Future Perspectives of Nutrigenomics Foods: Benefits vs. Risks

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Nutrigenomics, defined as the application of high-throughput genomics tools in nutrition research is now past its incubation phase. The poorly understood associations of diet and disease prevention in particular will likely be the single most important catalyst to its accelerated and continued growth. Whether the goal of matching foods to individual genotypes to improve the health of those individuals can be attained, and personalised nutrigenomic foods enter the world's food markets, depends on numerous hurdles being overcome: some scientific in nature, some technical and others related to consumer, market or ethical issues. Public adoption of new technologies is an important determinant for their success. Many of the drivers behind the trend in personalisation of food are now known, particularly ethical, legal, and social issues (ELSI) are the major drivers. Future development in the field of nutrigenomics undoubtedly will place its seemingly huge potential in better perspective. From the scientific responsibility point of view, one hopes that the new perspectives to be gained and progress to be made in this field will be so managed as to take the public at large on board, if we are to avoid another nutrition education disaster of the genetically modified organism type and dimension.

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Introduction
Fifty-four years ago, Watson and Crick described DNA as a double-helix structure. The publication of the human genome in 2001 represented a revolutionary breakthrough in health and nutrition research and its market applications. Both nutrients and non-nutrient components of foods, diets and lifestyle can affect every step in the flow of genetic information from gene expression to protein synthesis level. This transition may alter metabolic function of our body in a very complex ways. Like the pharmaceutical industry, the food industry now has an opportunity to position food and nutritional bioactives to promote health and prevent disease based on knowledge of the genetic make-up of individual consumers.

The new paradigm for the interplay between the human genome and its environment is the genome-food interactions. “Nutrition and food science are stepping into the genomic era, and it is becoming evident that nutrients and other food components are key factors in altering gene transcription, protein levels and functions and the metabolome, which eventually translates into a health or disease state on the basis of a given genome”². Thus, the nutrigenomics/nutrigenetics is an approach to nutrition and human health that takes into account and studies the effect of genetic differences in human responses to foods. Nutrigenomics is emerging at the same time as the functional food industry, a movement that is working toward foods that provide benefits beyond basic nutrition³.

Nutrigenomics is an emerging science with high consumer expectations, but the major concerns are whether the goal of matching foods to individual genotypes to improve the health of those individuals can be attained, and personalised nutrigenomic foods enter the world's food markets, depends on numerous hurdles being overcome: some scientific in nature, some technical and others related to consumer, market or ethical issues.

In this review, emerging paradigms of nutritional genomics are discussed as they relate to the functional food market. Emphasis is given on how genomics tools can be leveraged to produce better food to improve human nutrition and health and thereby deliver societal and economic benefits.

Pharmacogenomics vs Nutrigenomics
The boundary between the health effects and foods is becoming blurred everyday with the development of the concept of personalised functional food. The terms pharmacogenomics and nutrigenomics both

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have grown out at their genetic ancestors as large scale “-omics” technologies and can be used to individualise or personalise medicine or food. But, unlike pharmaceutical, food consumption does not deal with ‘single exposure-single time point’ effects, but the multiple dosing of complex mixtures of bioactive compounds, mostly at the low doses. It is very hard to detect all biological effects of a food component, food or diet. Thus, it is advisable to start with food components that are well characterized in terms of their metabolism, the cellular processes and health outcomes. The rapid advancement of analytical tools in transcriptomics, proteomics and metabolomics will enable not only increased detection sensitivity, but a greater range of effects. Thus, multiple minor changes taken together can be exposed with new bioinformatics approaches created with a broader sensitivity.

Drivers in functional foods

There are a number of drivers for functional foods, with trends emerging in market analyses. New Nutrition Business, for example, publishes “10 Key Trends in Functional Foods” on a regular basis. Although ‘nutrigenomic’ foods have yet to be mentioned specifically as such, many of the 2008 trends described in the marketing sense refer directly or indirectly to “personalisation” aspects. One recent market analysis on functional foods noted that although the industry is already crowded, there appears to be some splintering into subcategories based on consumer target markets (niche markets). Many of the drivers behind this trend in personalisation of food are changing demographics and social trends (more “singles” and childless couples), consumers awareness and subsequently increased scientific research-led clinical evidence for the efficacy of functional foods, increased nutrition-oriented marketing activity, particularly targeting health professionals, and the penetration of mass market distribution channels. The consumer’s preference for optimal health is an also a major driver for food choice and food production. Ethical legal and social issues are adding a new dimension in functionalised food development as a future driver.

Applications

Food is central to health, and advice on food consumption patterns is an important component of health promotion and the management of lifestyle related diseases such as obesity, heart disease and type-2 diabetes mellitus. We are now able to better appreciate that not only do foods deliver nutrients and other bioactive components, they also deliver them in an interactive matrix within single foods and then in whole diets.

Thus, while foods deliver nutrients that interact with genetic potential, not everyone is the same. While it may seem that there is enough similarity within populations to show effects of diet, there is a need to individualise advice, if we want to assure that the dietary strategy will benefit everyone. In addition, it must be remembered that people eat foods, not single nutrients in the diet and it is still this combination of food components that will have the ultimate effect. While there is a lot known about dietary fat and its effects on risk factors for chronic lifestyle related disease, there are numerous other food components that have implications for disease pathology. Put together, from a practice perspective, argues that there is not enough information to begin personalised nutrition on a grand scale just yet, but there is evidence of proof of concept in the case of dietary fat and lipid metabolism. The dietary polyunsaturated fatty acid (PUFA), for example is positively implicated in the management of risk factors and we can provide advice on useful whole diet models that assure a good balance of these fatty acids from targeted foods. We can also prescribe foods that contain bioactives known to be beneficial. In this manner, personalised advice takes the form of specific food-based advice that can be ultimately refined, as more knowledge on the nutrigenomics interface comes to hand.

Beyond agricultural application, the introduction of genomic technologies are now promising in food processing, food safety and quality assurance. In food processing, a relatively new application of these technologies is the discovery of ‘process markers’ to guide industrial processes or improve supply chain management. This application is very successful in tea manufacturing complex process and management of post-harvesting yellowing and short-life of broccoli. The safety evaluation of food components and the detection and identification of microorganisms during food spoilage are the major applications in food safety area. DNA finger printing is now being widely applied within the food industry as a means of authenticating plants, animals and packaged food products.
Food outcomes and attributes

The modern technologies at the molecular level have proven the scientific concept what Hippocrates uttered, “let food be your medicine and medicine your food” in 390 BC. There are indications from initial consumer’s studies that US consumers will accept functional foods based on nutrigenomic principles. Designed to address various health issues, these foods are likely to enter into consumer market over the next few decades. Two kinds of food outcomes are thought to emerge from research in the nutrigenomics area. Firstly, foods will result from “public good” information. This information will identify food components that are relevant to the needs of people with specific genetic conditions or predispositions. Presumably, they will need to either increase or decrease their consumption of these components. This information would be in public domain and freely accessible to all, especially to health professionals who provide dietary advice. Primary produce and minimally processed foods would also fit this category. Secondly, specifically manufactured nutrigenomic foods are likely to emerge on the market, developed in partnership with food industries and with protected intellectual property arrangements. These are likely to be processed foods, rather than commodities with specific brands capturing value.

The health professional of the future would need to have a very solid understanding of food composition and the bioactivity of food components. They would need to assess dietary intake with greater accuracy and be able to prescribe diets with more discrimination between foods and products. This would make a call on greater use of information technology, as food databases would need to be continually updated and made accessible. Food delivery systems would need to accommodate the discerning consumer and food labels would need to provide the information required.

Market: Current and future

The phrase “personalised foods” may conjure visions of nutrigenomic foods being developed by food companies for individual consumers, but this is unlikely due to problems of scale. Ronteltap et al. for example argues that “this is highly unlikely for foods that are made using high volume production technologies but is possible through the use of point-of-sale technologies, where (most likely) a beverage could be prepared using a combination of ingredients to suit an individual genotype”.

It is economically feasible that consumers with specific genetic profiles that may predispose them to particular disease or disease risk can be grouped, and so ‘nutrigenomic foods’ could be mass customised rather than individualised. This will depend on growing knowledge of the prevalence of genomic profiles, a process already begun with studies of single nucleotide polymorphisms (SNPs), as evidenced from a number of European Union-funded research initiatives, including LIPGENE and DIOGenes. Product diversification may depend on several factors, including market size and type, profit margins, level of value capture and the level of scientific validation required.

Bringing foods to the marketplace is always challenging, but in the case of functional foods, attention is always required for establishing the scientific evidence and then allowing for regulatory conditions. If nutrigenomic foods emerge as a completely new category of foods, there may be new needs in the areas of marketing and distribution of the foods, which will require additional business planning. As with the investment in any niche food, nutrigenomic foods will need to be high value products and extensive market research is necessary before undertaking production.

Consumer perceptions

Nutrigenomics is an emerging technology in the health maintenance and promotion area, represented by personalised food products and services. Besides advancing the fundamental understanding of diet–disease relationships, nutrigenomics could provide opportunities for the development of food products or dietary advice tailored to the nutritional needs of specific groups of consumers, or even individuals. Some authors have optimistically argued that these so called “personalised foods” will shift the global food market from a technology push into a consumer pull system. In this situation, the consumer's preference for optimal health is a major driver for food choice, and food production. In terms of 'cost-benefit perceptions', the benefits of nutrigenomics are potentially high, because it can be achieved with just nutrition as the tool. Health benefits relate to the wellness, improving performance (e.g., in sports) and ultimately longevity.

Few recent consumer studies have implicated the possibilities of the introduction of new foods accompanying the emerging knowledge in nutrigenomics. It is also highly likely that at least...
for preventive health effects, the total diet will remain the major factor, so individual foods will have to either be especially potent or play a major role in an overall food choice pattern that can be easily matched. For example, currently stanol enriched spreads can be effective in dietary strategies targeting cholesterol management, but they have to be consumed at defined levels and the total diet should remain low in fat. If the food does not deliver the purported effects, the consumer confidence will be lost, and this will affects the whole market. Delivery of messages and delivery systems for dietary management must be a well a considered accompaniment.

Whatever food products are developed, there must be some consideration for regional cuisine and food accessibility. Presumably, staples such as rice and bread would continue to form the backbone of various eating patterns. Fruits and vegetables are likely to remain significant, as more and more evidence emerges of their potential benefits. How the new products fit into the overall diet will be important. Finally, taste and the social context of eating will have an impact on the acceptability of these new products. Eating is a deeply entrenched social and cultural behaviour which is unlikely to be usurped by a medicalised form of consumption. The aim for a successful and ultimately more beneficial food supply is to ensure it fits within the picture of acceptable and enjoyable food consumption, made all the more enjoyable because it is ‘good for you’.

Ethical concerns

Nutrigenomics lies in the intersection of several fields in which ethical, legal and social issues (ELSIs) need urgent attention, if the desirable social outcomes are to be achieved from this promising science. Since it’s a high technology-backed discovery science, the consumer’s expectations are very high. The ‘biohype’ around the nutrigenomics foods and nutrigenetics tests are imminent and unavoidable, particularly in the early stages of evolution of a new idea. Practically, ‘biohype’ is already taking place through the aggressive marketing of nutrigenomics tests to the public, which many consider to be premature, raising concern over ELSIs. Five areas have been identified by international experts in the context of both basic nutrigenomics research and its clinical and commercial uses: i) health claims benefits arising from nutrigenomics, ii) managing nutrigenomics information, iii) delivery methods of nutrigenomics services, iv) nutrigenomics products, and v) equitable accessibility to nutrigenomics. Hence it is important to elevate the depth of debate to understand and management of this ‘biohype’ on diet-gene interactions using evidence-based research methodologies.

Is public health going private?

During the last 50 years, public health nutrition aims to develop “population-based strategies to promote good health through healthy diets”. The effective public health nutrition interventions generally rely on the notion of the “greatest good for the greatest number of the population”. But, with the advent of nutrigenomics and nutrigenetics principles, the future public health concept and policy need to be redesigned. The question is whether this new technology-driven functional foods will make an important difference to the health of the public. There is a new trend in industry to privatise the public health system.

Recently, it is reported that a large Dutch insurance company (VGZ) has signed an agreement of cooperation with Unilever and has described the initiative as a “promoter of public health”. They have promised to refund customer for three years, part of their premiums, up to 40 Euros a year, when they buy Unilever’s Becel pro-active products. In 2003, VGZ spent 92 million Euros for these purposes and following this business line, two other minor Dutch insurance companies (IZA and IZZ) have chosen the similar approach. This was a unique move, because normally insurance companies do not associate with disease prevention. The VGZ-Unilever venture seems an offspring of a marriage between modern bioscience and industry. There is convincing scientific evidences on the cholesterol lowering effect of plant sterol-based products, such as margarine, milk, yoghurt etc across the wide population, but it is still not enough at an individual level. Nevertheless, VGZ has announced (on its website) that it wants to take a lead role as a “promoter of public health” by saving money through health and conscious eating. This reflects some of the problems associated with the health tasks at hand and the nature of commercial relationships.

Regulation

In most of countries, food and drugs are regulated differently. One purported difference is that while food is a necessary requirement of survival of the
organism, even in the absence of ill health, pharmaceuticals contribute to survival only in a diseased condition. For genomics-driven functional foods, the case for using genetic information to inform dietary advice may be stronger than that for other foods. Traditionally, food is tested for safety, not for efficacy, unlike drugs. Since the boundary between food and drugs is increasingly thinned, their regulation will, arguably, increasingly need to consider for both safety and effectiveness.

Under current regulatory frameworks, the rules of the European General Food Law Regulation are applicable to all foodstuffs. Furthermore, legislation on dietetic foods, food supplements or novel foods, and two proposals on nutrition and health claims and the addition of substances to foods, may be applicable to nutrigenomics products, depending on their nature and their use. Currently, claims related to reducing risk of disease (or may be even curing disease) — the types of claims most likely to be useful for nutrigenomics-based products — are prohibited. Due to the amount of regulations and procedures to be followed, getting nutrigenomics products ready for the market will be an expensive and time-consuming process. This may have large impact on the type of companies able and willing to invest in nutrigenomics products.

The nutrigenomics and nutrigenetics are associated with aggressive pursuits in intellectual property protection, though policy makers may be undecided on how to regulate processes and products. There also is preliminary debate on whether proprietary discovery will impede new product development and the dissemination of healthier foods on the widest level in the future. In the EU, the US, Australia and Canada, genetic testing is coming under increasing scrutiny and governments are making efforts to standardize regulations. However, nutrigenetics tests are considered “lifestyle” tests, largely because they do not make clinical claims. The EU considers most genetic tests low risk and thus exempt from independent pre-market review. In Canada and Australia, there are even fewer controls. Currently, nutrigenetics tests are reviewed for neither analytical nor clinical accuracy. Very recently, the European Nutrigenomics Organisation (NuGo) has published the framework to advise scientists in some of the ethical issues surround nutrigenomics, such as storage of genetic data, with the long-term aim to produce a European standard. The guidelines are not a legal document and that the ethical approval for nutrigenomics research will depend on the legal standards developed in individual member states.

**Conclusion**

Nutrigenomics is a potentially promising development in emerging functional food and nutraceutical research. The value add now moves on to not just components with newly discovered functional properties, but also how these functional properties may interact with the genetic environment of the consumer. However, it is still in its infancy, and there are quite some uncertainties about its further development, both from technological and societal acceptance point of view. Healthcare practice and food product development will move on regardless and it is the partnership of science and practice that will enable a smooth uptake and translation of new knowledge in the field as it emerges. Steps in this direction, however, must be taken with caution and great care. There are ethical issues to consider, in terms of consumer confidentiality and rights to be fully informed. It will be increasingly necessary to communicate the extent of the lack of knowledge, as it is the extent of knowledge in the area to maintain trust, build effective partnerships (including with consumers) and, and most importantly, to do no harm. The potential, however, is almost utopian, as we move toward understanding the genetic details behind human biology and the way in which the consumption of food, one of life’s simplest and great pleasures can have such an enormous impact on life itself.

Future development in the field of nutrigenomics undoubtedly will place its seemingly huge potential in better perspective. From the scientific responsibility point of view, one hopes that the new perspectives to be gained and progress to be made in this field will be so managed as to take the public at large on board, if we are to avoid another nutrition education disaster of the genetically modified organism (GMO) type and dimension.

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