counseled and consented before a genomics interpretation tool is utilized and also so discussion can be made of where genomics is documented (when does it belong in the electronic health record vs being kept as part of an individual's private records that are not affiliated with any health insurance records or official documentation that can be utilized for discrimination?). It is also immensely important that if practitioners are going to obtain genomic information, they feel competent to counsel patients on how food, lifestyle, supplements, and medications can interact with their genome so that they feel empowered not doomed by their genomic data and understand that "their genomics is their history, not their destiny." In the case of Alzheimer's disease and cognitive impairment, working with an experienced clinical nutrition specialist or dietitian is often key to success since so many of the targeted potential intervention strategies involve changing diet and nutrient intake.

Food, mood, and metabolism

The use of personalized nutrition to optimize diet for individuals based on genetic variation, environment and needs to incorporate the added value of personalization beyond standard "healthy" advice that includes knowledge of differential responses to diet and variations in metabolome associations across phenotypes. Notable examples can be deciphered from the different patterns of key energy metabolism systems in response to polyunsaturated fatty acid manipulation in an animal model of metabolic syndrome compared to controls. Rats differentially bred for aerobic capacity yielded a "fit" phenotype and a metabolic syndrome-like phenotype (62). When both lines were fed either a high omega-6 or a high omega-3 diet that were otherwise identical in macronutrient composition, emerging results indicate that dietary interactions affected plasma leptin, ghrelin, adiponectin hormones, and the orexigenic cocaine amphetamine related transcript in the hypothalamus (62). These data demonstrated the ability of the same diet to have opposing effects in metabolically diverse phenotypes. In an observational analysis of 91 individuals with bipolar disorder and 76 non-psychiatric controls, all subjects maintained a 7-day diet record under the guidance and curation of a certified nutritionist and records were extracted into nutrient components using the Nutrition Data System for Research (NDSR, University of Minnesota); significantly lower intake of polyunsaturated fatty acids and variant linoleic acid metabolism were observed in in individuals with bipolar disorder. There was a significant association between dietary and plasma levels of linoleic acid and burden of disease measures in bipolar individuals (63, 64). In a follow-up study, the microbiome of the stools of individuals with bipolar disorder compared to controls found community- and species-level differences that also associated with polyunsaturated fatty acid intake and burden of disease measures (65). These data suggest that the gut microbiome may mediate effects of dietary linoleic acid on mood disorders.

To take the context of the gut microbiome further, an interesting and unique view of the gut ecosystem is depicted in Figure 4 (66). This presents a multifunctional redundancy of intrinsic property of an environment that is subject to fluctuations. The authors argue that the gut microbiota stability may be affected within a temporal framework and, in this context, bacteria turnover is a healthy feature expected in the gut. In order to ensure stability in the face of constant disturbance, microbiota species are continuously interchangeable by means of the metabolites produced by the action of gene products contained in the gut bacteria. Microbial genes and proteins and their metabolites in the gut grow from a simple structure in early life—usually dominated by bifidobacteria—to a complex structure in adults.

Microbiota species are interchangeable in terms of functions by means of the metabolites produced by the action of gene products contained in the gut bacteria. Metabolites produced by the action of microbiota are the downstream product of gene expression and metabolic activity and, therefore, they can be considered as a final output within the functional hierarchy. Metabolomics can thus provide a reliable snapshot of the actual functional state of the gut ecosystem. According to the model and the functional redundancy concept, the gut ecosystem is formed by a super species with a very large genome, composed of widely divergent microbial lineages whose genomes contain functionally similar sets of genes (represented by triangles) that would give rise to a coordinated single metabolic outcome (represented by circles). The diversity and abundance level of microbes, genes, proteins, and metabolites will influence energy balance, gut motility, inflammatory tone, mucosal integrity, appetite, and signaling, to cite but some. Also, note that the gut key player (i.e., pathogens) may also negatively influence the gut barrier, promoting inflammation (see components in the lower part of the figure) (66).

Besides considering microbial composition and function, it is important to consider, over time, the contribution of resistance (no changes in microbiota composition after being subjected to disturbance), resilience (restoration of the initial composition after disturbance), and functional redundancy (recovering of the initial function despite compositional changes). These modifications are produced along a continuum and are shaped by age, geography, lifestyle-related factors, and medication. For instance, redundancy in the infant gut may be higher than that found in the adult gut. Ongoing longitudinal studies are leveraging personal dense dynamic data (PD3) clouds (67) being collected from thousands of individuals. Most studies to date are designed to assess differences between means of groups stratified by a small number of features (treatment, phenotype, disease, etc.), if all other human heterogeneity is accounted for by randomization. However, this is unlikely enough for predictive value for the individual since similar clinical phenotypes may result from very different biological perturbations across individuals. The longitudinal PD3 clouds include clinical chemistries, metabolomics, proteomics, microbiomics,

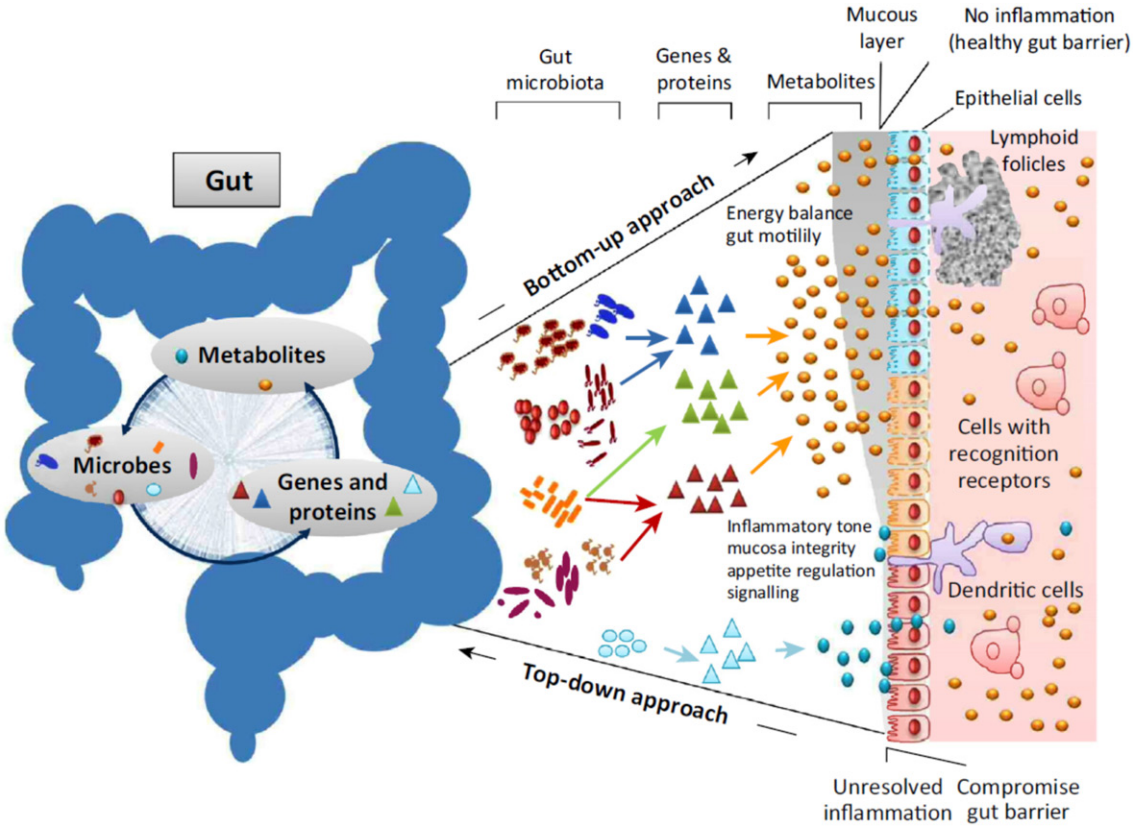

Figure 4. Model representing functional redundancy in the gut ecosystem. Microbiota species are interchangeable in terms of functions by means of the metabolites produced by the action of gene products contained in the gut bacteria. Metabolites produced by the action of microbiota are the downstream product of gene expression and metabolic activity and, therefore, they can be considered as a final output within the functional hierarchy. Metabolomics can thus provide a reliable snapshot of the actual functional state of the gut ecosystem. According to the model and the functional redundancy concept, the gut ecosystem is formed by a super species with a very large genome, composed of widely divergent microbial lineages whose genomes contain functionally similar sets of genes (represented by triangles) that would give rise to a coordinated single metabolic outcome (represented by circles). The diversity and abundance level of microbes, genes, proteins, and metabolites will influence energy balance, gut motility, inflammatory tone, mucosal integrity, appetite, and signaling, to cite but some. Also, note that the gut key player (i.e., pathogens) may also negatively influence the gut barrier, promoting inflammation (see components in the lower part of the figure) (66).

and genetics in order to follow everyone in high dimensional space. The systems biology approach can enable the understanding wellness states and identify wellness to disease transitions far before symptoms emerge so that relevant perturbed biological networks can be identified and targeted for reversal to wellness states. As observed by Simon Evans, the work supports the development of scientific wellness and its assimilation into predictive, preventative, personalized, and participatory health care of the 21st century. It is becoming very clear that autoimmune disease is a complex entity and may represent the result of a "perfect storm" of biological and environmental factors and that a systems-biology approach, utilizing a wider-lens perspective, will be required as these subjects are approached clinically.

Applying molecular DNA technology in the assessment of the gastrointestinal microbiota as part of an integrative approach to autoimmune disease

With the steady increase in the incidence of virtually every autoimmune disease occurring in the Western industrialized world, and standard treatment still relying mainly on symptom control using overt immune suppression which carry

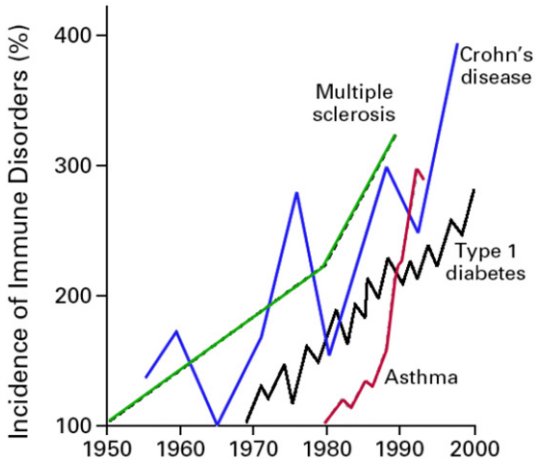

Figure 5. Rising incidence of autoimmune disorders (68).

significant side effects, clinicians are rightly looking for any advantage in the prevention and upstream management of autoimmune disorders.

The rising incidence of autoimmune disorders including multiple sclerosis, Crohn's disease, type 1 diabetes, and asthma is shown in Figure 5 (68, 69). With the concomitant explosion of research into the microbiome, and more

Table 1. Selected Predictive Antibody Tests (80).

Disease/Disorder	Autoantibody Tests	Positive Predictive Value	Years Prior to Clinical Diagnosis
Addison's disease	*Adrenal cortex antibodies	70%	10
Celiac disease	*Anti-tissue transglutaminase	50%–60%	7
	*Anti-endomysial antibodies	50%–60%	
	*HLA-DQ2 or DQ8 antigens	100%	
Hashimoto's thyroiditis	*Anti-thyroid peroxidase antibodies (postpartum)	92%	7–10
Primary biliary cirrhosis	*Anti-mitochondrial antibodies	95%	26
Rheumatoid arthritis	*Rheumatoid factor	62%–88%	14
	*Anti-cyclic citrullinated peptide	97%	
Scleroderma	*Anti-centromere antibodies	100%	11
	*Anti-topoisomerase I antibodies		
Sjogren's syndrome	*Anti-Ro and La antibodies	73%	5
Systemic lupus erythematosus	*RNP, Sm, dsDNA, Ro, La, and cardioliptin antibodies	94%–100%	7–10
Type I diabetes	*Pancreatic islet cell *Insulin	43%	14
	*65 kD glutamic acid decarboxylase	55%	
	*Tyrosine phosphatase-like protein	42%	
		29%	

specifically the gastrointestinal microbiota (GM), showing linkages between specific aberrant patterns (signatures) of dysbiosis and greater prevalence of specific chronic complex metabolic diseases, including autoimmune conditions, there is a natural desire to understand why these relationships may exist, whether they are simply associations or causal, and what mechanisms may underlie such relationships.

Examples of epidemiologic associations between gastrointestinal microbes and systemic autoimmune pathology include *Klebsiella:* ankylosing spondylitis; *Citrobacter, Klebsiella, Proteus,* and *Prevotella:* rheumatoid arthritis; *Bacteroidetes spp.:* arthritis in general; *Fusobacterium:* systemic sclerosis; *Mycobacteria:* psoriasis and Crohn's disease; *Yersinia:* Graves' disease and Hashimoto's disease; *Streptococcus:* pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS); *Chlamydia, Salmonella, Shigella, Yesrsinia:* reactive arthritis; *S Pyogenes:* rheumatic fever; *Camphylobacter jejuni:* Guillain-Barre syndrome; and *E coli, Proteus:* autoimmunity in general (70). PANDAS occurs when the immune system produces antibodies, intended to fight an infection, and instead mistakenly attacks healthy tissue in the child's brain, resulting in inflammation of the brain (basal ganglia section) and inducing a sudden onset of movement disorders, neuropsychiatric symptoms, and abnormal neurologic behaviors. Bacterial organisms in the GM may contribute to immune dysregulation and potentially the development of an autoimmune disorder in an individual by mechanisms that includes include gastrointestinal microbial-induced imbalances in Th17/Treg balance, molecular mimicry, and modulation of host proteins (71–75).

The hygiene hypothesis and changes in early environmental antigen exposure was postulated and briefly explored as a contributing factor in the emergence of the autoimmune epidemic in the Western industrialized societies (76). The various available testing methodologies for evaluation of the gastrointestinal microbiota was discussed and contrasted, including culture-based, next-generation sequencing (molecular) and quantitative PCR (qPCR; molecular) methods. The inherent limitations of culture-based methods (i.e., limited ability to assess anaerobic microbes and growth of microbes in transit after sample collection), and the strengths and weaknesses of next-generation sequencing microbiome versus a more targeted clinical/diagnostic-based qPCR method which quantitates the DNA of organisms was explored from the perspective of the clinician (77). Of interest, the culture-based methods are falling by the wayside, while next-generation sequencing testing may be most appropriate for research into the compositional signatures of the microbiota in various cohorts of subjects and quantitative molecular methods (qPCR) especially suited in helping clinicians to make clinical interventional decisions with individual patients. New opportunities for proactive screening for at-risk subjects for autoimmune disorders such as rheumatoid arthritis, ankylosing spondylitis, inflammatory bowel diseases, diabetes, multiple sclerosis, lupus, and others using emerging predictive antibody testing was reviewed and discussed from the perspective of the clinical nutritionist and the nutritionally minded physician. The various established predictive antibodies by disease, and their relative positive predictive value, are outlined in Table 1. Clinical experience suggests that the use of these testing methods can be more valuable if used in a truly predictive manner in patients with family history of autoimmune disease versus in a confirmatory fashion only after disease is suspected based on overt clinical presentation (78–80). Integrative medicine clinicians from various professional backgrounds and fields, including clinical nutritionist and the nutritionally minded physician, are encountering an ever-growing population of patients/clients with autoimmune-related disorders, especially women, who are seeking complementary care. These patients/clients are usually also receiving primary disease management from specialists such as rheumatologists. Health care providers of all types need to understand both benefits and risks of standard interventions as well as those of the evidence-based complementary and integrative approaches available. The autoimmune disease is a complex entity and may represent the result of a "perfect storm" of biological and environmental factors and that a systems-biology approach, utilizing a wider-lens perspective, will be required as these subjects are approached clinically (80). In the foregoing discussions, the reader can be aware that science and technology have lead the way to growing number of targeted therapies. Genetic disposition, environment and diet can turn genes on and off by modifying DNA (concept of a

process widely recognized as epigenetics). Where genes are turned on or off it is possible to modify a disease by targeting specific genetic mutations. Seminal references (81–90), are instructive in that they point to emerging bioinformatics world to foster awareness and the understanding of genomic information. For the consumer and patients there is need to embrace care and health management through new targets for pharmaceuticals and functional foods.

Conclusion

Genomics is a powerful tool that can help with the delivery of personalized medicine and personalized nutrition. Nutrigenetics/nutrigenomics conceptualize the research into the "relationship between genes and nutrients from basic biology to clinical practice." By understanding how genes alter the body's response to nutrition or how nutrition alters the body's response to defective genes, scientists are unlocking the codes to health and longevity. Profiling of genetic nutritional responses can help in the determination of which specific foods that give the best biological response, based on an individual's DNA. Nutritional genomics aims to develop a rational means to optimize nutrition through the identification of the person's genotype, and this defines the relationship between nutrients and human health. Individuals cannot change their genetics, but they can eat the right foods to support genetic predispositions and take the right supplements to support gene variations and promote normal cell function and structure. Poor diet can be a risk factor of disease. The understanding of the gut microbial community (from composition to functional perspectives), needs to be interwoven with genomic cross talk with active gene expression, protein synthesis (enzyme availability), and metabolism. Given that dietary components can alter gene expression, practitioners need to now understand that the degree to which diet influences health and disease depends upon an individual's genetic makeup. The advancement in the use of pharmacogenomics technology must continue to be defined and embrace diagnostic, prognostic, predictive characteristics of diseases benchmarked on variabilities of respective biomarkers. A network-biology approach depicting the gut microbiota is a constant reminder to practitioners that the continuously changing in the gut environment can help envision health as a reflection of the diversity and composition of gut microbiota and its metabolic status. The evidence based-outcome of discussions throughout the 2018 American College of Nutrition conference focused on "Personalized Nutrition: Translating the Science of NutriGenomics Into Practice." The reader is referred to the guidelines pertinent to pharmacotherapy, drug development (and with a context that potential impacts nutrition from the standpoint that the food already contain biomolecules that have to become systemically bioavailable in order to exert biopharmacological effect), and pharmacogenomics, available at the following U.S. FDA link: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM337169.pdf. The document refers to the presence of pharmacogenomics in premarket investigations and drug labeling and provides guidance and recommendations on when and how genomic information should be considered to address questions arising during drug development and regulatory review, including study design, data collection, and data analysis in early-phase trials. While the promise of pharmacogenomics in global health care and nutrition care needs is becoming apparent, there is need to ensure pharmacogenomics literacy. The net outcome would be that nutritionists, dietitians, doctors (physicians of all categories), nurses, pharmacists, and all health care professionals will have the knowledge base to both counsel and advise patients. The vein is to provide individuals with lifestyle recommendations that will help them enjoy optimal health and the highest possible quality of life.

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