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CLPG Gene Mutation: Molecular Mechanisms, Genetic Effects, and Applications in Animal Husbandry

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Abstract

Feed costs and carcass yields significantly influence the profitability and sustainability of sheep production. Therefore, the selection of animals with superior feed efficiency and high-quality meat production is essential. Genetic factors play a pivotal role in animal development and in determining phenotypic characteristics. Recent advances in genetic research have highlighted the substantial impact of various gene mutations on both physiological and morphological traits. Among these, the Callipyge (CLPG) gene mutation has garnered attention due to its association with muscle hypertrophy, demonstrating a distinctive genetic mechanism and pronounced phenotypic effects. The CLPG mutation promotes enhanced muscle development in sheep, particularly in the pelvic and lumbar regions, and is considered economically valuable. This trait is inherited through a unique epigenetic mechanism known as "polar overdominance." This article explores the molecular basis of the CLPG mutation, its physiological implications, and its potential applications in animal husbandry. Furthermore, the integration of this mutation into genetic selection programs, its influence on meat quality, and the ethical considerations surrounding its use are critically examined.

Keywords: Backbone Traits, Carcass Weight, Meat Production, Genetic Markers, Small Ruminants.

Introduction

Skeletal muscle mass represents a key economic trait, as muscle development and growth are critical for ensuring adequate meat production for human consumption. Consequently, understanding the (candidate) genes that regulate skeletal muscle development is essential for elucidating the molecular genetic mechanisms governing muscle growth and can support the meat industry in achieving its objective of enhancing meat yield (Mohammadabadi et al., 2021). In addition to physical traits, genetic factors also influence behavioral characteristics in animals (Sezer et al., 2023). Genetic research has gained increasing significance in the livestock sector as a means of improving productivity. An animal's genetic composition is determined by the

chromosomes it inherits from its parents, with each chromosome comprising numerous genes. Alterations such as extra, mutated, missing, or translocated genes can result in genetic disorders (Bilici, 2024). The complex nature of meat production traits in sheep is shaped by a combination of genetic and environmental factors that affect muscle growth, carcass characteristics, fat deposition, and the overall quality and quantity of meat (Kaseca et al., 2024; Revelo et al., 2023). Recent advancements in molecular genetics and genomic technologies have provided unprecedented insights into the genetic foundations of these economically important phenotypes (Zhu et al., 2025; Lou et al., 2024). Approaches such as genome-wide association studies (GWAS), transcriptome analyses, and candidate gene investigations have increasingly unraveled the complex genetic architecture underlying meat production traits, offering valuable markers and strategies for genetic selection (Liu et al., 2024). Among the genetic mutations known to enhance meat yield, the Callipyge (CLPG) gene mutation is of particular interest. First identified in 1983 in Dorset × Rambouillet crossbred sheep in the United States, this mutation gained attention due to its pronounced effect on muscle hypertrophy (Jackson et al., 1997). The presence of the CLPG mutation in certain sheep breeds presents significant potential for use in selective breeding programs. Advancements in molecular technologies have enabled the identification of genes associated with economically important traits and facilitated their application in genomic selection studies. In this context, molecular research plays a vital role in the field of animal husbandry (Bilici, 2024). Phenotypically, the single-nucleotide polymorphism (SNP) known as the Callipyge (CLPG) mutation manifests primarily as muscle hypertrophy in the pelvic and hind limb regions of sheep. Although not all muscles are affected, lambs carrying the mutation exhibit varying degrees of muscle enlargement. Callipyge lambs also display several commercially desirable meat quality traits, including higher meat yield percentages, larger loin areas, leaner carcasses, and well-developed limbs. At present, commercial meat sheep production commonly utilizes a two-way crossbreeding strategy, in which local breeds—characterized by strong reproductive performance, adaptability, and large body size—serve as the dam line, while imported high-performance meat breeds are used as sires. The resulting hybrid offspring are typically slaughtered for commercial purposes. Building upon this, a three-way crossbreeding system may be implemented, using an additional superior meat-producing sire as the terminal parent (Yang et al., 2015). The CLPG gene is recognized as a functional gene involved in regulating muscle development and meat tenderness in sheep (Chen et al., 2011; Jawasreh et al., 2019; Moriah et al., 2017). Mutations in this gene lead to muscle hypertrophy, particularly in the loin, hip, and leg regions (Cockett et al., 2005; Jackson et al., 1997; Koohmaraie et al., 1995). The objective of this review is to synthesize current research findings on the genetic influences affecting carcass composition and meat quality traits in sheep. It aims to offer a clear and concise overview of the existing body of knowledge and to highlight key discoveries from recent studies in this field.

Molecular Basis of the CLPG Gene Mutation

The Callipyge (CLPG) phenotype results from a mutation at the callipyge locus within the DLK1–DIO3 region on ovine chromosome 18. This region contains several paternally expressed genes, including *DLK1* and *RTL1*. The CLPG mutation leads to the overexpression of the *DLK1* gene, resulting in skeletal muscle hypertrophy, particularly in specific muscle groups such as the *gluteus medius*, *longissimus dorsi*, and *semimembranosus* (Cockett et al., 1996). The mutation was first identified in Dorset sheep in Oklahoma (Cockett et al., 1994). Sheep exhibiting this phenotype

show significantly increased muscle mass in the leg and loin regions; however, this hypertrophy is not uniformly expressed across all muscle groups, with the diaphragm and certain shoulder muscles showing no enlargement (Jackson et al., 1997). The CLPG locus, located in the telomeric region of chromosome 18, is inherited in a non-Mendelian manner known as polar overdominance. The callipyge phenotype is expressed only in heterozygous animals that inherit the mutation from their fathers, i.e., those with the +M/CLPG P genotype; where the superscripts M and P denote maternal or paternal inheritance of the alleles for both homozygous +M/+P and CLPG M/CLPG P, respectively. Animals that inherit the mutation from their mothers (CLPG M/+P) show normal muscle development (Cochett et al., 1996). The CLPG mutation is inherited in a pattern called polar overdominance, which differs from classical Mendelian inheritance. According to this pattern, phenotypic expression (muscle hypertrophy) occurs only in heterozygous individuals and when the mutant allele is of paternal (paternal) origin. Other combinations (MM, mm, mM) do not exhibit this phenotype.

Physiological and Phenotypic Effects

The phenotypic effects of the Callipyge (CLPG) mutation typically become evident within a few weeks after birth and continue to intensify until the onset of puberty. The observed muscle hypertrophy results from an increase in muscle fiber size (hypertrophy) rather than an increase in the number of muscle fibers (hyperplasia). While this condition contributes to enhanced meat yield, it may, in some cases, adversely affect meat tenderness and overall quality (Koohmaraie et al., 1995). Lambs carrying the CLPG mutation display a normal muscle phenotype at birth, with the hypertrophic characteristics emerging between approximately 4 and 6 weeks of age (Jackson, 1997). In contrast to the double-muscling gene mutation in cattle, which is expressed prenatally and often leads to dystocia, the postnatal onset of the CLPG phenotype does not increase the risk of birthing difficulties in sheep. Several studies have highlighted the production advantages associated with the callipyge phenotype, including increased *longissimus dorsi* muscle area (loin eye), improved lean meat composition, higher leg scores, elevated dressing percentages, and superior feed efficiency. However, Koohmaraie et al. (1995) reported that among all evaluated traits, tenderness of the *longissimus* muscle was the only characteristic negatively affected by the CLPG mutation.

Molecular Mechanisms and Genetic Effects

The CLPG mutation was initially identified in sheep exhibiting abnormal muscle development. The most distinctive characteristic of this mutation is its regulation through a parent-of-origin-specific gene expression mechanism known as genomic imprinting. Under typical conditions, both maternal and paternal alleles of a gene are expressed. However, in the case of imprinted genes, one allele—either maternal or paternal—is epigenetically silenced, and only the allele from the other parent is actively expressed. The CLPG mutation uniquely alters this imprinting mechanism. It is located within a locus on chromosome 18 that includes the *DLK1* and *GTL2* genes. When the mutated allele is inherited from the sire, the gene is expressed, resulting in skeletal muscle hypertrophy. In contrast, inheritance of the same mutated allele from the dam produces no observable phenotypic effect. This pattern of expression clearly indicates that the phenotypic manifestation of the CLPG mutation is dependent on paternal inheritance, with gene activation

occurring exclusively on the paternally derived chromosome. This mechanism can be summarized as follows:

• Mutated allele of maternal origin: Remains silent and has no phenotypic effect.

• Mutated allele of paternal origin: Expressed, leading to muscle hypertrophy and the "Callipyge" phenotype.

This imprinting mechanism is governed by a complex form of genetic regulation known as "transcriptional imprinting." The CLPG mutation enhances the expression of the *DLK1* gene while concurrently suppressing the expression of the *GTL2* gene. This dysregulation influences key signaling pathways involved in muscle development, ultimately promoting both an increase in muscle fiber size and, to some extent, fiber number. Consequently, a substantial increase in muscle mass is observed, particularly in the hind limbs, back, and shoulder regions of the affected animals.

Applications and Potential Benefits in Livestock Production

Studies conducted on various sheep breeds in Türkiye, including Kıvırcık and Karacabey Merino, have demonstrated a significant increase in neck muscle percentage in animals carrying the MN (heterozygous) genotype; however, no statistically significant differences were observed in slaughter weight or carcass yield (Esen et al., 2022). Similarly, a study conducted in Jordan reported that Awassi–Rambouillet crossbred (CRAW) sheep carrying the Callipyge mutation exhibited improvements in growth performance and in specific carcass components compared to purebred Awassi sheep, although reduced meat tenderness remained a concern (Jawasreh et al., 2019). In Pakistan, the presence of the CLPG mutation has been identified in some local breeds, such as Thalli, while it was absent in others, including Kajli and Lohi. This finding underscores the importance of considering genetic variation among local breeds in breeding programs (Shah et al., 2018). The muscle hypertrophy induced by the CLPG mutation offers considerable potential for the livestock industry. This mutation may serve as a valuable genetic marker in selective breeding programs aimed at increasing meat yield and improving carcass quality.

1. Enhancement of Meat Yield: Animals carrying the CLPG mutation exhibit up to a 30% increase in muscle mass compared to non-carriers, which directly contributes to higher carcass yields, particularly in animals raised for slaughter. In sheep breeding, the strategic use of this gene through appropriate parental combinations can optimize overall meat production.

2. Improvement of Carcass Quality: The CLPG mutation influences not only muscle mass but also certain physical properties of the meat. Although CLPG-carrying sheep possess larger muscle fibers, their meat typically contains lower fat content and has been reported to exhibit a relatively tender texture. These characteristics may be advantageous for producing lean meat, aligning with consumer preferences for healthier meat products.

3. Application in Selective Breeding Programs: The presence of the CLPG mutation can be accurately identified through genetic testing, enabling breeders to select animals that will transmit the mutated allele via paternal inheritance. For instance, mating a ram carrying the mutation with

a wild-type ewe is expected to produce offspring in which approximately 50% express the CLPG phenotype. This approach provides an effective tool for accelerating genetic improvement and facilitating the transmission of desirable traits to subsequent generations.

inheritance	Polar overdominance; only paternal heterozygotes are affected.
Muscle development	30-35% increase; tendency toward fast (IIb/IIx) fibers; compact carcass.
productiviy	Less fat, better feed efficiency.
Meat quality	Increased firmness; increased calpastatin levels; decreased proteolysis.
Racial differences	Variable effects in samples from Turkey, Jordan, and Pakistan; location-specific treatment is important.

Ethical and Economic Discussions

The increased muscle mass associated with the CLPG mutation may raise concerns from an animal welfare perspective. Excessive muscle development can result in complications such as dystocia (birthing difficulties) and impaired mobility. Additionally, the utilization of CLPG genotype animals may be constrained in market segments where meat flavor and texture are critical to consumer acceptance. While the CLPG (Callipyge) gene mutation offers notable economic advantages in animal husbandry, it simultaneously generates several ethical and economic debates. These discussions encompass a broad range of issues, from the welfare implications for genetically influenced animals to consumer perceptions and the sustainability of the livestock sector.

A principal ethical concern regarding the CLPG mutation pertains to animal welfare. The mutation's induction of muscle hypertrophy may negatively impact locomotion, as excessive muscle mass places additional strain on joints and the skeletal framework, potentially causing discomfort or pain. Such physical limitations can hinder the animals' ability to engage in natural behaviors, thereby diminishing their overall quality of life. Consequently, breeding programs employing this gene must carefully consider animal health and welfare.

Furthermore, increasing public and consumer sensitivity toward genetically modified organisms (GMOs) may render the use of the CLPG mutation ethically contentious. Although the mutation represents a naturally occurring genetic variation, its identification via genetic testing and deliberate propagation may be perceived by some consumers as an artificial intervention. This perception could affect the marketability of CLPG-derived meat products in a consumer environment increasingly favoring "natural" and "organic" labels.

Economically, the CLPG mutation substantially enhances muscle mass and meat yield, offering direct financial benefits to producers. The capacity to generate greater quantities of meat with reduced feed input can lower production costs and improve profitability. However, animals harboring this mutation may incur additional veterinary expenses, require specialized management, or suffer health-related losses. Therefore, the economic advantages of the CLPG mutation must be carefully weighed against these potential increased costs.

Although meat derived from animals carrying the CLPG mutation is characterized by low fat and high protein content, opinions differ regarding its texture and flavor. Some studies report that CLPG meat is firmer and exhibits increased tenderness, traits that may be favorable in certain markets but less appreciated in others. This variability in market acceptance constitutes a significant consideration influencing breeders' decisions to incorporate the CLPG gene in breeding programs. A precise understanding of consumer preferences and market demand is therefore crucial for the economic viability of this technology.
Furthermore, the overrepresentation of a single gene within animal populations may increase their susceptibility to diseases and environmental stressors, potentially threatening the long-term sustainability of the livestock sector. Consequently, preserving genetic diversity remains a fundamental principle of sustainable animal husbandry, necessitating the controlled and balanced utilization of advantageous genetic variants such as the CLPG mutation.

Conclusion and Future Perspectives

The CLPG gene mutation represents a notable genetic phenomenon, exemplifying a complex case of genomic imprinting and offering substantial potential to enhance productivity in livestock farming. A comprehensive understanding of the molecular mechanisms and genetic consequences associated with this mutation is essential for the development of effective selective breeding programs aimed at improving meat yield and carcass quality. Nonetheless, the potential adverse effects of the mutation on meat flavor and texture—such as increased toughness—warrant further investigation prior to its widespread commercial implementation. The genetic architecture underlying meat production traits in sheep constitutes a complex biological system, involving multiple interconnected pathways that regulate growth, muscle development, fat deposition, and skeletal formation. While the CLPG mutation holds significant promise for genetics-based selection strategies, its unique pattern of polar overdominance and influence on meat quality necessitate careful consideration. Emerging genome editing technologies may offer the possibility of mitigating the negative effects of this mutation while retaining its beneficial attributes. In the future, an enhanced understanding of genetic mechanisms such as those associated with CLPG is expected to facilitate the formulation of innovative approaches in animal genetics and breeding.

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