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Enhancing Dairy Cow Milk Fat Synthesis Genes with CRISPR-Cas9 Technology to Increase Dairy Product Yield

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Abstract This study explores the prospects and potential impacts of using CRISPR-Cas9 technology to improve the genes involved in milk fat synthesis in cows, aiming to increase dairy product yield. Dairy products hold a significant position in global diets, making it an urgent challenge to enhance dairy product production. Milk fat synthesis genes in cows play a crucial role in both the quality and quantity of dairy products. CRISPR-Cas9 technology, as an efficient and precise gene editing tool, provides a powerful instrument for improving cow genetics. By precisely editing genes related to milk fat synthesis, it is possible to enhance the milk fat synthesis capacity of cows, thereby increasing dairy product yields. Gene-edited cows also have the potential to improve milk fat quality, reduce environmental impact, enhance food safety, and bolster the sustainability of the dairy industry. However, gene editing raises ethical and legal concerns that require careful consideration. Ensuring safety and ethical compliance is a key challenge in future research and applications. In summary, the prospects for using CRISPR-Cas9 technology to improve cow milk fat synthesis genes are promising and have the potential to make significant contributions to meeting the growing global demand for dairy products.

Keywords CRISPR-Cas9 technology; Cow; Milk fat synthesis; Dairy product yield; Gene editing

Dairy products have long been a crucial part of human diet, offering rich nutritional value and delightful flavors. The dairy industry holds significant economic and social importance globally, providing not only high-quality proteins, fats, and vitamins to humans but also generating employment and economic opportunities for rural communities and agricultural economies, effectively supporting the sustainable development of rural society. However, the dairy industry faces growing demands, necessitating continuous improvement in both the quantity and quality of dairy products to meet global market needs. Lipid synthesis plays a vital role in dairy production, influencing not only the fat content but also the taste and texture of dairy products (Petitclerc et al., 2000). The regulation of lipid synthesis involves various factors such as diet, genetics, and environment. Nevertheless, the fundamental regulatory mechanism lies in gene control, where the genes related to lipid synthesis in cows play a crucial role. Therefore, enhancing the lipid synthesis genes in cows holds the potential to enhance dairy product yield and quality.

CRISPR-Cas9 technology stands as a powerful gene-editing tool, widely applied in fields such as medicine, agriculture, and biological research, providing unprecedented tools and opportunities for gene editing. In the medical field, it has been used to treat various genetic diseases, including cancer (Ma et al., 2023). In the field of agriculture, CRISPR-Cas9 technology has successfully been employed to improve plant varieties, enhancing resistance, yield, and quality (Hou et al., 2023). Despite the critical role of lipid synthesis in the dairy industry, the regulatory mechanisms of lipid synthesis remain not fully understood. This uncertainty hinders researchers from effectively improving the lipid synthesis process in cows. In the rapidly evolving dairy market, this slow progress is no longer practical. Therefore, the rapid and precise improvement of lipid synthesis genes in cows has become a significant issue. The emergence of gene-editing technology brings new opportunities to address this problem. Through CRISPR-Cas9 technology, researchers have the potential to quickly and accurately improve the lipid synthesis genes in cows, thereby enhancing the yield and quality of dairy products. The application of this technology in cow breeding holds immense potential, but whether it can successfully achieve this goal and whether it can have a positive impact on the dairy industry still requires in-depth research and validation.

This study aims to review the application of CRISPR-Cas9 technology in improving lipid synthesis genes in cows, analyzing its potential benefits and challenges, and exploring its prospects in the field of dairy production. The study will delve into the genes related to lipid synthesis in cows, the principles of CRISPR-Cas9 technology, and how this technology can be applied to cow gene editing. It will also focus on successful cases in this field and potential future trends, contributing to the sustainable development and innovation in the agricultural sector. To provide comprehensive information on this cutting-edge technology to the academic and industrial communities through in-depth research and review, in order to promote further research and application in the field of cow gene editing.

1 Importance of Dairy Cow Milk Fat Synthesis Genes

1.1 Functions of milk fat synthesis-related genes

The genes related to milk fat synthesis play a crucial role in the production and quality of dairy products. These genes encode various fatty acid synthesis enzymes and related proteins, controlling the types and amounts of fats in milk. Among them, three main genes are *ACACA*, *FASN*, and *SCD*, playing key roles in dairy cow milk fat synthesis (Kęsek-Woźniak et al., 2023).

The gene *ACACA* encodes Acetyl-CoA carboxylase, a critical enzyme in the fatty acid synthesis process. This process typically begins with tyrosine in milk, undergoes multiple biochemical reactions, and eventually synthesizes fatty acids. Acetyl-CoA carboxylase is the first key enzyme in this synthesis pathway, participating in the conversion of tyrosine in milk into lactic acid, further transforming into lactic acid ethyl ester, ultimately forming fatty acids. Improving the function of the *ACACA* gene can enhance the efficiency of this synthesis pathway, thereby increasing dairy product yield.

The *FASN* gene encodes Fatty Acid Synthase, a key player in fatty acid synthesis. Enhancing *FASN* function can increase the rate of fatty acid production, crucial for improving the efficiency of milk fat synthesis. The efficiency of milk fat synthesis is closely related to the quality and quantity of dairy products. By increasing the efficiency of milk fat synthesis, cows can produce more high-quality fats, thus improving the flavor and texture of dairy products.

The *SCD* gene encodes Stearoyl-CoA Desaturase, involved in converting saturated fatty acids into unsaturated fatty acids. Unsaturated fatty acids play a vital role in dairy products as they contribute to human health by reducing cholesterol levels and lowering the risk of cardiovascular diseases. Regulating the *SCD* gene can enhance the synthesis of unsaturated fatty acids, improving the nutritional value of dairy products.

The functions of dairy cow milk fat synthesis-related genes are crucial for the production and quality of dairy products. By improving the functions of these genes, it is possible to increase the yield and quality of milk fat, meeting the growing market demand and providing consumers with healthier and tastier dairy products. However, achieving these goals requires continued research and technological improvements to fully unlock the potential of dairy cow milk fat synthesis genes.

1.2 Relationship between dairy product quality and quantity

The quality and quantity of dairy products are closely related, and the functions of dairy cow milk fat synthesis genes have a direct and profound impact on both aspects. Improving milk fat synthesis genes can significantly increase the production of dairy products. Fat is one of the essential components of dairy products, and its content determines the yield of dairy products. The biosynthesis process of fatty acids is the core of milk fat synthesis, and dairy cow milk fat synthesis genes encode enzymes and proteins related to fatty acid synthesis. By improving the functions of these key genes, the synthesis rate of fatty acids can be increased, allowing cows to produce more milk fat. This not only increases the overall production of dairy products but also helps meet the growing market demand for dairy products, thereby enhancing the economic benefits of agriculture.

Improvements in milk fat synthesis genes also have a crucial impact on the quality of dairy products. The fatty acid composition in milk fat is one of the key factors determining the quality of dairy products. Different types and proportions of fatty acids directly affect the taste, texture, and nutritional value of dairy products (Figure 1) (Chen et al., 2004). For example, the content of unsaturated fatty acids can affect the taste of butter, while the content of saturated fatty acids can influence the texture and meltability of cheese. By regulating milk fat synthesis genes, a more precise fatty acid composition can be achieved to meet the quality standards of different types of dairy products and consumer preferences.

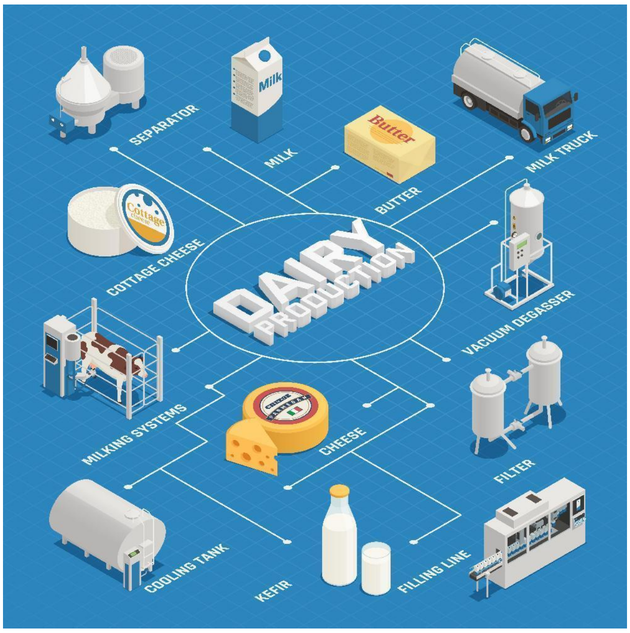

Figure 1 Dairy products

Improvements in milk fat synthesis genes also help increase the stability of milk fat, reducing oxidation and quality deterioration. This is crucial for extending the shelf life of dairy products and reducing food waste. By reducing oxidative reactions, milk fat can maintain a fresher and more stable state for a longer period, ensuring high quality during the distribution and sales of dairy products.

The functions of dairy cow milk fat synthesis genes have a direct impact on the quality and quantity of dairy products, which is of great significance to agriculture and the food industry. Further research into gene editing and related technologies can better meet the growing market demand, providing higher quality and more diverse dairy products while ensuring the sustainability and economic benefits of food production.

1.3 Limitations of existing research

Despite the widely recognized importance of dairy cow milk fat synthesis genes, there are still some limitations in current research aimed at improving these genes. Although CRISPR-Cas9 technology has achieved some success in dairy cow gene editing, there are still technical challenges. While CRISPR-Cas9 technology is highly accurate in targeted gene editing, its editing efficiency may not be sufficient for the needs of agricultural production when applied on a large scale. Improving gene editing technology to enhance editing efficiency remains an urgent task to ensure the desired gene changes in dairy cows. Precision is also a concern. In the CRISPR-Cas9 editing process, non-specific gene mutations or unexpected side effects may occur, posing potential risks to the health and productivity of dairy cows. Therefore, ensuring the accuracy and safety of editing is crucial. The issues of time and cost in gene editing also need to be considered. The high cost and cumbersome operating procedures may limit the feasibility of large-scale gene editing, especially for small dairy farms.

The genetic diversity of the dairy cow population is crucial for maintaining the long-term stability and adaptability of the population. However, gene-edited cows may lead to a reduction in genetic diversity. Introducing specific gene edits may cause certain genotypes of cows to proliferate widely in the population, reducing genetic diversity. This could make cows more vulnerable to future environmental changes and disease pressures, as reduced genetic diversity lowers population adaptability. Irreversible mutations may occur during the gene editing of cows, potentially having long-term effects on genetic diversity. Therefore, measures need to be taken to monitor and protect the genetic diversity of the dairy cow population to prevent unexpected negative consequences.

The importance of dairy cow milk fat synthesis genes in dairy product production cannot be ignored. By improving the functions of these genes, it is possible to increase the yield and quality of dairy products, meeting the growing market demand. However, current research still faces technical and practical challenges, requiring further investigation and exploration.

2 Application of CRISPR-Cas9 Technology in Agricultural Gene Editing

2.1 Development of CRISPR-Cas9

Understanding the historical development of CRISPR-Cas9 technology is crucial for a profound comprehension of its significance in agricultural gene editing. CRISPR (Clustered regularly interspaced short palindromic repeats) and Cas9 (CRISPR-associated protein 9) form a powerful duo that was initially discovered in the bacterial immune system, serving as a natural defense mechanism against viral invasions. Recognizing its potential for gene editing, researchers delved into in-depth studies of this system.

The history of CRISPR technology dates back to the 1990s (Mojica et al., 1993), when researchers first observed a unique DNA sequence in bacterial genomes playing a crucial role in the bacterial immune response. However, at that time, understanding of the functionality and applications of these DNA sequences was limited. In 2012, Jennifer A. Doudna and Emmanuelle Charpentier proposed the concept of using CRISPR-Cas9 for gene editing, marking the beginning of extensive research in this field (Jinek et al., 2012). In the following years, researchers continually improved CRISPR-Cas9 technology, enhancing its accuracy and efficiency. These improvements included introducing different variants of Cas proteins, such as Cpf1, and refining the precision of editing tools.

This discovery sparked widespread interest in the academic and biotechnological sectors, opening up a new avenue for scientists to precisely edit genomes. In the following years, CRISPR-Cas9 technology made significant progress and its application scope continued to expand. In the agricultural domain, CRISPR-Cas9 technology has been applied to enhance crops, endowing them with increased resistance to pests, drought, and diseases. Successful applications in other organisms have provided valuable experience and inspiration for applying CRISPR-Cas9 technology to to cow improvement, as similar principles and techniques can be applied to gene editing in different organisms, including cows (Edick et al., 2021).

The historical development of CRISPR-Cas9 technology is an exhilarating journey, evolving from the accidental discovery in the bacterial immune system to a powerful gene-editing tool, bringing a huge revolution to the fields of biological science and agriculture. This progression establishes a solid foundation for the application of CRISPR-Cas9 in dairy cow improvement, providing valuable insights for future research and practical implementations.

2.2 Principles of gene editing

Understanding the principles of gene editing is closely tied to comprehending the application of CRISPR-Cas9 technology in dairy cow improvement. Gene editing is a complex and precise engineering task (Horodecka and Düchler, 2021). Researchers initially select specific genes to edit, often related to milk synthesis, dairy product quality, and yield in the context of dairy cow improvement. To precisely edit target genes, researchers design guide RNA (gRNA) sequences capable of binding to specific regions of the target genes. The guide RNA directs the Cas9 protein to the vicinity of the target gene, ensuring that editing occurs at the correct location. Cas9 is an RNA-guided protein that, once bound to the guide RNA, can recognize and bind to specific sequences of the target gene. Once Cas9 binds to the target DNA, it induces a double-strand break. This marks the initiation of editing, as cells attempt to repair these breaks, usually through mechanisms like non-homologous end joining (NHEJ) or homology-directed repair (HDR). Ultimately, if the repair mechanism is successful or carefully designed by researchers, it may result in the desired genetic improvement, such as the insertion of specific gene sequences, removal of harmful gene mutations, or substitution of unfavorable genes (Figure 2).

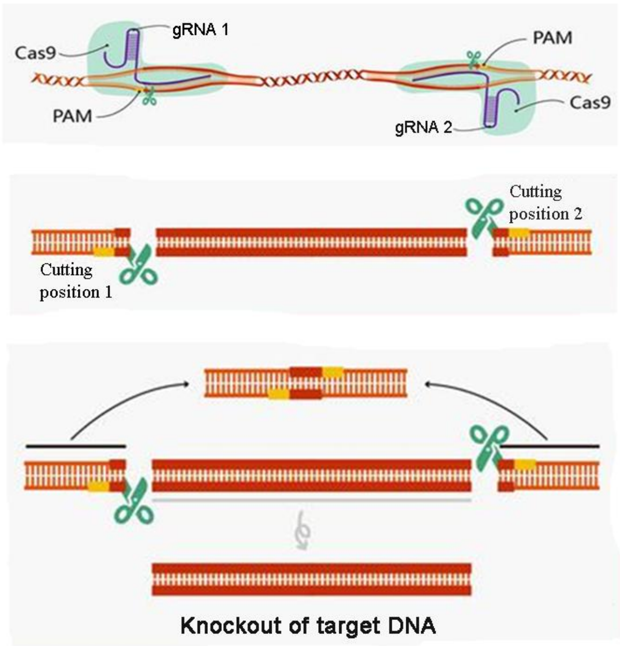

Figure 2 Gene editing process

The principles of gene editing involve selecting target genes, designing guide RNA to direct Cas9, and utilizing the cell's repair mechanisms to achieve precise editing of target genes. This process provides a powerful tool for dairy cow improvement, with the potential to enhance milk production and quality, marking a revolutionary advancement in the agricultural sector.

2.3 Prospects of CRISPR-Cas9 technology in dairy cow improvement

The prospects of CRISPR-Cas9 technology in dairy cow improvement have garnered widespread attention as it offers a new pathway for enhancing milk production and quality in dairy cow. CRISPR-Cas9 technology can be employed to boost the lipid synthesis capacity of dairy cow, directly impacting the fat content of dairy products. By editing genes associated with lipid synthesis, researchers can regulate the production and accumulation of fatty acids, thus increasing the fat content in milk. Through precise editing of key genes in the lipid synthesis pathway, scientists can achieve not only an increase in fat content but also adjust the fatty acid composition to produce healthier fats, such as dairy products rich in unsaturated fatty acids.

With the global population continually increasing and the dairy market expanding, the urgent need to enhance dairy production has become paramount in the agricultural sector. CRISPR-Cas9 technology provides new possibilities for achieving this goal. By editing genes related to both lipid synthesis and milk protein synthesis, scientists can improve the milk-producing performance of dairy cow. This includes not only increasing the daily milk yield per cow but also enhancing the protein content in dairy products. Improving the composition of milk proteins allows for the production of more diverse dairy products, such as high-protein yogurt, shakes, and dairy ingredients.

Increasing dairy production in cow can reduce adverse environmental impacts. By enhancing the milk production of individual cows, it becomes possible to achieve the same amount of dairy output with fewer cows. This reduces the resource demands of the dairy industry, including feed, water, and land, thereby alleviating the pressure on greenhouse gas emissions and land use. Improving the health and resilience of dairy cow reduces reliance on antibiotics and medications, contributing to a reduction in the risk of drug residues in dairy products.

Gene editing can lower the risk of potential pathogenic microorganisms and harmful substances in dairy products, thus enhancing food safety. Scientists can increase the efficiency of the immune system by editing genes in dairy cow, reducing the chances of cows contracting diseases and, consequently, lowering the potential risk of pathogens entering dairy products. Editing genes in dairy cow to decrease the levels of specific harmful substances, such as allergens, antibiotic residues, or carcinogenic substances, can further contribute to improving food safety.

Although CRISPR-Cas9 technology holds vast potential for dairy cow improvement, it faces challenges in its application, such as legal regulations and technical limitations. However, with continuous technological advancements and efforts from scientists, it is foreseeable that CRISPR-Cas9 will achieve more breakthroughs in the agricultural sector, providing significant improvements for the dairy industry. These prospects not only contribute to increasing dairy production quantity and quality but also aid in reducing environmental impact and enhancing food safety, thereby promoting sustainable development in the agricultural sector.

3 Research Methods and Case Studies

3.1 Specific applications of CRISPR-Cas9 in cow gene editing

The specific application of CRISPR-Cas9 technology in cow gene editing is a captivating field that has made significant progress. This technology allows scientists to precisely edit the genes of cows to enhance milk fat synthesis and increase dairy production.

In cows, a common application involves improving the efficiency of the milk fat synthesis pathway. For instance, scientists can edit genes related to fatty acid synthesis, such as *FASN* (fatty acid synthase), to increase the yield of milk fat. Additionally, they can edit genes associated with milk protein synthesis to improve the quality of dairy products. These edits can result in more fat and protein in cow milk, thereby enhancing the quantity and quality of dairy products.

3.2 Some successful case studies

Several successful case studies have demonstrated the potential of CRISPR-Cas9 technology in cow gene editing. These cases provide tangible evidence for enhancing cow milk fat synthesis genes to increase dairy production.

A research team successfully edited the *FASN* gene in cows, a key gene controlling fatty acid synthesis. By increasing the expression level of *FASN*, they achieved a more efficient milk fat synthesis pathway. This improvement led to a significant increase in daily milk production per cow, enhancing the efficiency of dairy product manufacturing.

Another case study focused on improving the quality of cow milk protein. Researchers used CRISPR-Cas9 technology to edit the cow's *β-lactoglobulin* (*β-Lg*) gene, reducing the risk of *β-Lg* allergies (Priyadharsini et al., 2023). This gene editing work improved the quality of dairy products, especially in the production of liquid milk and dairy products, reducing allergen content.

3.3 Current research

Despite significant achievements, the field of cow gene editing is continually evolving, with many ongoing studies involving broader gene editing targets and applications.

Some ongoing research aims to enhance cow resistance to diseases (Zhang et al., 2023). By editing immune-related genes, scientists hope to reduce the risk of cows contracting diseases, thereby lowering the use of drugs and veterinary expenses. Other studies focus on improving the functionality of dairy products. By editing genes related to the production of antioxidants or other beneficial compounds, researchers aim to produce more nutritionally rich and health-promoting dairy products. Some studies strive to enhance cow adaptability to different environmental conditions. This may include improving cow cold resistance (Wang et al., 2022) or heat resistance, thereby expanding the distribution range of cows in different geographical regions.

These ongoing studies represent the frontier of CRISPR-Cas9 technology in the field of cow gene editing. With advancements in technology and more successful cases, we anticipate seeing further innovations and improvements in the future, enhancing the efficiency of cow milk fat synthesis genes to meet the growing demand for dairy products and improve the sustainability of the food industry.

4 Summary

Gene-edited cows represent a revolutionary biotechnology with immense potential to enhance agricultural production, increase food yield and quality, reduce environmental impact, and enhance agricultural sustainability. Through CRISPR-Cas9 technology, scientists can precisely edit the genes of cows to increase milk fat synthesis efficiency, improve dairy production, and enhance the quality of dairy products. However, beyond these significant advantages, researchers must also recognize the challenges associated with gene-edited cows, including legal and regulatory issues, societal acceptance, and food safety concerns. Future research and applications need to consider these factors comprehensively to ensure the sustainable development and widespread application of the technology, while also safeguarding animal welfare and consumer interests.

Gene-edited cows have achieved significant milestones. Researchers have successfully edited multiple key genes in the milk synthesis pathway, such as *FASN* and *ACACA*, to enhance the efficiency of fatty acid and protein synthesis. Through gene editing, daily milk production in cows has significantly increased, providing a viable pathway to meet the growing global demand for dairy products. Successful cases of gene-edited cows further demonstrate the potential for diverse applications in various fields. Improving the milk synthesis pathway is crucial for increasing the production of fatty acids, with implications for the production of dairy products like butter and cream. Additionally, optimizing the milk protein synthesis pathway has positively impacted the quality and nutritional value of dairy products. On the other hand, by editing immune-related genes, researchers aim to enhance cows' resistance to diseases, reducing veterinary costs and medication use, which is crucial for the sustainability of agricultural production.

Despite these significant successes, the field of gene-edited cows faces several challenges. Firstly, the widespread application of CRISPR-Cas9 technology may lead to a reduction in genetic diversity. Frequent editing of cow genes may, to some extent, reduce the genetic diversity of the cow population, potentially making the entire population more vulnerable to new diseases or environmental changes. Therefore, measures need to be taken to balance the benefits of gene editing with the maintenance of genetic diversity, ensuring the overall health and stability of the cow population. Another crucial challenge is the inconsistency in international laws and regulations. There are differences in the legal and regulatory frameworks for gene edited cows among different countries and regions, which leads to legal and regulatory uncertainties. This makes cross-border cooperation and international trade more complex, which brings uncertainty to scientific research and agricultural production. The international community needs to strengthen collaboration to establish unified regulations and standards to ensure the safety and sustainability of gene-edited cow products. Only through international cooperation can the full potential of this technology be realized, promoting the sustainable development of the global food industry.

The long-term impacts and risks of gene-edited cows require further research. While the technology has shown many potential benefits in laboratory environments, more research is needed to assess its feasibility and sustainability under actual farm conditions. This includes comprehensive studies on the potential environmental and ecological impacts of cow gene editing to anticipate and address potential issues. In-depth research is necessary to better understand the potential impacts of this technology and how to manage potential risks.

Despite these challenges, gene-edited cows still have extensive development prospects. Future research and applications will focus on several key areas to further improve the efficiency and sustainability of cow milk synthesis. Research may emphasize fine-tuning gene editing to avoid unwanted side effects and maximize milk production capacity. This will involve more precise gene editing tools and deeper genomic research to ensure that edited gene changes have no adverse effects on the overall health of cows. Gene editing technology can also be combined with existing breeding methods to further enhance cow production capabilities. By combining gene editing and genomics, researchers can better understand the genetic traits of cows, allowing for more precise breeding. This means better selection and breeding of cows with high milk production potential, further increasing the yield and quality of dairy products.

In conclusion, gene-edited cows represent a promising field that can be used to increase dairy product yield and quality while reducing environmental impact. However, along with success come challenges, and through collaboration and innovation, gene-edited cow technology can achieve sustainable and responsible applications in agriculture, meeting the growing global demand for food. Future trends will focus on more precise gene editing, the integration of genomics and breeding, and the continuous evolution of regulations. Only through global collaboration among society, the research community, and governments can this vision be realized, achieving sustainable food production.

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