

17 April 2008

Re: Submission to Genomic Medicine Inquiry

1. We are submitting to the above inquiry in relation to the use of genetic profiling in the practice of nutritional therapy and to highlight some points which may be of interest.

Nutritional Therapy and Nutrigenomics

2. Nutritional therapy (NT) is the manipulation of the individual's environment through diet, nutraceuticals, lifestyle changes and education to promote optimum health, peak performance, disease prevention and patient care. In the US NT is known as 'functional medicine'.¹ Nutrigenomics is the science which looks at the relationship between nutrition and health at the molecular level. In 2004 Kaput and Rodriguez² proposed the now commonly quoted five tenets of nutrigenomics, *i.e.* that:

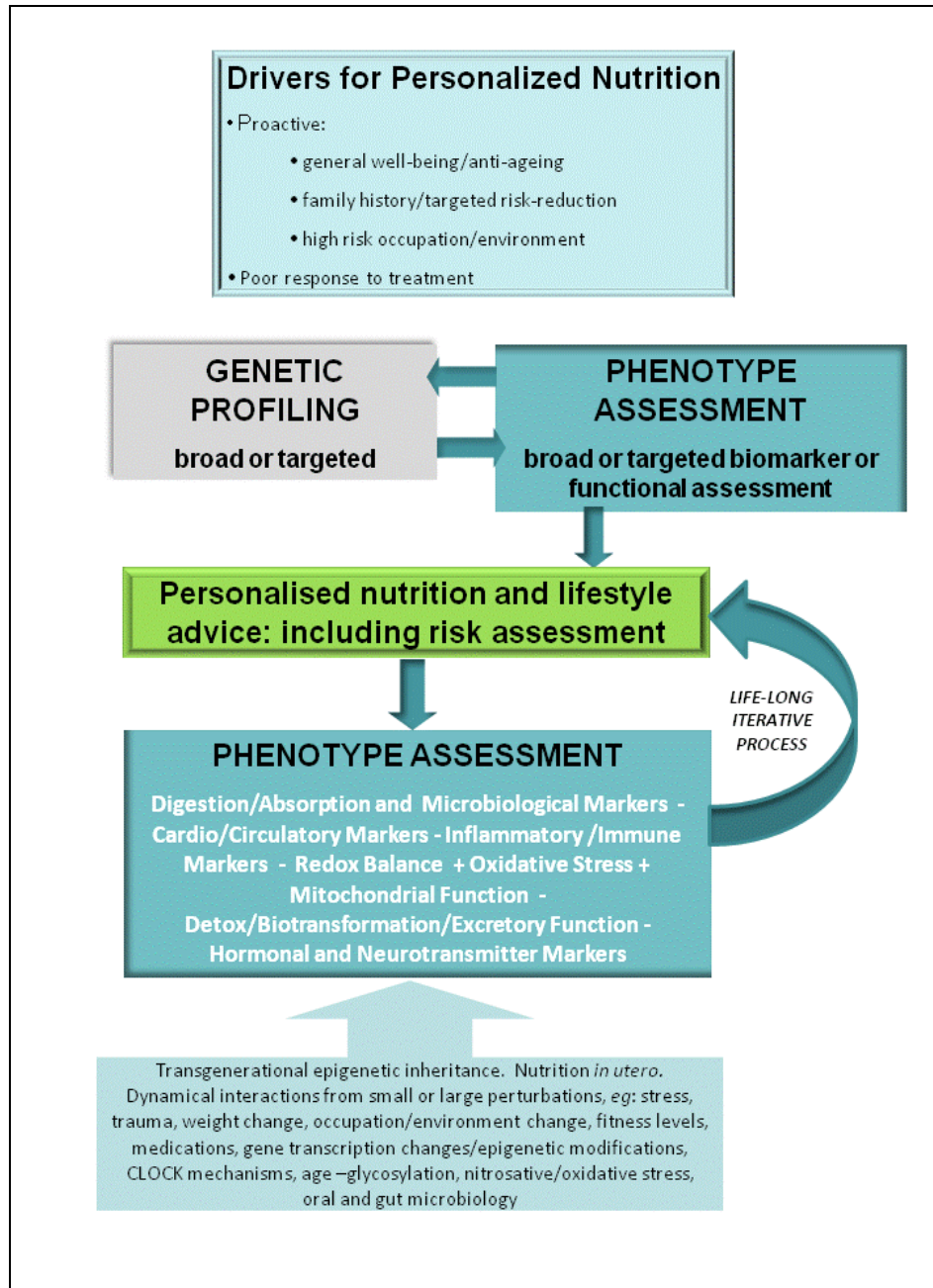
- common dietary chemicals act on the human genome, directly or indirectly, to alter gene expression or structure;
- under certain circumstances, and in some individuals, diet can be a serious risk factor for a number of diseases;
- some diet-regulated genes (and their normal, common variants) are susceptibility genes and likely to play a role in the onset, incidence, progression, and/or severity of chronic diseases;
- the degree to which diet influences the balance between healthy and disease states may depend on an individual's genetic makeup;
- dietary intervention based on knowledge of nutritional requirement, nutrition status, and genotype (*i.e.* "individualized nutrition") can be used to prevent, mitigate, or cure chronic disease.

3. The NT practitioner, using a personalized health model, may use genetic data to help inform practice to help reduce the risk of disease where the emergent phenotype results from the complex interaction between multiple genes (including epistatic and epigenetic) and environment, *i.e.* by identifying variants whose ultimate expression can be nutritionally modulated to benefit overall health status. Phenotype assessment is a core feature of NT

¹ <http://www.functionalmedicine.org>

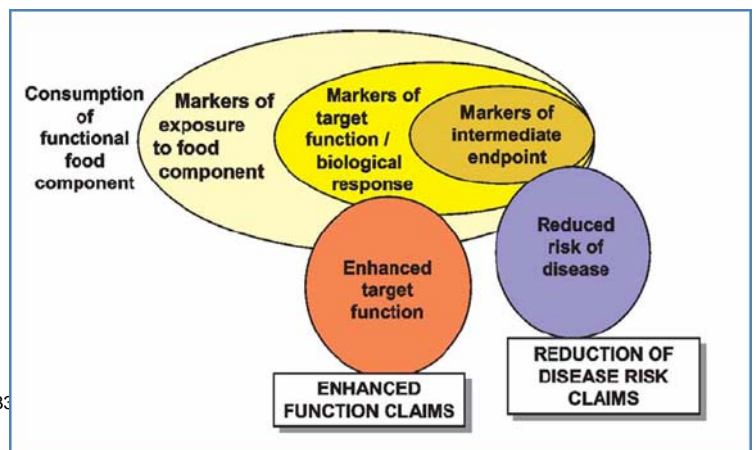
² Kaput J, Rodriguez RL. Nutritional genomics: the next frontier in the postgenomic era. *Physiol Genomics* 2004; 16(2):166-77.

practice: use of functional testing and other surrogate markers aids practitioner-client education in personal risk, which includes an appreciation of optimistic bias.



Disease-risk reduction and prevention in clinical practice and law

4. The principle of **disease risk reduction (DRR)**, as distinct from *prevention*, was incorporated into EU law in the 2006 Nutrition and Health Claims Regulation (NHCR), which



requires that all structure/function and DRR claims on foods and nutraceuticals must be preapproved by the EU Commission and meet a standard of substantial scientific agreement. The EU-funded PASSCLAIM project³ was tasked with establishing how claims would be substantiated: it identified a number of functional biomarkers, or surrogate end-point markers, to be used for DRR claims. The DRR paradigm recognises that chronic conditions are the product of multiple gene-environment influences. PASSCLAIM identified markers for: diet-related cardiovascular disease; bone health and osteoporosis; physical performance and fitness; mental state and performance; body weight, insulin sensitivity and diabetes; diet-related cancer; and gut health and immunity. DRR claims, as distinct from prevention claims, are *outside the scope of EU medical law*.

5. However there is **no legal definition of disease** in EU legislation, which has relied on the definition of a medicine (form and function) in borderline cases. As metabolomic technologies allow for earlier detection of changes outside the homeostatic range (with or without adverse sequelae), definitions of 'disease', 'nutrient', and 'essentiality' may need to be revisited, particularly as evidence continues to accumulate that some classic essential micronutrients (vitamins and minerals) and non-nutrients (food bioactives found in fruits, vegetables, grains, nuts, seeds and oils) act at the molecular and cellular levels to regulate gene expression (transcription and post-translational modification) and modulate inflammatory and immune pathways.⁴

Public 6. While basic biological requirements are universal, the extent of inter-ancestral and inter-individual variation in physiological demand for and response to nutrients fundamentally challenges the foundations on which population guidelines have been based such that the message may be disadvantageous in the case of some individuals or even sub-populations. This may include those in particular occupations who are exposed to environmental toxicants and whose nutritional status may impact on longer term outcomes.⁵ Nutritionists can no longer be confident about the advice given at the population level. Examples include:

❖ The human salivary amylase gene (AMY1) copy number varies significantly and has been positively correlated in a modern population with salivary protein levels where individuals from ancestral high starch-consuming populations have more AMY1 copies than those with traditionally much lower starch intake, implying that populations may have different optimal levels of starch intake.⁶

³ <http://europe.ilsa.org/activities/ecprojects/PASSCLAIM/>

⁴ Young VR (2002) 2001 W.O. Atwater Memorial Lecture and the 2001 ASNS President's Lecture: Human nutrient requirements: the challenge of the post-genome era. *J Nutr* **132**, 621-629

⁵ McGinty SA (2007) Toxicogenetics and nutrigenetics: biomarkers in occupational medicine and litigation. *Biomarkers in Medicine* **1**, 567-573

⁶ Perry GH, Dominy NJ, Claw KG, Lee AS, Fiegler H, Redon R, et al. (2007) Diet and the evolution of human amylase gene copy number variation. *Nat Genet* **39**: 1256-60

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❖ The success of low energy diets to reduce body weight may also be dependent on genetic variation: perilipin is a protein found in adipocytes and evidence suggests that those carrying the PLIN11482A variation are resistant to weight loss on a calorie-restricted diet.⁷

❖ For women participating in the Framingham Study, a gene-diet interaction was found between polyunsaturated fat intake and the APOA1 -75G/A variation. Carriers of the A allele had higher HDL-C (good cholesterol) with higher polyunsaturated fat (PUFA) intake (>8% energy from fat), whereas the G/G homozygotes had lower HDL-C associated with higher PUFA intake.⁸

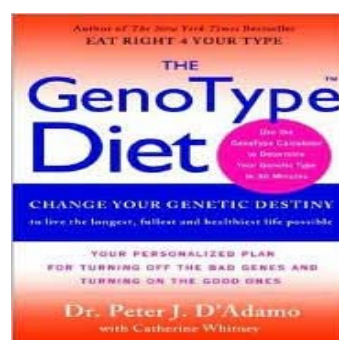
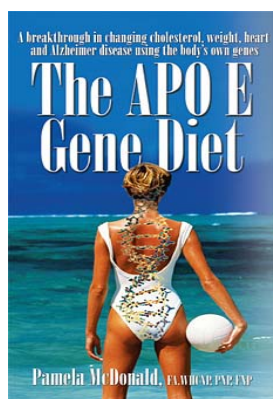
7. Awareness of the variability in the nutritional response may act as a driver towards personal health interventions separate from public health goals. At a workshop held in Washington DC in 2006 hosted by the US Institute of Medicine entitled "Nutrigenomics and Beyond: Informing the Future", IOM Director Harvey Fineberg spoke of the challenge that nutrigenomics poses the existing public health paradigm:

"...It is not just possible but likely that there are nutrients that affect some population groups differently than others, and public health guidelines will have to take such differences into account...A public health paradigm of universal education is going to have to be adapted to the scientific reality and scientific knowledge as it develops and unfolds."

8. While use of nutrigenetic profiling is still limited in the UK, the advent of popular diet books related to genotype have already appeared in the US and are likely to drive demand in the future, including in the arena of sports/performance nutrition.

www.apoegenediet.com

www.genotypediet.com



⁷ Corella D, Qi L, Sorli JV, Godoy D, Portoles O, Coltell O, et al. (2005) Obese subjects carrying the 11482G>A polymorphism at the perilipin locus are resistant to weight loss after dietary energy restriction. *J Clin Endocrinol Metab* 90(9):5121-6

⁸ Corella D, Ordovas JM. Single Nucleotide Polymorphisms that influence Lipid Metabolism: Interaction with Dietary Factors. *Annu Rev Nutr* 2005;25: 341-90.

About BANT, standards and regulation

9. BANT, set up in 1997, is the professional association for NT practitioners. With 2,000 members (including 1,000 students), it represents the interests of its members and NT more generally, and supports Continuing Professional Development programmes. Progress on NT regulation has been facilitated by The Prince's Foundation for Integrated Health, with funding from the Department of Health, through the Nutritional Therapy Council and, from summer 2008, through the new Complementary and Natural Healthcare Council (CNHC). Educational and practice standards have been set: in 2003 National Occupational Standards (NOS) were published by QCA/SQA; in 2004 the Core Curriculum and Learning Outcomes were published to meet the NOS; in 2006 a Grandparenting scheme was launched for entry to the national register; and in 2008 accreditation of courses is underway. The NTC Education & Training Committee has put together a first draft of competences for advanced practice using genetic profiling. Interim Standards of Proficiency anticipate underpinning knowledge in genetics, genomics and complexity science, as well as an appreciation of ethical, legal and social issues. Work will be taken forward in 2008/9 by the new Nutritional Therapy Board of the CNHC.