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Beyond Antibiotics: Harnessing Genetics and Genomics for Sustainable Mastitis Management in Dairy Cattle

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Abstract:

Mastitis remains one of the costliest diseases affecting dairy production, reducing milk yield, compromising animal welfare and increasing antimicrobial use. Conventional control measures, although essential, cannot fully prevent this recurrent infection because disease susceptibility is influenced by genetics. Precision breeding integrates genomic technologies such as quantitative trait loci mapping, genome-wide association studies, genomic selection, transcriptomics and other multi-omics approaches to identify animals with superior genetic resistance. Selection based on genomic estimated breeding values enables earlier and more accurate breeding decisions which reduces disease incidence and antibiotic dependence. Combined with effective management and veterinary care, precision breeding offers a sustainable strategy for healthier, more productive, and resilient dairy herds.

Keywords: Mastitis, genomic selection, transcriptomic, breeding

Introduction:

Mastitis remains one of the most economically important diseases affecting

the global dairy industry. Despite advances in dairy management, nutrition, housing and veterinary care, inflammation of the

mammary gland continues to reduce milk production, compromise animal welfare and increase production costs. Dairy cattle contribute nearly 80% of the world's milk production. Mastitis affects mostly affects cattle, buffaloes than sheep and goats. As the world's largest milk producer, India depends on healthy dairy herds to sustain food security, rural livelihoods and the growing dairy economy (FAO, 2021). Unlike many infectious diseases, mastitis is a multifactorial disorder resulting from interactions among pathogens, host immunity, genetics, environmental conditions and farm management. Consequently, even well-managed herds also experience recurrent infections if animals are genetically susceptible.

Conventional mastitis control relies on good milking hygiene, housing sanitation, vaccination, dry cow therapy and antimicrobial treatment. While these measures remain essential, growing concerns over antimicrobial resistance (AMR), treatment costs and recurrent infections have highlighted the need for sustainable long-term solutions (Kupczyński *et al.*, 2024). One such solution is precision breeding, which combines modern genomics with conventional breeding to identify and select animals carrying favourable genetic variants for disease resistance. Technologies such as quantitative trait loci

(QTL) mapping, genome-wide association studies (GWAS), genomic selection, transcriptomics and other omics now enable breeders to improve herd health while maintaining productivity. Rather than replacing conventional control measures, precision breeding complements them by gradually developing dairy populations that are naturally more resilient to mastitis and less dependent on antibiotic therapy.

Understanding mastitis: More than an udder infection

Mastitis is an inflammation of the mammary gland, most caused by bacterial pathogens entering through the teat canal. It results in substantial economic losses through reduced milk yield, poor milk quality, increased veterinary costs, premature culling and compromised animal welfare. The disease occurs in two forms. Clinical mastitis is characterised by visible signs such as swelling, pain, heat, abnormal milk and reduced milk production. Infection may involve only one quarter or several, but lesions remain specific to particular quarter because each quarter functions independently and early diagnosis with appropriate treatment can often prevent permanent damage. Subclinical mastitis, however, is more difficult to detect because affected animals show no obvious clinical signs. Since these animals continue producing contaminated milk and act as reservoirs of infection,

subclinical mastitis accounts for most economic losses in dairy herds.

A key indicator of udder health is the somatic cell count (SCC), which reflects the number of immune and epithelial cells present in milk. Healthy cows typically have SCC values below 100,000 cells/mL, whereas counts exceeding 200,000 cells/mL strongly indicate intramammary infection (Rupp and Boichard, 1999). Consequently, SCC has become an important tool for mastitis diagnosis, milk quality monitoring and genetic evaluation. Although antibiotics remain indispensable for treating bacterial mastitis, repeated antimicrobial use contributes to antimicrobial resistance and increases production costs. Moreover, chronic infections may cause irreversible fibrosis of mammary tissue, permanently reducing milk-producing capacity. These limitations emphasise that mastitis should not be viewed solely as a disease requiring treatment but as a multicausative disorder influenced by pathogen exposure, environmental conditions, management practices and the animal's genetic susceptibility. This understanding forms the basis for developing long-term preventive strategies such as precision breeding.

Why conventional control alone is not enough?

Conventional mastitis control has greatly improved udder health through hygienic milking practices, housing sanitation, balanced nutrition, vaccination, dry cow therapy and regular herd monitoring. These measures remain the cornerstone of mastitis prevention and have substantially reduced disease incidence in dairy herds. Despite these advances, mastitis continues to be one of the most prevalent and economically alarming diseases. The persistence of mastitis, even in well-managed farms, demonstrates that disease occurrence is influenced not only by pathogen exposure and management but also by the animal's inherent ability to resist infection.

Although antibiotics remain essential for treating bacterial mastitis, they are administered only after infection has developed, by the time tissue damage and production losses may already have occurred. Repeated antimicrobial use also increases treatment costs, milk withdrawal periods and the risk of antimicrobial resistance (AMR), a growing concern within the One Health framework (Kupczyński *et al.*, 2024). Likewise, currently available vaccines reduce disease severity but cannot provide complete protection against the diverse pathogens responsible for mastitis. These limitations

have shifted attention from treatment towards prevention. Rather than relying solely on therapeutic interventions, modern breeding programmes aim to enhance the animal's natural resistance to disease. Unlike antibiotics or vaccines, genetic improvement is a permanent and cumulative approach, allowing favourable alleles to be transmitted to future generations. Although breeding cannot replace good management, it offers a sustainable long-term strategy that complements conventional mastitis control (Shook, 1989). This paradigm shift—from treating mastitis to breeding animals that are naturally more resistant forms the basis of precision breeding.

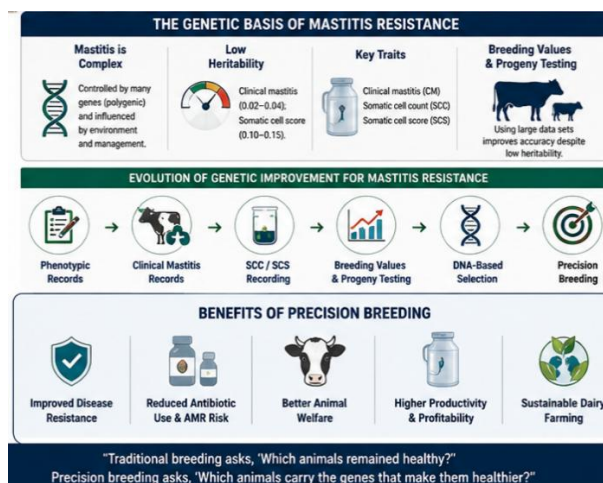
Can we breed dairy animals that are naturally resistant to mastitis?

The answer is yes but it is not straightforward. Unlike simple inherited traits, mastitis resistance is a polygenic trait, controlled by numerous genes that collectively influence immune function, inflammatory responses and mammary gland health. In addition, environmental factors such as pathogen exposure, nutrition, housing and management strongly influence whether disease develops. One of the greatest challenges is the low heritability of mastitis. Clinical mastitis has a heritability of only 0.02-0.04, indicating that environmental factors contribute more to disease occurrence than

genetics (Heringstad *et al.*, 2000). Consequently, selecting animals solely based on disease history results in slow genetic progress.

To improve selection accuracy, breeders rely on measurable indicators of udder health. The most widely used are clinical mastitis (CM) records and somatic cell count (SCC). During intramammary infection, immune cells migrate into the mammary gland, increasing the number of somatic cells in milk. Because SCC is routinely measured during milk recording, it serves as a practical indicator of udder health. For genetic evaluation, SCC is converted into somatic cell score (SCS), which has a slightly higher heritability (0.10-0.15) and is therefore more effective for selection (Rupp and Boichard, 1999). Breeders further improve selection accuracy by estimating breeding values, which predict an animal's ability to transmit favourable genes to its offspring. Historically, progeny testing of bulls provided reliable estimates of mastitis resistance based on the performance of hundreds of daughters (Shook, 1989). Several countries, particularly the Scandinavian dairy breeding programmes, successfully incorporated SCC and clinical mastitis records into national selection indices, demonstrating that disease resistance can be improved without compromising milk production (Heringstad

et al.,2000). Nevertheless, conventional selection remains relatively slow because it depends on phenotypic records collected after animals begin producing milk. This limitation has driven the adoption of molecular genetics and genomics, enabling breeders to identify genetically superior animals shortly after birth using DNA-based information. These advances have laid the foundation for precision breeding, where genomic information guides the selection of healthier, more resilient dairy animals.



Precision breeding in action: From DNA markers to genomic selection

The transition from conventional breeding to precision breeding marks a major milestone in livestock genetics. Traditional breeding relied on pedigree records and observable performance, whereas modern genomic technologies enable the identification of genetically superior animals at an early age, even before desirable traits are expressed. The first breakthrough came with the discovery

of QTLs-genomic regions associated with economically important traits. Unlike single-gene disorders, mastitis resistance is a polygenic trait, controlled by numerous genes with small individual effects. QTL mapping demonstrated that resistance has a measurable genetic basis and can therefore be improved through selective breeding. The Animal QTL Database currently reports more than 1,800 QTLs for somatic cell score (SCS) and over 500 QTLs for clinical mastitis (CM), illustrating the complex genetic architecture of mastitis resistance (Hu *et al.*,2013).

Although QTL mapping identified important genomic regions, these regions often contain many genes, making it difficult to identify the true causative variants. This limitation led to the adoption of genome-wide association studies (GWAS), which analyse hundreds of thousands of single nucleotide polymorphisms (SNPs) across the genome. Combined with high-density SNP chips and whole-genome sequencing, GWAS has enabled researchers to identify candidate genes involved in immune regulation, inflammation and mammary gland defence with much greater precision. These advances paved the way for marker-assisted selection (MAS) and, more importantly, genomic selection. While MAS relies on a limited number of DNA markers linked to favourable QTLs, genomic selection

simultaneously evaluates thousands of SNPs across the genome to estimate an animal's genomic estimated breeding value (GEBV). Because of its ability to capture the combined effects of numerous genes, genomic selection is effective for complex, low-heritability traits such as mastitis resistance. Importantly, breeding values can now be predicted shortly after birth using a simple DNA sample, allowing faster and more accurate selection of superior animals. Recent advances extend precision breeding beyond DNA sequence alone. Whole-genome sequencing, transcriptomics and other multi-omics approaches help identify functional genes and biological pathways associated with host immunity and udder health. When integrated with GWAS and QTL information, these technologies improve the identification of candidate genes responsible for disease resistance (Mackay, 2004).

Precision Breeding: Transforming Veterinary Practice and Sustainable Dairy Farming

Precision breeding extends beyond identifying disease-associated genes—it aims to produce healthier animals, reduce disease incidence and promote sustainable dairy production. Unlike therapeutic interventions that act after infection, genetic improvement gradually increases the frequency of favourable alleles within a

population, providing cumulative and permanent benefits across generations. Importantly, precision breeding complements rather than replaces conventional mastitis control. Good management practices, including hygiene, nutrition, biosecurity, vaccination and regular herd monitoring, remain essential. However, combining these measures with genetic improvement enhances the animal's natural ability to resist infection, resulting in more effective and sustainable disease control.

For veterinarians, this approach represents a shift from reactive disease treatment to proactive disease prevention. In addition to diagnosis and therapy, veterinarians are increasingly involved in interpreting genomic information, advising breeding decisions and collaborating with geneticists to improve herd health. As genomic technologies become more accessible, their role in precision breeding will continue to expand. Reducing mastitis through genetic selection also supports antimicrobial stewardship. Because mastitis is one of the leading causes of antibiotic use in dairy farming. Breeding animals with improved disease resistance can decrease antimicrobial use, lower treatment costs, reduce milk discard and contribute to global efforts to combat antimicrobial resistance within the One Health framework (Dhital *et al.*, 2026).

Beyond disease control, precision breeding improves animal welfare by reducing pain, chronic infections and premature culling while enhancing longevity and lifetime productivity. These health improvements translate into significant economic benefits through lower veterinary expenses, fewer replacement animals and improved farm profitability. Although precision breeding is also being explored in species such as dairy goats, where copy number variations (CNVs) and epigenetic mechanisms like DNA methylation are being investigated for disease resistance, practical implementation still requires further research. Moreover, genetic improvement should not be viewed as a standalone solution. The greatest success will come from integrating genomics with accurate phenotypic recording, sound management practices and continuous veterinary oversight. Ultimately, precision breeding is reshaping veterinary medicine by shifting the focus from treating mastitis after it occurs to preventing disease through informed genetic selection. This integrated approach promises healthier animals, reduced antibiotic dependence, improved farm sustainability and a more resilient dairy industry.



Future perspectives: Towards precision livestock health

Advances in animal genomics have transformed disease resistance breeding from a theoretical concept into a practical tool for dairy improvement. However, the future of precision breeding lies in integrating genomics with multi-omics technologies, artificial intelligence (AI) and digital livestock management systems. While genomic studies identify DNA variants associated with mastitis resistance, approaches such as transcriptomics, epigenomics, proteomics and metabolomics provide deeper insights into gene regulation, biological pathways and immune mechanisms. Integrating these datasets with genome-wide association studies and QTL mapping can improve the identification of reliable biomarkers for disease resistance. Similarly, AI and machine learning can combine genomic information with production records, health data, environmental measurements and

sensor-based monitoring to predict disease risk, optimise breeding decisions and develop herd-specific health strategies. As genotyping costs decline, national genomic breeding programmes and breed-specific reference populations will play an important role in expanding precision breeding, particularly in developing countries.

Emerging technologies such as gene editing, especially CRISPR-based approaches, offer potential opportunities for introducing favourable genetic variants; however, ethical, regulatory and economic challenges currently limit their application in food-producing animals. Therefore, genomic selection remains the most practical strategy for improving mastitis resistance in dairy populations.

Nevertheless, genetics alone cannot eliminate disease, as mastitis results from complex interactions among host genetics, pathogens, environment, nutrition and management practices. Future mastitis control will depend on integrating precision breeding with effective veterinary care, biosecurity, vaccination, nutrition and early disease detection. Veterinarians will increasingly work alongside geneticists, bioinformaticians and data scientists to translate genomic discoveries into practical herd health solutions, ultimately improving animal welfare, reducing antimicrobial use and promoting sustainable dairy production.

References:

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