Nutrigenomics: The Potential to Optimize Chronic Disease with SNP-Based Dietary Recommendations

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Abstract

In the individual, diet/nutrient-gene interactions are significantly impacted by common DNA sequence variations called single nucleotide polymorphisms (SNPs). SNPs alter the expression or activity level (ie, the Michaelis constant, K_M) of gene products, resulting in altered metabolism of and altered dietary requirements for nutrients, and can increase disease risk. However, whether one's genetic potential for health or harm will manifest as a phenotype is decided by the interplay among genes, diet, and lifestyle. Genes determine the range of possibilities, but nutrition and lifestyle choices significantly impact which genetic options are expressed and thereby influence whether individuals attain the optimal, normal, or detrimental potential in their genetic inheritance.

Nutrigenomic profiling can already identify SNPs that underlie individual variations in key nutrient requirements, as well as the likelihood of a positive response to specific dietary interventions. This article provides an introduction to several SNPs with well-documented effects on nutrient requirements and suggests how clinicians might begin to utilize the available data in this rapidly developing field to meet patients' unique needs.

Editor's note: *Please see the glossary at the end of this article for a more complete definition of the specialized vocabulary contained in the text.*

Nutrigenomics is the study of the bidirectional interactions between nutrients and genes. In the individual, the interactions between diet/nutrition and genes are significantly impacted by "common" (ie, present in at least 1% of the population) DNA sequence variations called single nucleotide polymorphisms or SNPs (pronounced "snips"). SNPs alter the expression or activity level (ie, the Michaelis constant, K_M) of gene products, resulting in altered metabolism of and altered dietary requirements for nutrients.[1] The K_M refers to how well and how easily an enzyme binds to its target. SNPs result in the production of enzymes with poorer binding affinity and therefore less activity (a decreased K_M).

Nutrigenomic research has revealed that human health and disease are shaped by a nature-meets-nurture etiology: SNPs that affect the activity of genes involved in basic cellular metabolism, maintenance, and repair functions can increase the risk of developing a disease. Yet, in most cases, having inherited a particular genetic variant or SNP connotes only susceptibility to a related pathological process. Whether one's genetic potential for health or harm will eventually manifest as a phenotype is decided by the interplay among genes, diet, and lifestyle.

Stated in another way, genes may determine the range of possibilities for function, but nutrition and lifestyle choices, such as smoking and alcohol consumption, significantly impact which genetic options are expressed, thereby influencing whether individuals will attain the optimal, the normal, or the detrimental potential in their genetic inheritance. Hence, where the "tire" of an individual's genetic inheritance hits the day-to-day "road" of diet and lifestyle determines whether the body's physiology is driven toward health or disease.[2,3]

Neither the current recommended dietary intakes (DRIs) nor most nutrition research reflects nutrigenomic understanding. In addition to the fact that the original DRIs were developed to prevent diseases of overt deficiency, a basic assumption underlying both the subsequent DRIs and most nutrition studies has been that all persons have "average" dietary requirements—yet, even in its relative infancy, nutrigenomic research clearly indicates this is not the case.

Nutrigenomic profiling identifies important SNPs that underlie individual variations in key nutrient requirements. Profiling also identifies the likelihood of a positive response to specific dietary interventions, which can enable the informed clinician to target those diet and supplement recommendations that are most likely to help prevent chronic degenerative disease and optimize health. Thus, nutrigenomic science has set a new standard. Merely avoiding deficiency is no longer an acceptable end goal.

This article provides an introduction to several SNPs with well-documented effects on nutrient requirements and a summary of a recent dietary and supplement intervention trials that suggests how clinicians might begin to use available data in this rapidly developing field to meet patients' unique needs.

How SNPs Impact Dietary Requirements

A substantive amount of research has confirmed that SNPs affecting folate metabolism, methylation, and the body's ability to utilize vitamin D also impact disease risk and that the potentially negative effects of such polymorphisms can be ameliorated by dietary recommendations and nutrient supplementation. Following is a discussion of several of these key SNPs.

Polymorphisms affecting folate requirements

MTHFR 677C→T

One of the most researched examples of a diet-SNP interaction involves the common (approximately 30% to 40% incidence) 677C→T (cytosine to thymine substitution) polymorphism of

the methylenetetrahydrofolate reductase (MTHFR) gene, which codes for a slow variant of the MTHFR enzyme, in which valine is substituted for alanine at position 222 and results in a reduction in enzyme activity. [1,4-6]

In subjects with the homozygous TT variant of the MTHFR genotype, the MTHFR enzyme has approximately 50% of the catalytic activity of the homozygous CC MTHFR wild type (the common genotype), whereas the heterozygous CT genotype has approximately 65% of the wild type's catalytic activity.[7-9]

This decreased enzymatic activity results in a reduced capacity to use folate to convert homocysteine to methionine and thence to S-adenosylmethionine (SAMe). Among its critical activities, SAMe, the universal methyl donor for a wide variety of biological substrates, plays a key role in the maintenance of genomic methylation patterns that determine gene expression and DNA conformation. SAMe is also necessary for the synthesis of myelin; membrane phospholipids; and the monoamine neurotransmitters serotonin, epinephrine, and dopamine; as well as for utilization of the antioxidant glutathione via glutathione S-transferase. For these reasons, folate deficiency results in high plasma levels of homocysteine, a cardiovascular and neurotoxic risk factor, as well as global DNA hypomethylation, single- and double-strand DNA breaks, chromosome breakage, point mutations in *KRAS* (an oncogene whose mutation-related activation plays a key role in neoplastic progression, especially in colorectal, pancreatic, and lung cancers), and a decrease in neurotransmitter levels.[10,11]

Carriers of 677C→T, both CT and TT but particularly those who are homozygous for this SNP, are at significantly increased risk for coronary heart disease (+19%) and have double the risk of having a child with neural tube defects unless they consistently consume higher-than-"normal" (ie, DRI, recommended) amounts of folate-rich vegetables, such as spinach or asparagus, and/or supplementwith folate.[10,11]

Folate insufficiency, and the resultant decrease in SAMe and increase in homocysteine levels, also have been recently recognized as a significant risk factor for Alzheimer's disease and other dementias.[12,13] In addition, folate insufficiency is associated with depression, with approximately one-third of depressed individuals having outright deficiency.[14]

On the positive side, both of the MTHFR 677C→T variants increase production of the form of folate that can be used to make thymidine, 1 of the bases in DNA, thus preventing potentially mutagenic uracil from being incorporated instead. When the Physician's Health Study examined the association between MTHFR Ala222Val SNPs (another way of referring to 677C→T; the 677C→T transition in the *MTHFR* gene results in an Ala222Val [alanine to valine] substitution in the polypeptide chain) and plasma folate concentrations in regard to colon cancer risk in 202 colorectal cancer cases and in 326 cancer-free controls, the results indicated a lowered risk for both cancers in MTHFR 677C→T carriers who were folate sufficient. In men with normal folate concentrations (serum folate >3 ng/mL) who were homozygous for MTHFR Ala222Val (ie, 677C→T), the risk of colon cancer was one-third that found in carriers of the wild-type CC alleles. In men who were folate-deficient, however, this protection was absent.[15]

Glossary[1,2]

Allele: One member of a pair or series of different forms of a gene. The individual's genotype for that gene is the set of alleles it has inherited. Since humans are diploid organisms (possess 2 copies of each chromosome), each human gene contains 2 alleles.

Dietary Reference Intake (DRI): In the early 1990s, the Food and Nutrition Board replaced the Dietary Reference Intake (RDA) with the DRIs, a family of nutrient reference values that includes 4 components: the Estimated Average Requirement, the Dietary Reference Intake, the Adequate Intake, and the Tolerable Upper Intake Level.

Functionally significant single nucleotide polymorphisms (SNPs): Although approximately 4.5 million SNPs have been identified within the human genome, only a small fraction alter gene function or expression and, therefore, might impact phenotype. Of the approximately 10 000 SNPs located within the coding regions of genes that cause a change in the peptide sequence (and are therefore called non-synonymous SNPs or nsSNPs), approximately 10% to 15% are projected to be potentially damaging, ie, functionally significant. Among SNPs located within the promoter regions (which are called regulatory SNPs or rSNPs), much less research has been done, but most are not thought to affect the overall activity of the protein or the gene expression. Based on 20 transcription factor (TF) sites with known alterations in TF binding to DNA, 245 potential TF sites in homologous genes have been identified and are currently being investigated.[3,4]

Haplotype: A group of gene alleles on a single chromosome that are closely linked and typically inherited together.

Heterozygous: A SNP containing 2 different alleles, 1 of which is the typical sequence of bases, ie, the "wild type" allele, which produces the most common (normal) phenotype, and 1 of which is an atypical base sequence, ie, the less common allele, often called a "variant" or a "mutant" allele.

Homozygous: A SNP in which both alleles contain the same sequence of bases.

Michaelis constant (K_M): The part of a formula that describes the kinetics of most enzymes. With SNPs, it refers to the binding affinity of the enzyme (how well and how easily it binds to its target).

Phenotype: Those options within an organism's genotype that are actually expressed; any observable characteristic or trait of an organism, eg, physical appearance or physiological or biochemical properties.

Polymorphism: Existence of a gene in several allelic forms in a population.

Other research has shown that folate-replete 677C→T carriers have a 1.2- to 3.0-fold reduced risk for colorectal cancer and a 4.3-fold reduced risk for acute lymphocytic leukemia.[16]

Alcohol consumption, however, removes the reduction in risk associated with 677C→T homozygosity for these cancers. In fact, individuals homozygous for MTHFR 677C→T who consume large amounts of alcohol are at even greater risk than those without the T allele who consume similar amounts. This is likely attributable to the fact that individuals homozygous for 677C→T are less able to compensate for the depletion of 5-methyltetrahydrafolate caused by alcohol, which results in alterations in methylation patterns that can alter oncogene expression.[10] Those with 677C→T heterozygosity were not evaluated in this study.

MTHFR 1298A→C

A second well-studied and common polymorphism (incidence approximately 31%) in the *MTHFR* gene, the mutation of 1298A→C (adenine to cytosine substitution, which leads to the replacement of Glu-429 by alanine in the enzyme), also decreases enzyme activity but not to the extent of the 677C→T variant. MTHFR 1298A→C is associated with only 68% of the normal (wild-type) activity. Even homozygosity for 1298A→C (CC) by itself does not result in elevated plasma homocysteine or lower plasma folate concentration (both of which occur in individuals homozygous for 677C→T); however, compound heterozygosity for 677C→T and 1298A→C (resulting in 677CT/1298AC) produces a similar biochemical profile to homozygosity for 677C→T.[6, 10]

In relation to colorectal cancer risk, homozygosity for 1298A→C appears to confer a slight reduction in risk in individuals with high folate or methionine intake, with a greater protective effect occurring among those carrying both C677C→T (either form) and the homozygous 1298A→C alleles[10]

As Le Chatelier's principle predicts, especially in individuals homozygous for MTHFR 677C→T, high folate intake is associated with increased production of SAMe, decreased plasma levels of homocysteine, and increased methylation of promoter sites in and transcriptional activity of tumor suppressor and DNA repair genes. High folate intake can restore methylation capacity in carriers of either the 677C→T or 1298A→C alleles, but DRI recommendations for folate (400 mcg) are likely to be insufficient for these individuals.[5,16,17]

Riboflavin intake above the DRI also should be considered in carriers of *MTHFR* SNPs. Riboflavin is a central component of the cofactor flavin adenine dinucleotide (FAD). Synthesis of the active form of folate (5-methyltetrahydrofolate, the prevailing folate species in serum) is FAD–dependent. Nutrigenomic research has revealed the 677C→T variants of the *MTHFR* gene have lower affinity for their flavin cofactors than the wild-type enzyme, thus 677C→T carriers need higher concentrations of riboflavin for sufficient catalytic activity to produce adequate 5-methyltetrahydrofolate.[18]

The key clinical takeaway message is that the activity of the reaction catalyzed by the *MTHFR* gene—and therefore the risks associated with the lessened MTHFR activity seen in carriers of 677C→T—can be markedly modified by providing higher than "average" amounts of folate, the substrate for MTHFR, and its cofactor riboflavin. This idea was first proposed by Bruce Ames, PhD, in his seminal paper on SNPs that discussed decreased coenzyme binding affinity and related nutrient needs and was recently reemphasized by leading nutrigenomics researcher Michael Fenech, PhD.[10] Basic biochemistry and other studies suggest that not only vitamin B_2 (riboflavin), but vitamin B_6, vitamin B_{12} (cobalamin), and choline may also be needed to optimize MTHFR–related methylation capacity in carriers of MTHFR SNPs. Homocysteine is metabolized through 3 vitamin B–dependent pathways: 2 paths are through the remethylation and recycling of homocysteine as methionine—a reaction catalyzed either by the enzyme betaine homocysteine methyltransferase (in which the cofactor betaine is derived from choline) or through the vitamin B_{12}–dependent enzyme methionine synthase—and the third path is through homocysteine being removed from the remethylation cycle by undergoing irreversible B_6–dependent transsulfuration to form cysteine.[19]

Glossary (continued)

RDA: See "DRIs," above.

rs12325817: Yet another SNP–naming convention. See "SNP naming conventions" below.

SNP: A single-nucleotide polymorphism (SNP, pronounced "snip") is a variation in the DNA sequence in which 1of the purine bases (A = adenine and G = guanine) or pyrimidine bases (T = thymine and C = cytosine) within a single nucleotide in the genome has been replaced by a different base. For example, in the methylenetetrahydrofolate reductase (MTHFR) gene 677C→T variant, cytosine has been replaced by thymine at nucleotide 677 of the MTHFR gene. Each variant sequence, in this case the versions containing C or T, is called an allele: Almost all common SNPs have only 2 alleles. One will be common in the population—the "wild type"—whereas the other, less common variant, is called the "mutant type."

SNP–naming conventions: SNP nomenclature is still not fully standardized; thus, the same SNP can be given different identifiers. The identical SNP may be named by reference to the change in its bases, eg, MTHFR 677C→T, or by the changes that result in the enzyme it produces; in this case, the MTHFR 677C→T SNP would be labeled Ala222Val. Or an "rs" identifier may be used. The "rs" naming convention is that of the SNP database at the National Center for Biotechnology Information, which acts as a public domain archive for a collection of polymorphisms in various organisms. This database maps each submitted SNP assay to the genome and assigns to each submitted SNP assay a RefSNP accession ID (rs number) that corresponds to the position in the idealized genome where the variation can be assayed.

Polymorphisms affecting methylation via choline requirements

Two related SNPs affect the body's ability to utilize and synthesize choline: MTHFD1 1958G→A and PEMT *rs12325817* (–774 G→C).

MTHFD1 1958G→A

Choline is an essential nutrient necessary for brain development, cell membrane structural integrity and signaling functions, methyl group metabolism, and neurotransmitter synthesis. Dietary choline deficiency decreases SAMe concentrations in tissues, resulting in hypomethylation of DNA and effects on gene transcription, genomic imprinting, and genomic stability. Fetal rodent brains from mothers fed choline-deficient diets show decreased gene promoter methylation that alters neurogenesis in the hippocampus for life.[20,21] Maternal deficiency of choline during pregnancy has been associated with a 4-fold increased risk of neural tube defects. Humans consuming insufficient choline develop fatty liver and liver and muscle damage.[22]

Another very common SNP (incidence 0.50) in an enzyme involved in folate metabolism, cytosolic MTHFD1 1958G→A (cytosolic 5,10-methylenetetrahydrofolate dehydrogenase 1958 G→A [guanine to adenine substitution]), increases the demand for choline as a methyl group donor and thus increases susceptibility to choline deficiency and its associated risks—this increase is less for those with just 1 A allele (GA) and more so for those with 2 (AA). In a recent study, 54 adult men and women ate diets containing adequate choline and folate then consumed a diet containing almost no choline, with or without added folate, for either 42 days or until they were clinically determined to be choline deficient. (Criteria for clinical choline deficiency were an increase in serum creatine kinase activity [>5 times] or an increase of liver fat [>28%] after consuming the low-choline diet; this resolved when choline was returned to the diet.)

More than half of the participants became choline deficient within less than a month. Carriers of both variants of the MTHFD 1958G→A allele were significantly more likely than noncarriers to develop signs of choline deficiency on the low-choline diet (OR =7.0) unless they were also treated with a folic acid supplement. Premenopausal women who were carriers of MTHFD 1958G→A were found to have a 15-times increased susceptibility to developing organ dysfunction on a low-choline diet.[23]

PEMT rs12325817 (–774 G→C)

In addition to diet, a portion of the human requirement for choline can be met via endogenous de novo synthesis of phosphatidylcholine catalyzed by phosphatidylethanolamine N-methyltransferase (PEMT) in the liver. Another common choline-related SNP (incidence 0.74) is found in the *PEMT* gene. More than 98 polymorphisms exist in this gene, but only the SNP *rs12325817* [–774 G→C], a guanine to cytosine substitution, is known to be functionally significant.

Since PEMT is induced by estrogen, premenopausal women who are heterozygous for PEMT *rs12325817* (–774 G→C) have sufficient estrogen to overcome its effects; however, in postmenopausal women with lower estrogen levels, this SNP greatly increases susceptibility to choline deficiency and its attendant risks.[20, 24]

Polymorphisms affecting vitamin D requirements

Vitamin D insufficiency has been shown to increase the risk for osteoporosis; prostate, breast, and colon cancer; cardiovascular disease, and immune-related diseases including asthma, insulin- and noninsulin-dependent diabetes, multiple sclerosis, Crohn's disease, Graves disease, and Addison's disease.[25-28] Vitamin D concentration can be impacted by vitamin D–receptor SNPs, including the restriction fragment length polymorphisms [RFLPs] BsmI, ApaI, TaqI, and FokI, which are found in the 3′-untranslated region (UTR) and the Cdx-2 polymorphism, which is found in the promoter area of the *VDR* (vitamin D [1,25- dihydroxyvitamin D3] receptor) gene.

VDR SNPs and Bone Health

The effects of VDR SNPs on bone metabolism, particularly in relation to osteoporosis risk, have received the most attention. In the initial studies on VDR polymorphisms and bone, the mutant or less common variant of the BsmI SNP, specifically BsmI BB, was associated with lower bone mineral density (BMD). However, most later studies have found no effect when looking at the BsmI, ApaI, and TaqI RFLPs singly but have noted an effect when looking at patterns of haplotypes combining these 3 adjacent RFLPs.

Overall, the research strongly suggests that the interindividual variability in intestinal absorption of calcium is dependent on VDR genotype. Carriers of the B(At) haplotype (BsmI B-allele, ApaI A-allele, and TaqI t-allele), which results in lower VDR activity, are at risk for decreased intestinal calcium absorption. So are carriers of the "f" allele, the variants of the FokI RFLP. The Ff and ff expressions do not appear to be linked to that of the other 3 RFLPs, so the f allele continues to be treated as a separate marker with individual effects.

Other associations for VDR SNPs have also been noted, including that the b allele (in the baT haplotype) has been associated with increased height. A positive association is that the A allele of the Cdx-2 A→G polymorphism appears to be protective: carriers of this SNP express higher levels of VDR in the intestine, resulting in higher calcium absorption and lessened risk for fracture. The G allele of this SNP, however, results in decreased transcription-factor binding activity and was associated with a 10% decrease in lumbar spine BMD in postmenopausal but not in premenopausal women.

VDR SNPs and Cancer

Prostate cancer: Vitamin D_3, acting directly through the VDR, is a key hormone involved in the regulation of cell proliferation in the prostate, and VDR polymorphisms can result in partial or complete resistance to vitamin D.[29] Striking associations have been noted between prostate cancer incidence and sunlight/ultraviolet (UV) exposure (expressed as latitude), leading to a significant amount of research investigating a relationship between VDR polymorphisms and prostate cancer. Nine studies have shown an association between BsmI, ApaI, and TaqI haplotypes and prostate cancer risk. Seven studies identified the baT haplotype as the risk allele, whereas, in 2 others, the BAt haplotype was associated with increased risk. In all cases, risk

associations were increased in subjects with low vitamin D levels.[26] Although not tied to specific *VDR* SNPs, small clinical trials have shown that supplementation with vitamin D_3 can slow the rate of prostate specific antigen rise in prostate cancer patients, demonstrating proof of concept that vitamin D_3 supplementation may be clinically effective in prostate cancer therapy.[30]

Breast cancer: Similar associations have been seen for breast cancer. Five studies involving a total of 1719 women identified the baT haplotype, and 3 studies involving a total of 875 women identified the BAt haplotype as the risk allele.[27]

When investigated singly, neither the TaqI nor the FokI polymorphisms have been found to increase the risk of breast cancer, although an association was noted between TaqI polymorphism and the risk of metastases. However, the BsmI SNP was associated with increased risk in 3 reports, and all the studies performed so far investigating a relationship between ApaI and breast cancer risk showed a link between this polymorphism and increased risk of malignant tumors.[26]

Studies measuring serum vitamin D metabolites in women who were followed up for many years indicate that low circulating vitamin D_3 levels are associated with increased breast cancer risk; thus, women carrying *VDR* SNPs associated with lessened vitamin D binding affinity may be at increased risk for breast cancer. Dietary and supplementation recommendations to promote endogenous levels of vitamin D_3 in the range of 75 nmol/L (30 ng/L) may have a protective function on mammary cells, thereby reducing breast cancer risk.[31]

Colorectal cancer: As early as 1980, a potential connection between vitamin D and colorectal cancer was noted, based on the observation that colon cancer mortality in the United States was highest in regions with the lowest amount of UVB exposure.[32] The link between colorectal cancer and sunlight exposure was later confirmed by several large studies comparing southern and northern parts of the United States. In an article titled, "Vitamin D as a Risk Reduction Factor for Colorectal Cancer," Grant and Garland suggest that 20% to 30% of colorectal cancer incidence is attributable to insufficient exposure to sunlight.[33]

Research on an association between BsmI-ApaI-TaqI haplotype polymorphisms and colorectal cancer suggests that the baT haplotype increases risk. In some studies, high levels of dietary intake of calcium and vitamin D have been associated with a reduced risk of colon cancer in BsmI BB *VDR* genotypes.[34,35] In the most recently published research, a case-control study of 250 cases and 246 controls, colon cancer cases were more frequently homozygous for the Cdx-2 A allele (9.2 vs 4.1%). Cdx-2 AA homozygotes were at significantly increased risk with an odds ratio of 2.27 after adjustment for age, sex, body mass index (BMI), nonsteroidal antiinflammatory use, and family history of colorectal cancer. Carriers of the FokI TT genotype were also at increased risk with an adjusted OR of 1.87. The 3-SNP Cdx-2-FokI-TaqI (A-T-G) haplotype also showed increased risk with an adjusted OR of 3.63.[36]

Of related interest is a study suggesting that postmenopausal hormone replacement therapy lowers colon cancer incidence via estrogen's activation of the VDR pathway and the resultant downregulation of inflammatory and immune-signaling pathways.[37] Treatment with soy isoflavones, eg, genistein, may have similar protective effects. In addition to its synthesis in the kidney, the antimitotic, prodifferentiating, and proapoptotic active metabolite of vitamin D, 1,25-(OH)(2)-D(3), is also produced via hydroxylation by colonocytes, which possess vitamin D–synthesizing (CYP27B1) and catabolic (CYP24) hydroxylases similar to those found in the kidney. Early in colon tumor progression, CYP27B1 and VDR expression increases, suggesting an autocrine/paracrine growth control in colon tissue as a physiological restriction against tumor progression. (Autocrine signaling is a type of cell signaling in which a cell secretes a hormone or chemical messenger that binds to autocrine receptors on the same cell, leading to changes in the cell. Paracrine signaling refers to the release of a hormone or messenger by endocrine cells into adjacent tissue rather than into the bloodstream.)

However, in human adenocarcinomas, expression of the catabolic CYP24 is also enhanced compared with adjacent normal mucosa. To maintain colonic accumulation of D_3, its catabolism needs to be restricted. In the rectal tissue of postmenopausal women, 17-beta-estradiol can elevate CYP27B1 expression. Phytoestrogens in soy, known to be estrogen receptor modulators, have been shown to decrease CYP24 expression. Both actions may underlie the observed protective effect of estrogens against colorectal cancer in women.[38]

Where the Nutritional Tire Meets the Genetic Road

A recent study found that using genetic information to personalize a patient's diet significantly improved weight management, resulting in better compliance, longer-term reductions in body mass index (BMI), and improvements in blood glucose levels. As part of their weight loss program, a group of patients (n=50, 22 female, 28 male) who had repeatedly failed at weight loss and were therefore attending a weight management clinic in Athens, Greece, were offered a nutrigenetic test that screened 24 variants in 19 genes involved in metabolism. Using algorithms to match characteristics (age, sex, frequency of clinical visits, and BMI at initial clinic visit), 43 controls were selected from other patients attending the clinic. BMI reduction and blood fasting glucose were measured at 100 and >300 days. All patients were put on a Mediterranean diet that was low in saturated fat and had a low glycemic load. After 300 days, individuals in the nutrigenetic group were more likely to have achieved and maintained weight loss (73%) than those in the comparison group (32%). Average BMI reduction in the nutrigenetic group was 1.93 kg/m^2 (5.6% loss) vs an average BMI gain of 0.51 kg/m^2 (2.2% gain) in controls. In those patients with a starting blood fasting glucose of >100 mg/dL, 57% (17/30) of the nutrigenetic group, but only 25% (4/16) of the control group, reduced levels to <100 mg/dL after >90 days of weight management therapy.[39]

Conclusion

We've long known that one man's optimal diet is another's route to disease, premature aging, and death—a seeming conundrum whose explanation is rapidly evolving as recent studies demonstrate gene-diet interactions so significant that they have lead to the creation of a new scientific discipline: nutrigenomics.

Food delivers not just calories, macronutrients, micronutrients, or antioxidant phytonutrients, but information. Food "speaks" to our genes, providing a snapshot of the state of affairs of the world in which we live. At the genetic level, the newscast provided by the foods we eat has a significant impact on what portions of our genome will be expressed, the phenotype we will display, how we age, and what diseases we develop.

As the above research indicates, the evolving field of nutrigenomics offers clinicians the possibility of truly personalizing and optimizing diet, supplement, and lifestyle recommendations to meet an individual's genetically unique needs. Currently available nutrigenomic testing analyzes key genes involved in the metabolism and transport of nutrients, removal of toxins, and protection from oxidation. Knowledge of the patient's specific pattern of genetic variation can greatly assist the clinician to provide genetically based recommendations that are most likely to optimize health and longevity.

For examples of the range of SNPs currently analyzed in nutrigenomic testing, see information about Genova Diagnostics (Asheville, North Carolina), sciona.com (Boulder, Colorado), and Suracell Inc (Montclair, New Jersey).

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