

Nutritional Genomics: Customizing Diet Plans According to Genetic Makeup

Emerging in the 1990s, nutrigenomics integrates the study of nutrients and genes into one scientific field.

BY LAURA SUAREZ, ASSOCIATE EDITOR

The notion that diet and disease are related is not new. In fact, many epidemiologic studies show that certain dietary components increase the risk of chronic disease.¹

Proteins, fats and carbohydrates, as well as a lack of key micronutrients and overconsumption of energy, are associated with the prevalence of chronic diseases such as type 2 diabetes, obesity, cardiovascular disease and several cancers and neurological disorders. Diet is also related to genetics, whereby dietary chemicals interact with susceptibility genes to create an individualized risk of disease. This may be expressed by gene multiplied by (X) environmental interaction. One classic example of this genotype-diet interaction is type 2 diabetes.²

Reporting in *Nutrition*, Jim Kaput, PhD, wrote: "The precise, statistical definition of gene-environment interaction is 'a different effect of an environmental exposure on disease risk in persons with different genotypes' or 'a different effect of a genotype on disease risk in persons with different environmental exposures.'"¹

STUDY OF GENES, DIET

These and similar findings sparked nutritional genomics, or nutrigenomics. Using principles from genomics – a field that is not quite 20 years in existence – nutrigenomics combines the study of an organism's genetic makeup with the study of dietary chemicals. Nutrigenomics has five tenants:²

- common chemicals from diet/nutrition directly or

indirectly act on the human genome to alter the expression or structure of the genes;

- diet is a risk factor for disease in certain individuals and in certain circumstances;
- the onset, incidence, progression and/or severity of chronic diseases may be influenced by genes, as well as their normal variants, that are regulated by diet;
- the genetic makeup of an individual may influence the intensity of dietary influence on health and susceptibility to disease; and
- using "individualized nutrition" as a dietary intervention to prevent, mitigate or cure chronic disease.

"Nutrigenomics is best explained by the concept of yin-yang," Dr. Kaput said in a recent interview with *Diabetic Microvascular Complications Today*. "A person's genetic makeup dictates how nutrients are metabolized and affect health, and likewise, nutrients influence or affect the expression of a person's genetic makeup."

Since the early 1990s, researchers have been studying nutrigenomics as a means to create individualized diet plans based on the way a person's genes interact to dietary and environmental elements. The idea is that by customizing diets according to genetic makeup, people can eat foods that will prevent the diseases to which they are most susceptible.

Nutritional genomics may lead to the prevention of all diseases. "Dietary intervention based on knowledge of nutritional requirement, nutritional status and genotype (ie, individualized nutrition) can be used to prevent, mitigate or cure chronic disease," Drs. Kaput and Raymond L.

Rodriguez, MD, wrote, adding that genes associated with chronic disease will first have to be identified and researched as to how they are regulated by nutrients.² Nutrigenomics has slowly entered the medical field, and it will continue to impact medicine in the future.

Researchers like Dr. Kaput, the president and chief scientific officer of NutraGenomics, Inc (Chicago), are currently working to link nutrients to specific gene sets. NutraGenomics is a research and development biotechnology company that identifies targeted therapies for chronic diseases including type 2 diabetes and obesity. The company uses a systems biology approach to identify diet-regulated genes. Finding a gene X nutrient relationship in humans is difficult, Dr. Kaput said in a recent interview, mainly due to the uniqueness of individual genetic makeups.

Approximately 99.9% of all human DNA is the same. Phenotypes that signify structural differences such as hair color, weight and response to nutrients are found in the 0.1% of DNA that is different. There are approximately 3 billion genetic base pairs, resulting in DNA sequences that differ at millions of bases in each person.³ These differences in gene sequences also determine disease susceptibility, and a person's response to their nutritional environment is caused by some of the millions of base pair differences in genes.²

DIABETES IS FIRST DISEASE

One of the first areas that will benefit from the use of nutrigenomics is diabetes, Dr. Kaput said. "It is my view that diabetes will be the first disease helped by nutrigenomics. There is great potential – if we can get enough research funds from the National Institutes of Health to proceed with well-designed nutritional genomics projects or from the pharma or food industries – to develop the tests and treatments."

Recent studies have indicated that several macronutrients can be traced to the prevalence of obesity and diabetes.² For instance, saturated fatty acids that increase LDL cholesterol may enhance the risk obesity and diabetes. Simple and complex carbohydrate intake, affecting blood glucose concentrations and glycemic index (GI), also increase the risk of type 2 diabetes and obesity. Evidence suggests that GI is associated with type 2 diabetes as well as coronary artery disease, colon cancer and breast cancer.² These associations have been shown in all but one case-controlled cohort study enrolling type 2 diabetic patients.

Other associated dietary risks for type 2 diabetes include consuming meat and eating a diet high in calories. "It is more likely that dietary imbalances, from micronutrient deficiencies to overconsumption of macronutrients or dietary supplements, are the modifiers of metabolism and potentiators of chronic disease," Drs. Kaput and

Rodriguez wrote.² "Although the complexity of food and genotypic variations appear daunting, molecular and genetic technologies may provide the means for identifying causative genes (or their variants) and the nutrients that regulate them."

Investigators at NutraGenomics are currently examining the relationship between genes and nutrients in type 2 diabetic patients. This process will have many variations, since type 2 diabetes can be caused by one of several pathways. Gene alteration along these pathways varies by individual, Dr. Kaput noted.

"Diet may not cure a type 2 diabetes mellitus patient, but it may help reduce symptoms, particularly with drugs," he said.

THREE PHASES

Dr. Kaput explained that there are three phases of nutrigenomics. First, as technology becomes available, diseases can be diagnosed more precisely with genetic testing. After genetic testing is perfected, healthy patients will be screened for disease susceptibility. In return, people may be able to plan their diet accordingly. "The problem [now] is that we don't have enough information to recommend diets," he said.

NutraGenomics and similar companies are working on ways to locate the genes that cause disease susceptibility. "Associating the variants of these genes with each molecular cause will allow a doctor to prescribe treatments for each individual," Dr. Kaput said. "Some of the recommended [treatments] will be for diet."

The last phase of nutrigenomics will be genetic testing at birth. This test will predict an individual's susceptibility to diseases as a "range of probabilities," Dr. Kaput explained, where drinking and smoking during life will produce a higher probability, and a healthy lifestyle including exercise and a healthy diet will produce a lower probability.

"Nutrigenomic approaches offer the best hope for understanding the molecular processes that maintain health and prevent disease development," Dr. Kaput wrote.¹

FIRST TO STUDY NUTRIGENOMICS

Kaput and other researchers including Willard Visek, MD, of the University of Illinois; George Wolff, MD, of the National Center for Toxicological Research; and Jose Ordovas, MD, of the nutrition and genomics laboratory at Tufts University, are among the first researchers to study nutrigenomics. Nutrigenomics "wasn't one discovery – just a realization that science had to be done differently," Dr. Kaput said.

As nutritional genomics continues to emerge, a new set of dietary recommendations will have to be established. "That is because we will have to test each patient,

be able to interpret a pattern of gene variants in 100 to 150 genes and develop specific treatments for common patterns," Dr. Kaput said.

Unlike current, generalized dietary recommendations intended for the whole public, new recommendations may have an estimated five to seven groups, which would each suggest their own set of treatments.

"If we can identify the best foods to keep an individual healthy, we should be able to delay the onset of disease," Dr. Kaput concluded. "If that can be done, each person would be responsible for the diets they eat to keep them healthy. But, unlike now, they would have real data rather than suggestions from population studies." ■

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WEIGHT GAIN IN ADULTHOOD IS A PRODUCT OF GENES, ENVIRONMENT

Genetic factors accounted for over 50% of the changes in BMI during middle age.

Reviewed by James C. Romeis, PhD

Varying body mass index (BMI) levels across a population of identical and fraternal twins suggest that genetics may contribute to the obesity epidemic.

In an attempt to determine the factors associated with obesity, investigators from the Saint Louis University (SLU) School of Public Health examined adult-onset weight changes in approximately 8,000 twins. They found that genetics was the reason for over 50% of the changes seen in weight. Environmental factors including diet and exercise were accountable for the other half, investigators said.

"We're not acknowledging the strength of genetic factors in our weight-loss strategies. You've got this genetic thing working against you that helps to explain why you're so heavy and why you may fail at diets and weight-loss programs," said James C. Romeis, PhD, lead investigator and professor of health services research at SLU, in a news release. Dr. Romeis published his findings in *Twin Research*. The study was funded by the National Institute on Aging.

BMI was calculated at baseline (1968) and between early adulthood and middle age. Changes in BMI were noted in 1987 and 1990. All patients were from the Vietnam Era Twin Registry. They were white, middle-aged, middle-class citizens who enlisted in the late 1960s. The male-male twin sets were either identical or fraternal, and 75% had normal BMIs during early adulthood (around 20 years old).

Twins experienced a gradual increase in BMI over 20 years. "Univariate data for each data period indicated that additive genetic factors accounted for between 63% and 69% of total variance in BMI," investigators wrote. They approximated what proportion of genetic factors influenced BMI and suggested that over half of the change in BMI was inherited and not from shared environmental factors.

Changes in weight were also tracked with the Cholesky longitudinal genetic analysis. Over 55% of patients were considered overweight or obese in 1990.

"While genetic vulnerability has probably not changed during the past few years, environments have, thus allowing for the genetic vulnerability to be expressed as what appears to be an alarming rate of increase," Dr. Romeis said. "Treatments and public health interventions need to recognize the magnitude of genetic factors if short-term and long-term interventions are to be effective." ■

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