



Genetics and Production of Safe, High-Quality Milk by Dairy Cattle

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A crucial part of the livestock industry is dairy cattle which contribute significantly to the livestock economy. Milk-fat traits of dairy cattle are related to the efficiency and quality of dairy cattle production, and their genetic breeding is also vital for the production of dairy cattle products. Presently, the dairy industry, particularly in developing countries, is shifting from quantity-based scale production to a quality- and efficiency-based scale. As a result, the level of dairy production and milk quality will inevitably be improved, leading to higher standards for the quality of dairy products. In view of the current situation and future trends in dairy development, it is of great significance to attach importance to the research on high-quality milk-production technology, meat-quality regulation and product quality and safety control.

The most common disease on dairy farms is bovine mastitis, which reduces milk production and affects milk quality. The infection occurs when pathogenic bacteria infiltrate the mammary gland through infection or environmental means. In actual samples, E. coli was found to have high rates of infection and prevalence, although it could be suppressed effectively by some antibiotics, such as gentamicin and tetracycline. However, E. coli isolates have shown severe resistance to many β -lactams, including penicillin, cephalothin and amoxicillin [1]. It is therefore important to explore other ingredients that can effectively inhibit Gram-induced inflammation and oxidative stress response. Accordingly, Liu et al. turned their attention to traditional Chinese herbal ingredients, the most prominent being Lycium barbarum polysaccharides (LBP), which exhibit antioxidant and anti-inflammatory properties both in vivo and in vitro. Through its activation of cytokine signaling-3 (SOCS3) and inhibition of mitogen-activated protein kinase (MAPK) signaling, LBP effectively alleviated E. coli-induced inflammation and oxidation in primary bovine mammary epithelial cells (pbMECs) [2]. These findings will enable us to conduct better research on the replacement of antibiotic-based treatments, and provide new ideas, technologies, and materials for the prevention and treatment of cow mastitis.

At the cellular level, microRNAs (miRNAs) are a class of endogenous non-coding RNAs. They have been shown to play an important role in cell differentiation, apoptosis, gene-expression regulation, and tumorigenesis. The inflammatory response is a complex process of inflammatory reactions that occurs in the body to various stimuli, including the release of inflammatory cytokines and chemokines, as well as the activation of corresponding signaling pathways. Additionally, miRNAs are vital to the immune system in that they can participate in and regulate the immune response, and suppress it by binding with target genes. With increasing research, miR-29 has emerged as a key regulator of liver lipid metabolism. The transient transfection of bta-miRNA29d-3p mimics and inhibitors in bovine mammary epithelial cells (BMECs) revealed that bta-miRNA29d-3p could regulate fatty-acid metabolism and TAG synthesis by regulating lipid-metabolism-related genes in BMECs and targeting glycerol-3-phosphate acyltransferase (GPAM) [3]. Meanwhile,



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Copyright: © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). based on mammary transcriptome analysis, a kind of miRNA, bta-miR-125a, has been identified as controlling bovine-milk fat production by targeting the 3' untranslated region (UTR) of serum amyloid A-3 (SAA1) mRNA. This miRNA can act as a positive regulator of lipid synthesis in mammary epithelial cells by targeting *SAA1* gene expression [4]. N6-methyladenosine (m_6A) methylation, a methylation modification found on mRNA molecules, has also been suggested to play a role in the development of lipid metabolism since it can change the mRNA levels of genes related to milk-fat metabolism. More importantly, genes and signaling pathways related to milk-fat metabolism have also been shown to be closely related to m_6A methylation. The above studies are expected to provide references for further research into mammary-gland development and milk-fat metabolism in ruminants [5].

A study by Zhang et al. investigated the effects of two metabolic-syndrome pathway genes, interleukin 6 receptor (*IL-6*) and leptin receptor (*LEPR*), on reproductive performance in dairy cows. Among the six SNPs they examined, five were significantly associated with at least one reproductive trait, including age at the first service, age at the first calving, the interval from calving to first insemination, and the calving ease in heifers and cows. Thus, IL6R and LEPR are considered to be important molecular markers for the genetic selection of reproductive traits in high-yielding dairy cattle [6]. In addition, *DDIT3* is also considered to be a novel gene that can regulate the mechanism of milk production traits, thus being used to regulate milk protein and fat traits of dairy cows. On the other hand, as a result of *DDIT3* silencing, inflammatory markers such as *IL-6* and *IL6R* were up-regulated, which means that lower *DDIT3* expression can prompt increased lipid accumulation and apoptosis through the up-regulation of *IL-6* expression [7].

The remaining concepts are discussed from the perspectives of molecular genetics, development, and selective breeding. In future production practices, it is important to pay special attention to mutations associated with abnormalities in dairy-cattle populations, such as defects in bovine leukocyte adhesion, complex vertebral malformations, and short spinal or short spinal lethal syndrome, as representative examples of inherited diseases [8]. Meanwhile, two variants of cofilin, cofilin-1 (CFL1, non-muscular type) and cofilin-2 (CFL2, muscular type), have been found in mammals, with a dual function on skeletal muscle fibers [9]. The acute phase response (APR) is a non-specific systemic response in which acute phase protein (APP) production changes. Hence, it is possible to use APP as a biomarker of inflammation. The rapid dynamics of serum amyloid A (SAA), one of the main APPs in dairy cows, also calls for special attention. Therefore, the breeding and reproduction stages should be controlled specifically with regard to genetics and gene selection [10]. In addition, beta-oxidation, an important metabolic process involving multiple steps, produces energy via the breakdown of fatty-acid molecules. Future studies can benefit from summarizing the importance of peroxisome β oxidation [11].

Taking common diseases of dairy cows as a starting point, this research enables the further analysis of the susceptibility of dairy cows to disease and the methods of mitigation. It also comprises an examination of some important regulatory factors that contribute to mRNA regulation, which provides suggestions for the improvement and enhancement of milk-fat traits. A greater emphasis is being placed on livestock production practices from the perspectives of genetics, reproduction, and breeding selection. In addition, fatty acid oxidation is summarized and the regulatory mechanism of fatty acids is analyzed in depth, providing new insights into future research on the genetics of milk-fat traits.

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References

- 1. Xu, T.; Cao, W.; Huang, Y.; Zhao, J.; Wu, X.; Yang, Z. The Prevalence of *Escherichia coli* Derived from Bovine Clinical Mastitis and Distribution of Resistance to Antimicrobials in Part of Jiangsu Province, China. *Agriculture* **2023**, *13*, 90. [CrossRef]
- Liu, R.; Zhu, H.; Zhao, J.; Wu, X.; Lu, X.; Xu, T.; Yang, Z. Lycium barbarum Polysaccharide Inhibits *E. coli*-Induced Inflammation and Oxidative Stress in Mammary Epithelial Cells of Dairy Cows via SOCS3 Activation and MAPK Suppression. *Agriculture* 2022, 12, 598. [CrossRef]
- 3. Zhao, X.; Li, J.; Zhao, S.; Chen, L.; Zhang, M.; Ma, Y.; Yao, D. Regulation of bta-miRNA29d-3p on Lipid Accumulation via GPAM in Bovine Mammary Epithelial Cells. *Agriculture* **2023**, *13*, 501. [CrossRef]
- 4. Cui, X.; Yuan, T.; Fang, Z.; Feng, J.; Wu, C. Bta-miR-125a Regulates Milk-Fat Synthesis by Targeting SAA1 mRNA in Bovine Mammary Epithelial Cells. *Agriculture* **2022**, *12*, 344. [CrossRef]
- 5. Xin, Z.; Zhang, T.; Lu, Q.; Yang, Z.; Chen, Z. Progress of m6A Methylation in Lipid Metabolism in Humans and Animals. *Agriculture* **2022**, *12*, 1683. [CrossRef]
- Zhang, H.; Sammad, A.; Shi, R.; Dong, Y.; Zhao, S.; Liu, L.; Guo, G.; Xu, Q.; Liu, A.; Wang, Y. Genetic Polymorphism and mRNA Expression Studies Reveal IL6R and LEPR Gene Associations with Reproductive Traits in Chinese Holsteins. *Agriculture* 2023, 13, 321. [CrossRef]
- Cui, X.; Li, C.; Wei, Z.; Meng, H.; Zhang, F.; Liu, Y.; Wu, C.; Yang, S. DDIT3 Governs Milk Production Traits by Targeting IL-6 to Induce Apoptosis in Dairy Cattle. *Agriculture* 2023, 13, 117. [CrossRef]
- 8. Marzanova, S.N.; Devrishov, D.A.; Turbina, I.S.; Marzanov, N.S.; Griffin, D.K.; Romanov, M.N. Genetic Load of Mutations Causing Inherited Diseases and Its Classification in Dairy Cattle Bred in the Russian Federation. *Agriculture* **2023**, *13*, 299. [CrossRef]
- 9. Sun, Y.; Ma, Y.; Wu, X.; Zhao, T.; Lu, L.; Yang, Z. Functional and Comparative Analysis of Two Subtypes of Cofilin Family on Cattle Myoblasts Differentiation. *Agriculture* **2022**, *12*, 1420. [CrossRef]
- 10. Trela, M.; Domańska, D.; Witkowska-Piłaszewicz, O. Diagnostic Use of Serum Amyloid A in Dairy Cattle. *Agriculture* **2022**, 12, 459. [CrossRef]
- Lu, Q.; Zong, W.; Zhang, M.; Chen, Z.; Yang, Z. The Overlooked Transformation Mechanisms of VLCFAs: Peroxisomal β-Oxidation. Agriculture 2022, 12, 947.

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