Nutrigenomics: Moving towards Personalized Nutrition for Obesity Prevention

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If you had the opportunity to simply provide a saliva sample, and in 6 weeks receive a list outlining your relative risk of developing type 2 diabetes and other diseases, would you take it? This opportunity is currently available from a US company called 23andme, which offers genetic testing to uncover disease risks using genetic markers with known associations. In response to public curiosity, commercial programs like 23andme and others apply genomic technologies, i.e. gene mapping and DNA sequencing, to disease prevention, but in truth they are only scratching the surface in the application of “omic” technologies to health. The term “omic” means “complete” or “all” based on a Greek suffix used to describe study areas in biology. Of the 50 or so “omic” terms coined so far, the field of nutrigenomics may soon be able to offer people more information on disease risk and prevention.

Nutrigenomics allows researchers to study diet-gene interactions, or more generally, the role of genes in response to changes in energy balance (food intake) or diet composition (micro- and macro-nutrients). What’s more, with nutrigenomics it may one day be possible to make personalized dietary recommendations based on genotype in order to help people lose weight, optimize their health, or help prevent disease onset/exacerbation, especially for at risk populations prone to obesity and type 2 diabetes.

The field of nutrigenomics consists of two distinct but related areas called nutrigenetics and nutrigenomics. Nutrigenetics is the study of how an individual's genotype affects their response to diet, whereas nutrigenomics is the study of how diet or specific nutrients affect gene expression, protein function, and subsequent downstream cell signalling pathways. Thus, it is now well accepted that to optimize health and prevent disease, one must consider environment and hereditary factors simultaneously. Importantly, nutrigenomic/nutrigenetic approaches allow researchers to study complex diseases like obesity and type 2 diabetes that are caused by a combination of genetic and environmental risk factors, such as diet.

It has been estimated that the heritability of obesity is between 40-70%; however, teasing out the cause of obesity is difficult because it is most commonly a polygenic (multi-factorial) disease with strong environmental factors. Polygenic forms of obesity are complex in nature where the adipose phenotype, a key tissue studied, is dependent on developmental, behavioural, environmental (e.g. diet composition), and genetic factors. In an effort to understand the causes of polygenic obesity, studies in the past few decades have unravelled genes that act as nutrient sensors, or genes that are implicated in obesity and diabetes pathogenesis. These findings have revealed that we have genes regulated by various micro- and macro-nutrients. For example, dietary fatty acids and their metabolites can bind directly to, and change the abundance/activity of specific transcription factors to control fat and carbohydrate metabolism. Moreover, nutrigenetic research in humans has revealed that in one's genotype there is genetic variation...
Nutrigenomics researchers make use of the HapMap database to identify haplotypes associated with diet-gene interactions in obesity and type 2 diabetes. For example, Mutch and colleagues looked at polymorphisms in two human fatty acid desaturase genes (Fads1/2), which encode desaturase enzymes responsible for altering tissue lipid profiles. Increased delta 5 desaturase activity (Fads1) may lead to a greater production of lipids like arachidonic acid and its pro-inflammatory derivatives, which are implicated in the pathogenesis of metabolic diseases including obesity and type 2 diabetes. Here, they looked at the relationship between SNPs for Fads1/2 and fatty acid desaturase activity in various ethnic populations from the Toronto Nutrigenomics and Health cohort. Most notably, they found a SNP in Fads1 where major/minor allele frequencies varied between Asians and Caucasians; however, regardless of ethnic background, carriers of the “T” rather than the “C” allele were associated with greater desaturase activity.

This study shows that there is genetic variation in the Fads gene locus in Caucasians and Asians, which is reflected by differences in desaturase activity. This research helps us understand why there are specific differences in people’s lipid profiles, and may eventually contribute to improved dietary strategies to manage obesity characterized by altered lipid profiles.

In addition to nutrigenetic research on haplotypes, human obesity is also being studied from a nutrigenomic standpoint (the effect of diet on genes). Mutch relates that associative nutrigenomic studies do not always agree probably because of differences in the population studied and the environmental factors affecting those populations. He goes on to propose that in order to further nutrigenomic research and reach the goal of personalized nutrition, large-scale clinical trials are needed to detect rare genotypes and elucidate diet-gene interactions. A recent large-scale European Framework VI clinical intervention study called Diet, Obesity and Genes (abbreviated as DioGenes), recruited over 548 obese subjects to complete an 8-wk low-calorie diet, and then selected a subset of 40 non-diabetic women to identify changes in adipose tissue gene expression (mRNA; transcriptome) that took place during the diet. Moreover, the study went further to identify unique gene expression profiles in those who maintained their new weight following the low-calorie diet, versus those who re-gained the weight following the intervention. Using bioinformatic software to identify gene sets, a distinct profile of genes that are up or downregulated in response to certain stimuli (e.g. oxidative stress), Mutch and his colleagues were able to tease out candidate pathways that were modulated by the low-calorie diet in both weight maintainers and weight re-gainers (see Figure 2). In short, the authors were able to conclude that there may be a genetic basis for the ability to maintain weight loss following the low-calorie diet in women.

In summary, current nutrition research in humans consists of cutting edge nutrigenetic studies like associative studies and large-scale clinical trials that identify differences in genetic variation among populations in order to better understand the role of diet in health outcomes.
that link haplotypes to disease states, and nutrigenomic studies like large clinical trials that aim to understand how dietary interventions affect gene expression and downstream signalling. These studies will unravel diet-gene interactions and identify the relative contribution of genetics and environmental factors in complex diseases like obesity (polygenic) and type 2 diabetes. Finally, researchers like Mutch hope to see their recommendations for personalized nutrition based on nutrigenomic research come to fruition in the next decade.

**Go Biological Process**

| Up-regulated Transcripts                                                                 | Down-regulated Transcripts                           |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------|
| response to light stimulus                                                                | response to hormone stimulus                        |
| negative regulation of cellular biosynthetic process                                     | negative regulation of apoptosis                     |
| negative regulation of mRNA processing                                                  | negative regulation of apoptosis                     |
| rRNA metabolic process                                                                  | cellular biosynthesis                                |
| ribosome biogenesis                                                                      | regulation of cell-cycle                              |
| regulation of rRNA metabolism                                                           | regulation of macromolecule biosynthetic process     |
| DNA metabolic process                                                                    | DNA metabolic process                                 |
| regulation of macromolecule biosynthetic process                                         | regulation of cellular biosynthetic process           |
| regulation of cellular biosynthetic process                                              | transport                                            |
| positive regulation of apoptosis                                                        | positive regulation of apoptosis                     |
| response to chemical stimulus                                                           | response to chemical stimulus                        |
| cellular biosynthesis                                                                     | cellular biosynthesis                                |
| generation of precursor metabolites and energy                                          | translation                                          |
| translation                                                                              | regulation of macromolecule biosynthetic process     |
| 41.4%                                                                                  | 38.5%                                                |

Figure 2: Bioinformatic output from Functional Network Analysis (© INSERM) showing the percent of up or down-regulated cellular pathways/processes from the Gene Ontology Biological Process database after weight loss in a treatment group of women compared to a control. This is done by analyzing microarray data of the transcriptome (unpublished data, image courtesy of Dr. D. Mutch).

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Anna is a PhD student at the University of Guelph in the field of nutrition, metabolism and exercise. Anna’s research revolves around studying the chronic inflammatory component of obesity, and understanding how long chain omega-3 polyunsaturated fatty acids like those found in fish oil decrease inflammation in adipose tissue. In her spare time, Anna likes to stay active hiking and travelling, and also enjoys freelance writing to encourage knowledge translation to the general public.