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Editorial

Nutritional genomics – "Nutrigenomics"

I have commented previously on what is perceived to have been the slowness, indeed reluctance, of nutritional science to incorporate concepts and technologies from the cutting edge of genomics and of molecular and cellular biology (Trayhurn, 1998). In the last 2–3 years it is apparent that this situation has changed. Indeed, the gap between nutritional science and the frontiers of biology have, in my view, been closing rapidly. This is partly because the importance of nutrition has been increasingly recognised by those in other fields such that they have begun to apply their expertise to nutritional issues. But in addition, those in nutrition have also come to appreciate the need to harness the developments that are taking place elsewhere.

The publication in February 2001 of the draft sequence of the human genome through the Human Genome Project, with parallel papers in *Nature* and *Science* (Lander *et al.* 2001; Venter *et al.* 2001), is in many ways a major milestone for nutrition as for other sciences. It has been followed by a draft of the mouse genome sequence (http://www.ensembl.org/Mus_musculus/; see Marshall, 2002), aiding the identification of the function of unknown human genes and their putative involvement in disease processes.

The human genome sequence is very much a beginning and not an end, a point emphasised by the publically-funded International Consortium (Lander *et al.* 2001). Their paper is not only a landmark publication scientifically, but also a model of scholarship, beginning as it does with a reference to Gregor Mendel and ending with a quotation from T.S. Eliot: "*We shall not cease from exploration. And the end of all our exploring will be to arrive where we started, and to know the place for the first time.*"

The sequencing of the human genome is a beginning since it provides a blueprint of biological potential, but does not tell us what actually takes place – in other words, what genes are expressed and what encoded proteins are synthesised in which tissues and under what circumstances. Additionally, the genome tells us nothing of functionally critical post-translational changes in proteins such as glycosylation or phosphorylation. It is, of course, *de rigeur* to talk of being in the 'post-genomic' era with the central task of biology now being 'functional genomics' – unravelling how genes and gene products operate. The more cynical have regarded functional genomics essentially as a form of repackaging of what biologists have always sought to do – to understand the full complexity of biological systems at different levels of organisation and how these systems are integrated. The words of Eliot are, perhaps, in practice especially apposite here.

The extent to which nutritional science has now aligned itself with functional genomics is illustrated by the very recent emergence of the new area of 'nutritional genomics', or 'nutrigenomics' as it is also termed. Indeed, over the last year or so there have been major developments in Europe such as the establishment of a 'Network for Nutritional Genomics' under the auspices of INSERM in France and a similar initiative 'The Centre for Human Nutrigenomics' in the Netherlands. Parallel initiatives have been taking place elsewhere, both on a national and a local level (e.g. the 'Nutrigenomic Network Potsdam-Berlin'). My own University has recently established the 'Liverpool Centre for Nutritional Genomics', bringing together a group of senior scientists involved in functional genomics in relation to a range of nutritional issues.

Nutritional genomics covers a broad canvas. It encompasses the interaction between nutrients and the expression of genes, harnessing techniques such as DNA microarrays and real-time PCR. It involves the characterisation of gene products and the physiological function and interactions of these products; the latter includes how nutrients impact on the production and action of specific gene products and how these proteins in turn affect the response to nutrients. As noted in a previous *Editorial*, proteomics is a key technology for the determination of the totality of gene products and their post-translational modification (Trayhurn, 2000).

One of the key opportunities for nutritional genomics is the exploration of the link between specific gene polymorphisms and the individual response to nutrients. Activity in this area is now developing and there is a long-term goal of providing personalised dietary advice based on the predicted response to nutrients derived from the genetic profiling of an individual. With the growing focus on the identification of SNPs (single gene polymorphisms) in humans, this is an increasingly realistic long-term target. There will, of course, be the issue of whether individuals will respond more to personal nutritional advice tailored to their own genetic profile, than when advised generally on the basis of the population as a whole.

Obesity is one area where the application of both genomic and nutritional genomic approaches has already been highly successful, and as such it provides an exemplar for nutrition as a whole. The most potent example comes

from the identification by positional cloning of the gene which in mutated form results in the obesity of the *ob*/*ob* mouse (Zhang *et al.* 1994). This in turn led to the discovery of a previously unknown hormone - leptin (and its receptors) – which provides a direct signal from adipose tissue to the brain, influencing food intake. It also resulted in a radical change in perspective on the physiological role of white adipose tissue – as an endocrine organ, and not just a site of lipid storage (see Trayhurn & Beattie, 2001). Mutations in the leptin and leptin receptor genes have subsequently been shown to be associated with obesity in humans (Montague *et al.* 1997; Clément *et al.* 1998; Strobel *et al.* 1998), while polymorphisms in several unrelated genes have been linked to increased body fatness (Arner, 2000).

Nutritional genomics/nutrigenomics will be a key area of nutritional science over the next decade. The significance of its rapid development lies not only in the problems that can now be addressed, but also as a reflection of the closing of the cultural gap between nutrition and the front-line of modern biology.

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