

Nutrigenetics — Building a Platform for Dietitians to Offer Personalized Nutrition **By Megan D. Baumler, PhD, RD, CD**

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Two men of the same age eat a diet low in fruits and vegetables and high in sodium and saturated fat. One develops hypertension, hypercholesterolemia, and eventually atherosclerosis, while the other lives a long life without such chronic disease. In another case, two postmenopausal women consume similar diets low in choline. One develops liver dysfunction due to the choline deficiency, but the other does not.

Why individuals experience different health outcomes even though they eat similar diets and practice comparable lifestyles is an important question that's been on the minds of nutrition and other healthcare experts in the medical community for decades. While it's long been suspected that genetics plays a critical role in determining how a person responds to dietary intake, only recently has research in the field of nutrigenetics demonstrated this.

Researchers hope that in the near future people will be able to receive personalized nutrition recommendations based on their genetic makeup to prevent chronic illnesses down the road such as cardiovascular disease and diabetes, known as polygenic diseases.

However, because there are several genes involved in the development of these and other polygenic illnesses, dietitians and other healthcare professionals don't fully understand the relationship between diet and disease risk, which stifles our ability to make personalized dietary recommendations as a preventive measure.

This continuing education course provides an overview of nutrigenetics field, discusses the evidence supporting the link between genotype and specific nutrient needs, and a reviews the current data highlighting the relationship between genotype and specific chronic diseases.

Nutrigenetics and Personalized Nutrition

Nutrigenetics is the study of the relationships among genes, diet, and health outcomes.¹ Nutrigenomics, a related but distinct field, is the study of how genes and nutrients interact at the molecular level. The field of nutrigenetics is relatively new. In 2003, the Human Genome Project, which identified all the genes in human DNA and determined the sequence of the 3 billion chemical base pairs that make up human DNA, was completed. Knowing the sequences of the human genome opened the doors to examine the relationship among an individual's genetic makeup, dietary intake, and health outcomes.

The excitement surrounding nutrigenetics stems from the notion that it's the foundation of personalized nutrition. Clearly, population-based dietary recommendations are helpful, but they

aren't adequate for all individuals since people respond differently to diets. Personalized nutrition bases dietary recommendations on genetic predisposition to disease. The idea is that once personalized nutrition is integrated into routine care, patients can be genotyped for specific genetic variations, made aware of their chronic disease risk and nutrient deficiencies, and given strategies to dramatically reduce their risk.

At present, personalized nutrition isn't widely practiced since genotyping doesn't occur routinely for polygenic diseases due to its lack of cost-effectiveness. A few private companies offer genotyping and personalized nutrition recommendations based on a handful of genetic variations, but whether this is effective in promoting health and preventing chronic disease hasn't been determined.

Interestingly, the genetic variation among individuals is minimal. Most people are approximately 99% genetically identical, with little variation in the roughly 3 billion base pairs that comprise the human genome.² However, this approximately 1% genetic variation leads to a wide variability of health outcomes, depending on dietary intake and other environmental exposures. Some of the genetic variation among individuals is in the form of single nucleotide polymorphisms (SNPs, pronounced "snips").

A SNP is the replacement of a single nucleotide (A, G, T, or C) in a gene sequence. If this replacement is in the part of the gene that codes for the protein product and if the replacement results in an amino acid substitution in the protein, then the SNP could result in a functional change in the protein. If the SNP is in the promoter area of the gene (the switch that turns the gene on and off), the codon replacement could result in a change in the expression of the gene.

People have two copies of each gene, thus people who have the SNP in both copies are likely to be more affected than people with one normal and one variant allele for the gene. The health consequences of the SNP depend on what the gene involved does. If the gene is important for metabolism, a functional SNP may result in a metabolic inefficiency (perhaps more nutrient precursor will be needed to make the desired product). If the gene with the functional SNP encodes for a hormone, the hormone may not work as well. Whether disease develops depends on the function that is perturbed.

Estimates show more than 10 million SNPs in the human genome exist; each individual has his or her own number and pattern of SNPs.³

Individual genetic variability affects a person's nutritional status in many ways. For example, a person's genetic sequence affects his or her nutrient requirements, energy utilization, appetite and taste, and risk of chronic disease in response to diet. Research is under way to determine how specific SNPs, or genetic variations, affect each of these aspects of nutrition.

Steven Zeisel, MD, PhD, director of the Nutrition Research Institute at the University of North Carolina at Chapel Hill, who conducts research in the field of nutrigenetics and has published hundreds of peer-reviewed articles, predicts that in five to 10 years, we'll know much more about SNPs and their effect on health in response to diet. "Knowledge in this field is increasing

exponentially,” Zeisel says. He believes individuals will soon be routinely genotyped for SNPs that affect nutritional status and receive dietary recommendations according to their genotype.

Zeisel believes that for personalized nutrition to be widely practiced, not only do researchers need to discover more SNPs that influence nutritional status, but computer software also must be developed to help dietitians make dietary recommendations based on an individual’s genetic composition. Thousands of SNPs are likely to affect nutritional status, and it will be impossible for dietitians to make comprehensive recommendations without specially designed software. Yet while the field of nutrigenetics is still young, researchers are making headway. Below is an overview of some of the evidence showing that genetic variation influences the interaction between diet and health outcomes.

Nutrient Requirements Based on Genotype

The USDA establishes the Dietary Reference Intakes for nutrients. These reference intakes, which include the Recommended Dietary Allowance (RDA), are set high to meet the estimated nutrient needs for normal physiologic function for the majority of the population. Although nutrient requirements vary from person to person, the RDAs appear to meet the needs of most people. Research is scarce on how genetics affects a person’s nutrient requirements, although some evidence on genotype and nutrient needs exists for a handful of micronutrients, including vitamin C, choline, and folate.

Vitamin C

Vitamin C is an essential nutrient that’s necessary for the synthesis of collagen and the inhibition of oxidative damage, which is characteristic of long-term diabetes complications. While vitamin C deficiency isn’t common in the United States, the inverse relationship between vitamin C status and chronic disease makes it one of the most important nutrients to obtain.

A recent study investigated whether genetic variations in the gene that codes for the enzyme glutathione S-transferase—which helps maintain the antioxidant capacity of vitamin C—had any effect on serum vitamin C status. Interestingly, individuals with at least one of two specific genetic polymorphisms within the glutathione S-transferase gene had an increased risk of serum vitamin C deficiency if they didn’t meet the RDA for vitamin C.⁴ This study suggests that it’s important for people with these polymorphisms to meet the RDA for vitamin C to maintain serum levels associated with normal physiologic function and prevent scurvy.

In the future, when individuals are genotyped, those who have these polymorphisms will receive this recommendation.

Choline

Choline is an essential nutrient that maintains cell membranes and sources of methyl groups, which are single carbons with three hydrogen atoms attached to them. A constant source of methyl groups is important for multiple biochemical reactions, including the synthesis of amino acids and neurotransmitters. Although choline is classified as an essential nutrient, some women can synthesize choline endogenously due to the enzyme phosphatidylethanolamine N-methyltransferase (PEMT). PEMT makes phosphatidylcholine in response to estrogen, thus decreasing the need for dietary choline, since phosphatidylcholine can be converted to choline.

A recent study demonstrated that a common SNP in the gene that codes for the PEMT enzyme increases the risk of liver or muscle dysfunction in people who are choline deficient.⁵ About one-half of women have the SNP that prevents the PEMT gene from responding to estrogen, thus increasing their dietary choline requirements. In this study, 80% of premenopausal women on a low-choline diet who had both copies of the SNP developed liver or muscle dysfunction compared with 43% of women with one copy of the SNP and 13% of those without the SNP.

In the future, those who have the PEMT SNP will be advised to consume the adequate intake of dietary choline to avoid liver or muscle dysfunction. Fortunately, choline deficiency is uncommon in the United States. However, PEMT is regulated by estrogen, putting postmenopausal women at increased risk of choline deficiency. So not only do these women have greater choline requirements, they're more likely to suffer health effects if they have the PEMT SNPs compared with women who aren't postmenopausal.

Folate

Folate is an essential nutrient that's necessary for the synthesis and repair of DNA. A strong association between folate status and the incidence of neural tube defects in newborns became apparent in the 1980s.⁶ While the underlying link between folate status and neural tube defects is still unclear, research has shown that individuals with a specific SNP in the enzyme methylenetetrahydrofolate reductase—necessary for the production of 5-methyltetrahydrofolate, which converts homocysteine to methionine—may have a higher folate requirement than those who don't have the genetic variation. These findings were based on reduced serum folate levels in response to the same dose of folic acid supplementation.⁷

The studies on vitamin C, choline, and folate clearly indicate that genetic variations affect an individual's nutrient requirements. In the case of these three nutrients, meeting the RDA is more important for people with specific genetic polymorphisms. Healthcare professionals won't know who these individuals are until they're genotyped, so dietitians can recommend only that everyone meet the RDAs for optimal health.

Preventing Chronic Disease Based on Genotype

Chronic illnesses such as cardiovascular disease, diabetes, and cancer are prevalent in developed countries. They can be attributed, at least in part, to lifestyle and environment factors, since our genes haven't changed appreciably over the last 100 years, although the incidence of chronic disease has skyrocketed. Furthermore, when individuals from cultures that have a low prevalence of chronic disease begin living in a culture with higher rates of chronic illness, their risk increases, suggesting that genetics aren't the sole risk factor.

Recent studies indicate that genetics affects whether a person will develop a chronic disease in response to diet and lifestyle. Fortunately, research also shows that people who are genetically predisposed to chronic disease won't necessarily develop the condition if they follow a specific preventive diet. In an age of personalized nutrition, individuals who are genetically predisposed to chronic disease will be advised to adhere to a preventive diet, since they'd be more likely to develop the disease.

Cardiovascular Disease

Connecting genetics to diet and heart disease began with apolipoprotein E (ApoE) in the mid 1980s.⁸ ApoE is a protein associated with lipids in the bloodstream and is involved in serum lipid metabolism. Individuals have one of three different forms of ApoE, depending on their genotype: ApoE2, ApoE3, or ApoE4. Those with ApoE4 (representing approximately 15% of the population) are more likely to have higher plasma concentrations of cholesterol.⁹ Interestingly, if a person with ApoE4 consumes a diet low in saturated fat, he or she is less likely to have high cholesterol despite the genetic predisposition.¹⁰ So for someone with ApoE4, consuming a heart-healthy diet may be more critical than for a person with ApoE2 or ApoE3. However, until these people can be identified, recommending a heart-healthy diet to everyone is imperative.

Apolipoprotein A1 (ApoA1) is another lipoprotein that plays an important role in serum cholesterol metabolism. One study found that a polymorphism close to the ApoA1 gene determines how polyunsaturated fatty acid (PUFA) intake affects plasma HDL cholesterol levels.¹¹ Those with a specific genotype for this polymorphism had increased HDL in response to an increased intake of PUFAs (greater than 8% of total calories). Individuals with a different genotype for this polymorphism had increased HDL cholesterol with a decreased intake of PUFAs (less than 4% of total calories). According to this study, it would make sense for some people to consume higher amounts of PUFAs than others, depending on genotype, to reduce cardiovascular disease risk. These findings demonstrate the complexity of the role of genes in the relationship between diet and health outcome.

Another genetic predisposition to cardiovascular disease involves a cluster of four SNPs in a common area on a particular chromosome (9p21). Humans have 23 pairs of chromosomes with each containing a portion of our DNA. Each of the four SNPs in 9P21 increases the risk of myocardial infarction (MI) by about 20%.¹² A study conducted in 2011 examined the effect of different diets on the relationship between the SNPs and the incidence of MI. Surprisingly, those who were genetically predisposed to MI didn't have an increased incidence of MI if they consumed a diet high in raw vegetables and fruits.¹² Those who were genetically predisposed and didn't consume many raw vegetables and fruits had the greatest incidence of MI. These findings indicate that following a certain dietary pattern may prevent an MI even for a person who's genetically predisposed. Understanding exactly who's at risk of MI based on these SNPs will be helpful for dietitians.

Many studies on genetics, diet, and heart disease focus on risk factors for heart disease rather than on the disease itself. Still, research suggests diet may have a strong impact on whether someone develops heart disease or its risk factors, despite genetic makeup. Moreover, depending on the genotype, different diets will work better for some than others. Once researchers clarify the connection between genetic variation, diet, and heart disease, dietitians will be able to make specific dietary recommendations to lower disease risk.

Diabetes

The prevalence of type 2 diabetes is increasing at a rapid pace. The National Diabetes Education Program reports that more than 25 million children and adults in the United States are living with diabetes, and the number of new diagnoses is increasing by 1.9 million each

year; type 2 diabetes account for roughly 95% of cases in adults. The role of diet and lifestyle in the prevention and management of diabetes has been established. However, the role of genetic variation among individuals in the prevention and management of this disease remains unclear. Researchers have discovered several polymorphisms strongly associated with type 2 diabetes risk and in some cases, this association may be modified by diet.

To date, a SNP in the transcription factor 7-like 2 protein gene has the strongest association with type 2 diabetes.¹³ People with the higher risk genotype for this SNP are approximately twice as likely to develop type 2 diabetes than those with the lower risk genotype for the SNP.¹⁴ Since the discovery of this association, several studies have demonstrated that the relationship between the genotype for the transcription factor 7-like 2 protein gene and diabetes outcome depends on diet and lifestyle. One study found that people with the higher risk genotype were 2.7 times as likely to develop type 2 diabetes when they consumed high glycemic index foods and a high glycemic load; those who ate low glycemic index foods and a low glycemic load were 1.6 times as likely to develop the disease.¹⁵ Therefore, people who are genetically predisposed to type 2 diabetes may decrease their risk of the disease if they consume a low glycemic load diet.

Other genes associated with type 2 diabetes risk include the sterol response element binding protein, the peroxisome proliferator-activated receptors, and the intestinal fatty acid binding protein.¹⁶ The proteins for which these genes code are important for multiple metabolic pathways, such as fatty acid synthesis, catabolism, and transport, all of which can affect insulin sensitivity. So the relationships between these genes and diabetes risk may be less direct and therefore more difficult to pinpoint particularly when different diets are taken into account. More research is needed to determine which diets may be more effective to reduce type 2 diabetes risk in people with specific genotypes.

Obesity

In 2007, while searching for a genetic link to diabetes, researchers found the gene associated with fat mass and obesity (FTO) to be significantly related to obesity in a series of studies that included almost 39,000 participants.¹⁷ Researchers found that a SNP within the FTO gene predisposed people to obesity. Individuals who had both copies (one from each parent) of the higher-risk SNP in the FTO gene (16% of study participants) were 7 lbs heavier and 1.67 times more likely to be obese compared with those who didn't have the higher-risk SNP. While this genetic association doesn't explain the obesity epidemic, it's the strongest genetic link to obesity risk. Nevertheless, because researchers believe the variation in BMI in the majority of the population is determined by genetics, more studies are needed on the genes involved in weight management.¹⁸

Interestingly, more recent studies have demonstrated that certain lifestyles and diets reduce the incidence of obesity even if individuals have the higher-risk genotype for the FTO gene or other genes linked to obesity. One study genotyped more than 20,000 people for 12 different SNPs associated with an increased obesity risk.¹⁹ Researchers found that a physically active lifestyle reduced obesity risk by 40% in those genetically predisposed. Another study showed that individuals who had a strong genetic predisposition to obesity reduced their risk when they consumed a diet low in saturated fat.²⁰

Future Outlook

As you know, two people who have similar lifestyles and environmental exposures can have very different health outcomes. Research suggests our individual genetic composition influences our health outcome in response to lifestyle and environmental factors. Researchers are making progress to understand the complex relationships among genes, diet, and disease risk. Personalized nutrition based on genetic composition isn't widely practiced in healthcare, but individuals seeking personalized nutrition beyond what their primary care provider offers can contact companies that sell cheek swab kits to collect DNA, which is sequenced for specific SNPs. Depending on their genotype for these SNPs, they can purchase specific dietary recommendations. The company GenoVive sequences DNA for 13 SNPs, each of which has been found in intervention studies to be associated with metabolism and weight management. Based on the person's genotype for each of the 13 SNPs, personalized dietary recommendations are offered with the goal of achieving a healthy weight.

For personalized nutrition to become cost-effective for widespread use, more of the genetic associations linked with diets and disease must be determined. Moreover, computer software must be developed to help dietitians provide personalized dietary recommendations based on thousands of polymorphisms for a single individual. Education and support programs that will help people adhere to the dietary recommendations are needed as well.

Meanwhile, you as the nutrition professional can help advance nutrigenetics by educating yourselves about the field and by determining whether certain diets are working for some clients and patients but not for others. These observations may indicate an underlying genetic link that's causing a client to respond to a specific diet and experience a positive health outcome. It's important to contact a researcher who has the tools to uncover this genetic link and explain your observations. This is how the discovery of a genetic association begins, for we need to understand more about the associations among genes, diet, and health outcomes for personalized nutrition to be part of routine care.

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Glossary of Terms

- **Base pair:** DNA consists of two complementary chains of nucleotides (adenine, guanine, cytosine, and thymine). A base pair is two complementary nucleotides (A and T or C and G).
- **DNA:** Deoxyribonucleic acid is a nucleic acid that contains genetic information.
- **Gene:** This is a sequence of DNA that encodes a protein.
- **Gene expression:** A gene is expressed when DNA is transcribed into messenger ribonucleic acid, called mRNA, which is usually then translated into a protein.

- **Genome:** This is the complete genetic content of an organism.
- **Genotype:** This is the specific sequence of a gene or genetic variation.
- **Nutrigenetics:** This is the study of the relationship among genes, diet, and health.
- **Nutrigenomics:** This involves the study of the interaction between nutrients and genes at the molecular level.
- **Single nucleotide polymorphism:** This is a point in the genome that differs by one base pair, which may or may not have any effect on an individual.

References

1. Ordovas JM, Mooser V. Nutrigenomics and nutrigenetics. *Curr Opin Lipidol*. 2004;15(2):101-108.
2. Levy S, Sutton G, Ng PC, et al. The diploid genome sequence of an individual human. *PLoS Biol*. 2007;5(10):e254.
3. Kruglyak L, Nickerson DA. Variation is the spice of life. *Nat Genet*. 2001;27(3):234-236.
4. Cahill LE, Fontaine-Bisson B, El-Sohehy A. Functional genetic variants of glutathione S-transferase protect against serum ascorbic acid deficiency. *Am J Clin Nutr*. 2009;90(5):1411-1417.
5. Fischer LM, da Costa KA, Kwock L, Galanko J, Zeisel SH. Dietary choline requirements of women: effects of estrogen and genetic variation. *Am J Clin Nutr*. 2010;92(5):1113-1119.
6. Mulinare J, Cordero JF, Erickson JD, Berry RJ. Periconceptional use of multivitamins and the occurrence of neural tube defects. *JAMA*. 1988;260(21):3141-3145.
7. Crider KS, Zhu JH, Hao L, et al. MTHFR 677C->T genotype is associated with folate and homocysteine concentrations in a large, population-based, double-blind trial of folic acid supplementation. *Am J Clin Nutr*. 2011;93(6):1365-1372.
8. Ordovas JM, Litwack-Klein L, Wilson PW, Schaefer MM, Schaefer EJ. Apolipoprotein E isoform phenotyping methodology and population frequency with identification of apoE1 and apoE5 isoforms. *J Lipid Res*. 1987;28(4):371-380.
9. Ordovas JM. Genetic influences on blood lipids and cardiovascular disease risk: tools for primary prevention. *Am J Clin Nutr*. 2009;89(5):1509S-1517S.
10. Corella D, Ordovas JM. Single nucleotide polymorphisms that influence lipid metabolism: interaction with dietary factors. *Annu Rev Nutr*. 2005;25:341-390.

11. Ordovas JM, Corella D, Cupples LA, et al. Polyunsaturated fatty acids modulate the effects of the APOA1 G-A polymorphism on HDL-cholesterol concentrations in a sex-specific manner: the Framingham Study. **Am J Clin Nutr.** 2002;75(1):38-46.
12. Do R, Xie C, Zhang X, et al. The effect of chromosome 9p21 variants on cardiovascular disease may be modified by dietary intake: evidence from a case/control and a prospective study. **PLoS Med.** 2011;8(10):e1001106.
13. Florez JC. The new type 2 diabetes gene TCF7L2. **Curr Opin Clin Nutr Metab Care.** 2007;10(4):391-396.
14. Zhang C, Qi L, Hunter DJ, et al. Variant of transcription factor #7-like 2 (TCF7L2) gene and the risk of type 2 diabetes in large cohorts of U.S. women and men. **Diabetes.** 2006;55(9):2645-2648.
15. Cornelis MC, Qi L, Kraft P, Hu FB. TCF7L2, dietary carbohydrate, and risk of type 2 diabetes in US women. **Am J Clin Nutr.** 2009;89(4):1256-1262.
16. Mutch DM, Wahli W, Williamson G. Nutrigenomics and nutrigenetics: the emerging faces of nutrition. **FASEB J.** 2005;19(12):1602-1616.
17. Frayling TM, Timpson NJ, Weedon MN, et al. A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. **Science.** 2007;316(5826):889-894.
18. Silventoinen K, Rokholm B, Kaprio J, Sørensen TIA. The genetic and environmental influences on childhood obesity: a systematic review of twin and adoption studies. **Int J Obes.** 2010;34(1):29-40.
19. Li S, Zhao JH, Luan J, et al. Physical activity attenuates the genetic predisposition to obesity in 20,000 men and women from EPIC-Norfolk prospective population study. **PLoS Med.** 2010;7(8):e1000332.
20. Corella D, Arnett DK, Tucker KL, et al. A high intake of saturated fatty acids strengthens the association between the fat mass and obesity-associated gene and BMI. **J Nutr.** 2011;141(12):2219-2225.

Examination

1. Nutrigenetics is the study of:

- A. the interaction between genes and nutrients at the molecular level.
- B. the role that genetic variation plays in the relationship between diet and health outcome.
- C. genetically modified foods.
- D. None of the above

2. What percentage of DNA is identical among all humans?

- A. 50%
- B. 75%
- C. 99%
- D. 100%

3. Why isn't personalized nutrition based on genetics widely practiced?

- A. It's not cost-effective.
- B. There aren't enough details about all the relationships among genes, diet, and health outcomes.
- C. Individuals aren't routinely genotyped by their healthcare providers.
- D. All of the above

4. How can dietitians contribute to the advancement of nutrigenetics and personalized nutrition?

- A. Become familiar with the research on nutrigenetics.
- B. Observe clients and patients to determine whether certain diets work for some but not others.
- C. Contact researchers about observations of clients and patients so the researchers can uncover the genetic link.
- D. All of the above

5. Which of the following statements about nutrigenetics is true?

- A. There are private companies that offer personalized dietary recommendations based on genetics.
- B. Personalized nutrition based on nutrigenetics is widely practiced.
- C. All people respond to diets similarly.
- D. The relationships among genes, diets, and health outcomes have been discovered.

6. Which of the following is an example of a genetic variation among individuals?

- A. Chromosome
- B. Gene
- C. Single nucleotide polymorphism (SNP)
- D. DNA

7. How might genetic variation affect an individual's nutritional status?

- A. Genetic variation doesn't impact nutritional status.
- B. Genetic variation may impact an individual's HDL cholesterol level in response to polyunsaturated fatty acid intake.
- C. Genetic variation dictates whether a person will develop a chronic disease despite dietary and lifestyle factors.
- D. None of the above.

8. If a client or patient says the diet you have recommended for him may not be effective because he's genetically unique, how might you respond?

- A. Acknowledge he's correct and tell him that the diet you're recommending will likely be effective regardless of genotype. However, you can't be certain until you know his genotype and further research is done in this area.
- B. Tell the client he isn't genetically unique.
- C. Tell the client the diet you have recommended has been shown to be effective for all genotypes.
- D. None of the above.

9. Which of the following statements regarding a SNP affecting nutrient requirements is correct?

- A. A SNP in the phosphatidylethanolamine N-methyl transferase gene decreases dietary choline requirements.
- B. A SNP in the methyltetrahydrofolate reductase gene may lower folate requirements.
- C. A SNP in the glutathione S-transferase gene makes it more important to meet the Recommended Dietary Allowance for vitamin C.
- D. All of the above

10. Which of the following statements regarding a SNP affecting chronic disease risk is correct?

- A. A cluster of 9P21 SNPs that increases risk of myocardial infarction
- B. A SNP in the gene associated with fat mass and obesity that predisposes people to cancer
- C. A SNP in the transcription factor 7-like 2 protein gene that doubles the risk of respiratory disease
- D. A SNP in a chloride channel gene that doubles the risk of obesity