Nutrigenomics: concept, advances and applications

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Received: 14-02-2015 Accepted: 13-08-2015 DOI: 10.5958/0976-0563.2015.00041.X

ABSTRACT

The interface between the nutritional environment and cellular/ genetic processes is referred to as Nutritional genomics or Nutrigenomics. It seeks to understand the effects of diet on an individual’s genes and health. Nutrigenomics seeks to provide a genetic understanding for how common dietary chemicals (i.e., nutrition) affect the balance between health and disease by altering the expression or structure of an individual’s genetic makeup. It is the science that examines the response of individuals to food compounds using post-genomic and related technologies (e.g. genomics, transcriptomics, proteomics, metabolomics etc.). Nutritional genetics is considered as the combination of nutrigenomics and nutrigenetics. Nutrigenomics is establishing the effects of ingested nutrients and other food components on gene expression and gene regulation. It will also determine the individual nutritional requirements based on the genetic makeup of the person (personalized diet) as well as the association between diet and chronic diseases which will help to understand the etiologic aspects of chronic diseases such as cancer, type-2 diabetes, obesity and cardiovascular disease (CVS). Nutrigenetics on the other hand identifies how the genetic makeup of a particular individual co-ordinates his or her response to various dietary nutrients. It also reveals why and how people respond differently to the same nutrient. The long-term aim of nutrigenomics is to understand how the whole body responds to real foods using an integrated approach termed ‘systems biology’. The huge advantage in this approach is that the studies can examine people (i.e. populations, sub-populations - based on genes or disease and individuals), food, life-stage and life-style without preconceived ideas. Nutrigenomic approaches will enhance researcher abilities to maintain animal health, optimize animal performance and improve milk and meat quality.

Key words: Nutrigenomics, Nutrient-gene interaction, Proteomics, and Post-genomics.

INTRODUCTION:

Nutritional genomics is the study of the interactions between our genetic makeup and the foods we consume, and the health outcomes that may occur. Nutritional genomics is a relatively new field of study that encompasses two distinct fields: nutrigenetics and nutrigenomics. Nutrigenomics focuses on how nutrients or non-nutritive bioactive components, such as enzyme inhibitors, found in the diet affect gene expression, protein and metabolite concentration and therefore metabolism, health status and risk of disease. Nutrigenomics is a discipline within nutritional genomics that studies the effects of foods on gene expression. This sounds complicated, but this should likely be understood with some of the familiar examples of nutrigenomics (De-Busk et al., 2005). For example, red wine has become something of a modern-day health food thanks to the fact that it contains resveratrol. Resveratrol is a nutrient that stimulates a gene that protects tissues from free radical damage. Another nutrient that affects your genes is folate, found in foods like fruits and green vegetables. Folate is a nutrient needed by the body to make DNA. When you do not take in enough folate, you have a higher risk of developing cancer. The fact, that common diet contains many bioactive substances that can through the interaction with receptors activate or modulate the transcription of target genes or directly cause the rearrangement of chromatin structure, is widely accepted, but not often recognized in the design and interpretation of genetic and epidemiologic studies.

The studies that follow the effect of a certain diet often disregard the possible effect of genetic variability within the studied cohort, on the other hand, some studies analyzing the effect of candidate gene polymorphism on the studied trait (for example blood pressure, obesity) do not include the diet interference, which can dramatically influence the resulting association. Nutritional genomics aims to resolve this evident discrepancy (Miggiano et al., 2006).

In a certain parallel to pharmacogenomics, the nutritional genomics focuses on the bioactive substances found in regular food and how those substances affect the balance between health and disease via the interaction with the individual’s genome. These are 5 basic principles of nutrigenomics (German, 2005):

1. Substances contained in the food (micro- and macro-nutrients) can directly or indirectly affect the human genome through changes in its structure and gene expression.

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2. Under certain circumstances and in some individuals, the diet can be an important risk factor for the development of the number of diseases.

3. Some genes regulated by active substances in the diet probably play a crucial role in the onset, incidence, progression and severity of the disease.

4. The degree to which diet influences the balance between health and disease may depend on individual’s genetic makeup.

5. Nutritional intervention is based on the knowledge of individual’s nutritional status and needs as well as genotype (individualized nutrition) and can be used for prevention, mitigation or healing the chronic diseases.

A nutrient is not merely a chemical component required for a particular metabolic function, but also that it plays an informational or signaling role in the cell. As with any system that transmits information, the signal must have a sensor or receiver that can accept, decode, and relay the information that has been transmitted. Cellular proteins that receive and transmit this information are termed “receptors.” The receptors then must relay this information via a transducing mechanism to the part of the cell that is capable of reprogramming the cell to adapt to the new environmental conditions. This reprogramming can occur in the cell nucleus or cytoplasm. It can involve changes in the expression of genes (transcription and translation), the stability of messenger RNA and protein, or the activity of proteins. The key principle behind nutrient control of gene expression is specificity. Each receptor must have the capability of binding a nutrient-signaling molecule with specificity and should initiate an adaptive change. It is reported that until recently, the regulation of gene expression in response to changes in nutritional environment was thought to be mediated primarily by hormones and/or the nervous system. However, the last decade has provided evidence that major (glucose, fatty acids, and amino acids) or minor (e.g., iron, vitamin) nutrients, or their respective metabolites, regulate gene expression in a hormone-independent manner (Allan Walker, 2004). Thus common dietary chemicals (nutrients) affect balance between health and disease by impacting the expression of genes.

**Nutrient-gene interaction**: There are 3 major conceptual groupings for thinking about nutrient-gene interactions:

1. **Direct interactions**: nutrients, sometimes after interacting with a receptor, behave as transcription factors that can bind to DNA and acutely induce gene expression.

2. **Epigenetic interactions**: nutrients can alter the structure of DNA (or of histone proteins in chromatin) so that gene expression is chronically altered.

3. **Genetic variations**: common genetic variations [single-nucleotide polymorphisms (SNPs)] can alter the expression or functionality of genes. All of these mechanisms can result in altered metabolism of and altered dietary requirements for nutrients.

Dietary chemicals can also affect gene expression directly or indirectly. At the cellular level, nutrients may:

- Act as ligands for transcription factor receptors
- Be metabolized by primary or secondary metabolic pathways, thereby altering concentrations of substrates or intermediates; or
- Positively or negatively affect signal pathways

**Macronutrients** A deficiency of essential nutrients can modify genetic expression.

**Carbohydrates**: The role of dietary carbohydrates in weight gain has become an important question in the public consciousness. Carbohydrates have been traditionally classified as simple (monomeric and dimeric) or complex (polymeric) on the basis of their chemical structure. A critical defect of this classification is its inability to predict the plasma glucose and insulin responses associated with different types of carbohydrates. The glycemic index, developed two decades ago (Jenkins et al., 2002), allows comparison of different foods based on their physiologic effects rather than on their chemical composition. A positive association between glycemic index and body weight has been shown in several short-term experimental studies and limited observational studies (Ludwig et al., 1999). The possible biologic mechanisms of glycemic index on body weight are...
thought to be related to insulin levels, hunger and satiation, and basic metabolic processes (Roberts, 2000). This finding is consistent with the hypothesis that with increased glycemic index, more insulin is produced and more fat is stored, suggesting that type of carbohydrate may be related to body weight.

Glucose, the most abundant monosaccharide in nature, provides a very good example of how organisms have developed regulatory mechanisms to cope with a fluctuating level of nutrient supply. In mammals the response to dietary glucose is complex because it combines effects related to glucose metabolism itself and effects secondary to glucose-dependent hormonal modifications, mainly pancreatic stimulation of insulin secretion and inhibition of glucagon secretion. In the pancreatic - cells, glucose is the primary physiological stimulus for the regulation of insulin synthesis and secretion. In the liver, glucose, in the presence of insulin, induces expression of genes encoding glucose transporters and glycolytic and lipogenic enzymes, e.g. L-type pyruvate kinase (L-PK), acetyl-CoA carboxylase (ACC), and fatty acid synthetase, and represses genes of the gluconeogenic pathway, such as the phosphoenolpyruvate carboxykinase gene. Although insulin and glucagon were long known as critical in regulating gene expression, it is only recently that glucose also has been shown to play a key role in transcriptional regulation.

Feeding high-energy diet to rats leads to early development of obesity and metabolic syndrome, apparently through an inability to cope with energy density of the diet (Selman et al., 2006). Obesity is associated with increase in mRNA levels for the oxyergic neuropeptides, NPY (neuropeptides Y), Ag RP (Agouti Related Peptide) etc. Hyperglycemia activated AGT gene expression in liver. It increased approximately 3 fold.

It is shown that in both animals and human subjects, reduced expression of CAPN3 was associated with elevations in circulating glucose and insulin concentrations, decreased carbohydrate oxidation and the accumulation of body fat, particularly in the abdominal region. The altered expression of CAPN3 contributes to the development of insulin resistance, obesity and type 2 diabetes. Lower levels of expression of calpain 3 in skeletal muscle were associated with reduced carbohydrate oxidation and elevated circulating glucose and insulin concentrations, and also with increased body fat and in particular abdominal fat. Therefore, reduced expression of calpain 3 in both humans and animals was associated with phenotypes related to obesity and insulin resistance (Walder et al., 2002). It is postulated that dietary carbohydrates and thyroid hormones are major regulators for expression of the lactase/phlorizin hydrolase in starved rats when they have a sustainable thyroid hormone level (Kuranuki et al., 2006).

**Dietary fats**: Fatty acids, in addition to their important role as energy-yielding nutrients, may exert a significant influence on the regulation of gene expression (Jump et al., 1999). Several rodent studies indicate that dietary lipids modulate the expression of genes in skeletal muscle, with an increase in the messenger RNA (mRNA) expression of genes involved in fatty acid metabolism after isoenergetic high-fat diets compared with low fat, high-carbohydrate diets (Samec et al., 1999).

The effect of altered dietary fat intake on the expression of genes encoding proteins necessary for fatty acid transport and ß-oxidation in skeletal muscle has been reported. A rapid and marked capacity for changes in dietary fatty acid availability to modulate the expression of mRNA-encoding proteins is necessary for fatty acid transport and oxidative metabolism. This finding is evidence of nutrient-gene interactions in skeletal muscle. Expression of hepatic gene expression related to lipid metabolism in broiler breeders declined sterol regulatory element binding protein 1 (SREBP-1), ATP-citrate lyase (ACL), fatty acid synthetase (FAS), malic enzyme (ME), acetyl-CoA carboxylase (ACC), and stearoyl-CoA (9) desaturase 1 (SCD1) genes in ad lib birds declined from their highest levels just prior to photo-stimulation to reduced levels as the birds came into and maintained egg production (Richard et al., 2003)

The effects of dietary fat on gene expression reflect an adaptive response to changes in the quantity and type of fat ingested. In mammals, fatty acid regulated transcription factors include peroxisome proliferator-activated receptors (PPARα, -β, and -γ), HNF4α, NFκB, and SREBP1c. These factors are regulated by:

(a) Direct binding of fatty acids, fatty acyl coenzyme A, or oxidized fatty acids
(b) Oxidized fatty acid regulation of G-protein–linked cell surface receptors and Activation of signaling cascades targeting the nucleus
(c) Oxidized fatty acid regulation of intracellular calcium levels, which affect cell signaling cascades targeting the nucleus.
At the cellular level, the physiological response to fatty acids will depend on:

(a) The quantity, chemistry, and duration of the fat ingested;
(b) Cell-specific fatty acid metabolism (oxidative pathways, kinetics, and Competing reactions);
(c) Cellular abundance of specific nuclear and membrane receptors
(d) Involvement of specific transcription factors in gene expression.

An important receptor that mediates the effects of dietary lipids on gene expression is the peroxisome proliferator-activated receptor alpha (PPARα), which is abundantly expressed in enterocytes. Nutrients impact gene expression mainly by activating or suppressing specific
transcription factors (Desvergne et al., 2006). The most important group of transcription factors involved in mediating the effect of nutrients and their metabolites on gene transcription is the super family of nuclear receptors, which is subdivided into six families of which the NR1 family is most relevant to nutrition. One important group of receptors that mediates the effects of dietary fatty acids and its derivatives on gene expression are the Peroxisome Proliferator Activated Receptors (PPARs, NR1C) (Sampath et al., 2005). Transcriptional regulation by PPARs requires heterodimerization with the retinoid X receptor (RXR; NR2B). When activated by an agonist, the PPAR/RXR heterodimer stimulates transcription via binding to DNA response elements (PPREs) present in and around the promoter of target genes. Besides up regulating gene expression, PPARs are also able to repress transcription by directly interacting with other transcription factors and interfere with their signaling pathways, a mechanism commonly referred to as transrepression.

Role of PPAR in intestinal fatty acid oxidation: It is well established that PPAR serves as a master regulator of fatty acid catabolism and regulate the following functions
- PPARα regulates intestinal cholesterol flux
- PPARα regulates intestinal nutrient transport and metabolism
- PPAR regulates intestinal motility
- PPARα diminishes effects of oxidative stress. Hence PPAR might be therapeutically valuable for patients with inflammatory bowel disease.

These mechanisms are involved in the control of carbohydrate and lipid metabolism, cell differentiation and growth

PUFA: Lipogenic enzymes in liver decreased as result of feeding a diet containing 60 % linoleic acid (Flick et al., 1977). Fatty acids stimulated the expression of adipocyte fatty acid binding protein (ap2) mRNA. In the 3T3-L1 adipocyte cell line, arachidonic acid (n-6) decreased SCD1 mRNA stability in a dose dependent manner (80% maximum repression), as did linoleic and eicosapentaenoic acids.

Protein: Protein is very essential for growth, to develop immunity, normal maintenance of body function and structure apart from reproduction and production. The function of protein in body is not only at macro level but it also functions at gene level. A variety or number of genes responds to dietary protein both protein quantity as well as quality influences gene expression. Insulin secretion was reduced in rats, which are fed with low protein diet due to reduction in pancreatic b-cell mass lower response of remaining β-cells to nutrients and lowered protein kinase activity (PKA). PKA is involved in potentiation of glucose induced insulin secretion by gastrointestinal hormones such as GIP and GLP-1. Low protein diet feeding to rats altered the many gene expression, which are responsible for proteins related to insulin biosynthesis, secretion and cellular remodeling. Normal insulin secretion is influenced by level of Protein Kinase C (PKC), K+ channel protein, calcium ion (Ca 2+) and PKAα. Increased ATP to ADP ratio achieved through glucose metabolism, close the K+ ATP channel, which leads to depolarization of b-cells. Depolarized β-cells opens the voltage dependent Ca 2+ channels which results in influx of calcium leads to exocytosis of insulin granules. Feeding low protein diet also increased expression of PFK in islets (tetramers M, P, L, and C) results in defective glucose metabolism; it further leads to deceased glucose induced insulin secretion. Feeding low protein diet decreases insulin level, it also acts through decreased movement of intracellular calcium.

Amino acids: The first step of protein translation is the formation of the 43s pre-initiation complex containing methionyl tRNA, eIF2, GTP. This is followed by the association of methionyl tRNA and eIF2 – GTP that bind to the 40s ribosomal sub unit. The GTP is hydrolyzed late in the initiation process, and eIF2 is released from the ribosome as an inactive eIF2 – GTP. The mechanism to regulate eIF2 activity may be at the level of the ribosomal protein S6 and eukaryotic elongation factor 2 (eEF-2) which is phosphorylated in response to many agents, including growth factors and hormones initiation process. Amino acids regulate protein translation through modulation of eIF2B activity, 4 E-BP phosphorylation and protein S6 phosphorylation. Protein and amino acids the response of IGFBP-2 gene expression to variations in nutritional status was rapid and different in several tissues of young chickens, which would help modulate the growth-promoting effect of circulating IGF-I by making the IGF-IGFBP complex (Kazumi Kita, 2002).

Caloric restriction: Early epidemiological studies neglected to account for the differences in energy content between carbohydrates and proteins (each at 4 kcal/g) and lipids (9 kcal/g). Virtually all association studies show an increased risk for common diseases with increased energy intake (Kant, 2000). Laboratory animal studies have consistently shown that reducing caloric intake is the most effective means to reduce the incidence and severity of chronic diseases, retard the effects of aging, and increase genetic fidelity (Uyeda et al., 2002). Energy balance may be monitored through changes in reducing equivalents. NAD also is a cofactor for Sir2, a histone deacetylase involved in chromatin silencing of nucleolar DNA, telomere, and mating type locus (Gasser et al., 2001). In mammals, other cellular targets, such as uncoupling proteins, and neuroendocrine peptides (e.g., leptin) of the central nervous system (CNS), are potential targets of regulation by caloric restriction.

Micronutrients: Vitamins are a class of organic compounds that are components of an adequate diet. They or their
derivatives function as coenzymes, cellular antioxidants, and/or regulators of gene expression. Various vitamins are recognized in human nutrition (Vitamins A, D, E, K, B₁₂, B₆, B₉, B₃, niacin, folacin, pantothenic acid, biotin, choline), with deficiencies or excesses in intake leading to changes in protein, nucleic acid, carbohydrates, fat and/or mineral metabolism. Thus, the integrity of physiological systems, including those associated with detoxification, cellular repair, immune processes, and neural and endocrine function, depends upon the nutritional and vitamin status of the host. For these reasons, it may be anticipated that the adequacy of the vitamin supply to cells and tissues would affect the development, progress and outcome of cancers.

Suboptimal intakes of specific micronutrients have been associated with CVD (B vitamins, vitamin E, carotenoids), cancer (folate, carotenoids), neural tube defects (folate), and bone mass (vitamin D) (Fairfield et al., 2002). B₉, B₁₂, serum homocysteine levels. Hyperhomocysteinemia is a risk factor and marker for coronary artery disease, but the mechanism(s) is not understood at the molecular level (Falk et al., 2001). Deficiency of vitamins B₁₂, folic acid, B₉, niacin, C, or E, or iron or zinc appears to mimic radiation in damaging DNA by causing single- and double-strand breaks, oxidative lesions, or both (Ames, 2001) and the various effects of micronutrient deficiency are presented in the Table below. Nutrient deficiencies are orders of magnitude more important than radiation because of constancy of exposure to milieu promoting DNA damage (Ames et al., 2001). Folate deficiency breaks chromosomes due to substantial incorporation of uracil in human DNA (4 million uracil/cell) (Blount et al., 1997). Single-strand breaks in DNA are subsequently formed during base excision repair, with two nearby single-strand breaks on opposite DNA strands leading to chromosome fragmentation.

Zinc is an essential trace element with cofactor functions in a large number of proteins of intermediary metabolism, hormone secretion pathways and immune defense mechanism. Zn is involved in regulation of small intestinal, thymus and hepatocytes gene expression. (Tako et al., 2003) MTF-I (Metal Responsive element Factor-I) is a Zn dependent transcriptional activator regulates metallothionin I and II through MRE (Menard, 1981). Zn dependent KLF4 transcription factor is involved in protein preparation of HT-29 cells. The other protein have Zn in it as constituents are ATP synthase, cytochrome c, a, NADP dehydrogenase I and II regulated by Zn.

In mammals, evidence is emerging that biotin participates in processes other than classical carboxylation reactions. Specifically, novel roles for biotin in cell signaling, gene expression, and chromatin structure have been identified in recent years. The activity of cell signals such as biotinyl-AMP, Sp1 and Sp3, nuclear factor (NF)-xB, and receptor tyrosine kinases depends on biotin supply. Consistent with a role for biotin and its catabolites in modulating these cell signals, many biotin-dependent gene products play roles in signal transduction and localize to the cell nucleus, consistent with a role for biotin in cell signaling. Postranscriptional events related to ribosomal activity and protein folding may further contribute to effects of biotin on gene expression. Finally, research has shown that biotinidase and holocarboxylase synthetase mediate covalent binding of biotin to histones (DNA-binding proteins), affecting chromatin structure; Biotinylated histones appears to play a role in cell proliferation, gene silencing, and the cellular response to DNA repair (Janos Zempleni, 2005). This observation suggests that biotin metabolites that have been considered “metabolic waste” in previous studies might have biotin-like activities. These new insights into biotin-dependent gene expression are likely to lead to a better understanding of roles for biotin in cell biology and fetal development. (Rodriguez, 2003)

PEPCK is vitamin A dependent enzyme involved in conversion of oxaloacetate to phospho enol pyruvate, one of the important steps in gluconeogenesis. Phosphoenolpyruvate carboxykinase (PEPCK) gene expression is decreased in vitamin A-deficient (VAD) mice. Vitamin A deficiency condition leads to changes in chromosomal structure of RARE (Retinoic Acid Responsive Element), which further leads to change in co regulator binding and activity. The reduction in RNA Pol II association is indicative of an interruption in the direct interactions of RNA Pol II with the PEPCK promoter, with general transcription factors and/or with co regulator molecules that contribute to the activation of the PEPCK gene. These results increase understanding of the molecular basis for decreased PEPCK gene expression in VAD mice in vivo and offer.

### Micronutrient deficiency and DNA damage

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<tr>
<th>Micronutrient</th>
<th>DNA Damage</th>
<th>Health Effects</th>
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<tbody>
<tr>
<td>Folic acid</td>
<td>Chromosome breaks</td>
<td>Colon cancer; heart disease; brain dysfunction</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>Uncharacterized</td>
<td>Same as folic acid; neuronal damage</td>
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<tr>
<td>Vitamin B6</td>
<td>Uncharacterized</td>
<td>Same as folic acid</td>
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<tr>
<td>Vitamin C</td>
<td>Radiation mimic (DNA oxidation)</td>
<td>Cataracts; cancer</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Radiation mimic (DNA oxidation)</td>
<td>Colon cancer; heart disease; Immune dysfunction</td>
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<tr>
<td>Iron</td>
<td>DNA breaks; radiation mimic</td>
<td>Brain and immune dysfunction; cancer</td>
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<tr>
<td>Zinc</td>
<td>Chromosome breaks; radiation mimic</td>
<td>Neurological symptoms; memory loss</td>
</tr>
<tr>
<td>Niacin</td>
<td>Disables DNA repair (polyADP ribose)</td>
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additional insight into the regulation of other retinoid-responsive genes (Kelly et al., 2003)

**Applications in animal sciences**

1. To develop animal feed/food matching to its genotype to benefit health and enhance normal physiological processes
2. To select nutrients fine tuned with the gene of the animal.
3. To understand the role of nutritional management in the performance (Production/disease) of the animal.
4. To understand the ageing process in animals.

**Implications on Animal Nutrition**

The central dogma of molecular biology states that DNA makes RNA and RNA makes protein. The application of molecular biology to understanding nutrient metabolism centers on identifying conditions that lead to the amplification of genetic information and synthesis of several copies of RNA and ultimately the initiation and progression of protein synthesis. The ultimate end point of these processes in livestock is a coordinated change in cellular and tissue metabolism to maintain homeostasis or to undergo homeorhesis to support a new physiological state. On these lines of action theoretically it is possible to control and prevent any disease or disorder having a genetic component by nutrient management and manipulation. Practically speaking, animal nutritionists have always been using dietary manipulations to affect and control the phenotype/performance. However the exact genetic cascade that was being targeted by such manipulations were not known.

The recognition that fatty acids are regulators of metabolism and act in the cell nucleus to control expression of genes for fatty acid synthesis has been extended to investigations on the origins of milk fat depression in dairy cows. It has been observed that the reduction in milk fat when fish oil is fed is linked to decreased mRNA abundance of acetyl CoA carboxylase, fatty acid synthetase, and stearoyl-CoA desaturase (also known as Δ⁹-desaturase). And also the potent action of trans-10, cis-12 CLA to reduce milk fat synthesis in lactating dairy cows involves a reduction in mRNA for acetyl CoA carboxylase, fatty acid synthetase, stearoyl-CoA desaturase, lipoprotein lipase, fatty acid binding protein, and glycerol phosphate acyltransferase. These changes are directly linked to a substantial reduction in lipogenic activity in explant cultures in vitro. These data provide understanding of the molecular basis for milk fat depression, a practical milk production problem that has been recognized for several decades.

In addition to knowing the minimal nutrient concentrations required to avoid deficiency, determination of optimal and toxic concentrations will be important. Nutritional effects on gene expression in different life stages and genotypes also must be a focus in companion animals. The importance of maternal nutrition during pregnancy on the gene expression and development of offspring was demonstrated in sheep. In pigs, nutrient excretion was shown to vary depending on breed, suggesting differences in metabolism due to genotype. Determination of nutrient requirements of dogs participating in different physical activities (e.g., dog sled racing, sprint racing or hunting/herding) also would be a worthy research venture.

However refinements in sample handling, statistical analysis, and hierarchical clustering of expressed transcripts and development of bovine-specific metabolic maps is necessary for greater understanding of the complex molecular basis of nutrient metabolism in support of milk production, growth and reproduction.

**Limitations**

As of yet, nutrigenomics is in its infancy. The tools to study protein expression and metabolite production have not yet developed to the point as to enable efficient and reliable measurements. Presently the accurate measurement of dietary exposure will be fundamental if we want to understand the interaction of nutrition with the genome. Transcript profiling using DNA micro arrays or candidate gene analysis is a static measure of the pool size of individual mRNA in a cell or tissue and does not provide any information on the dynamics of mRNA synthesis (Transcription) or RNA degradation (RNA stability). Determining the rate of mRNA synthesis typically involves use of nuclear run-on assays that measure the relative amount of new transcripts made from the previously initiated RNA polymerases and provides a measure of the in vivo rate of transcription of DNA to mRNA. Levels of some key proteins (e.g., the transferrin receptor) are regulated at the level of RNA stability; however, measures of RNA degradation rate are presently not easily attainable in vivo and therefore nutritional impacts on gene expression usually are only described for transcription rate and mRNA abundance.

All these technologies are still in the process of development. There is a need to develop guidelines and standards, which incorporate the state-of-the-art and enable and encourage researchers to apply the ‘omics’ technologies in ways that can be replicated, so that comparisons between laboratories can be made and which facilitate pooling of samples and data. Also once such research has been achieved, it will need to be integrated together in order to produce results and dietary recommendations. The prudent application of nutrigenomics hold great promise in countering this challenge and making desired manipulation of genome expression by nutritional intervention to boost up nutrient–gene status, a reality in years to come.

**CONCLUSION**

Nutrigenomics offers the potential of important health benefits for some individuals. Primary care physicians have minimal training in nutrition and genetics, and medical geneticists are in high demand and short supply. Dietetic practitioners are experts in nutrition science and interest in nutrigenomics is growing among members of this professional group. However, as with physicians, dietetics
practitioners would require considerable training to bring nutrigenomics into their practice capacity (Castle and Ries, 2007). In recent years, a high-resolution recombination map of the human genome has provided and increased the information on the genetic order of polymorphic markers and the SNP map of the human genome. It is hoped that the map of SNPs in the human genome will provide powerful molecular tools to decipher the role of nutrition in human health and disease and help defining optimal diets. Advanced genetic analysis in combination with twin studies may provide opportunities to understand the basis of complex traits and the role of individual genotypes on the development of polygenic diet-related diseases such as cancer and CVS (Boomsma et al., 2002). Thus nutrigenomics treats food as a major environmental factor in the gene–environment interaction, with the final aim to personalize food and nutrition and ultimately individualize strategies to preserve health, by tailoring the food to individual genotype (Iacoviello et al., 2008).

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