

## NEW ZEALAND - FERTILE GROUND FOR FUNCTIONAL FOODS AND NUTRIGENOMICS

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**ABSTRACT:** *Nutrition-related disorders including cardiovascular disease, diabetes and various cancers rank highly among the causes of death and disability in New Zealand, with significant differences between racial groups in disease susceptibility. While the bulk of the population are Caucasians, a significant proportion are of Polynesian origins, including both Maori and Pacific Island groups, with an increasing Asian immigrant population. Maori have significantly lower colon cancer and significantly higher stomach, breast, lung and pancreatic cancers in comparison with the rest of the population. Both diabetes and cardiovascular disease develop at an earlier age in both Polynesian and Asian groups as compared with those of Caucasian origin. Thus, dietary manipulation has the potential to significantly affect health and disease-related outcomes in the different racial groups of New Zealand. However, major dietary changes within the population are difficult to implement. Functional foods offer the solution of modifying the nutritive properties of foods that people already consume. New Zealand's high incidence of diet-related diseases makes it an ideal testing ground for new developments in functional foods. The key to these developments is nutrigenomics, which offers approaches powerful enough to explore the complex interactions between nutrients and biological systems, allowing the rational design of functional foods.*

**KEY WORDS:** : Cancer, Cardiovascular Disease, Diabetes, Functional foods, Nutrigenomics

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### INTRODUCTION

The relationship between diet and disease is well established. The Human Genome Project provided the promise of recognizing the genetic uniqueness of individuals, and its new challenge is to understand the nature of individual's interactions with their environment, especially diet. The emerging field of nutrigenomics integrates concepts of nutrition, molec-

ular biology and genomics, in order to study the interplay between diet and the activity of an individual's genes. Such ideals are moving into the commercial field. For example, the California-based company NutraGenomics, Inc. (<http://www.nutrigenomics.com>) advertise a customized workshop on nutritional genomics, which they base on 5 tenets, as follows:

- Improper diets are risk factors for disease
- Dietary chemicals alter gene expression and/or change genome structure
- The influence of diet on health and disease susceptibility depends upon an individual's genetic makeup
- Genes regulated by diet play a role in chronic diseases
- Intelligent nutrition – that is, diets based upon genetics, nutritional requirements and status – prevents and mitigates chronic diseases.

Whereas health and wellbeing are only one group of drivers in the functional food industry, they become of major importance in nutrigenomic studies, which focus on optimisation of a health outcome and avoidance of disease. The rationale for this approach is the recognition that health outcomes are not only a function of either diet or genetics, but a complex interplay between them. Understanding can lead to the rational development of functional foods to target key medical issues such as cardiovascular disease, cancer and diabetes, or debilitating disorders such as osteoporosis or arthritis. We suggest that the population mix, disease susceptibility and regulatory environment make New Zealand an outstanding testing ground for such products.

### DIET AND DIET-RELATED DISEASES IN NEW ZEALAND

A largely unpolluted environment, abundance of fresh food and agricultural-based economy in New Zealand has traditionally been assumed to provide the population with a healthy lifestyle and diet. However, an analysis of New Zealand food supply and consumption patterns in comparison with other OECD countries (Laugesen and Swinburn, 2000) suggests preferential eating patterns that coincide with high risks of diet-related diseases. For example, these authors calculated that on 1995 figures, the high *per capita* consumption of butter and meat fats led to the New Zealand food supply being ranked highest for thrombogenicity and third for

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atherogenicity among OECD countries. The high fat consumption makes the population susceptible to obesity, with consequent increases in the risk of cancer and diabetes (Hursting and Kari, 1999). While food preferences are slow to shift, consumers have responded to health messages with increases in fruit consumption, vegetable consumption and fibre intake between 1961 and 1995, and changes in the fatty acid profile of the diet (Laugeson and Swinburn, 2000).

Cardiovascular disease includes all diseases of the circulatory system including acute myocardial infarction, ischemic heart disease, valvular heart disease, peripheral vascular disease, arrhythmias, high blood pressure and stroke. Although the incidence of deaths from this class of diseases has been dropping somewhat over recent years (Capewell et al., 2000), nevertheless it represented approximately 40% of all deaths between 1996-1997, and was the leading chronic disease cause of hospitalisation in New Zealand (New Zealand Ministry of Health, in press). At an international level, it is also a major cause of death and disability (Murray and Lopes, 1997). Cancer leads to around 25% of all attributable deaths in New Zealand (New Zealand Ministry of Health, 1999). Obesity and diabetes are also very serious problems, and may enhance the probability of complications or of fatality from other diseases. Arthritis and depression are also at high levels in New Zealand, and both may be affected by diet.

### **POPULATION GROUPS AND FACTORS AFFECTING FOOD INTAKE**

Maori people, of Polynesian origins, representing around 14% of the population (Statistics New Zealand, 2001), are thought to have been in New Zealand for around 1000 years (Cambie and Ferguson, 2003). Although there is also a significant (and increasing) component of Pacific Island people (7%), as well as Asian immigrants into the country (7%), the bulk of the population are Caucasians of European descent.

There are differences between the groups in dietary intakes and food preferences (New Zealand Ministry of Health, 1999). Dietary surveys have generally suggested higher overall caloric intakes in the Polynesian groups. A National nutrition survey conducted in 1997 provided dietary data for Maori versus non-Maori (New Zealand Europeans and others) groups. In general, the intake of total energy, protein and fat was higher in men than in women, and higher for Maori than for non-Maori groups. The reasons for this may be partly economic. Food security is defined as "having enough, appropriate and acceptable food available". Parnell and co-workers (2001) found that New Zealand Europeans reported the most food security, Maori somewhat less, and Pacific people the least. This reduced food security led to the consumption of lower cost, higher fat foods. They suggested that not having enough food may be more prevalent in New Zealand than in the US or Australia.

The different population groups also have different risks of non-communicable disease. For example, cancer of the liver, stomach and [possibly] breast appear lower for the European groups as compared with those of Polynesian descent, while

that of the colon and prostate are higher (Tukuitonga et al., 1992; Ferguson, 2002). Both diabetes and cardiovascular disease develop at an earlier age and may be more severe in Polynesian groups as compared with those of Caucasian origin. For example, Simmons et al., 1996 surveyed residents from two districts of South Auckland, New Zealand, with a high proportion of Maori and Pacific Islands people, as well as interviewing patients with known diabetes. Their study revealed significant ethnic differences in diabetes and its care, at least in South Auckland. Maori and Pacific Islands patients were younger than Europeans at diagnosis, had a higher chance of having had their diabetes diagnosed in pregnancy, were less likely to be receiving antihypertensive or insulin therapy, were more likely to be blind, and were more likely to have received retinal photocoagulation.

There also seems to be significant differences among susceptibilities to disease in different population members, independent of race. Metcalf et al., 1999 considered levels of modifiable risk factors of coronary heart disease (CHD) survivors in a middle-aged New Zealand workforce. Their cross-sectional survey of 5,656 workers aged  $\geq 40$  included 73 individuals with a history of hospitalisation for CHD. Compared with those not showing evidence of disease, the CHD survivors reported higher total carbohydrate, dietary fibre, polyunsaturated fat intakes and ratio of polyunsaturated to saturated fat intakes. Total fat, saturated fat and monounsaturated fat intakes were lower than seen in the control group. They ate less red meat and less salt, and more fruit and cereal, milk and margarine. Despite this group moving to dietary measures considered beneficial for CHD, they had higher, similarly adjusted, mean serum total cholesterol, triglyceride and lower HDL-cholesterol levels, suggesting that they were dyslipidaemic. The authors suggested that high-risk CHD survivors would benefit from more aggressive measures aimed at correcting their lipid parameters.

Due to the rapid increase in the Asian population through immigration in recent years, combined with the diverse ethnic makeup of this broad category (44% Chinese, 26% Indian, 8% Korean, 5% Filipino, 4% Japanese, 3% Sri Lankan, 2% Cambodian, 2% Thai), there is, to date, little data on the eating habits and disease susceptibilities of this population within New Zealand. Addressing this current lack of knowledge will be important for the development of functional foods in New Zealand and may have far reaching implications for all Asian populations, who combined make up 60% of the human race.

### **GENETIC FACTORS AND INTERPLAY OF GENOTYPE AND DIET**

#### **Cancer**

Well-cooked meats are a major source of the dietary carcinogens known as heterocyclic amines, thought to be risk factors in colorectal and other cancer types (Snyderwine et al., 2002). The risk of cancer from heterocyclic amines may be modulated by host factors such as individual acetylator phenotype (Lang et al., 1994; LeMarchand et al., 2002). People

who have the rapid acetylator phenotype and eat high amounts of well-cooked red meats appear at significantly higher risk of colon cancer than other groups (Lang et al., 1994). It has been reported that approximately 93% of New Zealand Polynesians have a rapid acetylator phenotype, while most groups of European descent tend to have around 40% of individuals with this phenotype (McQueen, 1987)

Processed meats and N-nitroso compounds have also been associated with colon cancer risk (Norat and Riboli, 2001). CYP4502D6 is a polymorphic human enzyme that is involved in the activation of some, but not all, nitrosamines (Crespi et al., 1991). Wanwimolruk and co-workers (1992; 1998) compared genetic polymorphisms of debrisoquine (CYP2D6) in Polynesian compared with Caucasian groups from New Zealand. The Polynesian groups appeared to extensively metabolize debrisoquine, and showed a lower incidence of the poor metaboliser phenotype than New Zealanders of European descent. Again, there is likely to be a strong interplay between genes and environmental factors in this food safety issue.

Stomach cancer is also likely to be susceptible to both genetic polymorphisms and diet. The incidence of stomach cancer is high in Polynesian groups, and this has been associated with higher rates of *Helicobacter* infection and also a unique type of *Helicobacter* in the Polynesian groups (Falush et al., 2003). Both the susceptibility to and virulence of *Helicobacter* are susceptible to diet (Sivam et al., 1997).

Polymorphisms in DNA repair genes appear to be involved in a range of different cancer types. Goode et al., 2002, concluded that large, well-designed studies of common polymorphisms in DNA repair genes are important. These must also consider relevant exposures to dietary and environmental carcinogens likely to influence the probability of cancer in the presence of reduced DNA repair capacity.

### **Obesity, cardiovascular disease and diabetes**

Obesity is a key factor in the development of many cases of cancer, cardiovascular disease and diabetes, and is commonly attributed to lifestyle and dietary factors. However, it is becoming increasingly recognised that susceptibility to obesity may be at least partially genetically controlled. For example, Celi and Shuldiner (2002) suggest a central role of peroxisome proliferator-activated receptor gamma (PPAR gamma) in fat cell biology and in the pathophysiology of obesity, diabetes, and insulin resistance. Leptin is the product of the ob gene, and is a satiety factor secreted mainly in adipose tissue. As such, it is part of a signalling mechanism regulating the content of body fat (Shirasaka et al., 2003). While genetic and environmental effects to the individual may be important, there is also evidence that obesity may affect gene expression during foetal programming (Breier et al., 2001).

There is some evidence of racial differences in susceptibility to obesity in New Zealand. Simmons and Breier (2002) found that the offspring of Polynesian women are relatively hyperleptinemic as compared with European or Asian groups,

independent of birth size. Rush et al., 1997a and b showed significant differences between body mass index (BMI) criteria for obesity in Europeans as compared with Polynesians, and also showed that the resting metabolic rate (RMR) was significantly lower in Polynesian compared to Caucasian women. They suggested that this lower RMR may predispose Polynesian women to eventual onset of obesity.

While the dietary association with CVD is clearly important, several genes and variants have been associated with increased CVD risk, including some encoding components of the renin angiotensin system (Katsuya et al., 1995), mutations in the gene encoding the hepatic low-density lipoprotein LDL receptor protein (Jensen, 2002), apolipoprotein E, lipoprotein lipase and interleukin-6 (Stephens and Humphries, 2003) and leptin (Shirasaka et al., 2003). There is also a strong genetic component in diabetes, with at least 20 different chromosomal regions linked to human type 1 diabetes (T1D) (Pociot and McDermott, 2002) and a sizable number of genes linked to susceptibility to type 2 diabetes, including the calpain-10 gene (CAPN10) (Cox, 2002), the intestinal fatty acid binding protein (FABP2) (Weiss et al., 2002) and others. Wong et al. (2002) suggest that a locus on chromosome 20 q, close to D20S32e, may contribute to both insulin secretion and action in 12 members of a large Maori kindred with multiple affected members with type 2 diabetes. Therefore, cancer, obesity, cardiovascular disease and diabetes would appear important candidates for investigation using nutrigenomic approaches in New Zealand.

### **PRIORITIES IN FUNCTIONAL FOOD DEVELOPMENT**

Functional foods are increasing in popularity worldwide, with increasing numbers of consumers seeking foods that they perceive will deliver optimum health or better performance. There is an increasing tendency to view food as medicines, and an increased variety of products available. The more obvious ones provide low energy, fat, salt or cholesterol alternatives to regular food products, but some of the more innovative products rely on other properties. In particular, individual consumers diagnosed with a disease or early disease indicators, and who have consequently received specific dietary advice, are highly motivated and will pay premiums for branded foods with specific health claims. Sloan (2002) identified what she considered the ten major functional food trends (table 1). Flavour and cost appear major motivators in food selection, and functional foods may provide a realistic alternative to major dietary changes that are often difficult to implement.

Given New Zealand's strong background in agricultural and horticultural research and the recent emphasis by local funding agencies on innovative foods (Foundation for Research Science & Technology, 2003), New Zealand is ideally positioned to be at the forefront of functional food development. Functional foods already on the market include margarines with the potential to lower cardiovascular disease, "fibre-

**Table 1: Major classes of functional foods as identified by Sloan, 2002**

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|---|---|
| <ol style="list-style-type: none"> <li>1. Nutrient and speciality ingredient enhancement <ul style="list-style-type: none"> <li>• Fibre, iron, antioxidants and B vitamins</li> <li>• Bioavailability</li> </ul> </li> <li>2. Condition-specific marketing <ul style="list-style-type: none"> <li>• Heart, head and joint health</li> <li>• Obesity and diabetes</li> </ul> </li> <li>3. Lifestyle enhancers <ul style="list-style-type: none"> <li>• Energy</li> <li>• Immunity, stress and sleep</li> <li>• Mental performance and cognition</li> </ul> </li> <li>4. Sports market crossover (mainstream) <ul style="list-style-type: none"> <li>• Health – active – athlete – hardcore</li> </ul> </li> <li>5. Children's health <ul style="list-style-type: none"> <li>• Obesity and diabetes</li> <li>• ADHD</li> </ul> </li> <li>6. Gender, age and ethnic positioning <ul style="list-style-type: none"> <li>• Women's and men's health</li> <li>• The over 50s</li> </ul> </li> </ol> | <ol style="list-style-type: none"> <li>7. Weight, satiety and appetite suppression <ul style="list-style-type: none"> <li>• Low fat, low calorie</li> <li>• Super satiating foods</li> </ul> </li> <li>8. Functional snacks <ul style="list-style-type: none"> <li>• Moving toward medicine</li> </ul> </li> <li>9. Mother nature knows best <ul style="list-style-type: none"> <li>• Fresh whole foods with enhanced nutrients</li> <li>• Soy-based foods</li> <li>• Fish oils and omega 3</li> <li>• Whey protein</li> <li>• Pre and probiotics</li> </ul> </li> <li>10. Non-traditional foods <ul style="list-style-type: none"> <li>• Eye health</li> <li>• Oral health, etc</li> <li>• Whey protein</li> </ul> </li> </ol> |
|---|---|

enhanced” breads and yoghurts, and an increasing range of nutrient-enhanced fruits and vegetables. However, despite their potential health-enriching properties, they may not be reaching the groups at highest risk of diet-related disease, perhaps either due to a lack of awareness, or to the difficulty in convincing individuals who are yet to manifest acute disease of the need to change.

In all these areas, proof of efficacy is becoming increasingly important (Hasler, 2002) and the regulatory environments need to be able to adapt to the developments in functional foods. However, responsiveness in developing appropriate test methodologies, and a willingness to think innovatively in new areas means that New Zealand could anticipate to be at the forefront of setting the standards of the future.

### NUTRIGENOMICS

Despite the fact that good nutrition has long been recognised as perhaps the single most important factor in maintaining wellness, nutrition research has often been accused of lagging behind other fields of medical research (Trayhurn, 1998). However, nutrition research has embraced the growing field of genomics, recognising a tool at last powerful enough to explore the complex interactions between nutrients and biological systems, spawning the field of nutrigenomics.

Nutrigenomics encompasses the understanding of how nutrients affect health at the molecular level within the body and how these effects vary between individuals. The key technologies underlying nutrigenomics address these two overlapping areas. Firstly, genomics, including approaches such as DNA-arrays and RT-PCR, which examine the interactions between nutrients and gene expression, and proteomics, which determines the outcome of this altered gene expression on protein synthesis, activation and regulation, both examine the molecular mechanisms of nutrients, identify potential tar-

gets for nutritional intervention and establish suitable biomarkers for monitoring responses. Secondly, the characterisation of single nucleotide polymorphisms (SNPs) promises an understanding of the differences in response of individuals to nutrients at the genetic level.

As the field of nutrigenomics grows, it has been suggested that it will eventually be possible for an individual to be genetically profiled, identifying foods they should be eating or avoiding and which dietary supplements they should be taking (Peregrin, 2001). However, as the Western world's increasing obesity problem demonstrates, it can be extremely difficult to convince an individual to change their diet, even when specific causative foods have been identified. Therefore, the development of functional foods, guided by nutrigenomics research, offers a solution whereby people can continue to consume the foods they recognise and enjoy, which have had their nutritional content altered to better meet the needs of various identified subpopulations.

The diverse ethnic mix of the population with differing diet-related disease susceptibilities, the regulatory environment, the strong background in innovative agriculture with a new focus on the development of functional foods and the relative infancy of nutrigenomics combine to place New Zealand in the forefront of nutrigenomics research.

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