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Genomic Selection for Disease-Resistant Livestock: From SNP Markers to Precision Breeding

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Abstract:

Rising global demand for animal protein, alongside concerns over infectious diseases, antimicrobial resistance, and environmental sustainability, is driving the need for proactive health strategies in livestock production. Traditional measures such as vaccination, therapeutics, and biosecurity remain important but are largely reactive. Genomic selection provides a sustainable alternative by identifying and propagating animals genetically predisposed to disease resistance. The development of high-density SNP panels and genome-wide association studies has shifted breeding from phenotype-based selection to genome-informed prediction. Genomic breeding values (GEBVs), estimated from thousands of markers, enhance selection accuracy, particularly for low-heritability health traits like mastitis, bovine respiratory disease, and reproductive disorders. Early-life genotyping enables prediction of disease susceptibility before clinical expression, reducing treatment costs, antimicrobial use, and welfare risks. However, disease resistance is polygenic and influenced by gene interactions and environmental factors. Modern precision breeding therefore integrates multi-omics layers transcriptomics, epigenomics, proteomics, and metabolomics with advanced statistical and machine learning approaches to capture functional regulatory networks underlying immune competence. This shift moves beyond individual SNP effects toward systems-level understanding of resilience. By combining genomic information with functional biology and predictive modelling, genomic selection is advancing livestock breeding toward precision-based development of resilient herds that sustain productivity, enhance health outcomes, and support long-term sustainability.

Keywords: Disease Resistance, Genomic Selection, Genomic Breeding Values (GEBVs), Multi-Omics Integration, Precision Breeding

Introduction:

Rising global demand for animal protein, increasing pressure on natural resources, antimicrobial resistance, and the persistent threat of infectious disease outbreaks have intensified the search for sustainable solutions in animal agriculture. Traditional disease control strategies like vaccination, therapeutics, biosecurity, and culling remain essential, yet they are reactive by nature. For decades, animal breeding relied on pedigree records and observable performance. With the molecular revolution, marker-assisted selection and genomic selection transformed breeding from phenotype-based estimation to DNA-informed prediction. Today, genomic selection is widely regarded as one of the greatest success stories in livestock improvement, enabling accelerated genetic gain and improved prediction accuracy for economically important traits. Increasingly, its focus is shifting towards functional traits such as disease resistance, resilience, and immune competence. Disease resistance is inherently complex. Most health traits are lowly heritable, polygenic, and strongly influenced by environment. Yet advances in high-density SNP genotyping, genome-wide association studies (GWAS), single-step genomic BLUP, next-generation sequencing (NGS), and multi-omics integration have made it possible to identify genomic regions associated with susceptibility and resistance to infectious diseases. The trajectory is clear: livestock breeding is evolving from selecting markers to designing precision-bred, disease-resistant populations.

From Pedigree to SNP Panels: The Molecular Foundations of Genomic Selection:

The introduction of genomic selection by Meuwissen and colleagues in 2001 marked a paradigm shift in animal breeding. Rather than focusing on a few major genes, genomic selection estimates breeding values using thousands of SNP markers distributed across the genome. These genomic breeding values (GEBVs) capture the cumulative effects of many loci, including those with small individual effects but substantial collective influence. In dairy cattle, genomic selection dramatically shortened generation intervals and increased rates of genetic gain. Estimates suggest improvements of 20–100% in genetic progress compared to traditional systems. Importantly, genomic selection enabled progress for traits that are difficult, expensive, or ethically challenging to measure such as disease incidence.

Health traits pose unique challenges. They often have low heritability and binary expression (sick vs. healthy). In a landmark study on Holstein cows, Naderi et al. investigated genomic breeding values for clinical mastitis, claw disorders, and infertility using both genomic BLUP (GBLUP) and random forest models. Their work demonstrated that prediction accuracy depends heavily on training set composition, disease incidence representation, and choice of response variable (de-regressed proofs vs. pre-corrected phenotypes). They also showed that single-step GBLUP (ssGBLUP) which integrates pedigree, phenotypic, and genomic data can further improve accuracy when phenotyped but non-genotyped animals are available. These findings underscore a critical principle: genomic selection is not merely about genotyping; it is about intelligent data integration. Disease resistance prediction improves when models incorporate

comprehensive phenotypic and pedigree information alongside genomic markers.

Identifying the Genetic Architecture of Disease Resistance:

Genome-wide association studies have been central to identifying loci associated with disease resistance. By scanning the genome for SNPs linked to disease phenotypes, GWAS reveals candidate genes and quantitative trait loci (QTLs) that contribute to susceptibility or resilience. In dairy cattle, genomic investigations identified positional candidate genes associated with clinical mastitis (e.g., GAS1, GPAT3, CYP2R1), laminitis (SPINK5, SLC26A2), and endometritis (FGF12). Such discoveries illustrate that disease resistance is rarely governed by a single gene; rather, it emerges from networks involving immune signalling, tissue integrity, metabolism, and stress response pathways. Similarly, genomic applications in beef cattle disease prevention have identified markers associated with resistance to bovine respiratory disease (BRD), Johne's disease, mastitis, and other infectious conditions. Heritability of resistance to BRD, for example, ranges from 0.07 to 0.29, indicating that although environmental factors are substantial, genetic variation exists and can be exploited through selection.

The identification of SNP markers linked to disease traits enables early-life selection. Calves can be genotyped shortly after birth, and their genetic susceptibility to specific diseases can be predicted before exposure. This proactive strategy reduces reliance on antibiotics, lowers treatment costs, and enhances animal welfare. However, GWAS also has limitations. Many identified variants explain only a small fraction of genetic variance, and population structure can confound associations. Thus, while SNP discovery is essential, it represents only the first step toward precision breeding.

Beyond SNPs: Integrating Multi-Omics for Precision Breeding:

Genomic selection based solely on SNP variation captures only part of the biological story. Phenotypic expression arises from complex interactions among genomic variation, epigenetic regulation, transcriptomic activity, proteomic interactions, and environmental influences. Modern breeding systems increasingly recognize the necessity of multi-omics integration. As highlighted in the review on precision livestock breeding, genomic selection must expand beyond DNA variation to include transcriptomic, epigenomic, proteomic, and metabolomic information. Epigenetic modifications such as DNA methylation and histone modifications influence gene expression without altering DNA sequence. Transcriptomic analyses identify genes upregulated during immune response. Proteomics and metabolomics reveal downstream functional effects.

The editorial on omics technologies emphasizes that integration of these data layers improves understanding of gene networks and enhances breeding accuracy. Multi-omics approaches allow construction of regulatory networks explaining how genetic variants influence immune function and disease resilience. For example, RNA sequencing has revealed breed-specific SNPs influencing adaptive immunity and tolerance to infectious diseases of the mammary gland. Such insights allow more targeted

genomic selection, distinguishing between animals that resist infection and those that tolerate disease without productivity loss. Therefore, precision breeding is not merely genomic selection it is population-personalized breeding informed by comprehensive biological data.

Genomic Selection in Practice: Beef and Dairy Disease Resistance:

The practical application of genomic tools in beef cattle disease prevention illustrates how theory translates into herd-level benefits. Genomic selection identifies animals with superior immune function, reducing disease incidence and antibiotic use. Early detection strategies, combined with genomic data, enable tailored vaccination programs and improved biosecurity planning. In mastitis selection, somatic cell score (SCS) is a moderately heritable trait that serves as an indirect indicator of resistance. Incorporating SCS into genomic evaluations enhances prediction reliability and reduces mastitis prevalence. Similarly, genomic evaluation of claw disorders and infertility in dairy cows has demonstrated that appropriate training set design significantly influences prediction accuracy.

Yet genomic selection is not without challenges. Breed heterogeneity, crossbreeding systems, and smaller reference populations can reduce prediction accuracy in beef cattle compared to dairy populations. Maintaining genetic diversity is another concern; overemphasis on specific alleles may reduce adaptability to emerging pathogens. Thus, sustainable implementation requires balanced breeding objectives, large and representative reference populations, and continuous model refinement.

Toward Precision Breeding and Population Personalization:

The future of disease-resistant livestock breeding lies in precision and personalization. Precision breeding integrates genomic selection, multi-omics data, and advanced statistical models to tailor selection decisions to specific populations. Population-specific regulatory networks must be analysed to account for breed differences, environmental interactions, and gene–gene interactions. Emerging technologies such as genome editing further expand possibilities. While genomic selection reshapes allele frequencies gradually, genome editing allows targeted modification of specific loci. Although ethical and regulatory considerations remain, these tools highlight the trajectory toward designing resilient livestock genomes. Moreover, functional genomics clarifies mechanisms underlying disease resistance, moving selection beyond statistical association toward biological understanding. Integration of immune gene expression profiles, methylation patterns, and pathogen-host interaction studies strengthens predictive models. In essence, livestock breeding is transitioning from marker discovery to systems biology-based precision management.

Conclusion:

Genomic selection for disease resistance represents one of the most promising pathways toward sustainable livestock production. From early SNP marker discovery to advanced multi-omics integration, the field has evolved rapidly. Studies on dairy cow disease traits have demonstrated how training set

composition and statistical methodology influence genomic prediction accuracy. Broader omics frameworks emphasize that genomic selection must integrate regulatory networks across biological layers. In beef cattle, genomic applications already contribute to disease prevention, herd resilience, and reduced antimicrobial reliance. The journey from SNP markers to precision breeding reflects a broader transformation in animal agriculture. Disease resistance is no longer an unpredictable outcome observed after outbreaks; it is increasingly a trait predicted, selected, and strategically incorporated into breeding programs. The genetically resilient herd of the future will not arise by chance. It will be built through data integration, systems biology, and responsible genomic innovation ensuring healthier animals, reduced environmental impact, improved profitability, and enhanced food security in a rapidly changing world.

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