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From GWAS to Breeding Practice: Genetic Research on Improving Milk Production in Cattle

Qiyuan Ma ✉, Xiaofang Lin

Tropical Animal Center, Hainan Institute of Tropical Agricultural Resources, Sanya, 572025, China

✉ Corresponding author email: 1285899168@qq.comAnimal Molecular Breeding, 2024, Vol.14, No.1 doi: [10.5376/amb.2024.14.0004](https://doi.org/10.5376/amb.2024.14.0004)

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Abstract With the increasing global demand for dairy products, improving milk production in dairy cows has become one of the major objectives of animal husbandry. In this study, the genetic basis of milk production in dairy cows was analyzed in depth by Genome-wide association study (GWAS) method. Genomic data from thousands of dairy cows were collected in this study and several genetic markers significantly associated with milk yield were identified. These findings not only reveal key genes that influence milk yield, but also provide new directions for breeding practices. How the GWAS results can be applied to practical breeding, including the use of Marker-assisted selection (MAS) and Genomic selection (GS) techniques to improve selection efficiency, is further discussed. This study also discusses how to balance the goals of genetic diversity conservation and improved milk production during breeding, and the potential of emerging biotechnologies such as CRISPR/Cas9 in dairy cattle breeding. This study emphasizes the importance of sustainable breeding strategies and the need to consider ethical and social acceptability in the breeding process.

Keywords Genome-wide association studies; Cow milk production; Marker-assisted selection; Genomic selection (GS); CRISPR/Cas9

As one of the most widely consumed foodstuffs in the world, milk is not only loved for its rich nutritional value, but is also an important part of the agricultural economy in many countries. From vitamins to minerals to high-quality proteins, milk provides a range of essential nutrients for human health. Increasing milk production not only meets growing consumer demand, but also improves agricultural productivity and, in turn, economic development.

The history of genetic improvement as a traditional method of increasing milk production goes back thousands of years. Early breeding practices relied heavily on selecting those cows for breeding with high milk yielding traits. As genetics developed, a more systematic understanding of the relationship between milk yield and genetic factors began to emerge, which provided scientists with new tools and methods to optimize breeding strategies. By accurately identifying and selecting cows with desirable genetic traits, breeders are able to more effectively improve milk yield and other economic traits such as milk fat percentage and protein content.

In recent years, the emergence of genome-wide association study (GWAS) technology has brought revolutionary changes to the genetic research of milk production. GWAS technology can identify genetic markers associated with specific traits by analyzing millions of single nucleotide polymorphisms (SNPs) across the entire genome (Dong et al., 2023). The advantage of this method is that it can not only reveal the impact of individual genes on traits, but also reveal the multi gene interactions behind complex traits. In the field of animal breeding, GWAS technology has been successfully used to identify key genetic factors that affect milk yield, milk fat content, and protein content.

By integrating the research achievements of GWAS, breeding practice has entered a new era. Modern breeding strategies no longer rely solely on phenotype selection, but instead begin to use genetic markers for more precise gene selection. This method is called marker assisted selection (MAS), which allows breeders to predict the genetic potential of animals before they reach maturity. GWAS technology not only deepens the understanding of

the genetic basis for milk production, but also provides the possibility of achieving more efficient and precise breeding goals. The application of GWAS technology in animal breeding, especially in genetic research to improve milk production, has shown enormous potential and value. Through in-depth exploration of GWAS technology and its application in breeding practice, it can not only improve the yield and quality of milk, but also contribute to the sustainable development of agricultural production (Gong et al., 2021). With the advancement of technology and the deepening of research, genetic research will continue to bring revolutionary changes to agricultural production.

This study explores the genetic analysis of disease resistance in poultry and its application in poultry health management by integrating the latest advances in genetics, molecular biology, and genomics. Not only does it provide new scientific basis for the prevention and control of poultry diseases, but it also provides new ideas and methods for the sustainable development of the poultry industry. By deeply understanding the genetic resistance of poultry to diseases, we can more effectively address the challenges posed by poultry diseases and contribute to global food safety and public health.

1 The Principle and Application of GWAS Technology

1.1 Principles and Methods of GWAS Technology

Genome-wide association study (GWAS) are a powerful genetic research method aimed at identifying genetic variations that affect specific traits, such as disease susceptibility, crop yield, or animal production traits. GWAS analyzes the association between thousands of single nucleotide polymorphisms (SNPs) in individual genomes and specific traits to identify the genetic reasons behind trait differences. The core of this technology is that it does not require prior assumptions about the genetic basis of traits, allowing for unbiased identification of genetic markers related to traits across the entire genome.

GWAS research typically involves the following steps: collecting a sufficient number of samples and determining their genome-wide SNPs. For each SNP locus, statistical methods are used to compare the frequency differences among populations with different phenotypes (such as high and low milk production), in order to identify which genetic variations are associated with the traits of interest. Using bioinformatics tools and databases to perform functional annotation and biological interpretation of these associated genetic variations, exploring how they affect traits.

1.2 Application cases in the study of cow milk production

GWAS technology has been widely applied in genetic research on cow milk production. A specific example is the large-scale GWAS conducted in Holstein cows in the United States. The research team analyzed 294,079 Holstein cows that were lactating for the first time and successfully identified new additive and dominant effects related to five production traits (including milk yield), three fertility traits, and somatic cell fraction (Li et al., 2023). This study emphasizes the potential of GWAS technology in revealing the genetic basis of complex traits, particularly in economically important traits such as milk yield. Through this method, researchers can identify key gene regions that affect milk production, such as the DGAT1 gene, which is of great significance for understanding the genetic mechanism of milk production and formulating future breeding strategies.

Another study used the FarmCPU method to analyze 86,645 SNPs associated with milk production, somatic cell fraction, and body shape traits, ultimately identifying 95 genome-wide significant SNPs associated with milk production traits (Tong et al., 2023). These research results not only enhance the understanding of the genetic background of milk production traits, but also provide important genetic markers for future molecular breeding (Figure 1).

These research cases highlight the powerful ability of GWAS technology in identifying genetic variations associated with milk production. Through large-scale samples and advanced statistical methods, researchers are able to reveal the complex genetic network that affects milk production, providing scientific basis for breeding work to improve milk production. Although GWAS technology has shown great potential in identifying related genetic variations, the interpretation and application of its results still need to be cautious, especially when

considering the complexity of genetic diversity and environmental factors. Further research and validation are needed to successfully translate GWAS findings into practical breeding strategies.

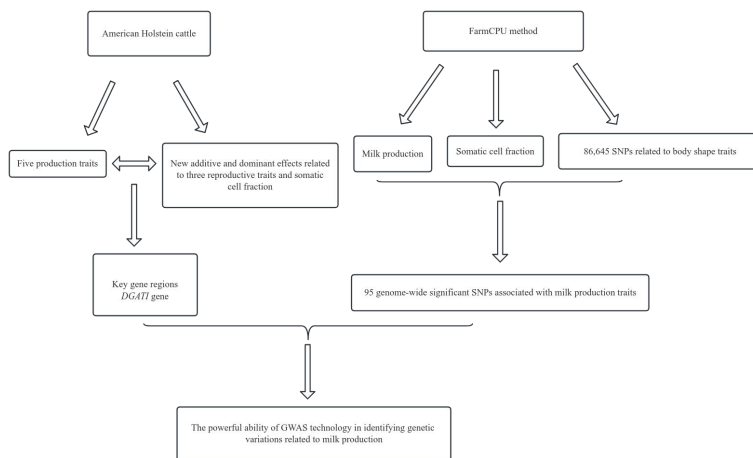


Figure 1 Application of GWAS technology in identifying genetic variations related to milk production

1.3 Advantages and limitations of GWAS technology

The main advantage of GWAS technology is its ability to identify genetic variations related to complex traits across the entire genome without requiring prior knowledge about candidate genes. This is crucial for understanding the genetic basis of complex traits, as these traits are often influenced by multiple genes and interactions between genes and the environment. GWAS can reveal unknown or unexpected biological pathways, providing a new perspective for the study of disease mechanisms and genetic improvement (Lu et al., 2021).

GWAS technology also has some limitations. It requires a large sample size to obtain sufficient statistical power, especially when it comes to small effect genetic variations. Many associations in GWAS results may need to be validated through subsequent research, as statistical associations are not directly equivalent to causal relationships. Although GWAS can identify genetic variations associated with traits, the biological functions and mechanisms of action of these variations often require further functional research to elucidate.

2 Transformation from GWAS to Breeding Practice

2.1 How GWAS identifies key genes and variations that affect milk production

Genome-wide association study (GWAS) are a powerful scientific approach that identifies genetic variations associated with specific traits such as milk yield by analyzing the entire genome. The core of this method is to find the statistical correlation between specific single nucleotide polymorphisms (SNPs) and traits. Through this approach, GWAS research can reveal which genetic variations have a significant impact on milk yield, providing scientific basis for breeding (Korkuć et al., 2020).

Sample collection and genotype analysis: The study began by collecting a large number of individual DNA samples. These samples come from cows with different milk yields. Using high-throughput sequencing technology for genotype analysis of these samples, thousands of SNPs were identified.

Statistical analysis: Statistical analysis is the core component of GWAS. Researchers used complex statistical models to compare the frequency distribution of SNPs in cattle herds with different milk yields. If a certain SNP has a significantly higher frequency in the high-yielding milk population than in the low yielding milk population, then this SNP may be related to milk yield.

Gene mapping and functional research: After identifying SNPs related to milk production, researchers will further investigate the gene regions in which these SNPs are located and how these genes affect milk production. This may involve research on the expression patterns, regulatory mechanisms, and biological functions of specific genes.

Through GWAS, scientists have successfully identified multiple key genes and variations that affect milk production. For example, genes such as DGAT1, GHR, and ABCG2 have been found to be significantly correlated with milk yield and milk fat content. These genes are involved in different biological pathways of milk production, including fatty acid metabolism, growth hormone signaling, and milk secretion.

2.2 Analyze how these genes and variations are used for selection and breeding strategies

How these findings can be applied to selection and breeding strategies is an important issue in modern animal husbandry, as genome-wide association studies (GWAS) have revealed key genes and variations that affect milk production. By applying the findings of GWAS to practical breeding, scientists and breeders can more accurately improve the yield and quality of milk.

Direct selection: the selection of breeding animals based directly on the presence of specific genes or SNPs. For example, if a SNP is positively correlated with high milk yield, then animals with that SNP will be preferentially selected for breeding.

Genomic selection (GS): Selection is based not only on individual genes or SNPs, but on the use of genome-wide information to estimate the genetic value of an animal. This approach allows for a more comprehensive consideration of the interaction of multiple genes and environmental factors that affect milk yield.

Mixed model evaluation: Combining phenotypic data, genotypic data and relevant genetic background information, statistical models are used to estimate the genetic potential of each animal, providing a more scientific basis for selection.

The application of GWAS technology has greatly contributed to the development of modern animal husbandry, especially in increasing milk production and improving dairy quality. By accurately identifying key genes and variants that affect milk yield, GWAS provides a strong scientific basis for breeding. Translating these scientific findings into practical selection and breeding strategies not only accelerates the rate of genetic improvement, but also improves breeding efficiency and economic benefits.

2.3 Example analysis: a case study of successful breeding

In Holstein dairy cows in China, a study conducted a genome-wide association study (GWAS) of traits including milk yield, fat and protein by using the Illumina BovineSNP150 BeadChip. The study identified ten significant single nucleotide polymorphisms (SNPs) associated with milk fat and protein, six of which were located within previously reported quantitative trait loci (QTL) regions (Yu et al., 2023). Specifically, the study confirmed the effect of the DGAT1 gene on milk fat and protein and identified several new candidate genes. These findings provide a valuable basis for molecular breeding in dairy cattle (Figure 2).

Another study utilized international breeding assessment data for GWAS to identify major loci affecting production traits and body size (Gutierrez-Reinoso et al., 2021). Analyzed using linear mixed models, the study identified 74 genome-wide significant SNPs associated with nine traits, which were distributed across 12 chromosomes. For example, traits affecting milk yield and body depth covered almost the same region on BTA25, highlighting significant SNPs and candidate genes including IGFAL, HAGH, and HS3ST6. By utilizing a large sample size of the global Brown Swiss population, this study provided insight into loci important for selection under the major production traits of this breed.

A study in Xinjiang Brown cattle focused on milk, reproductive and health traits using the FarmCPU method for GWAS and incorporating demographic corrections (Zhang et al., 2023). Twelve SNPs were associated with six of the ten traits studied, demonstrating the complexity of trait genetics. This study not only identified significant markers associated with traits such as percent fat and somatic cell score, but also mapped candidate genes in the vicinity of these SNPs, demonstrating the contribution of this study to understanding the genetic basis of important traits in dual-purpose cattle.

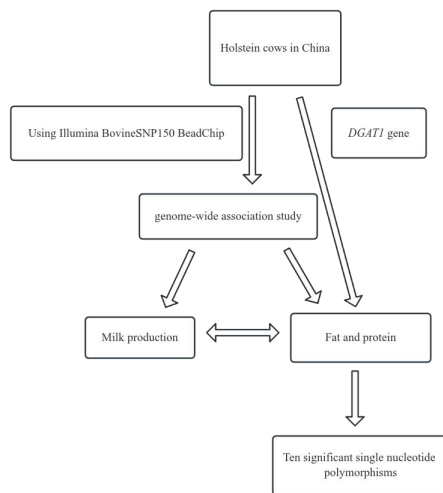


Figure 2 Breeding analysis of the whole genome association study of Holstein cows in china

These research examples illustrate how GWAS findings can guide dairy cattle breeding strategies, from identifying genetic markers for selection to understanding the genetic basis of complex traits. By integrating GWAS results into breeding programs, the dairy industry can achieve genetic improvements in milk yield and quality of cows, contributing to more efficient and productive dairy farming.

3 Challenges and Solutions in Breeding Practices

3.1 Balance between genetic diversity and breeding objectives

The balance between genetic diversity and breeding objectives is a complex and important topic in modern agriculture and animal husbandry. Genetic diversity is the basis for the health, adaptability and long-term survival of biological populations. It ensures that populations are able to adapt to environmental changes, resist diseases, and maintain their functions in the ecosystem. However, when pursuing specific breeding goals, such as increasing milk yield or improving traits such as meat quality, over-selection can lead to a narrowing of the genetic base, which can reduce the genetic diversity of populations.

Genetic diversity is not only essential for the conservation of wild species, but is equally important for plant and animal populations in agricultural production systems. It increases the resistance of populations to disease, enhances their adaptability to environmental change and contributes to the stability and sustainability of production systems. In breeding practice, maintaining genetic diversity means retaining more genetic variation, which is a potential resource for future breeding improvement (Huang et al., 2023).

Breeding goals are often focused on improving specific economic traits, such as increased yield, improved quality, or enhanced disease resistance. To achieve these goals, breeders may tend to select those best performing individuals for breeding, which often leads to a narrowing of the genetic base. How to maintain genetic diversity while pursuing breeding goals has become a major challenge in breeding.

Balancing genetic diversity and breeding objectives is a process that requires long-term attention and efforts. By adopting scientifically sound breeding strategies and utilizing modern biotechnology, not only can we achieve continuous improvement of breeding objectives, but we can also conserve and enhance the genetic diversity of populations, thus providing a solid foundation for future breeding efforts and biodiversity conservation. This is a sign of responsibility not only for current production but also for future generations and ecosystems (Figure 3).

3.2 Interaction between environmental and genetic factors

The interaction of environmental and genetic factors plays a complex and critical role in animal breeding, especially in dairy cattle breeding. Genetic factors determine the potential productive performance and adaptive capacity of an animal, while environmental factors such as feed quality, climatic conditions, and feeding

management directly affect the realization of these potentials. Understanding how environmental and genetic factors interact is essential for developing effective breeding strategies and management practices.

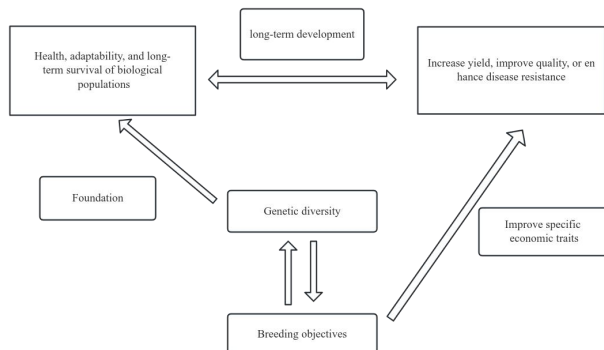


Figure 3 The interaction between balancing genetic diversity and breeding objectives

Environmental factors can significantly affect the phenotypic expression of an animal. For example, even cows with high genetic potential may not reach their maximum milk production potential under poor feeding conditions. In contrast, excellent feeding management and nutritional supplementation can help an animal to better realize its genetic potential. This phenomenon illustrates the direct influence of environmental factors on the expression of animal traits and the importance of improving environmental conditions to enhance production performance.

The interaction between genetic and environmental factors may lead to different responses to environmental changes in animals with different genetic backgrounds. This means that certain genetic variants may exhibit superior traits under specific environmental conditions. For example, some dairy breeds may be better adapted to cold climates, while others may perform better in tropical climates. Therefore, breeding strategies need to In order to optimize the interaction between environmental and genetic factors, breeders and breeders need to adopt a multifaceted strategy. The study of genetic-environmental interactions allows the identification of genetic markers with specific environmental adaptations, which provides the basis for molecular-assisted selection. Implementation of precision animal husbandry technologies, such as environmental monitoring and animal health tracking, allows real-time adjustment of husbandry management practices to the genetic needs of animals and environmental changes. Carrying out environmentally adapted breeding, i.e., selecting for breeding those animals that perform best under specific environmental conditions, can improve the overall fitness and productivity of populations (Figure 4).

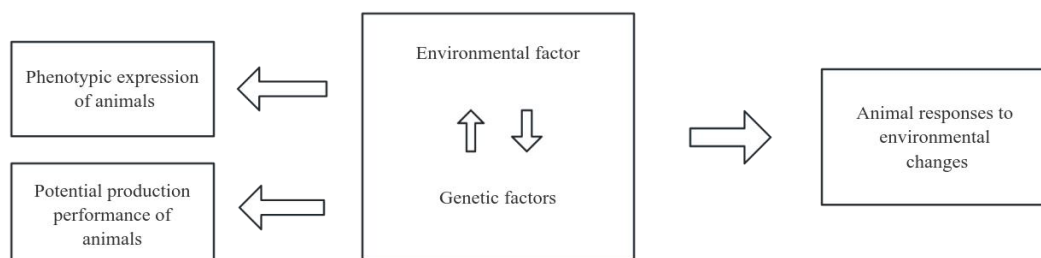


Figure 4 Performance of the interaction between environmental and genetic factors

The interaction of environmental and genetic factors has a profound effect on the production performance of dairy cows. By integrating genetic selection and environmental management, as well as using modern biotechnology, the development of the dairy industry can be promoted more effectively to maximize production performance and achieve sustainable development.

3.3 Methods of utilizing biotechnology to improve breeding efficiency

In modern animal husbandry, the use of biotechnology to improve breeding efficiency has become a trend. These technologies not only accelerate the breeding process, but also improve the accuracy of breeding, making it possible to produce animals that are better adapted to market demands.

Gene editing technologies, particularly the CRISPR/Cas9 system, offer the possibility of precisely modifying animal genomes. This technology can be used to directly alter specific genes that affect economically important traits, such as increasing milk production in dairy cows, improving meat quality in beef cattle, or increasing an animal's resistance to certain diseases. By precisely editing specific gene loci, it is possible to ensure that the altered genetic traits are inherited stably in the offspring, thus significantly improving the efficiency and effectiveness of breeding.

In vitro fertilization (IVF) and embryo transfer technologies have made it possible to obtain large numbers of offspring from animals with high genetic value. Through these techniques, it is possible to breed large numbers of superior breeds with high genetic potential without being limited by the natural reproduction rate (Su et al., 2023). Embryo transfer can also be used to conserve genetic resources across genera or to introduce superior genetic traits into different populations, thus accelerating the breeding process.

Genomic selection is a method of selection based on genome-wide information. By analyzing the entire genome, breeders can predict the genetic potential of an animal and make selection decisions accordingly. This method is more precise than traditional selection based on phenotypes or a limited number of genetic markers and can significantly improve the accuracy and efficiency of selection. Genomic selection has been used in the breeding of a wide range of animals, including dairy cattle, pigs and poultry.

Transgenic technology confers new traits or improves existing traits by introducing exogenous genes into the animal genome. This technology can be used to breed new breeds with specific advantages, such as high disease resistance, fast growth or high yield. Although transgenic animals face ethical and legal controversies and restrictions in some countries and regions, their potential to improve breeding efficiency and meet specific production needs cannot be ignored.

Early prediction of an animal's genetic potential can be achieved by identifying microsatellite or SNP markers linked to economically important traits. This marker-assisted selection method allows for genetic evaluation of animals at a very young age, resulting in early selection without waiting for the animals to grow up to exhibit the phenotype, significantly shortening the breeding cycle.

4 Future Research Directions

4.1 Prospects for the application of emerging technologies in milk yield genetics research

With the rapid development of gene technology, gene editing techniques such as CRISPR/Cas9 have begun to show great potential for application in dairy cattle breeding. These technologies allow scientists to precisely modify the genomes of dairy cows, which can directly affect milk yield and quality.

For example, the nutritional value of milk can be directly improved by precisely editing genes in the cow's genome that affect milk fat and protein content. Gene editing techniques can also be used to improve the health and disease resistance of cows and reduce the incidence of disease, thereby indirectly increasing milk production.

4.2 Role of big data and machine learning in breeding decision support

In the field of dairy cattle breeding, the application of big data and machine learning technology provides powerful data support for breeding decisions. By collecting and analyzing a large amount of data such as genetic information, production performance data, and environmental factors of dairy cows, machine learning models can help breeders predict the possible outcomes of different breeding strategies to make more scientific and precise choices (Hu et al., 2023).

For example, by analyzing historical breeding data, machine learning models can identify key genetic factors that affect milk yield and provide guidance for breeding. In addition, big data analytics can be used to monitor and predict the occurrence of diseases and provide decision support for the health management of dairy cows.

4.3 Sustainable breeding strategies and ethical considerations

Sustainable breeding strategies and ethical considerations are increasingly emphasized in the pursuit of increased cow yield and efficiency. Breeding strategies need to take into account environmental protection, such as reducing the impact of animal husbandry on the environment and protecting biodiversity; the breeding process also needs to pay attention to animal welfare to ensure that the health and welfare of dairy cows are not neglected. The application of emerging technologies such as gene editing has also triggered discussions on ethics and social acceptance, and how to balance technological advances with ethical considerations to ensure the responsible use of technology has become a non-negligible issue in breeding research.

With the continuous progress of science and technology, emerging technologies, big data and machine learning will play an increasingly important role in dairy cattle breeding research. Sustainable breeding strategies and ethical considerations will also guide the direction and methods of breeding. In the future, through the application and comprehensive consideration of these high technologies, dairy cattle breeding will be able to improve yield and efficiency while protecting the environment. In the field of modern dairy cattle breeding, with the rapid development of science and technology, the application of emerging technologies, such as CRISPR/Cas9 gene editing, big data analytics, and machine learning, as well as the emphasis on sustainable breeding strategies and ethical considerations are becoming the key factors that will drive progress in the field. The combined application of these technologies and methods will not only improve the efficiency and accuracy of breeding, but also realize the sustainable development of the dairy industry while safeguarding animal welfare and ecological balance.

5 Conclusion

The application of genome-wide association studies (GWAS) technology in the field of milk yield improvement has demonstrated its great contribution and potential. By accurately identifying genes and genetic variants associated with economically important traits such as milk yield, milk fat content and milk protein content, GWAS technology provides a strong scientific basis for breeding and greatly facilitates the development of dairy cattle breeding practices. This study will summarize the contribution of GWAS technology in improving milk yield and provide an outlook for future research and application (Yang et al., 2023).

GWAS technology emphasizes the importance of integrating scientific research with actual breeding practices. In the past, breeders often relied on traditional phenotypic selection and family line selection methods, which were effective but limited in accuracy and efficiency. The application of GWAS technology allows breeders to directly target specific genes affecting milk yield, greatly improving the accuracy and efficiency of selection. For example, variants in genes such as DGAT1 and GHR identified by GWAS have been shown to be closely associated with milk yield and milk fat content, making them important markers for breeding selection.

The application of GWAS technology has also provided new strategies and directions for breeding. By comprehensively analyzing the entire genome, GWAS not only identifies genes known to affect traits, but also reveals previously unrecognized related genes and genetic mechanisms. This offers the potential for a deeper understanding of the genetic basis of milk yield, as well as the development of new breeding goals and strategies. For example, recent studies have identified a number of new genes affecting mammary gland development and milk synthesis pathways that may be important breeding targets for improving milk yield in the future.

Looking ahead, there is still tremendous scope for the application of GWAS technology in improving milk yield. With the advancement of sequencing technology and the reduction of cost, it is possible to sequence the whole genome of more individual dairy cows, which will provide richer and more precise genetic information for GWAS and further improve the precision and efficiency of the study. Meanwhile, in combination with other emerging technologies, such as gene editing, GWAS discoveries can be translated into actual breeding results more quickly.

In addition, the application of big data analysis and machine learning technologies will make it more efficient to extract useful information from the large amount of complex data in GWAS, providing strong support for breeding decisions (Sermiyagin et al., 2020).

In conclusion, the contribution of GWAS technology in improving milk yield has been widely recognized, and its potential to combine modern biotechnology and information technology is still unfolding. Future research needs to further explore the application of GWAS in dairy cattle breeding and how to better translate the results of scientific research into breeding practices to achieve sustainable development and efficiency improvement in the dairy industry.

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