An Introduction to Nutrigenomics for the Renal Dietetics Professional

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Nutrigenomics has been identified as an important topic in renal dietetics practice and one that will demand new skills from the renal dietetics professional (1). The goal of this relatively new science is to understand the effects of specific nutrients on an individual's genes, and potentially apply research findings to decrease the incidence or manage the symptoms of chronic diseases (2).

The National Center for Minority Health and Health Disparities Center of Excellence for Nutritional Genomics designs research studies directed to delay, prevent and treat diseases which affect millions of Americans. These diseases include obesity, cardiovascular disease and type 2 diabetes (3). As the results of nutrigenomic research begin to appear in the media, dietetics professionals will need to help patients understand the relationship between nutrition and genes, and the impact of their interactions on health.

This article reviews the basic genetic principles underlying the science of nutrigenomics, examines the goals of nutrigenomic research and provides an example of possible applications for nutrigenomic research in the chronic kidney disease (CKD) population.

Basic Genetic Principles

Each individual's development and physiological functioning is controlled by genetic instructions contained in the double-stranded deoxyribonucleic acid (DNA) molecule. Genes are segments of DNA which carry genetic information in the form of a sequence of purine (adenine and guanine) and pyrimidine (cytosine and thymine) bases (4). Complementary base pairing between purines and pyrimidines (adenine to thymine and guanine to cytosine) stabilizes the DNA molecule and ensures that all information is duplicated on each strand.

In humans, DNA occurs in chromosomes within the cell nucleus. The set of 46 chromosomes containing approximately 20,500 genes and billions of DNA base pairs makes up the human genome (5). Genetic information in DNA is read and copied into ribonucleic acid (RNA) during the process of transcription. RNA specifies the sequence of amino acids assembled into proteins, such as enzymes and hormones, during the process called translation.

Free radicals and other oxidizing agents can change the sequence of bases or cause breakage in the DNA molecule (6). Even small changes in DNA, known as genetic variations or gene variants, may affect an individual's susceptibility to disease (7). Conversely, correct functioning of DNA depends on its interactions with various categories of protein. For example, enzymes called DNA ligases can repair broken DNA strands and are important in DNA replication (8). Polymerases bind DNA and copy the base sequence during transcription. Transcription factors are proteins that bind specific sets of DNA sequences, activating or inhibiting transcription of particular genes (9).

Previous research has shown that a number of food components influence health outcomes via genetic pathways and that genetic variation between individuals may determine how well a protein works (10). Supplementing the diet with selenium, an important component of the antioxidant enzyme glutathione peroxidase, has been linked with decreased incidence of some types of cancer in humans. However, due to genetic variation, some individuals have one amino acid substitution (leucine for proline) in their glutathione peroxidase molecules, which apparently increases their risk for lung cancer. Although the reason for this is unclear, it may reflect reduced ability of these individuals to utilize selenium.

Nutrigenomic Research Goals

Prevention of chronic disease is an underlying theme of nutrition research. However, most chronic diseases are probably the consequence of interactions among numerous environmental factors, multiple genes and their variants (11). An important goal of nutrigenomic studies is to identify the impact of nutrients on the genome for the purpose of promoting health (12). More specifically, nutrigenomics can increase our understanding of how nutrients affect gene expression and the role of genes in determining an individual's response to particular nutrients.

One of the challenges of nutrigenomic research is to separate the effects of large numbers of nutrients on each of the wide variety of targets within the human body. For this reason, simpler organisms have been used as model systems in nutrigenomic research (12). The presence of adipose-like tissue and a lipid transport system has made the fruit fly a suitable model for studying obesity and related diseases. In addition, methodologies used in medical and pharmacological research are being applied in nutrigenomics. These research strategies focus on identifying the information contained in a nutrient's molecular structure that activates a specific molecular pathway.

Research of this type has led to the identification of transcription factors as important intermediates between nutrients and gene expression (11,12). Transcription factors are produced as a result of a series of biochemical reactions initiated by the binding of an extracellular molecule, such as oxidized-LDL cholesterol, to receptors on the surface of a cell (11). Subsequently, these transcription factors enter the nucleus and bind to specific sequences of the genome, selectively switching particular genes on or off.

The nuclear receptor superfamily of transcription factors has been identified as an important group of sensors for nutrients and their metabolites (12). Transcription factors in this group bind fatty acids and cholesterol metabolites, and then bind specific DNA segments thereby influencing DNA transcription. Thus, nutrients are able to impact protein synthesis and metabolic processes via their interactions with these receptors.

Potential Application of Nutrigenomics in the CKD Population

During the past decade, a number of studies have indicated that omega-3 fatty acids in fish oils may be beneficial for patients with CKD. Treatment with fish oils appears to slow progression of renal disease in patients with a commonly occurring form of glomerulonephritis, while fish consumption is associated with decreased cardiac symptoms and reduced mortality rates in patients undergoing maintenance hemodialysis (13-18).

Renal disease progression has been linked to hypertension and obesity, both of which may damage vascular endothelial tissue, induce inflammation and disrupt renal filtration (19). When the vascular endothelium lining blood vessels are damaged, monocytes and absorbed lipids that accumulate in the walls of affected vessels become macrophages and secrete pro-inflammatory cytokines (20). Inflammation activates endothelial tissue, stimulating secretion of adhesion molecules and resulting in the attraction of more monocytes. Macrophages bind oxidized lipoproteins producing foam cells that may occlude small vessels.

Studies indicate that adding the omega-3 fatty acid docosahexaenoic acid to endothelial cell cultures allows its incorporation into cell membrane phospholipids, resulting in inhibition of endothelial cell activity and decreased production of adhesion molecules (20). There is also evidence to suggest that products of omega-3 fatty acid oxidation inhibit cytokine activity via a mechanism involving transcription factors belonging to the nuclear receptor superfamily. Thus, omega-3 fatty acids may exert transcriptional control over a number of endothelial pro-inflammatory genes, including those that encode adhesion molecules and cytokines in the vascular endothelium. This may provide a basis for therapeutic application of omega-3 fatty acids in the management of inflammatory processes (20-22).

Conclusion

Although evidence from nutrigenomic research is promising, it is currently considered insufficient to warrant the formulation of personalized nutritional recommendations based on genetic information (23). However, it is anticipated that as this type of research proceeds, interventions tailored to specific molecular mechanisms underlying health conditions will become increasingly feasible (11). Such interventions might include helping patients to understand disease states, as well as integrating diet and other lifestyle choices into a treatment plan. Renal dietetics professionals will require an understanding of the influence of specific food components on metabolic pathways, and there will also be a need for continuing education programs focusing on genetics and the application of nutrigenomics in the treatment of chronic disease (24). ◆

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