Imprinting of Candidate Genes Related to Intramuscular Fat Deposition in Animals

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Abstract

Intramuscular fat (IMF) content is an important factor for evaluating meat quality, playing a significant role in meat sensory qualities such as flavor, tenderness, and texture. IMF deposition is primarily regulated by three metabolic pathways: fat uptake, synthesis, and degradation. This article reviews relevant candidate genes affecting IMF deposition, preliminarily revealing the mechanisms influencing fat metabolism, aiming to provide a theoretical basis for future research on regulating IMF deposition.

Full Text

Candidate Genes Associated with Animal Intramuscular Fat Deposition

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Abstract

Intramuscular fat (IMF) content is a crucial factor in meat quality evaluation, significantly influencing sensory attributes such as flavor, tenderness, and marbling. IMF deposition is primarily regulated by three metabolic pathways: fatty acid uptake, synthesis, and degradation. This review synthesizes current research on candidate genes affecting IMF deposition and elucidates their roles in lipid metabolism, providing a theoretical foundation for future studies aimed at modulating IMF accumulation.

Keywords: intramuscular fat; lipid metabolism; candidate gene

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Intramuscular fat (IMF) content and its fatty acid composition play vital roles in meat quality, affecting both sensory characteristics (flavor, juiciness, and tenderness) and nutritional value [1]. The beneficial effects of IMF on meat quality have been demonstrated in pork [2], lamb [3], and beef [4], with visible fat marbling serving as a quality standard in many developed Asian and North American markets. IMF content depends not only on the number of precursor adipocytes that differentiate into mature IMF cells but also on lipid droplet accumulation within both IMF and muscle cells [1]. This deposition occurs when lipogenic metabolism exceeds lipolytic activity, and IMF accumulation capacity is regulated by three key processes: fatty acid transport, lipogenesis, and lipolysis. IMF formation is governed by spatiotemporally specific gene expression patterns, with environmental and nutritional factors primarily exerting their effects through modulation of these genes. Candidate genes involved in IMF deposition include those regulating fatty acid uptake, fatty acid synthesis, and lipid degradation. Research indicates that fatty acid transport is mainly mediated by fatty acid-binding proteins (FABPs) and fatty acid translocase (FAT/CD36), while lipogenesis is controlled by genes such as glucose-6-phosphate dehydrogenase (G6PDH), diacylglycerol acyltransferase 1 (DGAT1), fatty acid synthase (FAS), acetyl-CoA carboxylase (ACC), and stearoyl-CoA desaturase (SCD). Lipolysis-related genes primarily include hormone-sensitive lipase (HSL) and lipoprotein lipase (LPL). This review summarizes relevant domestic and international studies to provide a comprehensive overview of these candidate genes.

1. Candidate Genes in the Fatty Acid Uptake Process

IMF primarily resides in muscle membranes, including the perimysium, epimysium, and endomysium, and is mainly composed of triglycerides and phospholipids [5]. Consequently, regulating fatty acid entry into IMF cells is essential for providing substrates for IMF synthesis. Current research demonstrates that two candidate genes—FABP and CD36—play crucial roles in fatty acid uptake.

1.1 FABP

As members of the lipid-binding protein superfamily, FABPs exhibit tissue-specific expression. To date, nine distinct FABP types have been identified, all of which primarily regulate fatty acid uptake and intracellular transport [6]. Numerous studies indicate that FABP genes influence not only IMF deposition but also fatty acid composition. He et al. [7] first cloned and sequenced the duck liver-type fatty acid-binding protein (L-FABP) gene, then examined DNA polymorphisms in the exon region of L-FABP in 231 ducks to identify potential genetic markers for IMF. Their findings revealed that L-FABP promotes IMF deposition and increases C16:0 and C18:3 fatty acids in duck breast muscle. Kurian et al. [8] reported that L-FABP exhibits the highest affinity for palmitate, oleate, and arachidonate, suggesting that L-FABP proteins on the cell membrane most strongly bind C16:0 and C18:3 fatty acids to facilitate their intracellular transport. Lee [9] investigated the relationship between heart-type fatty acid-binding protein (H-FABP) gene polymorphisms and IMF content and fatty acid composition in Berkshire pigs, finding that HH and aa genotypes significantly increased IMF content. Cho et al. [10] suggested that H-FABP polymorphisms could serve as genetic markers for IMF content and backfat thickness in breeding programs, noting that while HH and Hh genotypes were associated with higher saturated fatty acid content, no H-FABP restriction fragment length polymorphism genotypes altered the n-6 to n-3 polyunsaturated fatty acid ratio. Research has confirmed that FABP promotes saturated fatty acid accumulation primarily because its binding affinity varies by fatty acid type, with greater affinity for saturated than polyunsaturated fatty acids [8]. Recent studies also link FABP genes to IMF deposition in ruminants. Hocquette et al. [11] demonstrated that adipocyte-type fatty acid-binding protein (A-FABP) gene expression serves as a reliable indicator of IMF deposition capacity in young Charolais bulls. Guo et al. [12] identified CIDEA, thyroid hormone-responsive gene (THRSP), acyl-CoA synthetase 1 (ACSM1), diacylglycerol acyltransferase 2 (DGAT2), and H-FABP as top-ranking candidate genes associated with IMF deposition in sheep.

Collectively, these findings indicate that FABP gene research has encompassed various animal species, and the positive role of FABP in IMF formation likely stems from its function as a fatty acid transporter that facilitates plasma fatty acid transport across membranes to triglyceride or phospholipid synthesis sites.

1.2 CD36

CD36 is a transmembrane glycoprotein that interacts with multiple ligands, including oxidized low-density lipoproteins and long-chain fatty acids, and is closely associated with lipid metabolism. However, research on CD36' s impact on IMF deposition remains limited, focusing primarily on cattle, with expression levels varying across different ages. Yang et al. [13] found that AMP-activated protein kinase (AMPK) regulates IMF synthesis by modulating CD36 distribution, whereby 5-aminoimidazole-4-carboxamide ribonucleotide (AICAR) activates AMPK, increases CD36 translocation to the plasma membrane, and consequently reduces cell surface CD36 expression, ultimately decreasing IMF content. Jeong et al. [14] reported a strong positive correlation between IMF content in the longissimus dorsi muscle of steers and CD36 gene expression. Conversely, Dalrymple et al. [15] observed minimal changes in CD36 expression in IMF from 3 to 30 months of age in Piedmontese × Hereford and Wagyu × Hereford crossbred cattle, though expression doubled between 25 and 30 months. The authors speculated that these discrepancies likely arise from breed differences or distinct crossbreeding combinations.

2. Candidate Genes in the Fat Synthesis Process

IMF synthesis involves fatty acid chain synthesis, elongation, and desaturation, as well as triglyceride formation. Key regulatory enzymes include G6PDH, which promotes NADPH generation, along with ACC, FAS, DGAT1, and SCD.

2.1 G6PDH

G6PDH catalyzes the dehydrogenation of glucose-6-phosphate to 6-phosphogluconate, a reaction that facilitates NADPH production for reductive biosynthesis of fatty acids and other lipids. Bonnet et al. [16] suggested that G6PDH activity is closely associated with IMF tissue deposition and marbling in beef cattle. Some studies report that IMF deposition occurs through modulation of G6PDH activity. Yang et al. [17] found that dietary nicotinic acid supplementation increased IMF deposition in steer longissimus dorsi, potentially by enhancing activity of NADPH-producing enzymes such as G6PDH and isocitrate dehydrogenase (ICDH) for de novo fatty acid synthesis. However, Zhao et al. [18] reported that daidzein increased IMF deposition in crossbred steers without altering G6PDH activity, and Choi et al. [19] reached similar conclusions. The relationship between G6PDH activity and IMF deposition remains controversial and requires further investigation.

2.2 ACC and FAS

ACC catalyzes the conversion of acetyl-CoA to malonyl-CoA and exists in two isoforms: ACCα, found predominantly in adipose tissue, and ACCβ, expressed in heart and muscle [20]. FAS is a key enzyme in endogenous fatty acid synthesis, primarily distributed in tissues with high lipid metabolism and hormone sensitivity, where it catalyzes the synthesis of long-chain fatty acids from acetyl-CoA and malonyl-CoA. De Jager et al. [21] found positive correlations between ACC and FAS gene expression and IMF content in steers, while Ward et al. [22] observed similar positive correlations between IMF content and expression of enzymes catalyzing saturated fatty acid synthesis (ACCα and FAS) in Angus cattle. These studies establish correlations between genes and IMF content, though future research should compare various candidate genes to identify major effect genes influencing IMF content. Additionally, FAS expression varies across muscle sites. Cui et al. [23] reported that FAS gene expression in muscle tissue of Beijing-You and Arbor Acres broiler chickens was highly positively correlated with liver fat content but not significantly associated with IMF content in breast or thigh muscle, suggesting that in poultry, FAS primarily influences liver fat deposition rather than IMF in breast and leg muscles.

2.3 DGAT1

DGAT1 is the rate-limiting enzyme catalyzing the synthesis of triglycerides from diacylglycerol and plays a crucial role in storing triglycerides within adipocytes. Recent research has extensively investigated how different DGAT1 genotypes affect IMF content. Anton et al. [24] found that Angus bulls with the DGAT1 AA/AA genotype exhibited higher IMF content compared to other genotypes in Hungary. Wu et al. [25] reported that DGAT1-(10433 and 10434) GC/GC, SCD1-878 CC, and SCD1-762 TT genotypes were primarily responsible for higher IMF content in beef cattle and could serve as genetic markers for IMF traits. They also speculated that homozygous cattle with the DGAT1-GC/GC genotype possess greater IMF content, though this hypothesis requires validation in additional homozygous animals. Li et al. [26] demonstrated that overexpression of porcine DGAT1 in skeletal muscle increased intramuscular triglyceride content and the percentage of lipid droplet surface area coverage, concluding that upregulating DGAT1 expression in skeletal muscle can enhance IMF content. This gene may prove valuable for developing transgenic pigs with higher IMF content and superior meat quality.

2.4 SCD

SCD is a transmembrane protein localized in the endoplasmic reticulum that catalyzes the formation of n-9 monounsaturated fatty acids by desaturating saturated fatty acids at the ninth carbon position. SCD gene research has focused primarily on ruminants. Avilés et al. [27] found that the SCD3-231 AA genotype in Spanish goats was associated with higher C16:1 fatty acid content in IMF, and similar correlations between SCD single nucleotide polymorphisms (SNPs) and C16:1 content have been reported in pigs [28] and cattle [29], primarily attributable to SCD' s desaturation activity at the ninth carbon position. Wu et al. [25] observed that SCD1-878 CC and SCD1-762 TT genotypes were associated with high IMF content in Chinese Simmental cattle and proposed that SCD1 SNPs could serve as genetic markers for cattle in northern and southern China. Thus, the SCD gene not only influences IMF content but also significantly affects IMF fatty acid composition.

3. Candidate Genes in the Fat Degradation Process

IMF degradation involves mobilization of lipids from IMF cells and hydrolysis of triglycerides in lipoproteins, primarily regulated by HSL and LPL genes.

3.1 HSL

Secreted mainly by adipose tissue, HSL directly acts on lipids as the rate-limiting enzyme in lipolysis. Ren et al. [30] found that HSL gene polymorphisms were highly correlated with muscle quality traits in Sujiang pigs, with AA genotype individuals showing higher IMF content compared to other genotypes, demonstrating that the A allele improves muscle quality and establishing HSL as a candidate gene for meat quality and carcass traits in Sujiang pigs. However, HSL expression varies among different sheep breeds. Qiao et al. [31] reported that HSL expression was negatively correlated with IMF content in Kazakh sheep but showed no significant correlation in Xinjiang fine-wool sheep. Xu et al. [32] examined PPARγ, FAS, and HSL expression in different carcass parts of fat-tailed and thin-tailed sheep, finding all three genes associated with fat deposition, particularly IMF regulation. These observations suggest that HSL primarily mobilizes lipids into free fatty acids and glycerol in muscle tissue, providing substrates for triglyceride synthesis in IMF cells while also supplying fatty acids for β-oxidation to meet muscle energy demands. Different breeds may utilize fatty acids through distinct pathways.

3.2 LPL

LPL is a key enzyme in fat deposition with dual functions: hydrolyzing triglycerides in chylomicrons and very low-density lipoproteins (VLDL) to produce free fatty acids for delivery to various tissues, and acting as a ligand to promote lipoprotein uptake. Several studies have reported correlations between LPL expression and IMF content. Wang et al. [33] found that LPL expression in muscle tissue was significantly positively correlated with IMF content in Laiwu pigs and extremely significantly correlated in Lulai Black pigs. Wang et al. [34] also confirmed that the C74T polymorphism in the LPL gene significantly increased IMF content, tenderness, and yellowness values in porcine longissimus dorsi muscle. Zhang et al. [35] used high-resolution melting curve analysis to examine the relationship between LPL gene polymorphisms and meat quality in broilers, revealing that the TT genotype produced higher IMF content (30% and 40%) compared to the CC genotype and suggesting that screening for meat quality genes could be an effective approach for modern breeding programs. These findings demonstrate that different LPL genotypes exhibit varying expression levels and correlations with IMF content.

IMF deposition manifests through increased IMF cell number, lipid droplet accumulation within IMF cells, and lipid droplet deposition within muscle cells. This dynamic process is regulated by candidate genes across three pathways—fatty acid uptake, synthesis, and degradation—though the specific regulatory mechanisms remain incompletely understood. Future research should employ molecular approaches to identify major effect genes and DNA molecular markers controlling IMF content to elucidate these regulatory pathways. Additionally, integrating nutritional modulation with genomics may fundamentally clarify how nutritional strategies regulate lipid metabolism genes to influence IMF deposition.

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