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Applications of Nutrigenomics in Animal Sectors: A Review

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ABSTRACT

Nutrigenomics is the study of gene expression or metabolic pathway depending on different food material. In recent year, nutrigenomics has gained special attention due to its great potentiality for treating chronic disease. In this review, we have emphasized the importance of nutrigenomics on human health and on animal farm, specially on pork and poultry industries. Types of food consumption are crucial factor for human health in term of specific nutrition related gene expression and this knowledge is important for preparation of personalized diet. Human genome project identified several polymorphic gene and few of them are involved in metabolic pathway. The present review demonstrated the metabolism related disease like lactose intolerance and phenylketoneuria which is occurred due to polymorphic nature of that particular gene. Due to high cost of raw material, feed efficiency in pork and poultry industries is a crucial factor. In several investigations, researchers have used different combination of food material to monitor the growth and health of pig and chicken but it needs more accuracy and better understanding. Though the food product development and field application technique has a long way to go, further development in the field of nutrigenomics will definitely show it's potentiality in the food market and the growth of individuals. A greater understanding of these mechanisms will lead us to a sustainable fisheries, more production and other aquaculture activities.

Key words: Nutrigenomics, human health, pork and poultry industry

INTRODUCTION

In last few decades, it is established that proper nutrition or diet can fight against several diseases. Nutrition genomics or nutrigenomics is the study to understand the nutritional effect on gene expression. In order to explore the importance of diet and diet formulation, it is necessary to understand the physiological, biochemical and metabolic pathways when observing the responses of organisms towards dietary components. The interaction between human gene and environmental factors that cause several human diseases was first investigated in USA (Amin *et al.*, 2012). Kaput *et al.* (2005) stated that individual differ from each other in their genetic makeup and thus their response against environmental stimuli varies greatly from one individual to another. Nowadays, advancement in molecular biology techniques provides us the opportunity to study the interaction between diets, metabolic pathway and gene expression. It is now well established that dietary requirement varies from one individual to another and thus random diet can cause different health related problem such as, body weight, blood pressure, blood sugar, etc. (Ordovas *et al.*, 2007). In a detail study Huang *et al.* (2011) stated that "The consumption of nuts, a diet high in carbohydrates and protein, green tea and red wine as well as the supplementation with policosanol

and red yeast rice extract can be considered for improvement of the lipid profile, while the supplements of guggulipid, garlic, chromium, vitamin C, magnesium-pyridoxal-phosphateglutamate, tocotrienols and absorbitol cannot be recommended". Whereas, in an another investigation Hori et al. (2011) demonstrated the correlation between diet and prostate cancer. There are several examples of nutrigenomics such as, lactose intolerance symptom which is characterized by insufficient production of lactase enzyme due to genetic variability in lactase gene (Swallow, 2003). People with lactose intolerance symptom are recommended for lactose free diet for better health. Phenylketonuria is an another classical example of nutrigenomics which is directly related to metabolic pathway disorder. Milner (2006) stated that proper diet can reduce the risk of disease in human. Several research groups are engaged in seeking to understand the relationship between dietary/nutritional factors and the expression of genes, metabolic and physiological changes in the body. This research will give us a better understanding of homeostasis in the body, the control and expression of genes and also the metabolic pathways involved in it. Not only human, nutrigenomics study is also important in different other sectors like poultry farm and pig meat industries. In recent year, the demand of chicken and pork is increasing rapidly. Feed efficiency is an important factor in these industries which can be achieved through nutrigenomics research. Till date this area is not so explore. A greater understanding of these mechanisms will lead us to sustainable fisheries more production and other aquaculture activities.

The nutrients and other components of food serve as the key factor in controlling gene expression and transcription (Sales *et al.*, 2014). It is not an approach to the basic nutrition provided by food but a rather wide area beyond it. It is already proved that pattern of gene expression varies from one individual to other due to single nucleotide polymorphism or SNPs (Dauncey, 2012; Norheim *et al.*, 2012). The types of food and its consumption quantity are thus very important for health and development of the body. Several research on nutrigenomics concluded that food with bioactive compounds are beneficial for health (Cozzolino and Cominetti, 2013). Nutrigenomics studies gives opportunities for fundamentally new approaches to nutritional research that enables global study of gene expression and its effects. In this present review, we have documented the importance of nutrigenomics in animal health and diet related gene expression.

NUTRIGENOMICS AND HUMAN HEALTH

Nutrigenomics has received much attention recently because of its potentiality for preventing, mitigating or treating chronic disease and certain cancers. It is already established that human genomes are identical about 99.9% and there is only 0.01% difference that occurs due to SNPs. Thorisson and Stein (2003) stated that there are about 3.1 million SNPS with high polymorphic nature present in human genome that create variability among individuals. Several studies indicated that different types of macronutrients (protein, carbohydrate), micronutrients (vitamins) and naturally occurring chemicals (flavonoids, coumarins, carotenoids) play potential roles in gene regulations. This SNP database can be used to identify genetic variants within population. Some types of cancer and cardiovascular diseases (CVD) are among the most evident pathologies sensitive to nutritional modulation (Kant, 2004; Sales *et al.*, 2014). Recognition of the dietary risk factors is important which will definitely help to reduce the impact of such factors in population. There are several diseases that are related to nutritional ingredients. Examples of some important cases are given below.

Cardiovascular disease: In recent year, food intake by individual has changed a lot which creates different health problem. Cardiovascular disease (CVD) is a chronic disease that is related to a group of abnormal condition such as obesity, hypertension and thrombosis. Apolipoprotein A-1 which is associated with High Density Lipoprotein (HDL) is produced by liver and intestine. A-1 HDL complex is responsible for cholesterol transport and are reported to be protective factors for CVD (Wilson et al., 1988). Apo A-1 encoding gene APOA1 is polymorphic in nature and has been studied deeply (Juo et al., 1999). Variation in this particular gene highly affects cholesterol transport and thus creates CVD. Sampath and Ntambi (2005) stated that Polyunsaturated Fatty Acids (PUFA) can induce the APOA1 gene. In this regards Dalmiel et al. (2012) stated that alteration in lipid metabolism might be a cause of CVD. Ordovas et al. (2002) conducted a detail study to explore the role of PUFA in cholesterol transport. They detected that individual carrying A allele in APOA1 gene increased the HDL concentration with increase of PUFA intake. Whereas, decreased level of HDL was detected in individual having G allele in APOA1 gene. De Pinho et al. (2014) stated that "The score for cardioprotective food was higher than that for foods that increase the risk of heart diseases, regardless of the presence of metabolic syndrome". So, personalized diet is very important for prevention of CVD.

Obesity: Obesity is the another health problem which is directly related to nutritional value. Researchers have established that not only environmental factors but genetic aspects are also important for many metabolic syndromes (Phillips, 2013). Energy balance in body is very important and this is controlled by several polymorphic genes encoding taste receptors. Loktionov (2003) reported that food intake is affected by several signalling molecules such as leptin, insulin and cholecystokinin and their corresponding receptors. While, Gaboon (2011) stated that several central energy regulators such as CART (cocaine and amphetamineregulated transcript), hypothalamic neuropeptide Y, melanocortin pathway factors etc. are highly polymorphic in nature and their expression varies depending on food stuff. So, formulated diet might be useful in obesity treatment as it can influence and control the gene expression.

Cancer treatment: The recent advancement in molecular biological techniques provides a new insight into a number of health related issue, including cancer. At present different types of treatment and therapies are available to combat with cancer but all these have side effects. As proliferation rate in cancer cell is much higher compared to normal cell, it requires more energy. To fulfill the energy requirement, it has modified its metabolic pathway. Unlike normal cell, cancer cell produce energy through glycolysis followed by lactic acid fermentation. So glucose has significant role in cancer cell. Changes in the expression of glucose responsive gene such as pyruvate kinase type M2 and phosphofructokinase1might be an alternative treatment of cancer (Yi et al., 2012; Luo and Semenza, 2012). Fruit and vegetables are primary sources of vitamins and mineral that have potential role in cancer prevention. Costa and Rosa (2011) Stated that folic acid present in fruit is converted to 5-methyltetrahydrofolate through several chemical process, which is then act as a precursor of methionine that helps in DNA mutilation. Thus, diet poor in folic acid may hamper DNA replication and cause cancer. The 1,25-dihydroxyvitamin D3 is the active form of vitamin D that regulate different body function including cell proliferation through Vitamin D Receptor (VDR) which shows polymorphism. Nicastro et al. (2012) stated that mutation in Fok1 (polymorphic form of VDR) can cause colorectal cancer. Several authors have reported the

importance of PUFA in disease treatment such as angiogenesis related gene expression (VEGF, MMP-2, PDGF) and cell proliferation related gene (PTEN, cyclin, p53, Wnt) that can modulate tumorigenesis (Schmitz and Ecker, 2008; Kang and Liu, 2013). In an investigation, Almendro and Gascon (2012) reported that several minerals have potential role in cancer development. For example, selenium (which stimulate the production of glutathione peroxidase enzyme and reduce the stress), prostacyclins (which protect DNA and lipid from oxidative damage) and zinc (which act on processes for the maintenance of gentic expression and stability) gain special attention. So, individual specific diets are necessary to reduce the health risk.

Hypertension: High blood pressure or hypertension is a serious problem that is associated with obesity and CVD. It is known that dietary sodium chloride is the responsive factor for hypertension. Luft and Weinberger (1997) reported that 15% population are sensitive to dietary salt and the remaining 85% individual has no such effect. Several polymorphic gene has been reported that play critical role in blood pressure regulation such as, angiotensinogen encoding gene (AGT) and aldosteron synthetase (CYP11B2) etc. (Luft, 2002). Dietary control of these genes might be a solution of hypertension.

Application of nutrigenomics in animal sector: In recent year, nutrition research gains a special attention due to its vast application in several branches of science. It is already proved that not only environmental cues but several other factors are associated with animal health. Nutritional genomics is a recent off-shoot of this genetic revolution. Tellez et al. (2014) stated that nutrigenomics is the junction that correlates diet, health and genomics in term of phenotypic effect. In particular, nutrigenomics is a broad field that include different others omics such as proteomics and transcriptomics (Costa and Rosa, 2011). The proper coordination between diet and omics is important key regulator in maintain animal health. Recent research indicated that bioactive material present in diet alone act as a transcriptional factor or interact with transcription factor and regulate the expression of metabolic genes (Sales et al., 2014). Several researchers reported that vitamin D, A and fatty acid can triggers transcription of gene by binding with nuclear receptor (Dauncey, 2012; Ronteltap et al., 2013). Current advancement in molecular biology has introduced several tools to explore the interaction between food and gene. Among these, DNA microarray has proved its potential. In general DNA microarray is a complex technique that measure the expression of genes or mRNAs level at a time. The principle of DNA array is hybridization of 2 standard DNA which is characterized by hydrogen or covalent bonding. The detection of gene expression is done by using several fluorescent probes which are categorized into 2 groups based on the principle of the array: single labeling and multiple labeling (Kato et al., 2005).

Pork industries: Nowadays, the nutrigenomics concept has been extensively used in different food production sectors such as pork industries, goatery farm and broiler chicken farm. The demand of pig meet is increasing rapidly due to huge globalization and increasing population all over the world. In recent year, a significant amount of cereals are consumed by biofuel companies for production of biodiesel and ethanol (Schmidt, 2007) which increase the prize of crops. So, reduction of raw material consumption in animal farm is important to get maximum benefit and this is only possible when we consider the nutrigenomics approach. Researchers are actively involved to increase the feed efficiency using different combination of feed. In a microarray study conducted by Wang *et al.* (2008) demonstrated that diet with glutamine supplement is better for piglets which

modulate expression of genes that are crucial for intestinal metabolism and function. Whereas, Guo et al. (2011) investigated the effect of dietary protein/carbohydrate ratio on fat deposition and gene expression (heart fatty acid-binding protein or H-FABP, peroxisome proliferator activated receptor γ or PPAR γ) in the mussel of pigs. Their result showed that low protein content in diet increase the intramuscular fat by regulation the above mentioned gene which enhances the quality of pig meet. Intestinal microbiota play a critical role in host nutrition and health. Feed efficiency of animal is highly dependent on the composition of these microbiota which is directly related to metabolism. In general, pigs are unable to produce endogenous enzyme for Resistant Search (RS) and thus seek helps from intestinal microbiota which convert it to short chain fatty acid. Haenen et al. (2013) stated that diet with high RS modulate the microbial composition in colon and caecal which stimulate the expression of monocarboxylate transporter 1 (SLC16A1) and glucagon (GCG). Feeding strategy is one of the most important factor that control the quality of meat, safety and nutritional value. In a detail study Park et al. (2012) determined the effect of different dietary fat like beef tallow, soybean oil, olive oil and coconut oil on pig health using DNA microarray and real time PCR. Result of their investigation demonstrated the over expression of insulin pathway related genes such as cAMP-dependent regulatory, protein kinase type II alpha (PRKAR2A) and the catalytic subunit of protein phosphatase 1, beta isoform (PPP1CB) in olive oil treated groups. Later on Kim et al. (2014) also reported the dietary fat related gene expression in growing-finishing pig. Not only fat, dietary proteins are also important for maintaining pig health. Schwerin et al. (2002) conducted a feeding experiment in pig with 2 types of dietary protein: casein and soy protein. They observed that expression of several genes such as organic anion transporter polypeptide 2, calnexin, glutathione-S-transferase and peptide methionine sulfoxide reductase were much more in pigs fed with soy protein than casein protein. In a similar study, Meadus et al. (2014) reported the hepatic gene expression of Cytochrome 8b1 (CYP8B1), aldehyde dehydrogenase 2 (Aldh2) and thiosulfate transferase (TST) in pigs fed with Camelina sativa. Nutrition related gene expression in pig is very important to optimize the feed efficiency (Table 1). Till date there are scanty of report regarding the pig nutrition. Better understanding of this area will help to promote growth, increase production and enhance meat quality.

Table 1: Diet related gene expression in pig

Feed intake	Gene expression	References
Wheat bran based diet	Cationic AA transporters and myosin	Garcia <i>et al.</i> (2015)
Maternal dietary protein	Myostatin gene	Liu <i>et al.</i> (2011)
Diet with high (18%) and low (14%) protein	High protein reduce the expression of acetyl	Zhao <i>et al.</i> (2010)
	CoA carboxylase (ACC), Fatty Acid Synthase	
	(FAS) and sterol regulatory element	
	binding protein 1c. High protein stimulates	
	the expression of lipoprotein lipase (LPL),	
	carmitine palmtoyltransferase-1B (CPT-1B),	
	peroxisome proliferator-activated receptor γ	
	(PPARy) and adipocyte-fatty acid binding proteins	
Diet with high cholesterol	Hepatic gene expression	Cai <i>et al.</i> (2015)
High protein (26%) and low protein	Lower expression of monocarboxylate	Tudela <i>et al.</i> (2015)
(18%) diet with or without	transporter 1 and higher expression of	
fermentable carbohydrate	TNF-a and IL-8 with high protein diet	
Diet with high and low energy content	High energy content diet up-regulated the	Dal Monego <i>et al.</i> (200
	expression of NADH dehydrogenase ubiquinone	
	1 beta 9, pyruvate kinase, enolase 3, muscle	
	creatine kinase and isocitrate dehydrogenase 3	

Poultry industries: Like pig meat, the demand of broiler chicken is also increasing rapidly. Feed optimization in chicken farm is a very crucial job in term of health and production and this is not possible without considering nutrigenomics research. Naji et al. (2014) stated that nutrigenomics play a critical role in broiler production through various aspects such as (a) Correlates nutrition and genetics in breeding programs (2) Epigenetics, 1 of the branch of nutrigenomics helps to improve broiler performance (3) Increase feed efficiency iv. deliver better health and v. increase meat quality. For past few years, several nutritional programs have been conducted to explore the effect of diet on neonatal and early-life periods. Researchers have demonstrated that fasting in post hatch chicken for a period of 24 h has adverse effects which reduce body weight and meat quality in adult broilers (Gonzales et al., 2003; Halevy et al., 2000). However, Everaert et al. (2010) stated that chick growth and development can be accelerated with proper diet supplemented with low protein. Particularly, nutrigenomics research will lead to the implementation of improved precision feeding strategies by the poultry industry. Recently, in a study carried out by Jiang et al. (2014) reported that nicotinic acid plays an important role in lipid metabolism in female chicken of two brioler strain: Arbor Acres (AA) and Beijing-You (BJY). The result of their investigation also correlates the expression pattern of hepatic genes apolipoprotein A-I (ApoA-I) and apolipoprotein B (Apo B) with varying amount of nicotinic acid in feed. Apart from bioactive material in feed, several trace elements and vitamins are also considered to be the determinant factors for health. Li et al. (2009) reported that vitamin E act as a transcriptional regulator of gene involved in lipid oxidation and antioxidant gene expression in broiler chicken which reduce stress and enhance meat quality. Similarly, Kaiser et al. (2012) stated that vitamin E containing diet can enhance the immune protection against bacterial lipopolysaccharide associated infection in chicken. Nutrigenomics data analysis also showed that algae based diet can reduce the stress profile in chicken through nutrigenomics data analysis (Xiao et al., 2011). Like vitamin E, different types of minerals such as zinc can actively regulates the transporter gene in intestine of broiler chicken and the expression pattern is directly related to the amount of zinc in feed. Whereas, selenium was reported to be a key regulator of gender specific gene regulation in chicken (Brennan et al., 2012). Furthermore, Yuan et al. (2011) reported that diet with 80% Mintrex-Zn/Mn reduce the fecal mineral excretion without compromise in the growth performance. Several others research also reported various diet related gene expression in chicken (Table 2). Antibiotics, vaccines and other

Table 2: Diet related gene expression in chicken

Feed intake	Gene expression	References
Diet with immunomodulators like ascorbic acid, 1,3-1,6 β-glucans and corticosterone	Cytokine gene expression (IL-1 β , IL-2,toll-like receptors 4 and 15) in spleen	Kumar et al. (2011)
Comparison between organically grown feed and conventionally grown feed	The 49 genes were found to be differentially regulated in jejunum. Genes related to immune system (chemokine ah221, B-G protein, immunoglobulin heavy chain) were also differentially expressed	De Greeff <i>et al.</i> (2010)
Feed with mannan-oligosaccharides	Expression of 77 protein synthesis gene, including superoxide dismutase 1, lumican, β 2-microglobin, apolipoprotein A-1, fibronectin 1 etc	Xiao <i>et al.</i> (2012)
Poultry feed containing lead	Down regulation of all sugar, peptide and amino acid transporters. Up regulation of stress related genes	Ebrahimi et al. (2015)
Diet supplemented with high and low nutrient (HN and LN)	Different gene expression in two groups: Yellow-Feathered Chicken (WYFC) and White Recessive Rock Chicken (WRRC) The gene expressions of Rheb, TOR, S6K1 and 4E-BP1 in muscle were the highest in the WYFC fed with low nutrient LN diets are optimal for the long-term housing of chickens	Wang <i>et al.</i> (2013)

therapeutic agents are randomly used in poultry farm to combat with disease, which increase the coast. Diet based tool might be an alternative technique to reduce poultry mortality. Till date, it is a new area of research. More investigation should be conducted to explore the nutrition related genetic network in animal. In this regards, nutrigenomics database will be the potential tool.

FUTURE SCOPE OF NUTRIGENOMICS

New tools available in modern research allow nutritionists to screen genetic background through transcriptomics, proteomics and metabolomics and develop dietary strategies targeted nutrition. Actually, nutrinenomics approach can be divided into 3 ways (1) Gene switching, (2) Emphasis gene-protein relation and (3) Influence of food ingredients on gene expression. To evaluate the interaction between diets and genes, DNA microarray techniques and quantitative real-time Polymerase Chain Reaction (PCR) can be applied. Two dimensional gel electrophoresis might be an important tool to explore the effect of individual amino acid on protein composition that leads to safe usage of transgenic fish in our nutrition. The division of biomarker nutrigenomics is a revolutionary new way to view the food and the pharmaceutical capabilities of the food to reverse disease and slow down the process of ageing (Bhatt and Sharma, 2011). In order to get desired health, genes specific nutritional factors should be targeted (Kore et al., 2008). In Japan, about 350 items have been approved as food for specified health use by the Japanese Ministry of Health, Labour and Welfare. Each item has a specific health claim, such as food for hypertension, high cholesterol, diabetes, etc. based on clinical studies. Nutrigenomis is a recent subject and there are scanty of report regarding the nutrition related gene expression. More research should be conducted to explore the genetic polymorphism and nutrition related gene expression for preparation of personalized diet.

CONCLUSION

Nutrigenomics, emerging as a new era of research, promises us better development of functional food and nutraceutical research. Nutrigenomics is widely used for studying different human disease like heart-related disorders, hypertension, obesity, as well as diet-related disorders. Gene-diet relation revealed that the adiponectin gene polymorphism contributes to insulin resistance. Further development in the field of nutrigenomics will definitely show its potentiality in the food market and the growth of individuals. This nutritional research is not only for application in laboratories but for a better development of food for society. Thus, it is essential to take care of public awareness on these matters. In field application, the manufacturers need regulation and guidance to improve safety reliability and health benefits on the products. To overcome diet related diseases and promote health, we can develop Food Based Dietary Guidelines (FBDG). In this post-genetic era, the genes we inherit cannot be altered but we can change their response to their environment through nutrigenomics in order to achieve desired results.

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