

Does Your Diet Fit Your GENES?

The latest trend in nutrition counseling will match your genotype to a personalized food plan for improved health and performance.

Want a sneak peek at the kind of diet advice you might expect to get in the year 2025? Well, first you'll need to prick your finger for a blood test or urinate in a cup and send the specimen to a lab, where it will undergo protein and DNA analysis. A few days later, you'll get an e-mail that outlines your personalized, comprehensive food plan, based on the specific needs of your genetic profile.

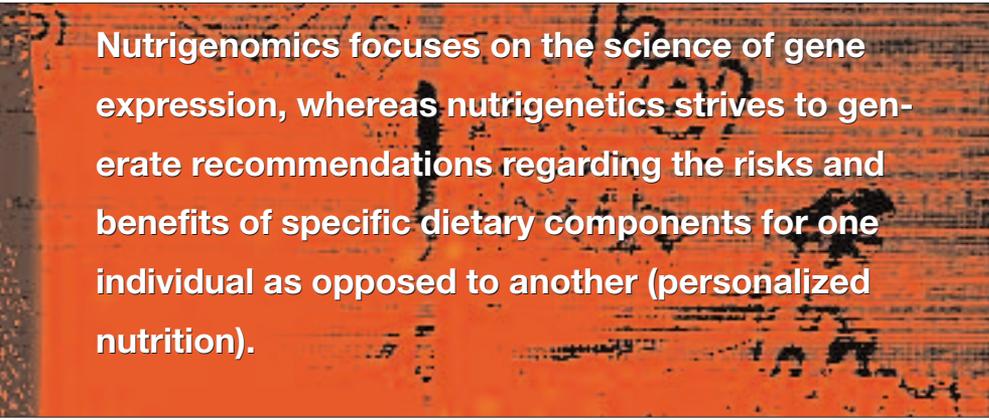
Sounds far-fetched? Researchers have been investigating the concept of "personalized" nutrition for decades. Today, supermarket shelves boast special formulations of vitamins and food products geared to particular populations; for example, nutrition drinks for older adults and soy-spiked oatmeal for menopausal women. It is not an exaggeration to say that the whole approach to nutrition is in the process of changing.

By Amy Paturel, MS, MPH

The Times They Are A-Changing

Researchers are learning that manipulating diet based on certain genetic variants may help you achieve and maintain optimal health, whether the aim is disease prevention or peak performance. While managing health through tailored nutrition programs may be a lofty goal, the truth is we have already begun the journey. Case in point: the government's newly implemented MyPyramid, a dietary approach that recognizes—some would say even celebrates—individual differences.

“MyPyramid is a positive, if only a ‘baby,’ step toward the concept of personalized nutrition,” says Dave Schmidt, PhD, president and chief executive officer of the International Food Information Council (IFIC). “Moving dietary guidance from a one-size-fits-all approach to MyPyramid, which offers 12 different diets based on several demographic factors (such as height, weight and activity level), is real progress.”



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Defining the Human Genome

For decades, scientists have been trying to understand the **human genome**, which, put simply, is the DNA sequence that results in the uniqueness of each human being. The Human Genome Project began in 1990 with worldwide scientific collaboration and was completed in 2003. Likened in scientific significance to putting a man on the moon, the Human Genome Project has provided an “instruction manual” to the human being's 30,000-plus genes.

“Now that we've crossed that bridge [i.e., identifying those genes], there's no turning back,” says Raymond Rodriguez, PhD, director for the NCMHD Center of Excellence in Nutritional Genomics and professor of molecular cell biology at the University of California, Davis. Since genetics cuts across all health-related disciplines, this instruction manual will become the basis for preventing and treating disease and promoting wellness.

We now know that any two individuals share 99.9% of their DNA profile (University of California, Davis 2004). Interestingly, it is the remaining 0.1% of each person's profile that is responsible for our different responses to environmental factors, such as air pollution or pesticides. Those different responses often involve a change in **nucleotides**, or genetic building blocks. Responses that involve a change in a single nucleotide within the genetic material and occur in more than 1% of the population are called **single nucleotide polymorphisms (SNPs)**.

Think of SNPs as being variations in the human recipe. They can be used to create a map showing the relative positions of the

known genes on the chromosomes of a given species. In fact, a consortium of pharmaceutical companies and academic institutions are currently mapping human SNPs. While the initial target of this effort is drug development, diagnostic applications are already being designed and nutritional applications are not far behind.

Forging a New Nutrition Science

In the last half of the 20th century, researchers focused on understanding the functions of essential nutrients and the roles of micronutrients (e.g., vitamins and minerals). Scientists discovered how carbohydrates and fats contributed to the onset of diseases such as diabetes and cardiovascular disease. They learned which vitamins and minerals helped reduce the risk of disease. Still, scientists were baffled as to why some individuals who regularly consumed high-fat diets showed no evidence of arterial blockage, while others who ate a healthier diet had cholesterol

levels that were off the charts. Although the researchers suspected that genetic differences were the key, it was quite a challenge to identify cellular, molecular and genetic-level mechanisms for such varied responses. Enter the field of genomics.

Advances made in the field of **pharmacogenomics** (i.e., the study of drugs developed according to genotype) have underscored the importance of genotype–environment interactions. These advances illustrated how individual genetic variation in human populations could affect the efficacy of a drug and the severity of its undesirable side effects. This concept of per-

sonalized medicine has now extended to nutrition. Using the same tools and concepts pioneered in the pharmacogenomics field, scientists are currently examining how individuals respond to their nutritional environment. It's now accepted that nutrients alter molecular processes, such as DNA structure, gene expression and metabolism—which may, in turn, alter the onset, development and/or progression of a host of diseases.

“Individual genetic differences in response to dietary components have been evident for thousands of years,” says Rodriguez. “The classic examples are lactose intolerance and alcohol intolerance.” For example, people who lack the intestinal enzyme to digest certain proteins in milk have difficulty consuming dairy products. Similarly, some people have a specific variation to what is known as chromosome 2, and this variation causes an allergic reaction to alcohol.

Nutritional Genomics 101

Just as ultraviolet rays and smoking can alter genes and cells in the body, so too can food chemicals and various nutrients. Consider what happens biologically when you eat a meal. Until recently, most scientists thought food had one job: to provide energy for cells. Although that is the way most dietary chemicals respond in the body, others bind to proteins that are instrumental in “turning on” certain genes. According to the underlying concept of nutrigenomics, a diet that is severely out of balance will cause gene expressions that make us vulnerable for chronic disease. Where the idea of “intelligent nutrition” comes in is in

helping restore the body's equilibrium.

The science of nutritional genomics seeks to provide a molecular understanding of how dietary chemicals, such as antioxidants, affect health by altering the expression or structure of a person's genetic makeup. There are two terms that are widely used within the field of nutritional genomics: nutrigenomics and nutrigenetics. **Nutrigenomics** is the term used to describe the exploration of which genes and proteins in the body are activated under different circumstances and how environmental factors influence gene activation. The term **nutrigenetics**, on the other hand, is used to describe how we inherit specific traits and how differences among those traits are explained by variations in our genes. To contrast the two, nutrigenomics focuses on the science of gene expression, whereas nutrigenetics strives to generate recommendations regarding the risks and benefits of specific dietary components for one individual as opposed to another (personalized nutrition).

Diet is a significant risk factor for a number of diseases, but the degree to which diet influences the balance between health and disease depends, at least in part, on a person's genes. Theoretically, then, dietary intervention—based on nutritional requirements, nutritional status and genotype—can be used to prevent, mitigate or cure chronic disease. In the future, scientists will be able to help people better manage their health and well-being by matching their diet with their unique genetic makeup.

“Food intake is the environmental factor to which we are all exposed permanently, from conception to death,” says Jose M. Ordovas, PhD, director of the Nutrition and Genomics Laboratory at Tufts University. “As such, dietary habits represent a key environmental factor that modulates gene expression throughout our lives.”

A Matter of Privacy

Most experts expect that the real-world application of nutrigenomics, or personalized nutrition, will result in significant cost savings for consumers, employers, government and third-party insurance providers through its effects on disease prevention. However, other experts caution against rushing to embrace the science before there has been a detailed investigation of its moral and ethical implications. There's concern that employers or insurers could use genetic information against those who are at high nutritional risk for disease.

According to Dave Schmidt, PhD, president and chief executive officer of the International Food Information Council (IFIC), “Consumers are generally positive about the potential benefits of personalized nutrition.” However, Schmidt cited a 1997 survey commissioned by IFIC in which two-thirds of the people polled said they would not undergo genetic testing if they thought that health insurers and employers would be able to access the results.

If and when genetic testing becomes commonplace, the collection, storage and use of genetic information will be a highly controversial issue. And since genetic tests could be relevant to blood relatives, physicians might face situations in which they must choose between keeping patient confidentiality and providing potentially useful information to other members of the same family.

The Ethnic/Ethical Debate

The theory that genetic markers distinguish one ethnic group from another is at the philosophical heart of nutrigenomics. The idea that there could be biological relevance to race is being hotly debated.

Take the case of certain tribes of Native Americans today: According to Rodriguez, more than half of all Pima Indians in Arizona currently have type 2 diabetes, compared with only 7% of the state's Caucasian residents. The Pima tribe's ancestors lived in regions with great seasonal variations in weather and food availability, and consequently their lifestyle required extreme physical efforts simply to find food. Today, the tribe no longer forages for sustenance and instead has come to rely on a steady diet of foods that are high in carbs, fat and sodium, all of which contribute to insulin resistance. There are many other examples of this ill fit between certain cultures and certain diets, suggesting some interplay between genes and nutrition.

“If you're from Northern European ancestry, you can probably digest milk; if you're [from] Southeast Asia, you probably can't,” says Rodriguez. “So the likelihood that you tolerate milk depends on the degree to which you have Northern European blood.”

In another instance, many Japanese immigrants developed extremely high levels of blood cholesterol after relocating to the United States. The Masai tribes of East Africa are a further example, because they have developed new health problems since abandoning their traditional meat, blood and milk diet for one based on corn and beans.

Personalizing Nutrition for the Masses

Ordovas has identified 40 or so genes known to affect cardiovascular health. He estimates that there may be hundreds of genes that will eventually be used in a “risk analysis” database. However, whether those genes ultimately manifest in a real health risk will also depend on an individual's lifestyle habits and age. For example, in an obese person, a gene that affects weight gain may also trigger the gene that monitors blood lipids to express high levels of LDL cholesterol and triglycerides. However, if the person is lean, the beneficial gene could prevail.

Because humans share more than 99% of their DNA, the minor differences that do exist among ethnic and racial groups are responsible for human diversity, such as hair and skin colors, height, weight and all other “gene-based” variations. Some of the small differences also involve medically important variations, including susceptibility to disease.

For example, minor genetic differences may account for why some women are more sensitive than others to environmental carcinogens. Many researchers argue that the link between alcohol and breast cancer risk is largely related to a person's genetic profile. According to Rodriguez and others, researchers have identified a genetic factor that influences the association between excessive alcohol consumption and breast cancer risk.

Other research suggests a relationship between the ability to process milk proteins and puzzling neurological diseases, such as autism and schizophrenia. Scientists have speculated that a genetic intestinal enzyme flaw in some individuals may lead to an inability to properly digest proteins found in certain dairy products. This flaw may cause the body to produce morphine-like compounds that are absorbed by areas of the brain linked to

autism and schizophrenia.

In the future, single bioactive compounds may be delivered in a variety of forms to counteract these kinds of developmental anomalies. For instance, a lactose-intolerant individual who lacks an essential intestinal enzyme needed to hydrolyze milk proteins may soon be able to get that enzyme in a pill form. The same may hold true for women who are at high risk for breast cancer and may need to ingest a different enzyme before consuming alcohol.

“I’m confident that nutrigenomics will eventually provide significant information that can truly improve an individual’s health outlook,” says Schmidt. “The question is whether consumers will truly use the information they obtain if it means a major change to their diet or lifestyle that they don’t find to be as tasty or enjoyable [as what they’re used to].”

Putting Personalized Diets Into Practice

Just as fitness professionals personalize exercise regimens based on clients’ physical levels and fitness goals, nutritionists will someday make nutritional recommendations based on individuals’ genetic differences and underlying disease risks.

Like exercise guidelines, these personalized diets will probably not be all that different from one another, explains Rodriguez. In other words, food plans for clients won’t deviate too much from the fruit- and vegetable-heavy diet recommended by the U.S. Department of Agriculture.

“At a basic level, some of the advice resulting from nutrigenomics or personalized nutrition may sound a lot like the U.S. Dietary Guidelines,” says Schmidt. “Most people are aware that family history and other factors may dictate a more specialized diet than is generally recommended.”

The people who will benefit most from personalized nutrition will be the approximately 20% of people at the far ends of the spectrum: those at the top, who don’t have to worry much about what they eat; and those at the bottom, who need to follow special diets or take specific supplements. In practical terms, this means that if you are among the population whose cholesterol count doesn’t respond to diet, you’ll be able to indulge in the occasional bacon and egg sandwiches. You’ll take only the vitamins your body needs and in the right doses. And there’s a real chance of extending your life, by postponing the onset of diseases to which you’re naturally susceptible. The question: Where do you fall in the spectrum?

The Perils and Pitfalls of Personalized Nutrition

The field of nutrigenomics has the potential to revolutionize

Additional Resources

Books

- DeBusk, Ruth. 2003. *Genetics: The Nutrition Connection*. Washington, DC: American Dietetic Association.
- Rodriguez, Raymond. Forthcoming. *Nutritional Genomics: Discovering the Path to Personalized Nutrition*.
- Willett, Walt. 2001, 2005. *Eat, Drink and Be Healthy: The Harvard Medical School Guide to Healthy Eating*. Free Press.

Websites

- <http://nutrigenomics.ucdavis.edu/>: NCMHD Center of Excellence for Nutritional Genomics, University of California, Davis
- www.nutrigenomics.nl: Centre for Human Nutrigenomics

the way Americans approach wellness and disease management. By elucidating genetic profiles of individuals and formulating diets for the prevention or treatment of disease, nutrigenomics promises to provide new opportunities for consumers whose genetic susceptibility to specific diets and diseases are known. That’s the good news.

Unfortunately, there is a darker side to nutrigenomics: Some experts worry that beyond offering obvious improvements in public health and quality of life, nutrigenomics presents a new way for marketers to exploit the public. Once scientists have identified small subgroups based on their SNPs, manufacturers will be able to create products to target the unique needs of these groups and market products directly to them.

“There’s certainly potential for misleading claims and for overpromising benefits to consumers before we have enough knowledge to make such projections,” warns Schmidt. “Some [consumers] may spend significant sums for false hope or a sense of security when there may just not be enough evidence to prove a benefit.”

The potential market for nutrigenomics products is bound to be huge. In fact, the *Nutrition Business Journal* projects that sales within the nutrigenomics industry could one day reach \$20 billion (Berberich 2005). A few companies are already leading the pack to provide gene-based dietary recommendations. A quick search on the Internet will turn up numerous websites that provide dietary, lifestyle and health risk assessments. Some already solicit DNA samples (usually from a cheek swab) and make nutrition product and lifestyle recommendations based on selected genotypes. In fact, according to a report published by the Institute for the Future, a strategic research firm, 33% of the U.S. population will be making adjustments to their diets based on nutrigenomics by 2010 (Gillies 2003).

As it stands today, however, not all of the nutrients in foods have been characterized. “There are probably thousands of chemicals

present in foods, still classified as nonnutrients, that may play a significant role in gene regulation, health and disease,” says Ordovas.

Peering Into the Future

Clearly, nutrigenomics is still in its infancy, and comprehensive personalized diets based on genotype may be a decade or two down the road. For now, fitness professionals should continue to gear clients toward a dietary approach that is healthy for the majority of genotypes, as this majority is the basis for current federal dietary recommendations and the revamped MyPyramid.

In addition to diet, clients should be constantly reminded of the importance of an active lifestyle in maintaining health. “Perhaps the next field to emerge will be ‘kinetogenomics,’” says Rodriguez. “Trainability is a complex phenotype that includes muscle mass, muscle type and metabolism, all of which are controlled by genes—which is not all that different from nutrition.”

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