

Nutrigenomics and gene regulation in animals- a review

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Abstract

Nutrigenomics studies the effect of various nutrients and bioactive compounds in feed/food on gene expression and gene regulation. Increased urbanization and human population along with heavy competition for feed grains between humans and animals lead to a search for an innovative solution by which a small quantity of feed gives maximum production and improve animal health. This innovative solution is possible through Nutrigenomics. It is a new science seeking to understand the influence of dietary components on the Genome, Transcriptome, Proteome, and Metabolome. Nutrigenomics determines the individual nutritional requirements as per the genetic makeup of the animal as well as the association between diet and chronic diseases. Supplementation of different nutrients in different proportions leads to improvement in animal production, growth rate, and health performance by enhancing an immune response in animal body through alteration of gene expression and gene regulation. It may be possible to get desired health and productive performance by targeting the specific gene through nutritional manipulation. Nutrigenomics focused on a balanced and healthy diet to prevent diseases and improves animal health and quality of life. It also helps in the improvement of animal performance, immunity and delay in the ageing process. Further, it provides a better understanding of the mechanisms involved in disease susceptibility and reduces health care costs. Nutrigenomics is still the young and emerging tool for rapid and effective evaluation of nutritional strategies that provides a valuable tool for producers to differentiate and identify nutritional strategies to maximize profitability by enhancing animal performance.

Keywords: Gene expression, Gene regulation, Nutrients, Nutrigenomics

Introduction

The study of the consequences of the influence of nutrients and other bioactive food components on the expression of the genetic material is called Nutrigenomics. As per Bionaz *et al.*, 2015, it is defined as the study of the genome with reference to influences of nutrition on the expression of genes. It is a new science in which the influence of nutrients on the Genome, Transcriptome, Proteome, and Metabolome can be studied (Bordoni *et al.*, 2021). The omics revolution leads to the field of nutrigenomics, i.e. the study of the genome-wide influences of various nutrients through alteration in protein, mRNA, and metabolite expression (Reddy *et al.*, 2018). Nutrigenomics gives an idea about the effects of dietary nutrients and bioactive food components on gene expression and gene regulation. It studies the effects of dietary nutrients on cellular gene expression and ultimately, decides the animal phenotype. In addition to nutrient metabolism, nutrition interacts with genes and alters the expression of genes involved in the regulation of animal performances. Individual nutritional requirements based on the genetic makeup of an individual as well as the interrelationship between diet and chronic diseases will also possible to determine in the nutrigenomics study. Nutrigenomics is one of the upcoming sciences that also have the potential to provide knowledge about new areas of health and disease management (Namra *et al.*, 2020). A Nutrigenomics study will identify the genes that give physiological responses to diet and the genes in which polymorphism occurs (Li *et al.*, 2014). It is an emerging scientific discipline that identifies the influence of environmental factors on gene expression (Evangelakou *et al.*, 2019). The concept of nutrigenomics shows tremendous promise for an improved understanding of the effects of dietary intake on health. The dietary exposures altered in individuals with genetic variants in metabolic pathways provide knowledge regarding great potential for personalized nutrition advice. However, dietary intake assessment remains inadequate instead of considerable resources that have gone into improving technology for the measurement of the genome and biological systems (Katherine *et al.*, 2013). The excitement about nutrigenomics comes from a growing awareness of the potential for modifications of food or diet to improve health and minimize the risk of diet-related diseases (Neeha and Kinth, 2013). Hence, the objective of this review is to provide a brief introduction about nutrigenomics and how it works in the field of animal sciences.

Nutrigenomics- opportunities

Due to increased urbanization and the human population, the demand for animal products has been increasing day by day. Also, there is heavy competition between human beings and animals for cereal feeds that leads to an increase in demand for animal products. To satisfy the increased demands of animal products there is a need for an innovative solution to convert a small amount of feed for better production; this may be possible via 'omics' technology.

Omic Sciences

Genomics, proteomics, Inomics, Metabolomics, Phenomics and transcriptomics are the different omic sciences. In Genomics studies, DNA sequencing, genetic mapping, genetic profiling, recombinant DNA technology and structural and functional analysis of genomes are included while, studies of protein identification and quantification, post-translational modifications are included in proteomics. Metabolomics is related to studies of metabolite profile, metabolic intermediates, hormones and other signalling molecules. However, RNA sequencing, expression profiling and transcriptional regulation studies are included in transcriptomics. Evaluation of morphological, biochemical and physical traits, establish a link between genetics, epigenetics and environmental factors carried out in phenomics. Whereas, Inomics is related to the study of element profiling, biochemical regulation and element interactions (Deshmukh *et al.*, 2014).

How does nutrigenomics works?

With a normal animal diet, the genetic information in a strand of DNA is copied into a new molecule of messenger RNA in the transcription process that serves as blueprints for protein synthesis during the process of translation. In the process of translation, there is translation of the sequence of a messenger RNA (mRNA) molecule to a sequence of amino acids during protein synthesis. The type of protein formed decides the cell structure and function i.e. phenotype of an animal that leads to the generation of biological response in an animal body. This all process is involved in the gene expression process. Any alteration in gene expression will lead to alteration in biological response in an animal body. Deficiency, undernutrition, overnutrition affects gene expression and gene regulation. Through normal diet,

nutrients act as dietary signals that are signalling through sensor mechanisms that lead to the formation of normal genotype. Further normal genotype leads to the formation of a normal phenotype that maintains homeostasis in an animal body. If the supplementation of nutrients in animal diet is normal but there is metabolic stress or pro-inflammatory stress on the animal body that leads to the formation of sensitive genotype through nutrient sensor signalling. Sensitive genotype produces a sensitive phenotype that will responsible for the onset of disease in an animal body (Gonzalez *et al.*, 2015).

These processes are controlled by the basic genetic make-up, external factors such as Disease and Environmental toxins or specific nutrients. Researchers can extract “specific messenger RNA (mRNA)” from tissue at any stage to measure the effect of a nutrient on gene expression instead of measuring the effect of a specific nutrient on animal performance or the physiological response at the end of the study. By using gene chips, the mRNA amount present that relates to the relative amount of copies of known genes could be measured. Gene is “up-regulated”, “down-regulated” or “unaffected” as a result of a specific dietary change can be determined by using contrasting colour labels.

Nutrients in the diet of an animal affect gene expression directly or indirectly through metabolites formed during metabolism or through the signal transduction process.

Dietary aspects examined in nutrigenomics studies (Nowacka-Woszek, 2020)

1. **Type of diet-** Under the type of diet dietary aspects included are undernutrition, overnutrition, macro and micro-element supplementation, type of protein and fat source, macro and micro-element deficiency.
2. **Life period during the study to be carried out** – it includes prenatal period, the period after weaning, lactation period and adult life period.
3. **Duration of the dietary regimen-** it includes Short-term and long term dietary regimens.
4. **Study of genome functioning-** includes the study of effects at gene transcript level or protein level or due to DNA methylation or due to histone modifications.
5. **Phenotype study-** it includes the study of metabolism changes, production traits and animal health status.

Regulation of gene expression by dietary glucose

Glucose in presence of insulin induces gene expression in the liver encoding glucose transporters and glycolytic and lipogenic enzymes, eg. Acetyl-CoA carboxylase (ACC). It is a known fact that insulin and glucagon has a critical role in regulating gene expression, but recently it was found that Glucose also has a key role in transcriptional regulation.

When glucose concentrations increased in liver cells that lead to an increase in the secretion of enzymes like pyruvate kinase and acetyl-CoA carboxylase. Therefore, there is an increased flux of glucose metabolites into fatty acid synthesis. Further, In pancreatic β -cell, the transcription of pyruvate kinase and the insulin gene is induced by glucose. Glucose also stimulates the transcription of specific genes that augment the cellular content of the corresponding mRNA and protein and thereby affects gene expression. A sugar signalling mainly goes through the carbohydrate-responsive element-binding protein (ChREBP) (Haro *et al.*, 2019).

Regulation of gene expression by dietary fat

The effect of dietary fat on gene expression depends upon the quantity and type of fat ingested. After ingestion of fat in the animal body, there is the formation of fatty acids in the animal body and these fatty acids are acts as i) a precursor of eicosanoids, ii) as ligands for nuclear receptors, PPARs and iii) as a controller of the nuclear content of SREBP1c (Wan *et al.*, 2017). Genes regulation by fat could be carried either by direct binding of (oxidised) fatty acids, fatty acyl-coenzyme A or oxidised fatty acid (eicosanoid) regulation of cell surface receptors and that of intracellular calcium levels as well as activation of signalling cascades (Jump, 2001; Segers *et al.*, 2017). The quantity, chemistry and duration of the fat ingested will decide the physiological response to fatty acids at the cellular level. The type of dietary fat supplemented affects the fatty acid composition and insulin signalling-related gene expression in the *longissimus dorsi* muscle of pigs (Park *et al.*, 2012).

Regulation of gene expression by dietary protein

Shortage of mRNA necessary for expression of the fatty acid synthase gene in the adipocytes occurs due to protein-rich diets that results in the moderation of total body fat. Dietary proteins

regulate gene expression by the GCN2/activating transcription factor 4 (ATF4) and mTORC1 pathways by sensing amino acid concentrations (Jump, 2001; Soheli, 2020). Zhang et al., 2014 reported that supplementary dietary protein increased IMF accumulation mainly to increased intramuscular lipogenic gene expression and decreased lipolytic gene expression.

Regulation of gene expression by dietary minerals

As similar to other nutrients, mostly minerals are involved in several gene expressions “Bivalent metals” has a strong influence on gene expression. Both parenteral and oral zinc and cadmium applications enhance the transcription rate of the metallothionein (MT) gene in intestinal tissue (Ouellette *et al.*, 1982). Zinc could regulate gene expression directly by regulating transcription and indirectly by physiological modulation of responsive genes through secondary mediators that affect the transcription process (Cousins, 1998). Cadmium prolongs the half-life of MT mRNA in hepatocytes. This effect on the half-life prolongation of MT mRNA is tissue specific. Cadmium has a stronger influence on gene expression than that of zinc, and the intensity of the gene expression effect is higher in spermatocytes and spermatids than in hepatocytes and fibroblasts (De *et al.*, 1991). Iron influences transferrin and ferritin concentrations by exerting an effect on mRNA stability and the translation rate (Bremner and Beattie, 1990).

Regulation of gene expression by dietary vitamins

Vitamins are micronutrients required in minute quantity and they have a role in gene expression. Biotin has a role in the synthesis of various essential proteins (enzymes) at the gene level. Vitamin C is also plays role in hepatic gene expression.

Vitamin A regulates gene expression through its retinol and retinoic acid form. The most important target tissues for Vitamin A action are in the adrenal glands, testes, cerebellum, kidneys, prostate, cerebral cortex, skin and viscera. After retinoic acid binds to its receptor, it will stimulate the transcription and translation of vitamin A-responsive genes, including some involved in cell differentiation (also in the secretion of growth hormone, glycerolphosphate dehydrogenase and leptin production among others). Vitamin A deficiency leads to a negative influence on hepatic PEPCK gene expression in mice. Oral supplementation of retinoic acid restores that expression (Scribner *et al.*, 2005).

Vitamin D directly binds to DNA at Vit.D responsive elements as a homodimer or heterodimer and activates gene transcription. Vitamin deficiency downregulates the mitochondrial transcription whereas, Vitamin D supplementation upregulates the mitochondrial transcription (Machado *et al.*, 2019). According to Jiang *et al.*, 2013 supplementation of Nicotinic acid influenced the lipid metabolism and related gene expression and when supplemented with 120 mg Nicotinic acid/kg, some pharmacologic actions on lipid metabolism appeared. On supplementation of nicotinic acid changes in body weight and fat deposition appeared to be associated with hepatic expression of adiponectin.

Applications of nutrigenomics

- i) To develop animal feed/food matching to its genotype
- ii) To select nutrients fine-tuned with genes of an animal
- iii) To understand the role of nutritional management in the performance of an animal
- iv) To understand the nutrient-gene interaction
- v) To understand the ageing process in animals
- vi) To understand the relation of nutrigenomics and immune response
- vii) To understand the interrelationship between nutrigenomics and diseases in animals
- viii) To understand the role of nutrigenomics in animal reproduction

Conclusion

Nutrigenomics is a new tool to define nutritional strategies for feeding animals as per their genotype make-up. Different nutrients affect gene regulation and gene expression that decides the phenotype of an individual that is responsible for different biological responses in an animal body. This developing tool could improve animal performance, health, growth rate, immune response and ultimately increased profitability in Animal husbandry. Further, on-farm trials are necessary to make a final conclusion about nutrigenomics and improvement in animal health and performance.

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