

# Application of Nutrigenomics for Enhancement of Body Growth in Ruminants

**M. Mondal\*, M.K. Ghosh**

ICAR-National Dairy Research Institute, Eastern Regional Station, Kalyani, West Bengal, India

## Abstract

*Many a times different animals fed with the same diet may perform differently and it is due to differences in ability of nutrients to interact within the biological systems affecting molecular pathways resulting in differences in body weight gain, production or reproduction performances. For better understanding of the above processes, nutrigenomics and endocrinomics; two emerging fields that are of great help to discover the differential expression and function of genes occur with different diets, have come up. Nutrigenomics is dealt with the effects of each and every bioactive chemical in foods and supplements that alter gene expression in an animal. On the other hand, nutrients alter the hormonal inter milieu of the animal thereby 'turn on' or 'turn off' of a particular set of pathways affecting 'switching on' or switching off' of a defined set of genes (Endocrinomics). Hence, there is always a crosstalk between nutrigenomics and endocrino-genomics. This paper highlights the importance of nutrigenomics and endocrinomics, and their interactions during the process of growth in domestic animals in general and bovine species in particular.*

**Keywords:** Endocrine genomics, transcriptome, microarray, nutritional genomics, diet-gene interaction

**\*Author for Correspondence** E-mail: drmmondal@gmail.com

## INTRODUCTION

Livestock farming, an important part of Indian agriculture, contributes significantly to Indian economy in terms of household nutritional security and increased household income thereby poverty alleviation. In India, the livestock sector alone contributes nearly 25.6% of value of output at current prices of total value of output in agriculture, fishing and forestry sector.

The overall contribution of livestock sector in total GDP is nearly 4.11% at current prices during 2012–13 [1]. As per the 19th livestock census, India has the world's largest numbers of bovine population (299.9 million heads) [1]. As estimated, the rapidly growing world human population will require around 67% more protein of animal origin by 2050 than it is today. Recent studies indicated that an increase in consumer's income in fast-growing BRICS (Brazil, Russia, India, China, and South Africa) countries consisting about 50% of global population is supposed to induce important changes in the amount and types of food consumption. Hence, the livestock sector can significantly contribute towards

augmenting rural livelihood, poverty alleviation, and food security [2]. However, developing and fostering livestock systems that require low to moderate amounts of economical and external inputs and will significantly enhance production potential are key features of sustainable development. Sustainable livestock development, including diversifying livestock production, is a pragmatic approach to address both hunger and food security [2].

Among all domestic animals, Indian ruminants including cattle and buffaloes hold the greatest promise and potential for fulfil the expected demand of animal protein in near future. Though we have the largest numbers of livestock population in the world, the Indian bovines suffer from some of the inherent problems like; (1) late maturity (2) poor estrus expressivity/anoestrus/repeat breeding, and (3) long postpartum calving intervals etc. Age at puberty influences production efficiency in animals. The slow growth rate and thus late maturity of dairy cattle and buffaloes leads to a great economic loss at organized as well as unorganized dairy farms in India. Sexual

maturity is directly related to growth of an animal rather than age; and faster growing calves reach sexual maturity at an early age. Heifers that grow faster, show short prepubertal period and calve at younger age, have greater life time productive efficiency with higher fecundity than heifers exhibiting slow growth rate, long prepubertal period and calving at older age [3].

Over the last decade, advances in the biochemical technologies available for examining functional genomics have provided a number of new molecular tools for evaluating responses to nutritional strategies. These tools are largely based on an understanding of the expression and control of specific genes and gene products and have led to the development of the sciences associated with nutrigenomics [4].

Bioactive food compounds can interact with genes affecting transcription factors, protein expression and metabolite production. The study of how genes and gene products interact with dietary chemicals to alter phenotype and conversely, how genes and their products metabolize nutrients (Nutrigenomics) is important to produce enough quantity of food of animal origin that is needed to feed huge human population in near future [5].

## **NUTRITIONAL GENOMICS OR NUTRIGENOMICS**

Traditional nutrition research involves in determination of requirement of specific nutrients, ration formulation and monitoring of performance upon feeding the specific nutrients/ration. Emergence of nutritional biochemistry leads to the assessment of targeted metabolic pathways such as carbohydrate or lipid metabolism where small molecule and enzyme assays could monitor the specific effects of diet. More recently with the development of the field of molecular biology, researchers have been able to study the impact of diet on the organism at the molecular level.

The concept of “nutrigenomics” developed at the turn of the 21st century to describe the trend in human nutrition research towards individualized dietary formulation. Nutrigenomics has since focused on how diet impacts the expression of genes and the

development of specific diseases including diabetes, obesity, and heart disease. In reality, the scope of this field is significantly larger. The interaction of an organism with its nutrition source is an intimate and complex physiologic affair that is typically based on changing *inter milieu*. The regulatory control mechanisms of these processes can be based at all levels from genetics and gene expression to the feedback of specific metabolites.

## **DEFINITION OF NUTRIGENOMICS**

Nutrigenomics, or nutritional genomics, is a multidisciplinary science that combines information from genetics, nutrition, physiology, pathology, molecular biology, bioinformatics, biocomputation, sociology, ethics, and other disciplines. We believe that understanding diet-nutrient interactions in different individuals will help explain and help alleviate health disparities hence, this knowledge applies to national and international societal issues in personal and public health.

“The new science of nutrigenomics teaches us what specific foods tell your genes. What you eat, directly determines the genetic messages your body receives. These messages, in turn, control all the molecules that constitute your metabolism: the molecules that tell your body to burn calories or store them. If you can learn the language of your genes and control the messages and instructions they give to your body and your metabolism; you can radically alter how food interacts with your body, lose weight, and optimize your health” [6].

## **APPLICATION OF NUTRIGENOMICS**

### **Characteristics of Bovine Genome**

Recently, whole genome sequencing of bovine further paves the way to nutrigenomics and endocrinomics research. The bovine genome is composed of 29 autosomes and two sex chromosomes, and contains approximately three billion nucleic base pairs [7]. Bovine genome is similar in size to that from other mammals. Mapping strategies have resulted in many complimentary markers that have helped define the structural nature of the genome, and sequencing studies have identified and cataloged well over 300,000 expressed sequence tags (ESTs) in gene bank.

### 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 antioxidants, other nutrients have shown to be potent signaling molecules and act as nutritional hormones and some photochemical of plant origin acts as a modulator of animal health and production. Genes are turned on and off according to metabolic signals that the cell receives from internal factors, e.g. hormones, and external factors, e.g. nutrients. Numerous dietary components can alter genetic events, and thereby influence health. In addition to the essential nutrients, such as carbohydrates, amino acids, fatty acids, calcium, zinc, selenium, and vitamin A, C and E; there is a variety of nonessential bioactive components that seem to significantly influence health. These essential and nonessential bioactive food components are known to modify a number of cellular processes associated with health and disease prevention, including hormonal balance, cell signaling, cell cycle control, apoptosis, and angiogenesis. Often bioactive food components will modify several processes simultaneously [8].

### Nutrigenomics in Animal and Feed Sciences

The aim of transcriptomics in nutrigenomics 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 over 30000 genes in humans [9]. 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. 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 [10]. Use of a microarray was also allowed brain gene expression changes in response to different amounts of omega-3 polyunsaturated fatty acids in diets of rats to be revealed [11]. The authors concluded that PUFA enriched diets

lead to significant changes in expression of several genes in the central nervous tissue, and these effects appear to be mainly independent of their effect on membrane composition.

The experiments demonstrated the ability of cDNA microarray technology to study levels of gene expression in response to nutrition in an intact animal system [12]. DNA microarray technology allows the simultaneous analysis of the expression of large numbers of genes, improving greatly the performance of traditional methods for gene expression analysis [13]. DNA array technology (or so-called DNA chip technology) is currently the most powerful tool in transcriptomics, which enables the measurement in parallel and in tens of samples, of the expression of up to 50,000 transcripts [14]. The integration of microarray analysis into basic and applied nutrition and food research provides new insights into the effects of nutrition and food ingredients like fats, carbohydrates, proteins, carotenoids, vitamins, minerals, flavonoids and xenobiotics at the molecular level [9]. The relationship between specific nutrients or diet and gene expression may help to identify these effects and facilitate the prevention of common diet related diseases.

In the context of nutrition and micronutrient research in livestock species, transcriptomic methods have been popularly applied; however, it has been widely discussed albeit primarily in other studies using cell lines and animal models. Under such type of approach, a multitude of genes regulated at the mRNA level by dietary components has been identified and this, in turn, has provided new insights into the biological processes affected by nutritional parameters. In livestock species, the major application of nutrigenomics tools is to how effectively being utilized for dairy and meat industries.

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 and the role of gut microflora on nutritional diet intake in ruminants. Study of Ron *et al.* 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, lactation and involution [15]. The bovine cDNA microarray for beef industry was mainly investigated for muscle fibre number and fibre composition of muscle is largely determined during prenatal development. Study of Lehnert *et al.* provided a detailed description of molecular events accompanying skeletal muscle differentiation in the cattle, as well as gene expression profiling for muscle growth and development and developmentally regulated in bovine foetal muscle [16]. Their study also highlights the developmental expression pattern of *FSTL1* and *IGFBP5*, which have previously been implicated in myogenesis regulation, as well as describing the changing representation of a recently-described ncRNA (*NEAT1* orthologue) in developing cattle muscle.

### Nutritional Genomics in Ruminants

Genetic predisposition and nutritional management requires reproductive performance and fertility in dairy cattle. This is particularly important during the transition period and early lactation, when the animal is particularly sensitive to nutritional imbalances. Byrne reported that 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 [17]. Many of these changes in expression could be predicted from observed changes in animal growth and physiology during normal nutrient restriction [18]. 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.

Gene expression studies will allow for the identification of pathways and candidate genes responsible for economically important traits. 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 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. There is very scarce 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 is shown to alter protein synthesis at transcriptional level. 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 lead 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.

### Identification of the Regulatory Elements of Genes

Hormones often effect changes in their target tissues by altering the expression of specific sets of genes. At the DNA level, these temporal, spatial, and quantitative changes in

gene expression are controlled by various regulatory DNA sequences such as promoters, enhancers, insulators, and silencers [19–20]. The identification and characterization of regulatory DNA sequences that mediate the actions of hormones and their signaling pathway genes therefore constitute an important focus of hormonal research. Traditionally, regulatory DNA sequences have been investigated on a gene-by-gene basis, using a variety of approaches including deletion constructs, DNA footprinting, and gel shift assays. With the availability of genome sequences, novel strategies for the large-scale, computer-based *in silico* identification of regulatory sites are becoming feasible [21].

### mRNA Expression Profiling

The majority of cells in an individual organism share an identical set of genes. Nevertheless, these cells display an astonishing phenotypic diversity that is further enhanced by a multiplicity of developmental stages and physiological or pathological states. This diversity of cellular phenotypes encountered within an individual is almost entirely due to differences in the patterns of gene expression. Consequently, the study of changes in gene expression over time and space, as well as in response to hormones represents a challenging area of hormonal research. Traditional experimental methods, such as Northern blot analysis, differential display, and subtractive hybridization, were the standard tools that researchers used to identify differentially expressed genes. These approaches produced either lists of differentially expressed genes or, at most, semiquantitative estimates of transcript frequencies in different biological samples. This situation changed with high-throughput sequencing of cDNAs, including studies of ESTs and the serial analysis of gene expression (SAGE). These methods allowed scientists to quantify the occurrence of thousands of transcripts in libraries prepared from different cells or tissues. Based on the resulting data, the relative expression of different genes within a biological sample could be assessed. Databases containing information on ESTs derived from different tissues or cell lines can be analyzed to estimate the relative abundance of transcripts [22]. Using digital differential display or electronic

subtraction, a computational assessment of transcript frequencies in different samples (e.g., with or without nerve growth factor treatment) can be used to explore differential gene expression [23]. With the introduction of DNA array technologies, powerful tools for global studies of gene expression have become available to individual laboratories [24]. Microarray technologies have also been applied to investigate a number of endocrine tissues and hormone-regulated processes.

### CONCLUSIONS

Combinatorial approach of nutrigenomics and endocrinomics to increase animal productivity holds promise. The availability of genomewide assays that interrogate hundreds of thousands of DNA variants will facilitate the understanding of how genomic variation affects the interaction of diet with the physiological response of the animal. Nutrigenomics approaches this interaction by evaluating how the effects of specific diets, nutritional restriction, or excess nutrients influence DNA damage, the epigenome, and gastrointestinal microbiota. New resources to identify the factors affecting these processes will enhance the work that is critical to unravel these interactions in cattle. Endocrine concepts and the re-emergence of signaling as a primary means of understanding the complex interactions of genes may shape the new bioinformatics tools that are needed for the analysis of pertinent data, as well as direct the development of new biomolecules that are tailored to genomic-translational information.

### COMPETING INTERESTS

The authors declare that they have no competing interests.

### REFERENCES

1. *19th Livestock Census*. All India Report, Ministry of Agriculture. Department of Animal Husbandry, Dairying and Fisheries, Krishi Bhavan, New Delhi, India. 2012; 1–130p.
2. Naveena BM, Kiran M. Buffalo Meat Quality, Composition, and Processing Characteristics: Contribution to the Global Economy and Nutritional Security. *Animal Frontiers*. 2014; 4: 18–24p.

3. Hoffman PC, Funk DA. Applied Dynamics of Dairy Replacement Growth and Management. *J Dairy Sci.* 1997; 75: 2504–2516p.
4. Swanson KS, Schook LB, Fahey GC. Nutritional Genomics: Implications for Companion Animals. *J Nutr.* 2003; 133: 3033–3040p.
5. Kaput J, Ordovas JM, Ferguson L. The Case for Strategic International Alliances to Harness Nutritional Genomics for Public and Personal Health. *Brit J Nutr.* 2005; 94: 623–632p.
6. Hyman M. *Book on Ultra-Metabolism: The Simple Plan for Automatic Weight Loss.* New York: Atria Books; 2006; 24p.
7. Lewin HA. The Future of Cattle Genomics: The Beef is Here. *Cytogen Gen Res.* 2003; 102: 10–15p.
8. Törrönen R, Marjukka K, Kaisa P. Nutrigenomics-New Approaches for Nutrition, Food and Health Research. *Nutrigenomiikka.* 2006; 20: 3–43p.
9. Müller M, Kersten S. Nutrigenomics: Goals and Strategies. *Nat Rev Genet.* 2003; 4: 315–322p.
10. Takamatsu K, Tachibana N, Matsumoto I, *et al.* Soy Protein Functionality and Nutrition Analysis. *Biofactors.* 2004; 21: 49–53p.
11. Kitajka K, Sinclair AJ, Weisinger RS, *et al.* Effect of Dietary Omega-3 Polyunsaturated Fatty Acids on Brain Gene Expression. *Proc Nat Acad Sci USA.* 2004; 101: 10931–10936p.
12. Masotti A, Letizia da Sacco, Gian Franco Bottazzo, *et al.* Microarray Technology: A Promising Tool in Nutrigenomics. *Critical Reviews Food Sci Nutri.* 2010; 50: 693–698p.
13. Spielbauer B, Stahl F. Impact of Microarray Technology in Nutrition and Food Research. *Mol Nutr Food Res.* 49: 908–917p.
14. Corthesy-Theulaz I, den Dunnen JT, Ferre P, *et al.* Nutrigenomics: The Impact of Biomics Technology on Nutrition Research. *Ann Nutr Metab.* 2005; 49: 355–365p.
15. Ron M, Israeli G, Seroussi E, *et al.* Combining Mouse Mammary Gland Gene Expression and Comparative Mapping for the Identification of Candidate Genes for QTL of Milk Production Traits in Cattle. *BMC Genomics.* 2007; 8: 183–193p.
16. Lehnert SA, Reverter A, Byrne KA, *et al.* Gene Expression Studies of Developing Bovine Longissimus Muscle from Two Different Beef Cattle Breeds. *BMC Dev Biol.* 2007; 7: 95–98p.
17. Byrne KA, Wang YH, Lehnert SA, *et al.* Gene Expression Profiling of Muscle Tissue in Brahman Steers during Nutritional Restriction. *J Anim Sci.* 2005; 83: 1–12p.
18. Jones KL, King SS, Iqbal MJ. Endophyte-Infected Tall Fescue Diet Alters Gene Expression in Heifer Luteal Tissue as Revealed by Interspecies Microarray Analysis. *Mol Reprod Dev.* 2004; 67: 154–161p.
19. Burke LJ, Baniahmad A. Co-Repressors 2000. *FASEB J.* 2000; 14: 1876–1888p.
20. Zhan HC, Liu DP, Liang CC. Insulator: From Chromatin Domain Boundary to Gene Regulation. *Hum Genet.* 2001; 109: 471–478p.
21. Pennacchio LA, Rubin EM. Genomic Strategies to Identify Mammalian Regulatory Sequences. *Nat Rev Genet.* 2001; 2: 100–109p.
22. Adams MD, Kerlavage AR, Fleischmann RD, *et al.* Initial Assessment of Human Gene Diversity and Expression Patterns Based upon 83 Million Nucleotides of cDNA Sequence. *Nature.* 1995; 377: 3–174p.
23. Lee NH, Weinstock KG, Kirkness EF, *et al.* Comparative Expressed-Sequence-Tag Analysis of Differential Gene Expression Profiles in PC-12 Cells before and after Nerve Growth Factor Treatment. *Proc Natl Acad Sci USA.* 1995; 92: 8303–8307p.
24. Ferea TL, Brown PO. Observing the Living Genome. *Curr Opin Genet Dev.* 1999; 9: 715–722p.

### Cite this Article

Mondal M., Ghosh M.K. Application of nutrigenomics for enhancement of body growth in ruminants. *Research & Reviews: Journal of Veterinary Science and Technology.* 2016; 5(1): 1–6p.