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Applications of nutrigenomics in animal health, production and reproduction

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Abstract

Increase in demand of animal products leads to search of new feeding strategies that can give more production in less feed. This could be possible through omic technology through the nutrigenomics. Nutrigenomics is nothing but the study of effect of nutrients on gene expression and gene regulation. By following new feeding strategies it is possible to downregulate the genes responsible to stress in animals that are responsible in inducing diseases and low production and upregulate the genes that will improve fertility and production through nutrient-drug interaction. Supplementation of energy, certain amino acids, vitamins, minerals and nutritional regulation would lead to improve production, reproduction and health performance in animals by reducing the disease occurrence through improving the immunity and increase in synthesis of necessary enzymes and hormones. Nutrigenomics tool could become useful in increasing profitability in animal husbandry by improving animal health, production, product quality and reproduction.

Keywords: Animal health, nutrigenomics, production and reproduction

Introduction

Recently there has been a huge development in molecular genetics techniques allowing the study of genome function on a large scale. These advances have been leading to a reduction in costs and greater accessibility and contributed to the development of new disciplines that would fall within the generic term "Nutritional Genomics".

Nutrigenomics studies how food/feed nutrients affect animal metabolism by altering gene expression and gene regulation. It involves many fields *viz*; nutrition, bioinformatics, genomics, molecular biology, functional genomics, epidemiology, and epigenomics (Benitez *et al.* 2017) [3].

Malnutrition, whether overnutrition or undernutrition, can have long-term consequences on human and animal health. Overnutrition leading to obesity, reproductive problems and cardiovascular diseases is an increasing global problem (Laddu and Hauser, 2019) [16]. However, undernutrition causes calorie, macronutrients, and micronutrients deficiencies that can result in serious chronic diseases (de Luca *et al.* 2017) [7].

The objective of this review is to discuss the applications of nutrigenomics and how various nutrients affect or improve the health, production and reproduction in animals by altering gene expression.

Applications of nutrigenomics (Ghormade *et al.* 2011) [9]

i) 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.

ii) To select nutrients fine-tuned with genes of an 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.

iii) To understand the role of nutritional management in the performance of an animal

Gene expression studies will allow for the identification of pathways responsible for economically important traits. Dietary manipulations and nutritional strategies are key tools for influencing production. Provides new tools; clearly understand how nutritional management can be applied to address disease, performance and productivity in birds and animals.

Sucrose and lactose supplementation leads to an increased expression of genes for sodium hydrogen exchanger isoforms 1 and 2, and ATPase isoform 1 in ruminal epithelial cells that further leads to decreased ruminal acetate and increased ruminal butyrate proportion. This decreased acetate proportion leads to low milk fat syndrome in animals (Oba *et al.* 2015) [20].

Providing Forage-based diet leads to greater production of polyunsaturated fatty acids (PUFAs) that results in the activation of FABP4, FASN, and PPARG by PUFAs. Which further leads to increased concentration of PUFA in beef referred as healthy food and increased PUFA leads to increase in intramuscular fat deposition in beef cattle. Addition of Fatty acids in diet of bovines leads to activation of intracellular transport/ channeling, and key transcription factors associated with lipogenesis. These factors are PPARG and SREBF2. Therefore addition of fatty acids in the diet of bovines resulted into milk fat biosynthesis in bovine mammary glands (Osorio and Moisa, 2019) [21]. As per Bionaz *et al.* (2015) [4], providing unsaturated long chain fatty acids in animal diet results into the activation of peroxisome proliferator-activated receptors (PPAR) and milk fat synthesis.

Supplementation of Methyl donors (e.g., choline, methionine, folic acid, B₂, B₆, and B₁₂) to animals during transition phase resulted into increase in the synthesis of SAM(S-adenosyl methionine) that has role in various biological processes, including transsulfuration, polyamine biosynthesis, DNA methylation and histone methylation that upregulates the Met and PPAR α through DNA methylation and therefore, there is Improvement in milk yield and dry matter intake. Further, supplementation of PUFAs, insulin, Arginine activates PPAR γ in the intramuscular preadipocyte of a beef steer leads to upregulation of their lipogenesis-related target genes and increase fat deposition in steer body. However, supplementation of PUFAs, insulin, Arginine in lactating animals activates PPAR α in the liver as well as activation of the PI3K/Akt/mTOR signalling pathways that will improve milk protein synthesis (Osorio and Moisa, 2019) [21].

Amino acids supplementation in the diet leads to the activation of sterol regulatory element-binding protein 1 (SREBP1) that results into regulation milk protein synthesis (Bionaz *et al.* 2015) [4]. Methionine restriction and low protein diets (5% and 10%) will GCN2/ eIF2 α /ATF-4/FGF-21transduction pathways and received metabolic response in the form of hyperphagia, increased energy expenditure, lipolysis and thermogenesis (Haro *et al.* 2019) [11].

High concentrate in the diet of animals downregulates the genes ACSL1, ACSS1 & 2, ACACA, FAS, SCD, FADS2, and SREBP1 and higher DNA methylation in the mammary gland that will decrease the milk fat in goat milk (Tian *et al.* 2017) [27].

iv) To understand the nutrient-gene interaction

Direct interactions: Nutrients after interacting with a

receptor, behave as transcription factors that can bind to DNA and induce gene expression. Direct interactions involve a short term trigger and cause the acute modification of the transcription process. This effect generally disappears once the exposure to the specific nutrient has been stopped.

e. g. Vitamin A interacts with retinoic acid receptor and the resulted in transcription activation or inhibition of gene expression.

Epigenetic interactions: Nutrients can alter the structure of DNA so that gene expression is altered Epigenetic mechanisms are mediated either by DNA methylation or by histone methylation or acetylation. Such epigenetic modifications can lead to gene expression changes that are remains long life and can be transmitted to the coming generations.e.g. High dietary fats can raise the chances of diabetes even in offspring.

Genetic variation: Common genetic variations such as single- nucleotide polymorphisms (SNPs) can alter the expression or functionality of genes.

v) To understand the ageing 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.

Aging results from the dysregulation of the neuro-endocrine system by chronic exposure to physical, biological, or emotional stress, which may overburden or damage the organism's adaptive capacity, leading to "adaptation diseases" and ultimately death. DNA methylation has an important role in regulation of gene expression, maintaining DNA stability and integrity in the normal ageing process

Restricted calorie/energy in the animal diet increases activity of DNA methyltransferase 1 that corrects the decreased methylation level during ageing and stops the E2F-1 factor from binding to p16INK4a promoter, causing down-regulation in p16INK4a resulted into induction of longevity of life (Alam *et al.* 2019) [2].

Supplementation of folate, vitamin B₁₂, niacin, vitamin E, retinol, and calcium reduces DNA damage and induces longevity of life whereas, the high level of riboflavin, pantothenic acid, and biotin in the diet increases DNA damage and induces ageing process (Ladeira *et al.* 2017) [15].

vi) To understand the relation of nutrigenomics and immune response

Nutrition is the "key element" of health maintenance, particularly for the immune system. A deficiency of an essential nutrient will eventually affect the body's performance. Immune system is particularly sensitive to deficiencies, and once the immune system is compromised, negative consequences follows.

According to (Higdon, 2000) [12] Supplementing Vitamin A converted into retinoic acid that activates *trans*-RA/RAR α signalling pathway that promotes the conversion of naïve

CD4 T-lymphocytes into effector T-lymphocytes–type 1 helper T-cells (Th1) and induces the production of proinflammatory cytokines by effector T-lymphocytes which stimulates the immune response in animal body.

Vitamin C supplementation leads to secretion of gene regulatory monooxygenase and dioxygenase enzymes those involved in decrease DNA methylation and Histone methylation, hypoxia-inducible factor-1 α (HIF-1 α) that regulates gene transcription and cell signalling pathways and resulted into modulation of immunity (Carr and Maggini, 2017) [6].

Selenium deficiency leads to adverse effect like enhancement of stress through up-regulation of specific gene expression & signalling pathway and Hampere genes responsible for detoxification mechanism and protection from oxidative damage that alter protein synthesis at transcriptional level and decrease in immune response (Rao *et al.* 2001; Kore *et al.* 2008) [24, 14].

Probiotics in the diet of an animal increases the expression of innate immune receptor, TLR2 as well as inhibiting the production of TH1/TH2 cytokines leads to enhanced innate immune response in animal body (Adjei-Fremah *et al.* 2018) [1].

vii) To understand the interrelationship between nutrigenomics and diseases in animals

High fat in the diet of an animal increases risk of metabolic disorders by increasing methylation in the promoter domains of fatty acid synthase (*FASN*), and a mitochondrial protein of the electron transport chain (*NDUFB6*) as well as triggering the durable epigenetic changes in genes that control regulation of intake, such as; opioid receptors and dopaminergic pathways (Murdoch *et al.* 2016) [19].

Supplementation of folate, vitamin B₁₂, niacin, vitamin E, retinol, and calcium reduces DNA damage that prevents genotoxicity and carcinogenicity whereas, the high level of riboflavin, pantothenic acid, and biotin in the diet increases DNA damage that leads to increased chances of genotoxicity and carcinogenicity (Mead, 2007) [18]. Folic acid deficiency affects DNA methylation and leads to increase chances of cancer occurrence. Fatty acids that are related to binding to the transcription factor and deficiency of fatty acids leads to obesity. Vitamin D deficiency affects mRNA stability and increases risk of kidney diseases.

Flavones increases mRNA synthesis that leads to increase in the chances of Cancer occurrence. Theaflavins decreases the mRNA synthesis that leads to Arthritis.

According to (Mead, 2007) [18] antioxidant bioactives, such as plant phenols, vitamins, carotenoids, and terpenoids reduces the release of pro-inflammatory cytokines and inhibits the expression of COX-2 and iNOS genes by the suppression of NF- κ B activation in macrophages and reducing the process of sustained inflammation that prevents occurrence of chronic inflammatory diseases in animals.

Iron influences transferrin and ferritin concentrations by exerting an effect on mRNA stability and the translation rate (Bremner and Beattie, 1990) [5]. Both parenteral and oral zinc or cadmium application enhance the transcription rate of the metallothionein (MT) gene in intestinal tissue that will protects from heavy metal toxicity, DNA damage, and oxidative stress (Ouellette *et al.* 1982) [23].

viii) To understand the role of nutrigenomics in animal reproduction

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.

High energy diet reduces the hypothalamic expression of NPY1R and of β -arrestin1 leads to lowering sensibility of the hypothalamus to NPY action that hastens the puberty in youngones (Diniz-Magalhães *et al.* 2017) [8].

Supplementation of conjugated linoleic acid increases *PTEN* gene expression through activation of PPAR γ in granulosa cells and attenuated the phosphorylation of Akt and thereby regulating granulosa cell functioning that leads to improved proliferation and steroidogenesis and improved fertility (Sharma and Singh, 2012) [26].

Wang *et al.* 2014 [28] reported that supplementation of arginine leads to translational knockdown of SLC7A1 mRNA and enhance embryo and extra embryonic membranes development.

Protected vitamin B complex supplementation in cows during transition phase and early lactation period upregulates the genes like OXTR, MUC5B, MUC1, IL1B, SPP, TRD, FZD8, and FOLR1 resulted into early implantation of embryo & early embryonic development in the endometrium (Kaur *et al.* 2019) [13].

Zinc deficiency leads to i) compromise in zinc-activated gene transcription of critical mitogenic signals, ii) impaired mitogenic hormone signal transduction and iii) hampered DNA synthesis. Collectively this all leads to hampered cell division and growth in animal body (MacDonald, 2000) [17].

Future of nutrigenomics

Nutrigenomics new tool for nutritional research in mitigating the problems related to animal's health and production. In coming year's innovations in nutrition research with use of various molecular technologies will definitely update our basic understanding of nutrient gene interrelationship and help to define new methods for managing production. Finally by targeting the specific gene through nutritional manipulation, it may be possible to get the desired performance in terms of health as well as production. Discovery of "gene markers" related to economically important traits; improved by dietary regimens.

Conclusion

It is inferred that "Nutrigenomics" a valuable tool that affect alters gene expression through nutritional manipulation. This tool could be useful to identify nutritional strategies to maximize animal performance in terms of improvement in production, health and reproduction.

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