

Nutritional Regulation of Gene Expression in Animals: Feeding Beyond Nutrients

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SUMMARY

Animal nutrition has traditionally focused on providing adequate energy, protein, vitamins, minerals, and water to support growth, reproduction, maintenance, and production. However, advances in molecular biology have revealed that nutrients serve not only as sources of energy and structural components but also as important biological signals that regulate gene expression. This interaction between nutrition and the genome forms the basis of nutrigenomics, which explores how dietary components influence gene activity and how genetic variation affects an animal's response to nutrients. Nutritional regulation of gene expression represents a major shift from simply meeting nutrient requirements toward strategically using diets to optimize biological functions at the molecular level. Nutrients and their metabolites can regulate genes involved in metabolism, immunity, growth, reproduction, stress responses, and tissue development. Understanding these mechanisms can improve animal health, feed efficiency, productivity, product quality, and sustainability, supporting the development of precision nutrition strategies for modern livestock production.

INTRODUCTION

Gene expression is the process by which genetic information encoded in DNA is converted into functional molecules, primarily proteins and functional RNA. It occurs mainly through **transcription**, where DNA is transcribed into messenger RNA (mRNA), followed by **translation**, where mRNA directs protein synthesis. Although most cells contain the same genetic material, selective activation or suppression of genes enables specialized cellular functions. Gene expression regulates essential processes such as growth, metabolism, immunity, reproduction, and tissue development. It is influenced by genetic and environmental factors, particularly nutrition. Nutrients and their metabolites can modify gene activity, thereby affecting animal health, productivity, feed efficiency, and physiological responses.

How Do Nutrients Regulate Genes?

Nutrients act not only as sources of energy and building blocks but also as **biological signalling molecules** that regulate gene expression. After digestion and absorption, nutrients and their metabolites interact with receptors, transcription factors, enzymes, hormones, and intracellular signalling pathways, thereby activating (**upregulating**) or suppressing (**downregulating**) specific genes. A major mechanism involves transcription factors that bind to DNA and control the transcription of target genes. Nutrients also regulate gene activity through **epigenetic mechanisms**, including DNA methylation, histone modification, and non-coding RNAs such as microRNAs, without altering the DNA sequence. Nutrients such as folate, choline, methionine, vitamin B₁₂, and betaine provide methyl groups required for DNA methylation, influencing long-term gene expression, particularly during foetal development, growth, and stress. Nutrition further affects hormones such as insulin, IGF-1, growth hormone, thyroid hormones, leptin, and glucagon, which regulate genes involved in growth, metabolism, reproduction, appetite, and immunity. Nutritional regulation is dynamic and reversible; dietary changes can rapidly alter gene activity. Thus, **nutrigenomics** enables precision nutrition strategies to improve animal health, feed efficiency, productivity, disease resistance, product quality, and environmental sustainability.

Nutrients That Influence Gene Expression

Nutrients are increasingly recognized as **molecular regulators** that influence gene expression in addition to fulfilling their conventional roles as sources of energy and essential building blocks. Through interactions with transcription factors, nuclear receptors, signalling pathways, and epigenetic mechanisms, nutrients regulate the expression of genes involved in growth, metabolism, immunity, reproduction, stress adaptation, and product quality. The major nutrient groups that influence gene expression are discussed below.

1. *Proteins and Amino Acids*

Proteins supply amino acids required for tissue synthesis, enzyme production, hormone formation, and numerous physiological processes. Beyond these structural roles, several amino acids function as **metabolic signalling molecules** that regulate gene expression and cellular metabolism.

Among the essential amino acids, **lysine, methionine, leucine, threonine, tryptophan, and arginine** play particularly important regulatory roles. **Leucine** activates the **mammalian target of rapamycin (mTOR) signalling pathway**, stimulating genes responsible for protein synthesis, skeletal muscle growth, cell proliferation, and nutrient utilization. **Arginine** enhances the production of nitric oxide and polyamines, thereby regulating genes involved in immune responses, vascular function, wound healing, and reproductive performance. **Methionine**, besides being a limiting amino acid in many livestock diets, serves as a precursor of **S-adenosylmethionine (SAM)**, the principal methyl donor required for DNA methylation and epigenetic regulation of gene expression. **Lysine** influences muscle protein deposition and lean tissue development through its effects on anabolic pathways. Adequate dietary protein and balanced amino acid supplementation promote the expression of genes involved in muscle accretion, milk protein synthesis, intestinal development, immune competence, and antioxidant defence, ultimately improving feed efficiency, growth performance, and production efficiency.

2. *Fatty Acids*

Dietary fatty acids are not only concentrated sources of energy but also important signalling molecules that regulate lipid metabolism, inflammation, and immune function at the genetic level.

Polyunsaturated fatty acids (PUFAs), particularly **omega-3 (α -linolenic acid, EPA, and DHA) and omega-6 (linoleic acid and arachidonic acid) fatty acids**, regulate gene expression primarily by activating **Peroxisome Proliferator-Activated Receptors (PPARs)** and other lipid-sensitive transcription factors. These receptors control genes involved in fatty acid oxidation, lipid synthesis, adipocyte differentiation, glucose metabolism, inflammatory responses, and energy homeostasis.

Omega-3 fatty acids generally suppress the expression of pro-inflammatory genes while enhancing genes associated with antioxidant defence and immune regulation. In dairy cattle, they improve milk fatty acid composition, reproductive efficiency, and immune function. In poultry and swine, dietary PUFAs enhance meat quality, improve feed conversion efficiency, and reduce inflammatory stress.

Balanced dietary lipid nutrition therefore contributes not only to energy supply but also to metabolic regulation and improved production performance through gene-mediated mechanisms.

3. *Vitamins*

Several vitamins function as **gene-regulating molecules** by acting through nuclear receptors that directly control transcription of target genes.

Vitamin A, in the form of **retinoic acid**, binds to **Retinoic Acid Receptors (RARs)** and **Retinoid X Receptors (RXRs)**, regulating genes involved in embryonic development, epithelial tissue integrity, vision, immune function, and cellular differentiation.

Vitamin D interacts with the **Vitamin D Receptor (VDR)** to regulate genes responsible for calcium and phosphorus homeostasis, bone mineralization, muscle function, and innate immunity. Vitamin D also influences genes associated with antimicrobial peptide synthesis and inflammatory responses.

Vitamin E, although primarily recognized as an antioxidant, indirectly regulates genes involved in oxidative stress responses and immune function by protecting cell membranes from oxidative damage.

Several **B-complex vitamins**, including **folate, vitamin B₁₂, riboflavin, and pyridoxine**, participate in one-carbon metabolism, supplying methyl groups necessary for DNA methylation and epigenetic regulation of gene expression.

Vitamin deficiencies may impair normal gene regulation, resulting in reduced growth, compromised immunity, reproductive disorders, poor skeletal development, and decreased production performance.

4. Minerals

Minerals are indispensable components of numerous enzymes, transcription factors, and antioxidant systems involved in gene regulation. Many trace minerals influence gene expression either directly through transcription factors or indirectly by maintaining cellular homeostasis.

Zinc is a structural component of more than 300 enzymes and numerous **zinc-finger transcription factors**, which regulate DNA binding and transcription of genes involved in growth, immune function, cell proliferation, and tissue repair.

Selenium forms part of **selenoproteins**, including glutathione peroxidase and thioredoxin reductase, which regulate antioxidant defence, thyroid hormone metabolism, and immune-related gene expression.

Copper participates in oxidative enzymes involved in connective tissue formation, iron metabolism, antioxidant protection, and immune regulation.

Chromium enhances insulin sensitivity and influences genes associated with glucose metabolism, nutrient partitioning, and stress responses.

Other minerals such as **iron, manganese, magnesium, iodine, and calcium** also regulate numerous metabolic pathways by supporting enzyme activity, hormone synthesis, and intracellular signaling.

Balanced mineral nutrition improves antioxidant capacity, disease resistance, fertility, milk production, growth performance, and overall metabolic efficiency through coordinated regulation of gene expression.

5. Plant Bioactive Compounds (Phytochemicals)

Plants contain numerous biologically active compounds known as **phytochemicals**, which possess nutrigenomic properties despite not being classified as essential nutrients.

Important phytochemicals include **polyphenols, flavonoids, tannins, saponins, carotenoids, terpenoids, curcumin, resveratrol, catechins, and essential oils**. These compounds influence gene expression by modulating intracellular signalling pathways such as NF- κ B (Nuclear Factor Kappa B), Nrf2 (Nuclear Factor Erythroid 2–Related Factor 2), MAPK (Mitogen-Activated Protein Kinase), AMPK (AMP-Activated Protein Kinase), and PPAR (Peroxisome Proliferator-Activated Receptor) pathways, which regulate inflammation, oxidative stress, immune function, apoptosis, and energy metabolism.

Polyphenols and flavonoids enhance the expression of antioxidant genes while suppressing pro-inflammatory cytokine genes. Condensed tannins influence genes involved in rumen microbial activity, nitrogen utilization, methane production, and parasite resistance. Essential oils regulate genes associated with gut integrity, digestive enzyme secretion, and microbial balance, thereby improving nutrient digestibility and intestinal health. Because of their antimicrobial, antioxidant, and anti-inflammatory properties, phytochemicals are increasingly being used as **natural alternatives to antibiotic growth promoters** in sustainable livestock production systems.

6. Carbohydrates and Energy Supply

Although often viewed primarily as energy sources, carbohydrates also regulate gene expression through glucose-mediated signalling pathways. Blood glucose concentrations influence insulin secretion, which activates intracellular pathways such as **PI3K-Akt** and **mTOR (Mechanistic Target of Rapamycin)**, regulating genes involved in glucose uptake, glycogen synthesis, lipid metabolism, and protein synthesis.

In ruminants, fermentation of carbohydrates produces **volatile fatty acids (VFAs)**—acetate, propionate, and butyrate—which serve not only as energy substrates but also as signaling molecules. **Butyrate**, in particular, functions as a **histone deacetylase (HDAC) inhibitor**, promoting beneficial epigenetic modifications that enhance intestinal development, rumen epithelial maturation, and immune function.

Proper dietary energy balance therefore supports optimal metabolic gene expression and improves growth, lactation, and reproductive performance.

Benefits in Livestock Production

Understanding nutritional regulation of gene expression allows nutritionists to formulate diets that maximize an animal's genetic potential.

Some important benefits include:

- Improved growth rate and feed conversion efficiency.

- Enhanced milk, meat, and egg production.
- Better reproductive performance and fertility.
- Stronger immune function and disease resistance.
- Improved meat and milk quality.
- Greater tolerance to heat stress and environmental challenges.
- Reduced nutrient losses and environmental pollution.

Applications in Precision Livestock Nutrition

Advances in molecular biology, genomics, and artificial intelligence are transforming livestock feeding. Scientists can now identify genes associated with desirable production traits and design precision feeding programmes that complement an animal's genetic profile.

For example, dairy cows can receive diets tailored to improve milk composition, broiler chickens can be fed to enhance muscle growth, and pigs can be provided nutrients that regulate genes associated with lean meat production. These precision nutrition strategies improve productivity while reducing feed costs and environmental impacts.

Future Prospects

The integration of nutrigenomics, genomics, metabolomics, and precision farming technologies is expected to revolutionize animal production. Future feeding programmes will increasingly focus on individual animal requirements rather than herd averages. Such approaches will improve production efficiency, animal welfare, and sustainability while reducing greenhouse gas emissions and dependence on antibiotics.

Although nutrigenomics is still an emerging discipline in livestock production, continued research promises innovative feeding strategies that will enable animals to achieve their full genetic potential.

CONCLUSION

Nutrition is no longer viewed merely as a source of energy and nutrients. It is now recognized as a powerful regulator of gene expression that influences growth, metabolism, immunity, reproduction, and productivity. By understanding how nutrients interact with genes, livestock producers can adopt more precise and sustainable feeding strategies. As nutrigenomics continues to evolve, nutritional regulation of gene expression will become an indispensable tool for improving animal performance and ensuring sustainable livestock production.

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