Biological Functions of Polyunsaturated Fatty Acids and Their Applications in Animal Production[1] Postprint

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Abstract

Polyunsaturated fatty acids (PUFA) are important nutrients that constitute essential components of cell membrane phospholipids and exhibit extensive biological functions in biological systems. They can regulate lipid metabolism and immunity, possess anti-cancer properties, prevent and treat cardiovascular diseases, promote growth and development, and modulate gene expression. This article elaborates on the sources and biological functions of polyunsaturated fatty acids and briefly discusses their current application status and prospects in animal production.

Full Text

Biological Functions of Polyunsaturated Fatty Acids and Their Application in Animal Production

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Abstract: Polyunsaturated fatty acids (PUFA) are essential nutrients that serve as crucial components of cell membrane phospholipids. They exhibit extensive biological functions in biological systems, including regulation of lipid metabolism and immunity, anti-cancer activity, prevention and treatment of cardiovascular diseases, promotion of growth and development, and modulation of gene expression. This review elaborates on the sources and biological functions of PUFA and discusses their current application status and future prospects in animal production.

Keywords: polyunsaturated fatty acids; biological functions; animal production; application

Polyunsaturated fatty acids (PUFA) are essential fatty acids that the body cannot synthesize de novo. Their biological functions and relationship with human health have become a focal point of international attention and research in recent years. Numerous studies have demonstrated that PUFA play important roles not only in maintaining biological membrane structure and function, enhancing immune function, promoting growth and development, and regulating lipid metabolism and related gene expression, but also in reducing thrombosis, decreasing the incidence of cardiovascular diseases, and combating cancer [1-3].

In recent years, with reduced production costs, the application of PUFA in animal production has garnered increasing attention. Research on PUFA has gradually extended from apparent performance indicators such as growth performance, antioxidant capacity, and immune function to molecular regulatory mechanisms. More underlying factors related to PUFA growth mechanisms have been discovered, such as the regulation of lipid metabolism-related gene expression and anti-cancer mechanisms, providing a theoretical basis for their application in animal production practice. This review summarizes the sources, biological functions, and applications of PUFA in animal production.

1. Sources of PUFA

PUFA are defined as straight-chain fatty acids containing two or more double bonds with carbon chain lengths of 18–22 carbon atoms. They mainly include the n-6 series linoleic acid (LA, C18:2) and arachidonic acid (AA, C20:4), and the n-3 series linolenic acid (LNA, C18:3), eicosapentaenoic acid (EPA, C20:5), and docosahexaenoic acid (DHA, C22:6). LNA can be further divided into α-linolenic acid (ALA, C18:3n-3) and γ-linolenic acid (GLA, C18:3n-6).

LA and LNA are primarily found in vegetable oils. For example, soybean oil and safflower oil contain high levels of LA, perilla seed oil and linseed oil are extremely rich in ALA, and evening primrose oil and comfrey seed oil contain substantial amounts of GLA. Additionally, most marine algae, microorganisms, and lower fungi contain considerable LNA (Table 1). AA is widely distributed in animal tissues, being present in the brain, liver, blood phospholipids, and adrenal glands of many animals, and lower fungi, especially *Mortierella* species, also contain large amounts of AA. EPA and DHA are mainly found in marine organisms such as high-fat fish and seaweed, and are almost undetectable in common terrestrial plant and animal oils [4]. Some fungi, shellfish, and crustaceans also contain substantial DHA.

2.1 Effects on Cell Membrane Function

PUFA play a vital role in the composition of all cell membranes, maintaining the homeostasis of normal membrane protein function and influencing cell membrane fluidity, thereby regulating cell signal transduction processes and gene expression in different cell types [6]. Studies have shown that PUFA can alter cell membrane lipid composition, inhibit the growth of Caco-2 cells, increase membrane fluidity, and exhibit dose-dependent effects [7]. Nair et al. [8] demonstrated that n-3 PUFA can alter membrane phospholipid fatty acid composition, thereby regulating second messenger signal transduction processes in cardiac myocytes. However, because the unsaturated double bonds of PUFA are susceptible to free radical attack and peroxidation, excessive PUFA intake can enhance lipid peroxidation in vivo and reduce cell membrane fluidity. Yehuda et al. [9] found that LA and ALA themselves affect neuronal membrane fluidity indices, reducing cholesterol (TC) content in neuronal membranes, decreasing membrane fluidity, and increasing cellular susceptibility to damage and death, thereby impairing normal cellular function. Additional research indicates that DHA and EPA can affect sperm cell membrane structure, conferring favorable fluidity to the sperm plasma membrane, participating in protein-mediated cellular responses in the membrane, influencing lipid mediator production, cell signal transduction, and gene expression [10].

2.2 Effects on Lipid Metabolism

n-3 PUFA can inhibit the activities of fatty acid synthase (FAS), diacylglycerol acyltransferase (DGAT), and hydroxymethylglutaryl-CoA (HMG-CoA) reductase, promote fatty acid oxidation and decomposition, inhibit triglyceride (TG) synthesis, downregulate hepatic low-density lipoprotein (LDL) receptors, suppress TC synthesis, and reduce TC absorption, thereby decreasing serum TG and TC levels [11-12]. Li et al. [13] reported that dietary supplementation with appropriate amounts of LA can reduce serum TC and LDL levels in meat rabbits. Haug et al. [14] found that dietary fish oil supplementation decreased plasma TG content while reducing hepatic TG and very-low-density lipoprotein (VLDL) synthesis. Furthermore, PUFA can stimulate peroxidases and induce uncoupling proteins (UCP) in mitochondria, enhancing mitochondrial β-oxidation and accelerating blood lipid clearance and decomposition while reducing body fat deposition [15]. Research has shown that dietary fish oil can induce peroxisomal fatty acid oxidation in skeletal muscle and increase UCP-3 content by twofold, thereby reducing fat and protein deposition [16].

2.3 Effects on Gene Expression

Dietary PUFA regulate various gene expressions in the body, thereby influencing anabolic processes in animals. Sterol regulatory element-binding protein-1c (SREBP-1c) is a key nuclear transcription factor that regulates lipid metabolism-related gene expression, primarily participating in the regulation of hepatic fatty

acid and TG biosynthesis and metabolism. PUFA possess the ability to modulate SREBP-1c levels and expression. Studies have confirmed that PUFA can inhibit SREBP-1c gene expression, thereby suppressing the transcription of hepatic lipogenic genes and lipid biosynthesis, with n-3 PUFA demonstrating more pronounced inhibitory effects than n-6 PUFA [17]. Conversely, overexpression of SREBP-1c promotes hepatic lipogenic gene expression but has no significant effect on TC synthesis-related genes [18]. Foretz et al. [19] demonstrated that in isolated hepatocytes, SREBP-1c overexpression is a major factor affecting both fatty acid synthesis gene expression and insulin-induced glucokinase gene expression. FAS is a large molecular protein complex with multiple catalytic functions that catalyzes the synthesis of fatty acids from acetyl-CoA and malonyl-CoA, serving as a key rate-limiting enzyme in hepatic fatty acid synthesis. Its regulatory mechanism for animal lipid metabolism-related gene expression primarily occurs at the transcriptional level, and it is regulated by SREBP-1c. FAS expression is consistent with SREBP-1c levels. Experiments have proven that reduced hepatic SREBP-1c levels lead to decreased expression of hepatic FAS and acetyl-CoA carboxylase-1 (ACC-1), thereby reducing hepatic lipid accumulation [20].

Adipose triglyceride lipase (ATGL) in adipose tissue is an important rate-limiting enzyme that catalyzes the first step of TG hydrolysis, converting TG into glycerol and free fatty acids. Comparative gene identification 58 (CGI-58) is an ATGL activator that enhances ATGL activity, and the N-terminal tryptophan-rich structural domain of CGI-58 is essential for regulating proper CGI-58 localization and ATGL activation function. Therefore, both play important roles in lipid metabolism [21]. Additionally, PUFA increase thermogenesis and reduce body fat deposition while maintaining glucose metabolic balance by upregulating mitochondrial UCP-3 transcription, inducing genes encoding proteins involved in fatty acid oxidation, and downregulating the transcription of genes encoding other proteins, as shown in Figure 1 [Figure 1: see original paper] [22-23].

2.4 Effects on Immune Function

The immunomodulatory functions of PUFA have been demonstrated in both human medicine and animal studies. Dietary PUFA supplementation can regulate lymphocyte proliferation, receptor and molecule expression on cell membranes, antigen presentation, and natural killer cell activity, thereby influencing cellular immune responses. Singer et al. [24] demonstrated that n-3 PUFA reduce interleukin-1 (IL-1) and interleukin-2 (IL-2) secretion in mouse lymphocytes, increase tumor necrosis factor-α (TNF-α) production in macrophages, and decrease natural killer (NK) cell activity. In contrast, n-6 PUFA increase IL-2 production while reducing TNF-α production and NK cell activity in mice, consistent with the findings of Chavali et al. [25]. These results demonstrate that n-3 PUFA possess immune-enhancing properties, whereas n-6 PUFA have opposite effects. Merzouk et al. [26] reported that both EPA and DHA reduced

concanavalin A (Con-A)-stimulated lymphocyte IL-2 secretion while enhancing IL-4 production, thereby inhibiting T lymphocyte proliferation and reducing immunity. Furthermore, n-3 PUFA can modulate cytokine secretion by altering signal transduction or cytokine gene expression and protein translation processes, thereby affecting immune function. Fritsche et al. [27] found that mice infected with live *Listeria* or sterile phosphate-buffered saline (PBS) and fed an n-3 PUFA diet showed significantly decreased mRNA expression of IL-2, interleukin-12 (IL-12), interleukin-1β (IL-1β), and interferon-γ (IFN-γ) in spleen tissue. Since IL-12 and IFN-γ play major roles in innate and adaptive host defense, these findings indicate that n-3 PUFA can effectively protect against infectious diseases.

2.5 Effects on Cancer

With improving living standards, food safety has become an increasing concern. EPA and DHA, as important components of PUFA, exhibit anti-cancer, anti-atherosclerotic, lipid-lowering, and cardiovascular-protective effects, with their cancer-inhibiting properties receiving particular attention. The primary mechanisms involve inhibiting the biosynthesis of arachidonic acid-derived eicosanoids, affecting transcription factor activity, gene expression, and signal transduction processes, altering estrogen metabolism, regulating free radical and reactive oxygen species production, and influencing insulin sensitivity and cell membrane fluidity [28]. Colas et al. [29] found through in vitro experiments that dietary DHA supplementation reduced tumor angiogenesis prior to enhanced responsiveness to anthracyclines, suggesting that DHA chemosensitivity is manifested through inhibition of tumor vascular responses in mammary tumor hosts. Bougnoux et al. [30] reported that DHA supplementation during anthracycline chemotherapy significantly increased survival rates in metastatic breast cancer patients without any detectable toxic side effects. Additionally, studies have shown that oral administration of EPA to rats with methylcholanthrene (MCA)-induced sarcoma reduced tumor volume, with further research revealing significantly decreased vascular endothelial growth factor (VEGF) mRNA expression levels in liver tissue, indicating that EPA exerts anti-tumor effects by inhibiting VEGF expression [31].

2.6 Effects on Cardiovascular Disease

PUFA can protect animals against atherosclerosis, reduce blood TG levels, inhibit platelet aggregation, and prevent thrombosis, thereby decreasing the incidence of cardiovascular diseases [32]. Renaud et al. [33] conducted a dietary intervention study in French farmers, replacing butter with rapeseed oil and ALA-enriched margarine, which resulted in significantly increased EPA content in plasma lipids and platelet phospholipids and significantly reduced platelet aggregation after two years. PUFA also exert clear effects on arterial thrombosis formation and platelet function. PUFA released from platelet membrane phospholipids can be converted by cyclooxygenase into thromboxane A (TXA),

which promotes platelet aggregation and vasoconstriction. In contrast, PUFA released from vascular wall membrane phospholipids can be enzymatically converted into prostacyclin (PGI), which inhibits platelet aggregation and induces vasodilation. The balance between these two substances regulates platelet and vascular function. Therefore, PUFA have therapeutic and preventive effects on cardiovascular diseases.

2.7 Effects on Growth and Development

PUFA can promote fetal and infant growth and development. The brain represents a major proportion of body size and weight in fetuses and infants, and AA and DHA, as the predominant fatty acids in the brain, are crucial for fetal development and infant growth. Their deficiency can lead to slow growth and development of fetal brain cells and even cause incomplete development of the fetal central nervous system, affecting metabolism. Obesity is a significant factor affecting human health in modern society, with its incidence having doubled over the past two decades and this trend continuing to rise. PUFA are closely associated with obesity development, and since obesity is related to both dietary fat quantity and fatty acid composition, altering dietary fatty acid profiles can help mitigate obesity development. Animal studies have found that n-3 PUFA can alter body composition and reduce body fat accumulation, thereby maintaining weight balance [34]. Additionally, supplemental n-3 PUFA during pregnancy and lactation can increase fetal birth weight, promote growth and development, reduce the risk of preterm delivery and other complications during pregnancy [35].

3.1 Application in Poultry Production

As an important nutrient, PUFA can improve feed conversion efficiency, promote protein synthesis, reduce fat deposition, decrease feed-to-weight ratio, increase PUFA content in poultry muscle, alleviate lipid peroxidation, improve meat quality, and thereby enhance animal growth performance. Sanz et al. [36] added tallow and sunflower oil to broiler diets, finding that compared with the tallow group, the sunflower oil group showed significantly reduced abdominal fat deposition and lower hepatic FAS activity, indicating decreased hepatic fat synthesis. López-Ferrer et al. [37] found that adding high levels of fish oil to broiler diets increased PUFA content in chicken thigh meat, particularly long-chain n-3 PUFA, while reducing saturated fatty acid (SFA) and monounsaturated fatty acid content, with only slight changes in total n-6 PUFA content, consistent with the findings of Hrdinka et al. [38]. Ding et al. [39] reported that dietary n-6/n-3 PUFA ratios of 3:1 and 6:1 significantly reduced hepatic malondialdehyde (MDA) and nitric oxide (NO) contents in growing Yangzhou geese, decreased damage to hepatocyte membrane structures, and improved antioxidant capacity. PUFA also participate in lymphokine and antibody secretion and the generation of new immune cells, and their deficiency may affect the normal development of immune organs, making them crucial for poultry immune function. Hughes

et al. [40] demonstrated that because n-3 PUFA inhibit the mitogenic response of T cells and spleen cells, excessive dietary n-3 PUFA can reduce immunity. Friedman et al. [41] showed that adding PUFA from different sources to broiler diets revealed a quadratic relationship between dietary PUFA levels and antibody quantity in broiler chicks on days 11–14, indicating that appropriate PUFA supplementation can enhance immunity, while excessive or insufficient amounts can suppress immune responses.

3.2 Application in Swine Production

Dietary PUFA can be directly incorporated into body fat without hydrogenation after digestion and absorption. Therefore, adding PUFA to pig diets can increase PUFA content in pork tissues, which reduces the oxidative stability of lipids and myoglobin, making muscle fat more susceptible to oxidative rancidity and off-flavor development during storage and processing, thereby decreasing meat quality and economic benefits. For pregnant sows, dietary PUFA can not only affect the fatty acid composition in the sow' s body but also influence the fatty acid composition of colostrum and milk, which subsequently affects the fatty acid composition of offspring tissues, providing piglets with abundant available fatty acids, increasing energy supply to piglets, improving piglet survival and growth rates, and enhancing sow reproductive performance. Missotten et al. [42] reported that dietary n-3 PUFA enrichment not only directly affects fatty acid composition in pig organs and tissues but also indirectly influences meat fatty acid composition by affecting fatty acid synthesis enzyme expression. Tilton et al. [43] found that compared with the control group, adding 10% tallow to lactating sow diets reduced C10:0, C14:0, C16:0, C16:1, and LNA contents in sow milk while increasing C18:0 and C18:1 contents, thereby increasing sow carcass weight and piglet weaning weight. Ci et al. [44] reported that feeding sows diets containing 8% corn oil from 7 days before farrowing to weaning significantly increased ALA content in colostrum while reducing C20:3n-6 and EPA contents, with no significant differences in other fatty acid types. In contrast, LA and C20:2n-6 contents in longissimus thoracis (LT) muscle were significantly elevated, while C16:1n-7, C17:1n-7, C20:3n-6, AA, and DHA contents were reduced. Compared with the control group, total PUFA and n-6 PUFA contents and n-6/n-3 PUFA ratios in colostrum and LT muscle were significantly increased, while n-3 PUFA content was significantly decreased. Additionally, PUFA can improve sow immunity and enhance piglet immunity by increasing milk immunoglobulin content, thereby improving piglet survival and birth weight and effectively reducing pre-weaning mortality. Bontempo et al. [45] reported that adding conjugated linoleic acid (CLA) to sow diets during gestation and lactation increased immunoglobulin G (IgG) content in sow serum and colostrum, enhancing immunity in both sows and piglets.

3.3 Application in Ruminant Production

Increasing research has found that applying PUFA in ruminant production can not only improve lactation performance by regulating milk fatty acid composition but also enhance meat tissue fatty acid composition and meat quality, thereby increasing the nutritional value of ruminant products. Zhong et al. [46] demonstrated that adding whole cottonseed to dairy cow diets significantly increased long-chain PUFA content in milk, optimized milk fat composition, improved milk quality, and increased milk yield and fat percentage. Collins et al. [47] found that adding flaxseed oil to lamb diets significantly reduced n-6/n-3 PUFA ratios in muscle and subcutaneous fat while significantly increasing PUFA/SFA ratios. Additionally, research has shown that adding flaxseed to beef cattle diets can increase PUFA, particularly ALA, content in muscle and tissues while reducing n-6/n-3 PUFA ratios [48]. Moreover, due to the biohydrogenation of PUFA and the toxic effects of free fatty acids on methanogens and protozoa, adding PUFA to ruminant diets can effectively reduce methane emissions in the rumen. Studies have shown that adding LA and LNA separately or in combination can significantly reduce methane production, with effects becoming more pronounced as LNA content increases [49].

3.4 Application in Aquaculture

PUFA are essential fatty acids for fish and crustaceans and can be converted into long-chain highly unsaturated fatty acids through desaturation and carbon chain elongation, playing important roles in their growth, development, and reproduction. Levine et al. [50] reported that PUFA are particularly important for the early development of brachyuran crabs, with DHA and EPA significantly improving larval survival and growth rates. Chandge and Paulraj [51] found that adding LA or LNA to feed improved the growth rate, feed conversion ratio, protein efficiency, and protein utilization of Indian white prawns (*Penaeus indicus*), with the 2% LNA group showing significantly higher growth rates than the 1% LNA group. Additional research has shown that n-3 PUFA can regulate fish immunity and disease resistance by altering the expression levels of immune-related genes [52]. These findings demonstrate that dietary PUFA supplementation can promote aquatic animal growth, improve protein utilization, enhance reproductive performance, and strengthen immunity.

PUFA exhibit high application value in enhancing animal immunity, improving antioxidant capacity, regulating lipid metabolism, combating cancer, and preventing cardiovascular diseases. In livestock production, research on the molecular biological mechanisms by which PUFA regulate animal fat deposition can help us more rationally regulate animal nutrition, improve animal product quality, and obtain greater economic benefits. However, the mechanisms underlying many physiological functions of PUFA remain incompletely understood, and further investigation is needed regarding their optimal dietary supplementation levels, as well as potential differences in feeding effects among different breeds, sexes, and physiological developmental stages.

References

[1] PATTERSON E, WALL R, FITZGERALD G F, et al. Health implications of high dietary Omega-6 polyunsaturated fatty acids[J]. Journal of Nutrition and Metabolism, 2012, 2012: 539426.

[2] PETRIK M B H, MCENTEE M F, JOHNSON B T, et al. Highly unsaturated (n-3) fatty acids, but not α-linolenic, conjugated linoleic or γ-linolenic acids, reduce tumorigenesis in Apc(Min/+) mice[J]. The Journal of Nutrition, 2000, 130(10): 2434–2443.

[3] HABERMANN N, SCHÖN A, LUND E K, et al. Fish fatty acids alter markers of apoptosis in colorectal adenoma and adenocarcinoma cell lines but fish consumption has no impact on apoptosis-induction ex vivo[J]. Apoptosis, 2010, 15(5): 621–630.

[4] GARG M L, LEITCH J, BLAKE R J, et al. Long-chain n-3 polyunsaturated fatty acid incorporation human atrium following supplementation[J]. Lipids, 2006, 41(12): 1127–1132.

[5] ZHOU Tongyong, REN Fei, DENG Li, et al. Research progress on γ-linolenic acid and its physiological and biochemical functions[J]. Guizhou Agricultural Sciences, 2011, 39(3): 53–58.

[6] DAS U N, Jr. Essential fatty acids: biochemistry, physiology and pathology[J]. Biotechnology Journal, 2006, 1(4): 420–439.

[7] NANO J L, NOBILI C, GIRARD-PIPAU F, et al. Effects of fatty acids on the growth of Caco-2 cells[J]. Prostaglandins, Leukotrienes and Essential Fatty Acids, 2003, 69(4): 207–215.

[8] NAIR S S D, LEITCH J, GARG M L, et al. N-3 polyunsaturated fatty acid supplementation alters inositol phosphate metabolism and protein kinase C activity in adult porcine cardiac myocytes[J]. The Journal of Nutritional Biochemistry, 2001, 12(1): 7–13.

[9] YEHUDA S, RABINOVITZ S, CARASSO R L, et al. The role of polyunsaturated fatty acids in restoring the aging neuronal membrane[J]. Neurobiology of Aging, 2002, 23(5): 843–853.

[10] CALDER P C, YAQOOB P. Understanding omega-3 polyunsaturated fatty acids[J]. Postgraduate Medicine, 2009, 121(6): 148–157.

[11] NESTEL P J. Fish oil and cardiovascular disease: lipids and arterial function[J]. American Journal of Clinical Nutrition, 2000, 71(1): 228S-231S.

[12] BROUGHTON K S, MORGAN L J. Frequency of (n-3) polyunsaturated fatty acid consumption induces alterations in tissue lipid composition and eicosanoid synthesis in CD-1 mice[J]. The Journal of Nutrition, 1994, 124(7): 1104–1111.

[13] LI Ronggang, MA Mingwen, WANG Chunyang, et al. Effects of dietary linoleic acid supplementation on growth performance, immune indices and lipid metabolism in meat rabbits from weaning to 2 months of age[J]. Chinese Journal of Veterinary Science, 2011, 31(11): 1676–1680.

[14] HAUG A, HØSTMARK A T. Lipoprotein lipases, lipoproteins and tissue lipids in rats fed fish oil or coconut oil[J]. The Journal of Nutrition, 1987, 117(6): 1011–1017.

[15] TAKADA R, SAITOH M, MORI T, et al. Dietary gamma-linolenic acid-enriched oil reduces body fat content and induces liver enzyme activities relating to fatty acid beta-oxidation in rats[J]. The Journal of Nutrition, 1994, 124(4): 469–474.

[16] BAILLIE R A, TAKADA R, NAKAMURA M, et al. Coordinate induction of peroxisomal acyl-CoA oxidase and UCP-3 by dietary fish oil: a mechanism for decreased body fat deposition[J]. Prostaglandins, Leukotrienes and Essential Fatty Acids, 1999, 60(5/6): 351–356.

[17] TERAN-GARCIA M, ADAMSON A W, YU G, et al. Polyunsaturated fatty acid suppression of fatty acid synthase (FASN): evidence for dietary modulation of NF-Y binding to the Fasn promoter by SREBP-1c[J]. Biochemical Journal, 2007, 402(3): 591–600.

[18] SHIMANO H, HORTON J D, SHIMOMURA I, et al. Isoform 1c of sterol regulatory element binding protein is less active than isoform 1a in livers of transgenic mice and in cultured cells[J]. The Journal of Clinical Investigation, 1997, 99(5): 846–854.

[19] FORETZ M, GUICHARD C, FERRE P, et al. Sterol regulatory element binding protein-1c is a major mediator of insulin action on the hepatic expression of glucokinase and lipogenesis-related genes[J]. Proceedings of the National Academy of Sciences of the United States of America, 1999, 96(22): 12737–12742.

[20] HOWELL G, DENG X, YELLATURU C, et al. N-3 polyunsaturated fatty acids suppress insulin-induced SREBP-1c transcription reduced trans-activating capacity LXRα[J]. Biochimica et Biophysica Acta: Molecular and Cell Biology Lipids, 2009, 1791(12): 1190–1196.

[21] GRUBER A, CORNACIU I, LASS A, et al. The N-terminal region of comparative gene identification-58 (CGI-58) is important for lipid droplet binding and activation of adipose triglyceride lipase[J]. Journal of Biological Chemistry, 2010, 285(16): 12289–12298.

[22] CLARKE S D. Polyunsaturated fatty acid regulation of gene transcription: a mechanism to improve energy balance and insulin resistance[J]. British Journal of Nutrition, 2000, 83 Suppl 1: S59–S66.

[23] MASCARÓ C, ACOSTA E, ORTIZ J A, et al. Control of human muscle-type carnitine palmitoyltransferase I gene transcription by peroxisome

proliferator-activated receptor[J]. Journal of Biological Chemistry, 1998, 273(15): 8560-8563.

[24] SINGER P, RICHTER-HEINRICH E. Stress and fatty liver-possible indications for dietary long-chain n-3 fatty acids[J]. Medical Hypotheses, 1991, 36(1): 90-94.

[25] CHAVALI S R, FORSE R A. Decreased production of interleukin-6 and prostaglandin E2 associated with inhibition of delta-5 desaturation of ω-6 fatty acids in mice fed safflower oil diets supplemented sesamol[J]. Prostaglandins, Leukotrienes and Essential Fatty Acids, 1999, 61(6): 347-352.

[26] MERZOUK S A, SAKER M, REGUIG K B, et al. N-3 polyunsaturated fatty acids modulate in-vitro T cell function in type I diabetic patients[J]. Lipids, 2008, 43(6): 485-497.

[27] FRITSCHE K L, ANDERSON M, FENG C, et al. Consumption of eicosapentaenoic acid and docosahexaenoic acid impair murine interleukin-12 and interferon-γ production in vivo[J]. The Journal of Infectious Diseases, 2000, 182(Suppl.1): S54-S61.

[28] Larsson S C, Kumlin M, Ingelman-Sundberg M, et al. Dietary long-chain n-3 fatty acids for the prevention of cancer: a review of potential mechanisms[J]. American Journal of Clinical Nutrition, 2004, 79(6): 935-945.

[29] COLAS S, MAHÉO K, DENIS F, et al. Sensitization by dietary docosahexaenoic acid of rat mammary carcinoma to anthracycline: a role for tumor vascularization[J]. Clinical Cancer Research, 2006, 12(19): 5879-5886.

[30] BOUGNOUX P, HAJJAJI N, MAHEO K, et al. Fatty acids and breast cancer: sensitization to treatments prevention metastatic re-growth[J]. Progress Lipid Research, 2010, 49(1): 76-86.

[31] JHO D, BABCOCK T A, HELTON W S, et al. Omega-3 fatty acids: implications for the treatment of tumor-associated inflammation[J]. The American surgeon, 2003, 69(1): 32-36.

[32] FERNANDEZ M L, WEST K L. Mechanisms by which dietary fatty acids modulate plasma lipids[J]. Journal of Nutrition, 2005, 135(9): 2075-2078.

[33] RENAUD S, NORDOY A. "Small is beautiful" : alpha-linolenic acid and eicosapentaenoic acid in man[J]. The Lancet, 1983, 1(8334): 1169.

[34] RUZICKOVA J, ROSSMEISL M, PRAZAK T, et al. Omega-3 PUFA of marine origin limit diet-induced obesity reducing cellularity adipose tissue[J]. Lipids, 2004, 39(12): 1177-1185.

[35] DROUILLET P, KAMINSKI M, DE LAUZON-GUILLAIN B, et al. Association between maternal seafood consumption before pregnancy and fetal growth: evidence for an association in overweight women. The EDEN mother-child cohort[J]. Paediatric and Perinatal Epidemiology, 2009, 23(1): 76-86.

[36] SANZ M, LOPEZ-BOTE C J, MENOYO D, et al. Abdominal fat deposition and fatty acid synthesis are lower and β-oxidation is higher in broiler chickens fed diets containing unsaturated rather than saturated fat[J]. The Journal of Nutrition, 2000, 130(12): 3034–3037.

[37] LÓPEZ-FERRER S, BAUCELLS M D, BARROETA A C, et al. n-3 enrichment of chicken meat. 1. Use of very long-chain fatty acids in chicken diets and their influence on meat quality: fish oil[J]. Poultry Science, 2001, 80(6): 741–752.

[38] HRDINKA C, ZOLLITSCH W, KNAUS W, et al. Effects of dietary fatty acid pattern on melting point and composition of adipose tissues and intramuscular fat of broiler carcasses[J]. Poultry Science, 1996, 75(2): 208–215.

[39] DING Luoyang, CAI Miaoying, WANG Mengzhi, et al. Effects of dietary ω-6/ω-3 polyunsaturated fatty acid ratio on liver lipid peroxidation and hepatocyte ultrastructure in geese[J]. Chinese Journal of Animal Nutrition, 2012, 24(10): 1976–1982.

[40] HUGHES D A, PINDER A C. n-3 polyunsaturated fatty acids inhibit the antigen-presenting function of human monocytes[J]. American Journal of Clinical Nutrition, 2000, 71(1): 357S-360S.

[41] FRIEDMAN A, SKLAN D. Effect of dietary fatty acids on antibody production and fatty acid composition of lymphoid organs in broiler chicks[J]. Poultry Science, 1995, 74(9): 1463–1469.

[42] MISSOTTEN J, DE SMET S, RAES K, et al. Effect of supplementation of the maternal diet with fish oil or linseed oil on fatty-acid composition and expression of Δ5- and Δ6-desaturase in tissues of female piglets[J]. Animal, 2009, 3(8): 1196–1204.

[43] TILTON S L, MILLER P S, LEWIS A J, et al. Addition of fat to the diets of lactating sows: I. Effects on milk production and composition and carcass composition of the litter at weaning[J]. Journal of Animal Science, 1999, 77(9): 2491–2500.

[44] CI L, SUN H L, HUANG Y P, et al. Maternal dietary fat affects the LT muscle fatty acid composition progeny at weaning finishing stages pigs[J]. Meat Science, 2014, 96(3): 1141–1146.

[45] BONTEMPO V, SCIANNIMANICO D, PASTORELLI G, et al. Dietary conjugated linoleic acid positively affects immunologic variables in lactating sows and piglets[J]. The Journal of Nutrition, 2004, 134(4): 817–824.

[46] ZHONG Rongzhen, GAO Yanxia, LI Qiufeng, et al. Effects of dietary whole cottonseed proportion on lactation performance and milk fatty acid composition in dairy cows[J]. Chinese Journal of Animal Nutrition, 2012, 24(4): 762–768.

[47] COLLINS C L, DAVIS J J, SINCLAIR A J, et al. Dietary flaxseed improves the fatty acid composition of lamb tissues[J]. Asia Pacific Journal of Clinical

Nutrition, 2004, 13(Suppl.1): S52.

[48] SCOLLAN N D, DHANOA M S, CHOI N J, et al. Biohydrogenation and digestion of long chain fatty acids in steers fed on different sources of lipid[J]. Journal of Agricultural Science, 2001, 136(5): 345–355.

[49] ZHANG Chunmei, YI Xianwu, YUAN Zhipeng, et al. Effects of adding different ratios of linoleic acid and linolenic acid on in vitro rumen fermentation and methane production[J]. Chinese Journal of Animal Nutrition, 2008, 20(2): 223–227.

[50] LEVINE D M, SULKIN S D. Nutritional significance of long-chain polyunsaturated fatty acids to the zoeal development of the brachyuran crab, *Eurypanopeus depressus* (Smith)[J]. Journal of Experimental Marine Biology and Ecology, 1984, 81(3): 211–223.

[51] CHANDGE M S, PAULRAJ R. Requirements of linoleic and linolenic acid in the diet of Indian white prawn *Penaeus indicus* (H Milne Edwards)[J]. Indian Journal of Geo-Marine Sciences, 1996, 27(3): 402–406.

[52] ZUO R T, AI Q H, MAI K S, et al. Effects of dietary n-3 highly unsaturated fatty acids on growth, nonspecific immunity, expression of some immune related genes and disease resistance of large yellow croaker (*Larmichthys crocea*) following natural infestation of parasites (*Cryptocaryon irritans*)[J]. Fish & Shellfish Immunology, 2012, 32(2): 249–258.

Note: Figure translations are in progress. See original paper for figures.