NUTRIGENOMICS –EMERGING TOOL FOR THE PREVENTION OF DISEASES

J. Raju, P. Ravi Kanth Reddy, B. Priyanka, J. Narasimha and P. Guru Vishnu
P.V. Narsimha Rao Telangana Veterinary University, Hyderabad
E-mail: drrajuj@gmail.com (*Corresponding Author*)

Abstract: Nutrigenomics, the junction between health, diet, and genomics, can be viewed as the blend of molecular nutrition and genomics. Nutrigenomics will provide a far better understanding of how nutrition affects metabolic pathways and homeostatic regulation, how this regulation is disrupted in the early stages of diet-related disease, and the extent to which individual sensitizing genotypes lead to such diseases. Ultimately, nutrigenomics will certainly lead to evidence-based nutritional intervention approaches for preventing diet-related disease.
Keywords: Nutrigenomics, health, cardiovascular diseases, cancer, diabetes.

Introduction

During the past ten years, nutrition research has experienced an important paradigm shift from epidemiology and physiology to molecular biology and genetics. This is chiefly a consequence of three factors which have resulted in an increasing realization that the implications of nutrition on health and disease can never be understood without a thorough understanding of how nutrients act at the molecular level.

Firstly, the completion of several large genome projects markedly transformed the research agenda by drawing attention to the great importance of genes in human nutrition, and has provided loads of new genetic information to be explored. Second, there is an ever increasing recognition that micronutrients and macronutrients will be potent dietary signals that influence the metabolic programming of cells that have a vital role in the control of homeostasis (Francis et al., 2002). Finally, nutrition researchers have gradually started to realize that genetic predisposition could be an important contributor to the main causes of death that are related to diet, such as cardiovascular disorders, diabetes type II and cancers (Willett, 2002) .

The connection between diet and health is well established. Renewed awareness in which dietary constituents are biologically active and the manner they exert their consequences has been fuelled by the development of nutritional genomics (Elliott and Ong, 2002).

What is nutrigenomics?

Della Pena, in 1999, who defines for the very first time nutritional genomics as the fundamental technique to gene discovery which is presently best suited to substances of nutritional significance that are synthesized or collected by plants and other organisms (Ordova's and Corelli, 2004). This is a concept which focuses on role of nutrient-gene interaction. According to Chavez et.al, (2003) Nutrigenomics is the study of molecular relationships between nutritional stimuli and the response of the genes. Müller and Kersten, (2003) described the nutrigenomics as 'the application of high-throughput genomic tools in nutrition research. Nutrigenomics will promote a better knowledge of how nutrition can affect metabolic pathways and homeostatic control; how this regulation is disrupted during the early stage of a diet-related disease, and to what level individual sensitizing genotypes induce such disease's(Müller and Kersten, 2003).

Five tenets of Nutrigenomics

1) Dietary ingredients influence the human genome, either directly or indirectly, to alter gene expression or structure; 2) Under particular circumstances and in some persons, diet may be a crucial risk factor for several diseases; 3) Certain diet-controlled genes will likely contribute in the onset, incidence, progression, and/or severity of chronic diseases; 4) The degree to which diet influences the balance between healthy and disease states can be dependent upon on an individual's genetic makeup ; 5) Dietary intervention depending on knowledge of nutritional requirement, nutritional status, and genotype (i.e. personalized nutrition) may be used to prevent, minimize or cure chronic diseases (De Busk et al., 2005).

Nutrigenomics and the omic technologies

Genomics tools can be utilized in two distinct, but complementary, approaches in molecular nutrition research. The first approach is the conventional hypothesis-driven strategy: specific genes and proteins, the expression of which is determined by nutrients, are discovered using molecular tools like genomics(covering DNA), transcriptomics(RNA), proteomics(protein) and metabolomics (metabolites) - which eventually enables the regulatory pathways by which diet influences homeostasis to be identified (Müller and Kersten, 2003). In coming future, these models might offer the solution to understanding the relations between metabolic and inflammatory signaling paths.

The second approach, which is mainly theoretical at this point, is the systems biology approach: gene, protein and metabolite signatures which are connected with specific nutrients, or nutritional regimens, are catalogued, and might offer 'early warning' molecular

biomarkers for nutrient-induced modifications to homeostasis (Müller and Kersten, 2003). The first strategy will offer us with thorough molecular data on the relationship between nutrients and the genome, while the second strategy could be very important for human nutrition, provided the problem in of collecting tissue samples from 'healthy' individuals.

Considering these two broad strategies, the following objectives of nutrigenomics research can be identified: the elucidation of the relationships between nutrient-related regulatory pathways and proinflammatory stress pathways, to know the means of metabolic dysregulation that causes diet-related diseases; the identification of genotypes which are risk-factors for the development of diet associated human diseases (such as diabetes, hypertension or atherosclerosis) and quantification of their effect; and the application nutritional systems biology to develop biomarkers of early metabolic dysregulation and susceptibility (stress signatures) which are influenced by diet(Müller and Kersten, 2003).

Applications of nutrigenomics

In cardiovascular diseases

Cardiovascular disease (CVD), the largest cause of morbidity and mortality globally, is a complex multifactorial disease that is affected by genetic factors and environmental factors like diet. Nutrigenomics research shows the effect of genotype on the responsiveness to dietary factors or nutrients that could minimize CVD risk (Corella and Ordovas, 2009). Nutrigenomics becomes a reality in dietary personalization, in cardiovascular medicine, and consequently in optimizing CVD treatment and prevention. Hyperlipidemia is often associated with atherosclerosis and coronary heart disease. Therapy involves c as modifications in the patient's diet, physical exercise and therapy with pharmaceuticals like statins. However, individuals respond differently to the treatment.

 One single nucleotide polymorphism (-75 G/A) in the apolipoprotein A1 gene in women is linked to an increase in High density lipoprotein-cholesterol levels with the increase in the dietary intake of polyunsaturated fatty acids (PUFA). Individuals with the A variant showed an increase in the protective HDL (good cholesterol) levels following an increased consumption of PUFA when compared to individuals with the G variant having same quantities of PUFA. The genetic outcome was reversed, however, in women who ate more polyunsaturated fatty acids (PUFA) relative to saturated fats (SF) and monounsaturated fats (MUFA). In men, this type-of-fat effect was substantial when alcohol consumption and tobacco smoking were taken into account in the analyses (Corthésy, 2005).

In cancer

Diet is an important modifiable environmental factor, influence cancer risk and tumor behavior. About 30-40% of all the cancer cases are influenced by diet however; the exact amount is not known and is dependent upon the specific variety of cancer and the specific components of diet. Many studies suggest that prostate, breast, colon, liver and lung cancers are coupled to the dietary intakes (Davis and Milner, 2004).

Bioactive ingredients present in fruits and vegetables can protect against carcinogenesis by several mechanisms such as obstructing metabolic activation through increasing detoxification. In-vitro research studies and preclinical models have demonstrated many constituents of plant foods can modulate detoxification enzymes; examples are flavonoids (e .g. quercetin, rutin, and genistein), phenols (e.g. curcumin, epigallocatin-3-gallate and resveratrol), isothiocyanates, allyl sulfur compounds, indoles, and selenium (Keum et al., 2004; Milner, 2001).

Rodent models provide opportunities for identifying targets: Current advancements with mouse strains possessing cancer linked genes that are overexpressed or inactivated offered researcher with new models for understanding the carcinogenesis process and evaluating preventive approaches. For instance, a mutation of the p53 tumor suppressor gene is among the most often noticed genetic lesions in human cancer, accounting for; 50% of all human tumors analyzed to date. Hursting et al. noticed in p53-knockout (p532/2) mice that energy restriction (60% of the control intake of carbohydrate energy) enhanced the latency of spontaneous tumor development by 75%, reduced serum insulin-like growth factor-1 and leptin levels, and considerably slowed thymocyte cell cycle traverse and triggered apoptosis in immature thymocytes. Still other research illustrates the impact of the tumor suppressor gene p21 in evaluating the response to a diet rich in fat and low in vitamin D and calcium and how the allele from each parent can influence the size of the response with regard to longevity. Collectively, both animal and human findings offer an indication that genetic history can significantly control the process where bioactive food substances are absorbed, are metabolized, and impact molecular targets. It is thought that increased focus on genetic pathways and molecular targets will boost the nutrition community to discover sites of action of several bioactive food constituents across different tissues.

In diabetes

Type-2 diabetes is a metabolic disease involving impaired carbohydrate, protein, and lipid metabolism. This is additionally connected to sedentary life style and consumption of 'wrong' foods. We know that certain foods which are rich in sugar and white starches can produce the

symptoms of diabetes even worse. However, diabetes patients may have different responses to particular foods owing to their different genes. For instance, a report discovered that physicians advise modifications to diet and an increase in physical exercise for type 2 diabetic patients, but only 20% of patients can actually control symptoms by these interventions. This is where nutrigenomics might help control type-2 diabetes (Kaput et al., 2007). Nutrigenomics can come to help through clinical diagnostics for phenotypes such as insulin level and glucose tolerance, as well as through metabolomics diagnostics wherein diabetes biomarkers (biochemical compounds viz. glucose, cholesterol, creatine, and fatty acids that indicate the susceptibility and advancement of the disease) are assessed. Researches demonstrated that 'over expression' of SREBP -1a and SREBP-1c (t-RNAs that trigger genes involved in the synthesis and uptake of cholesterol, fatty acids, and triglycerides) play a vital role in the progression of diabetes. In the same way, some fibers modulated cholesterol absorption in the digestive tract, thus performing a significant role in describing nutrient bioavailability. This may help researchers discover the complex relationship of diet-gene interaction of the diabetic person and offer more efficient dietary strategies.

Similarly, nutrigenomics might help in formulating treatments for type-2 diabetes through personalized diet. And they happen to be more efficient than certain drugs. For instance, the drug, rosiglitazone, frequently used by type-2 diabetics, is known to modify lipid metabolism in liver tissues and adipose tissues resulting in liver toxicity with long term use. However, nutrients present in certain diets possess the similar metabolic pathway as the said drug, but without its negative effects. Well-known nutritional studies evaluating the response of an intervention group to controls offered the same diet without specific nutrients. Simple examples examined serum lipid alterations due to a high fat vs. control diet or determined variations in nutrient intakes between groups of individuals who have a disease (cases) versus those that do not (i.e. controls). Outcomes of these studies are averages of all members of the control and all members of the interference group (Kaput et al., 2007).

In eye diseases

There is the latest discovery on the connection of nutritional and genetic factors in age-related eye diseases: age-related macular degeneration (AMD; a degenerative disease of the retina) and cataract (opacification of the lens). The eye is specifically sensitive to oxidative stress due to direct exposure to light. Antioxidants, such as zinc, vitamin C, and E, possess a protecting effect in AMD and probably in cataract. In addition, two carotenoids, lutein and

zeaxanthin, might have a more precise role in the eye: they accumulate in the retina, wherein they form the macular pigment, and in the lens. Finally, docosahexaenoic acid (an omega-3 polyunsaturated fatty acid) is especially vital for the retina, where it exerts structural, functional and protective actions (Delcourt, 2007).

Conclusion

Nutrigenomics, the junction between health, diet, and genomics, can be viewed as the blend of molecular nutrition and genomics. Nutrigenomics will provide a far better understanding of how nutrition affects metabolic pathways and homeostatic regulation, how this regulation is disrupted in the early stages of diet-related disease, and the extent to which individual sensitizing genotypes lead to such diseases. Ultimately, nutrigenomics will certainly lead to evidence-based nutritional intervention approaches for preventing diet-related disease.

References

(1) Chavez, A., & de Chávez, M. M. (2003). Nutrigenomics in public health nutrition: short-term perspectives. European Journal of Clinical Nutrition, 57, S97-S100.

(2) Corella, D., & Ordovas, J. M. (2009). Nutrigenomics in cardiovascular medicine. Circulation: Cardiovascular Genetics, 2(6), 637-651.

(3) Corthésy TI, Nutrigenomics: The Impact of Biomics Technology on Nutrition Research, Ann Nutr Metab, 49, 2005, 355-365.

(4) Davis CD, Milner J, Frontiers in nutrigenomics, proteomics, metabolomics and cancer prevention, Mutat Res, 551(1-2), 2004, 51-64. 11.

(5) DeBusk, R. M., Fogarty, C. P., Ordovas, J. M., Kornman, K. S. (2005). Nutritional genomics in practice: where do we begin? J Am Diet Assoc; 105:589–98.

(6) Delcourt, C. (2007). Application of nutrigenomics in eye health. In *Nutrigenomics-Opportunities in Asia* (Vol. 60, pp. 168-175). Karter Publishers.

(7) Elliott, R., & Ong, T. J. (2002). Nutritional genomics. *Bmj*, *324*(7351), 1438-1442.

(8) Francis, G. A., Fayard, E., Picard, F. & Auwerx, J. Nuclear receptors and the control of metabolism. Annu. Rev. Physiol. 65, 261–311 (2002).

(9) Kaput J, Noble J, Hatipoglu B, Kohrs K, Dawson K, Bartholomew A, Application of nutrigenomic concepts to Type 2 diabetes mellitus, Nutrition, Metabolism & Cardiovascular Diseases, 17, 2007, 89-103

(10) Keum YS, Jeong WS, Kong AN, Chemoprevention by isothiocyanates and their underlying molecular signaling mechanisms, Mutat Res, 555(1-2), 2004, 191-202.

(11) Milner JA, A historical perspective on garlic and cancer, J Nutr, 131(3s), 2001, 1027S-1031S.

(12) Müller M, Kersten S. Nutrigenomics: goals and strategies. Nat Rev Genet. 2003 Apr; 4(4):315

(13) Ordovas, J.M., Corella, D. (2004) Nutritional genomics. Annu. Rev. Genomics Hum. Genet. 5, 71-118

(14) Willett, W.C. Balancing life-style and genomics research for disease prevention. Science 296, 695–698 (2002).