

Nutrigenomics

From promise to practice

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NUTRIGENOMICS, A TERM DERIVED FROM 'nutrition' and 'genomics', analyses the interactions of nutrients/dietary bioactive components with the genome. The purpose of nutrigenomics is to comprehend the body's response to various diets and food through various high-throughput 'omics' techniques—including genomics, transcriptomics, proteomics and metabolomics.¹ Genomics makes use of techniques such as recombinant deoxyribonucleic acid (DNA) and DNA sequencing methods to sequence, assemble and analyse the structure and function of genomes. Transcriptomics, also known as 'gene expression profiling' is the study of the transcriptome encoded by the genome in a given cell population using DNA microarray technology.² Proteomics is the study of the structure and function of proteins and is a vital component of functional genomics. Apart from being used in the analysis of gene expression in tissues, proteomics can also be used for the identification of new protein biomarkers that can be detected in plasma.³ Metabolomics is an emerging field of 'omics' research that studies metabolite levels in the metabolome (a set of small-molecule metabolites) and their changes over time in response to stimuli. Metabolic abnormalities could be detected in individuals by the quantitative non-invasive analysis of human body fluids (such as urine, blood and saliva) to detect physiological alterations in response to the toxic effects of chemicals, visible in the form of lesions in the liver or kidneys.⁴ Transcriptomics has, however, helped in understanding the complex interactions between genetic and environmental factors in order

to design nutritional interventions.⁵ The 'omics' applied to nutrition will ultimately lead to the discovery of biomarkers for early diagnosis as well as to the design of personalised diets that encompass bioactive food components of great health benefit.²

With the success of the Human Genome Project and advances in technologies, a significant amount of information has been amassed related to human genes and their mechanisms. In turn, nutrigenomics is a new and evolving field which forms a junction between health, diet and genomics to analyse patterns of gene expression, protein expression and metabolite production triggered by nutrients.⁶ It examines the characteristic behaviour of cells towards a particular nutrient and its influence on homeostasis. Nutrigenomics is also involved in the discovery of certain genes and markers during the initial-stages of diet-related diseases.

Nutrigenomics increases our knowledge about the mechanisms by which nutrition affects the metabolic pathways underlying homeostatic control. Subsequently, this can be used to determine naturally occurring chemical agents in food that could prevent the onset of diseases such as obesity, type-2 diabetes and cancer. The nutrients present in the diet are received as signals by the sensory system of the various cells in the body which are interpreted by the cells to gene expression, protein expression and metabolite production. Hence, different diet patterns elicit a variety of gene and protein expression and metabolite production. Such diet-induced patterns and their effects are described by nutrigenomics as "signature dietary patterns". Micronutrients and macronutrients are

potent dietary signals that influence the metabolic programming of cells that play a crucial role in the control of homeostasis.

Nutrigenomics, which studies the interactions between different types of food and the genome, can aid in selecting foodstuffs that are vital to health. One of the emerging fields of research to use nutrigenomics is complementary alternative medicine (CAM). CAM is defined as a method of treatment that is used together with (complementary) or instead of (alternative) traditional medicine and includes meditation, spiritual healing, energy therapy (magnet therapy and light therapy), massage therapy, acupuncture, herbal preparations (*Ayurveda*), dietary supplements, yoga, acupressure, movement therapies, naturopathy and homeopathy.⁷⁻⁸ CAM research has identified a number of active compounds from various herbal and dietary products and evaluated their anti-disease (e.g. anti-cancer) properties; these include polyphenols from green tea, resveratrol from grape seed/skin, anthocyanin and pigments from numerous flowers, algae, fruits and vegetables. The common property of these compounds is their anti-oxidant/free radical scavenging ability. Our previous study demonstrated that some of these compounds induce high free-radical formation, prevent cell growth and cause apoptosis selectively in cancer cells, but not in normal cells.⁹ A number of CAM studies have focused on the effects of individual compounds derived from herbs/plants used at 'bioavailable' concentrations. However, only a few studies, including our own work, have explored the effects (synergistic, additive or antagonistic) of the combination of these compounds in diseases.⁹ Interestingly, each of these individual compounds, when used in combination, have been found to target multiple signalling pathways in the cell.⁹ Oral administration of CAM natural medications has shown to have the great advantage of low toxicity and positive effects on various diseases.¹⁰⁻¹¹

In Oman, with high rates of consanguinity, the risk of developing genetic disorders, including inborn errors of metabolism is widespread.¹² The rapid advances in nutrigenomic technology will ultimately lead to breakthroughs in the treatment of various genetic disorders. Inherited mutations in specific genes can predispose the individual to diseases. The risk of developing cancer can be

markedly increased if there is a gene-diet interaction. Twin studies showed that the probability of identical twins developing the same cancer is less than 10%, indicating that the environment is an important factor in cancer susceptibility. For example, studies have shown that familial susceptibility is only responsible for relatively rare cancer variants.¹³ In addition, most twin studies make the assumption that both twins are exposed to the same environment and the absence of any environment-genotype interaction.¹³ Differences in epigenetic modifications between twins can also explain the differences in susceptibility between twins.¹⁴

As nutrition is a major component of the environmental conditions which can putatively interact with the genotype to bring about a phenotypical change, any disease or condition that is associated with genetic and/or nutritional components can be targeted for nutrigenomic studies in order to test whether dietary intervention can affect the outcome. Differences in genetic makeup (genotype), as well as nutrient deficiencies, are factors in various diseases, including cancer, cardiovascular, digestive and inflammatory diseases. Nutrigenomics is addressing why some people can control disease with diet, whereas others require drugs. Therefore, nutrigenomics is expected to significantly contribute to personalised medicine.

The expected benefits from nutrigenomics are tremendous and encompass: (1) a better understanding of the toxicity and safety profile of macro- and micronutrients; (2) the prevention of certain diet-associated diseases; (3) the enjoyment of otherwise less healthy food by individuals whose health is not likely to be affected; (4) the avoidance of unhelpful dietary supplements that are routinely used by certain people, and (5) the prevention of diseases and an increase in life expectancy.

Despite its recognised future potential benefits, nutrigenomics nevertheless raises a number of ethical issues and risks that are similar to 'genethics' or ethics in genetics: (1) a predisposition to develop a disease might trigger anxiety and stress in the individual; (2) the privacy of the patient might be jeopardised (for instance in deciding who should know the results); (3) potential discrimination against affected individuals by employers, health insurance companies, family, etc.; (4) the crucial need for well-qualified physicians to interpret nutrigenomic reports and make the appropriate

decisions, and (5) other unrecognised risks.

Despite its early positive impact and the very few diet-gene interactions that have been well characterised to yield useful information (e.g. obesity), far more research is needed before nutrigenomic expectations become a reality. Understanding the mechanisms by which some components in food interact with certain genes that can predispose to metabolic diseases would help people to avoid certain types of food; this can subsequently lead to the prevention of certain diseases. Furthermore, knowing the right amount and the type of specific nutrients that our body requires would positively impact the management of our health. Although studies conducted in this field have been costly and difficult, the results are deemed to be helpful for the advancement of medical technologies pertaining to health care (personalised medicine) and weight management.

Ongoing nutrigenomic studies in our laboratory aim to establish the relationship between various combinations of powerful specific natural compounds that can target specific diseases (e.g. a combination of phytochemicals specific to treat cancer). More interestingly, in addition to understanding the basic molecular mechanisms of action of certain compounds in cancer, functional nutrigenomics will ultimately lead to the identification and validation of candidate gene targets that can pave the way towards the design of anti-cancer therapeutic strategies.

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