

Review Article

Nutrigenomics and its Applications in Animal Science

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Abstract

Nutrigenomics applies genomic technologies to study how nutrients affect expression of genes. With the advent of the post genomic era and with the use of functional genomic tools, the new strategies for evaluating the effects of nutrition on production efficiency and nutrient utilization are becoming available. Nutrigenomics plays an efficient role in various fields of animal health like nutrition, production, reproduction, disease process etc. Nutrigenomic approaches will enhance researchers' abilities to maintain animal health, optimize animal performance and improve milk and meat quality.

Key words: Nutrigenomics, Genotype, Nutritional management

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Introduction

In recent years, nutritional research has moved from classical epidemiology and physiology to molecular biology and genetics. Following this trend, nutrigenomics has emerged as a novel and multidisciplinary research field in nutritional science that aims to elucidate how diet can influence animal health.¹

It is already well known that bioactive food compounds can interact with genes affecting transcription factors, protein expression and metabolite production. The application of modern molecular biology techniques has the potential to revolutionize animal nutrition, as opportunities to integrate the information coded in the genome to applied animal nutrition because; production is the goal of animal nutritionists. "Genomics" is the study of the functions and interactions of all genes in the genome; "nutrigenomics" applies genomic technologies to study how nutrients affect expression of genes. The study of how genes and gene products interact with dietary chemicals to alter phenotype and, conversely, how genes and their products metabolize nutrients is called nutritional genomics or "Nutrigenomics".² It is expected that nutritional genomics will be a key area in nutritional research over the next decade³ and that nutrigenomic studies will be very useful for elucidating the roles of food components in obesity,⁴ coronary heart diseases⁵ and cancer prevention.⁶ From a nutrigenomic perspective, nutrients are dietary signals, detected by the cellular sensor system, that influence gene and protein expression and, subsequently, metabolite production.⁷ Thus, nutrigenomics is the two way interaction of individual genetic and specific dietary components that may alter gene expression and, ultimately, transcription of an enzyme or other protein. Further, when nutrigenomics is combined with metabolic information (metabolomics), whole animal

assessment may be achieved and provides the opportunity for corrective intervention via specific nutrients and other compounds.⁸

With the advent of the post genomic era and with the use of functional genomic tools, the new strategies for evaluating the effects of nutrition on production efficiency and nutrient utilization are becoming available. New tools that examine the regulation of metabolism at the level of gene expression are being used to examine nutritional effects of dietary components and nutritional strategies. These tools will allow much more rapid evaluations of the relationship between diet and their key biological functions and also promise to provide methods for detecting fine differences in nutrient quality, and may eventually be used to evaluate not only supplementation and management practices in livestock production systems, but also the nutritional value of feed ingredients.⁹

From the research perspective, to explore the effect of dietary components on the genome, the crucial stages of nutrigenomics are transcriptomics, proteomics and metabolomics. Application of these modern research tools, known as "omics" technologies, should yield new knowledge on the course of molecular processes in animal organisms and a more precise evaluation of the biological properties of feeds.

Applications of Nutrigenomics in Animal Science

1) **To develop animal feed/food matching to its genotype.** The goal of nutrigenomics or nutritional genomics is to develop foods and feeds that can be matched to genotypes of animals to benefit health and enhance normal physiological processes. Using gene chips that contain the genetic code of animal, researchers can measure the effects of certain nutritional supplements, and how they alter the gene interactions of the body.

2) To select nutrients fine-tuned with genes of animal. Nutrigenomics is not altering the genetics of an animal nor to genetically modify the animal rather we are altering the activity of genes switching on good genes and keeping bad ones switched down. Through nutrigenomics we are carefully selecting nutrients for fine-tuning genes and DNA present in every cell and every tissue of an animal. For example, keeping stress response genes switched down with proper nutrition so that the animal is healthier, more productive.

3) To understand role of nutritional management in performance (production/disease) of animal. Gene expression studies will allow for the identification of pathways and candidate genes responsible for economically important traits. Dietary manipulations and nutritional strategies are key tools for influencing ruminant production. There is a usual belief that nutrition and genetic makeup both strongly influence the reproductive performance of milking animals. This is particularly important during the transition period and early lactation, when the animal is particularly sensitive to nutritional imbalances. Nutrigenomics and nutritional genomics are providing new tools that can be used to more clearly understand how nutritional management can be applied to address disease, performance and productivity in animals. In the changing scenario of ruminant's nutrition the objective of nutrigenomics is to study the effects of diet on changes in gene expression or regulatory processes that may be associated with various biological processes related with animal health and production. In studies of steers under nutritional restriction due to intake of poor quality feeds, expression of specific genes associated with protein turnover, cytoskeletal remodeling, and metabolic homeostasis was clearly influenced by diet.¹⁰ These studies provide application of nutrigenomics to resolve the molecular

markers important in nutrition research. There is vary scares information about effect of diet on expression of genes related to productive or reproductive traits of livestock, it may be possible to begin to understand the importance of the relationship between individual nutrients and the regulation of gene expression. To understand this concept of nutrigenomics a study of diet induced gene expression is discovered in which selenium deficiency shown to alter protein synthesis at transcriptional level.¹¹ It leads to adverse effect like enhancement of stress through up-regulation of specific gene expression and signaling pathway. On the other hand genes responsible for detoxification mechanism and protection from oxidative damage were hampered, these consequences ultimately leads to alteration of phenotypic expression of related symptoms of selenium deficiency. From the above example it is apparent that possibly nutrigenomics can be used to identify the specific markers to manipulate gene expression through use of nutrients or their combinations so as to improve productive as well as overall animal performance. Nutrigenomics will be a path-breaking tool through identification of pathways and candidate genes responsible for dietary induced diseases and ultimately reduction in production losses due to these diseases in animals. The discoveries of gene markers related to economically important traits like milk, meat, wool production etc whose expression can be improved by dietary regimens is a need of today's nutrigenomic research, which will help for sustainable livestock production.

4) Nutrient-Gene interaction. The diet has long been regarded as a complex mixture of natural substances that supplies both the energy and building blocks to develop and sustain the organism. However, nutrients have a variety of biological activities. Some nutrients have been found to act, as radical scavengers known as antioxidants and as such are

involved in protection against diseases. Other nutrients have shown to be potent signaling molecules and act as nutritional hormones.⁷ Some of the plant secondary metabolites also known as photochemical act as a modulator of animal health and production.

5) To understanding the aging process in animals. A nutrigenomic approach can be applied to understanding the aging process in companion animals. Healthy adult animals given the same foods can be studied to identify the gene expression and biochemical differences characteristic of the aging process. Foods for senior animals can then be rationally designed and evaluated for their ability to modify gene expression profiles in animals to more closely reflect those found in healthy adult animals, which has the potential to improve health and quality of life. In addition, canine and feline nutrigenomic studies may provide evidence that nutrigenomics can improve health and quality of life for humans.

6) Nutrigenomics and immune system. The concept underlying nutrigenomics is that nutrition is the key element of health maintenance, particularly for the immune system, so that an optimum level of nutrition will ensure optimum animal health. A deficiency of an essential nutrient will eventually affect the body's performance. The immune system is particularly sensitive to deficiencies, and once the immune system is compromised, negative consequences follows.

There is a defined relationship between production and immune status of animals. Higher the production, more sensitive is the immune system of animal. Two decades ago, the main aim of animal nutritionists was to design ration so to avoid deficiencies. Deficiency is now rare in modern livestock production systems. So we can now move to the next stage rather than merely preventing deficiency, we can strive to actually meet the animal's exact requirements from its diet, in order that it can meet its genetic potential.

8) Nutrigenomics and diseases.

Essential nutrients and other bioactive food components can serve as important regulators of gene expression patterns. Macronutrients, vitamins, minerals, and various phytochemicals can modify gene transcription and translation, which can alter biological responses such as metabolism, cell growth, and differentiation, all of which are important in the disease process. Genome wide monitoring of gene expression using DNA microarrays allows the simultaneous assessment of the transcription of thousands of genes and of their relative expression between normal cells and diseased cells or before and after exposure to different dietary components. This information should assist in the discovery of new biomarkers for disease diagnosis and prognosis prediction and of new therapeutic tools.

Many diseases and disorders are related to suboptimal nutrition in terms of essential nutrients, imbalance of macronutrients, or even toxic concentrations of certain food compounds. There are multietiological diseases which are due to interaction of different nutrients along with several genes¹² Due to remarkable diversity in all living beings differences in food digestion, nutrient absorption, metabolism, and excretion have been observed and genetic diseases in these processes have been reported. The functional integrity of gene is mainly depends on metabolic signals that the nucleus receives from internal factors, e.g. hormones, and external factors, e.g. nutrients, which are among the most influential of environmental stimuli. Genomes evolve in response to many types of environmental stimuli, including nutrition. Therefore, the expression of genetic information can be highly regulated by, nutrients, micronutrients, and photochemicals found in food.¹³

9) Nutrigenomics and reproduction.

The science of nutrigenomics has begun to use information obtained from basic

studies of the genome to evaluate the effects of diet and nutrient management schemes on gene expression. Preliminary studies have shown the value of such techniques and suggest that it will be possible to use specific gene expression patterns to evaluate the effects of nutrition on key metabolic processes relating to reproductive performance. While the effects of nutrition on fertility are only partially understood, modern nutrigenomics will undoubtedly play a key role in developing strategies for addressing some of the limitations in reproductive performance.

Currently, oligo based and cDNA microarray techniques make it possible to understand many of the factors controlling the regulation of gene transcription and globally evaluate gene expression profiles by looking at the relative abundance of gene-specific mRNA in tissues. These techniques provide an unprecedented amount of information and are only now being used to examine key reproductive, developmental, and performance characteristics in cattle. They also promise to provide a tremendous amount of new information that can be used to understand and diagnose key issues that limit reproductive performance.¹⁴

Nutrigenomics and the omic technologies

The sequencing of the genomes has led to the development of a whole new scientific methodology. These new areas of scientific study usually include the 'omics' suffix. The technical developments have given us novel tools enabling high throughput genome wide approaches. These tools form the basis of the biomics era; genomics (covering DNA), transcriptomics (RNA), proteomics (protein), metabolomics (metabolites) and systems biology (integrating all of these), with bioinformatics enabling the storage, integration and analysis of the overwhelmingly complex data set produced.

Nutrigenomics aims to determine the influence of common dietary ingredients on the genome, and attempts to relate the resulting different phenotypes to differences in the cellular and/or genetic response of the biological system.¹⁵ More practically, nutrigenomics describes the use of functional genomic tools to probe a biological system following a nutritional stimulus that will permit an increased understanding of how nutritional molecules affect metabolic pathways and homeostatic control. Nutrigenetics, on the other hand, aims to understand how the genetic makeup of an individual coordinates their response to diet, and thus considers underlying genetic polymorphisms. It embodies the science of identifying and characterizing gene variants associated with differential responses to nutrients, and relating this variation to disease states. Therefore, both disciplines aim to unravel diet/genome interactions; however, their approaches and immediate goals are distinct. Nutrigenomics will unravel the optimal diet from within a series of nutritional alternatives, whereas, nutrigenetics will yield critically important information that will assist clinicians in identifying the optimal diet for a given individual, i.e. personalized nutrition.

Role of transcriptomics in nutrigenomics

The transcriptome is the complete set of RNA that can be produced from the genome. Transcriptomics is the study of the transcriptome, i.e. gene expression at the level of the mRNA.

Using either cDNA or oligonucleotide microarray technology, it describes the approach in which gene expression (mRNA) is analysed in a biological sample at a given time under specific conditions. It is the most widely used of the "omics" technologies. Regulation of the rate of transcription of genes by food components represents an intriguing site for regulation of an individual's phenotype.¹⁶ A host of essential nutrients

and other bioactive food components can serve as important regulators of gene expression patterns. Macronutrients, vitamins, minerals, and various phytochemicals can modify gene transcription and translation, which can alter biological responses such as metabolism, cell growth, and differentiation.

The aim of transcriptomics is to determine the level of all or a selected subset of genes based on the amount of RNA present in tissue samples. Transcriptomics is concerned with the expression of genes in animals. In precise experiments conducted on animals, the scope of investigation is usually restricted, for example to assess the influence of dietary components on the transcript level of selected organs, as demonstrated in Table 1.

The use of a microarray containing probes for the over 8000 genes present in the liver of rats demonstrated that about 33 % of the genes of rats fed a soya protein diet differed from those of casein fed animals.¹⁷ Significant differences were observed in the gene cluster concerned with lipid metabolism, and in the gene related to energy metabolism, transcription factor, and anti-oxidation enzymes. In similar experiments carried out by Tachibana *et al.*, (2005),¹⁸ compared with casein, soya protein changed the expression of 120 genes involved in lipid metabolism, antioxidant activity and energy metabolism. Endo *et al.*, (2002) also reported that various dietary protein sources resulted in a difference in expression of about 281 genes in rat liver, suggesting a nutritional function for protein components.¹⁹

In dairy industry, an effective utilization of microarray technology was beneficial to study mammary gland tissues (milk production and udder health), muscle growth and development and myogenesis process (beef production) and the role of gut microflora on nutritional diet intake in ruminants (health and food safety). Study

of Ron *et al.*, (2007) has effectively been hybridized Affymetrix microarray (MG-U74v2) in identification of 249 differentially expressed probe sets common to the three experiments along the four developmental stages of puberty, pregnancy,²⁰ lactation and involution. In context to candidate genes for milk production traits, a total of 82 expressed genes were identified in mammary gland tissue with at least 3-fold expression over the median representing all issues tested in Gene atlas.

In pork industries, the impact of advanced nutrigenomics tools has been discussed for the economic benefits and to improve human nutrition and health. In pig, nutrigenomics tools were effectively utilized in analysis of regulation of myogenesis and its biochemical pathways.²¹ Combination of biochemical pathway and microarray results revealed the biological insight of porcine myogenesis process is controlled by two distinct waves, i.e. Notch signaling pathway and the WNT signaling pathway. Recent study on porcine microarray expression profiling in 16 tissues revealed the interaction between gene and tissue for differentially expressed genes targeted differentially for each tissues's transcriptome.²² Evidence from the recently published transcriptomics based nutritional studies performed in livestock species suggests that, with appropriate study design, it is feasible to apply transcriptomic methods successfully in animal feed and nutritional research. However, newly emerged nutrigenomics tools like gene expression based biomarker development still poses a major challenge and the use of expression profile 'signatures', rather than single genes, may provide an eventual solution for this information should assist in the discovery of new biomarkers for disease diagnosis and prognosis prediction and of new therapeutic tools.

Role of proteomics in nutrigenomics

Proteomics is the study of all the proteins in a particular cell, tissue or compartment.²³ The major tools of proteomics are two dimensional (2D) gel electrophoresis and mass spectrometry (MS). Proteomic analysis was quite effective and useful to evaluate the effect of dietary methionine on breast-meat accretion and protein expression in skeletal muscle of broiler chickens.²⁴ Via a tandem mass spectrometer, a total of 190 individual proteins were identified from *Pectorali major* muscle tissue; three of them were recognized which differed distinctly between the treatment proteome and could be considered as potential biomarkers regulated by a methionine deficiency in broiler chickens.

Role of metabolomics in nutrigenomics

Metabolomics represents the final step in understanding the function of genes and their proteins. The aim of metabolomics is to determine the sum of all metabolites (other substances than DNA, RNA or protein) in a biological system: organism, organ, tissue or cell (Müller and Kersten, 2003). Techniques employed to investigate the metabolome include nuclear magnetic resonance (NMR)

spectroscopy, high performance liquid chromatography (HPLC) and gas chromatography-mass spectrometry (GC-MS). These methods are capable of resolving and quantifying a wide range of compounds in a single sample. The main characteristics of these new technologies were miniaturization, automation, high throughput and computerization.²⁵

As in the case of transcriptomics and proteomics, the scope of metabolomic analysis is mainly restricted to the assessment of the influence of dietary components on the metabolome of selected organs or tissue in animal nutrition studies. In experiments performed by Bertram *et al.* (2006) metabolomic analysis was implemented to detect the changes in the biochemical profiles of plasma and urine from pigs fed with high-fibre rye bread.²⁶ Two diets with similar levels of dietary fibre and macronutrients, but with contrasting levels of wholegrain ingredients, were prepared from whole rye and fed to pigs. Using an explorative approach, the studies disclosed the biochemical effects of a wholegrain diet on plasma betaine content and excretion of betaine and creatinine.

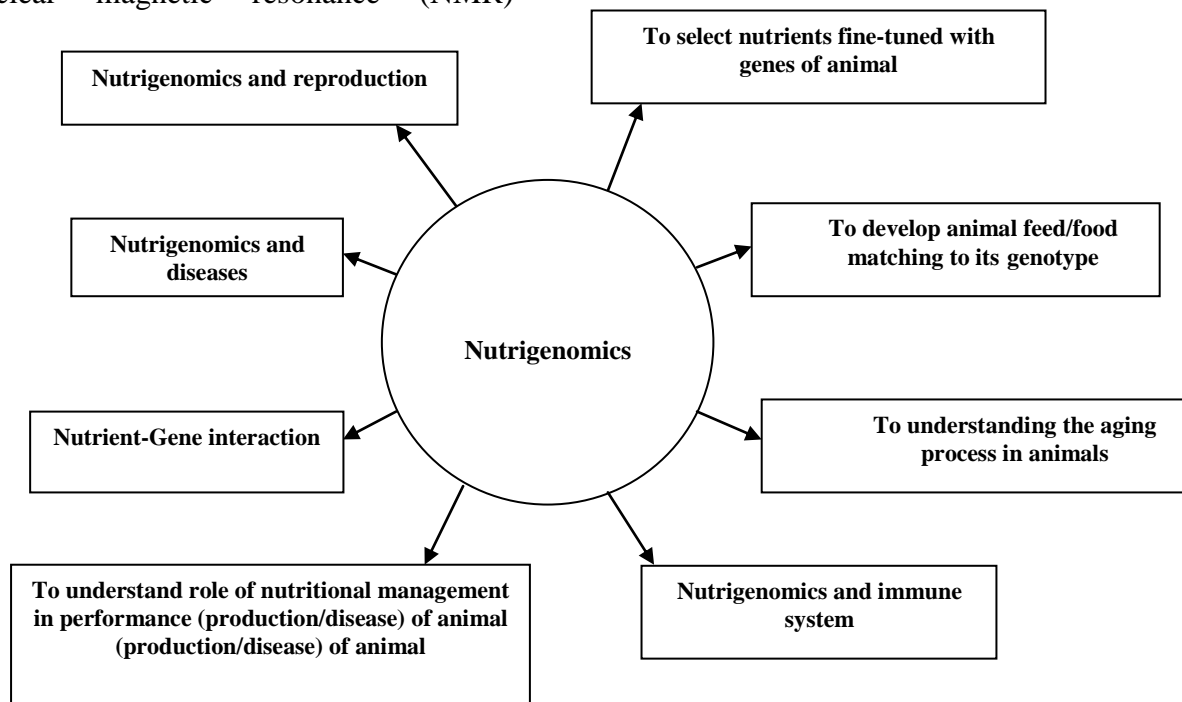


Fig 1. Schematic overview of integration of Omics technology in animal feeding and nutritional research

Table 1: Influence of Dietary Components on The Transcript Level

Omic technology	Nutrigenomics		
	Technique	Nutritional Research	Animal Feeding
Transcriptomics	DNA Microarrays, Oligonucleotide probes, spotted cDNA products	Nutrient-related diseases and predispositions; Individualized food; Functional food; Diagnosis	Quality of animal feedstuff; Quality of animal products; Optimization of nutrient/diets requirements; Food safety assessment
Proteomics		Post transitional modification; Protein-protein interaction; Bioprocess cultivation conditions; Food quality control; Functional food; Diagnosis	
Metabolomics	Nuclear magnetic resonance (NMR) spectroscopy, High performance liquid chromatography (HPLC); Gas chromatography-mass spectrometry (GC-MS)	Understanding the function of genes and their proteins; Resolving and quantifying a wide range of compounds in a single sample (diet); Detect the changes in the biochemical profiles of plasma, urine etc from animal fed with diet prepared; To determine the sum of all metabolites (other substances than DNA, RNA or protein) in a biological system: organism, organ, tissue or cell	

Conclusion

Nutrigenomic approaches will enhance researchers' abilities to maintain animal health, optimize animal performance and improve milk and meat quality. Nutrigenomics is a rapidly emerging science still in its beginning stages. It is uncertain whether the tools to study protein expression and metabolite production have been developed to the point as to enable efficient and reliable measurements. Also once such research has been achieved, it will need to be integrated together in order to produce results and dietary recommendations. All of these technologies are still in the process of development.

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