

An overview of gene-nutrient interactions

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We are near the end of human structural genetics. The Millennium draft sequence identifies over 90% of the 3 billion base pairs of DNA carried in every cell: the total assemblage of genes, or *genome*. International partners in the Human Genome Project are now working to eliminate gaps and ambiguities, to produce a 'gold standard' sequence by 2003. The genome sequence will be an immensely valuable resource, and its high publicity has produced a revolution in nomenclature: omes are the new isms and ologies. Nutritionists, who thought they were studying metabolism or physiology, are now told that the basic information of the genome turns nutrients and their metabolites into living cells or organs (the *metabolome*) which, in turn, are integrated into a living human being (the *phenome* or *physiome*).

Actually, the structural genome by itself does not tell all that much. We need *functional genomics* to tell us what gene products do: and which may not be obvious from their sequence. Also, the genome is the same in all cells but the subset of genes expressed is not. Much more needs to be known about the control of transcription, whereby the information encoded in our genes is copied onto messenger RNA (mRNA), forming the *transcriptome* (the complete set of mRNA). One method of control is DNA imprinting by methylation; the *methylome* is the complete set of DNA methylations in a cell type. After transcription, mRNA changes before translation to proteins can take place. Non-coding regions (introns) are removed from between the coding regions (exons) by splicing. Often, the same initial transcript can be spliced in many different ways (the current record, for a neuroprotein gene, is about 50,000 permutations). Editing of mRNA can sometimes remove a base encoded by DNA, and replace it by another. Thus, the final members of the transcriptome are not simple copies of the genome. Also, topping and tailing of the end regions of mRNAs influences rates of protein translation. Proteins, once translated, can be cleaved or have their constituent amino-acids significantly modified. The complete set of protein molecules in a cell (the *proteome*), therefore, is at least an order of magnitude greater than the complete set of genes (about 30,000). International proteomic consortia are already in place, but technical problems (proteins will not form convenient paired strands, as nucleic acids do) will ensure that progress is much slower than with genomics.

Genomics and proteomics are 'big science'. Nutritionists can intelligently choose small important genetic items to generate hypothesis-led research. Of course, as non-reductionist scientists, we have much experience in elucidating aspects of the metabolome and physiome, with cell cultures, animal models and nutritional interventions in humans. But now we can maximise our research potential by a systematic, genome-up approach to the study of nutrition.

Indeed, it could be argued that nutrition is not at the edge of the gene, but rather is centre stage. Dietary components make substantial contributions to the stability of DNA, can affect the regulation of gene expression, and may have roles in genetic imprinting; the methylome is a function of folate status. Moreover, nutritional requirements are influenced by variability within the genome; mostly by single nucleotide polymorphisms (alternative bases), which occur about once every 1000 base pairs. These are defined as polymorphic variants or alleles (alternative forms of a gene) when they occur in at least 1% in the population. Such mutations close to or within a gene may influence the amount, structure and function of the gene product; this in turn can influence nutritional requirements, and susceptibility to degenerative disease.

The objectives of this overview are to delineate some of the complex each-way gene-nutrient interactions, to provide examples of nutrients that are involved in such interactions, and to show some of the opportunities available to nutritionists to advance the discipline of nutrition in the post-genomic era.