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Genetics of disease resistance in livestock: Mechanisms, genomic tools and future perspectives

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Abstract
Livestock diseases remain one of the most significant constraints to sustainable animal production worldwide, particularly in developing countries where livestock forms the backbone of rural livelihoods. Infectious, parasitic and emerging diseases reduce productivity, compromise animal welfare, threaten public health and impose heavy economic losses. Conventional disease control strategies such as vaccination, chemotherapy and biosecurity, although essential, face biological, logistical and economic limitations. Consequently, increasing attention is being directed toward exploiting the inherent ability of animals to resist, tolerate or remain resilient to disease. Advances in quantitative genetics, genomics, immune-genomics and gene-editing technologies have transformed our understanding of host-pathogen interactions and opened new avenues for breeding healthier and more resilient livestock populations. This article comprehensively reviews the concepts of disease resistance, tolerance and resilience; the economic and welfare implications of livestock diseases; limitations of conventional control strategies; genetic and genomic approaches to disease resistance; emerging technologies such as CRISPR-Cas9; and future prospects within a One Health framework. Integrating genetic improvement with sound veterinary practices is essential for achieving sustainable, climate-resilient and economically viable livestock production systems.

Keywords: Livestock diseases, disease resistance, disease tolerance, disease resilience, genomics, sustainable livestock production

Introduction
The term “disease” literally denotes a state of “dis-ease,” reflecting a deviation from normal physiological structure and function (Bishop, 2020) [3]. In livestock, disease manifests as impaired growth, reduced milk and meat production, poor reproductive performance, compromised welfare and increased mortality. Infectious and parasitic diseases continue to pose major challenges to livestock production globally, with a disproportionately high impact in developing countries such as India, where livestock supports millions of small and marginal farmers (Perry & Grace, 2019) [9].
Diseases such as Foot and Mouth Disease (FMD), Brucellosis, Peste des Petits Ruminants (PPR), Lumpy Skin Disease (LSD), mastitis, tick-borne diseases and gastro-intestinal parasitism result in substantial economic losses. These losses include direct costs such as mortality, reduced productivity and treatment expenses, as well as indirect and intangible costs related to trade restrictions, culling, loss of genetic potential and reduced farmer confidence (Kramer & Conroy, 2020) [8]. Estimates suggest that disease-related losses may account for approximately 20% of livestock sector turnover in developed countries and up to 35-50% in developing regions (Perry & Grace, 2019) [9].
Beyond economic impacts, livestock diseases have important implications for public health and food security. Many livestock diseases are zoonotic, including Brucellosis, Tuberculosis and Anthrax, posing serious risks to human health and underscoring the importance of disease control within a One Health framework (FAO, 2022) [5]. In the context of climate change, intensification of production systems and increased global trade, disease risks are expected to escalate, necessitating innovative and sustainable approaches to animal health management.

Disease resistance, tolerance and resilience

Modern veterinary and animal breeding sciences distinguish clearly between disease resistance, tolerance and resilience, concepts that are central to understanding host responses to infection (Doeschl-Wilson *et al*., 2018) [4].

Disease resistance refers to the ability of an animal to prevent infection or to limit pathogen replication following exposure. Resistant animals either do not become infected or rapidly eliminate the pathogen through effective innate and adaptive immune responses, thereby reducing pathogen load and transmission within populations (Bishop, 2020) [3].

Disease tolerance describes the ability of the host to withstand infection with minimal adverse effects on health or performance, even when pathogen burden remains high. Tolerant animals experience reduced tissue damage and maintain physiological homeostasis despite infection (Doeschl-Wilson *et al*., 2018) [4].

Resilience refers to the capacity of an animal to maintain acceptable levels of productivity, such as milk yield, growth or reproductive performance, in the face of disease challenge. Resilient animals may become infected and even exhibit clinical signs but continue to perform relatively well under disease pressure (Windig & Calus, 2018) [13].

These strategies represent distinct biological responses: resistance targets the pathogen, tolerance minimizes host damage, and resilience emphasizes sustained productivity. Recognizing these differences is critical for designing breeding objectives and disease management strategies tailored to specific production systems.

Economic, welfare and production implications

Livestock diseases impose substantial economic burdens at farm, regional and national levels. Resistant animals generally require fewer treatments, exhibit lower mortality and reduce pathogen circulation within herds, resulting in direct cost savings (Azam *et al*., 2021) [1]. Tolerant and resilient animals contribute to production stability in endemic disease environments, which is particularly valuable in smallholder and low-input systems.

Improving disease resistance also has important implications for animal welfare, as healthier animals experience less pain, stress and suffering. From a public health perspective, reducing disease incidence in livestock lowers the risk of zoonotic transmission and decreases reliance on antimicrobial drugs, thereby mitigating antimicrobial resistance and reducing drug residues in animal products (Rauw, 2018) [10].

Conventional approaches to disease control and their limitations

Traditional disease control strategies rely on vaccination, biosecurity, chemotherapy and improved management practices. Vaccination remains a cornerstone of preventive veterinary medicine and has been highly effective for many diseases when properly implemented (FAO, 2022) [5]. Mass vaccination campaigns have demonstrated success in controlling diseases such as FMD, PPR and LSD.

However, vaccination-based disease control faces several limitations. Effective vaccines may not be available for all pathogens or strains, immunity may be short-lived, and cold-chain and logistical constraints often limit coverage in extensive and pastoral systems (Perry & Grace, 2019) [9]. Diseases such as mastitis and parasitic infestations depend heavily on management practices rather than vaccination.

Chemotherapeutic control, although effective in the short term, contributes to the growing global problem of antimicrobial resistance and environmental contamination. These limitations underscore the need for complementary, sustainable strategies, including genetic approaches to disease resistance.

Genetic basis of disease resistance

Natural variation in disease susceptibility exists across all livestock species. When animals are exposed to the same pathogen under similar environmental conditions, some individuals resist infection or tolerate pathogens better than others due to differences in immune system genes and regulatory pathways (Bishop, 2020) [3]. This genetic diversity forms the foundation for improving disease resistance through selective breeding.

Host genetics influence multiple aspects of immunity, including pathogen recognition, inflammatory responses, antigen presentation and tissue repair. Both innate and adaptive immune responses are under genetic control and exhibit heritable variation (Zhao *et al*., 2023) [14]. Indigenous and locally adapted breeds often display greater resistance or tolerance to endemic diseases, reflecting long-term natural selection and adaptation to local environments (FAO, 2022) [5].

Recent advances in Genome-Wide Association Studies (GWAS) have enabled the identification of specific genetic markers associated with resistance to infectious and parasitic diseases in cattle, sheep, goats and pigs. These markers are often linked to immune response pathways, making them valuable targets for genetic selection (Azam *et al*., 2021; Becker & Daetwyler, 2019) [1, 2].

Genomics and disease resistance: The new frontier

1. Genomic selection

Modern genomic technologies, including whole-genome sequencing, high-density genotyping and transcriptomics, are revolutionizing livestock breeding. Genomic selection allows identification of animals with superior immune competence and disease resistance at an early age, even before exposure to pathogens, thereby improving selection accuracy and accelerating genetic gain (Schaeffer & Gianola, 2022) [11].

Beyond breeding, genomic technologies support applied disease-management strategies such as tailored herd health plans, targeted vaccination programs and early detection of disease susceptibility. Integration of genomic data with precision livestock farming tools enables proactive disease management, reducing dependence on antibiotics and improving animal welfare and sustainability (Azam *et al*., 2021) [1].

2. Immuno-genomics and CRISPR/Cas9 technologies

Immuno-genomics integrates genomic and transcriptomic data to elucidate how host genes are expressed in response to infection. This approach has enhanced understanding of host-pathogen interactions and facilitated identification of key resistance and tolerance genes (Kong *et al*., 2022) [7].

Gene-editing technologies such as CRISPR/Cas9 represent a major scientific breakthrough in genetic disease control. CRISPR enables precise modification of genes associated with disease susceptibility, including insertion of beneficial genes such as “NRAMP1” linked to tuberculosis resistance, and deletion of host receptors exploited by pathogens, such as “CD163” involved in Porcine Reproductive and Respiratory Syndrome (PRRS) (Hetzel & Thorley, 2023) [6].

Notably, CRISPR-based approaches have been used to generate pigs completely resistant to Classical Swine Fever by targeting viral replication pathways, demonstrating the potential of gene editing where vaccination is limited or ineffective (Hetzel & Thorley, 2023) [6]. Despite its promise, ethical, regulatory and societal considerations remain significant challenges to widespread adoption.

Balancing disease resistance with productivity

A key challenge in breeding for disease resistance is balancing health traits with productivity. Immune responses require energy and nutrients, potentially diverting resources from growth or milk production (Rauw, 2018) [10]. Consequently, breeding programs increasingly emphasize resilience and tolerance alongside resistance to achieve balanced genetic improvement.

Integrating health, productivity, fertility and adaptability traits into breeding objectives is essential for long-term sustainability, particularly under changing climatic conditions and increasing disease pressure.

Field-level challenges and constraints

Despite rapid technological advances, practical implementation of genetic resistance strategies faces several challenges. Accurate phenotyping of disease traits under field conditions is difficult and costly, especially for diseases with low incidence or variable exposure. Limited infrastructure, lack of trained personnel and inadequate recording systems further constrain adoption of genomic tools in developing countries (Azam *et al*., 2021) [1].

Additionally, resistance to one pathogen may not confer protection against others, and pathogen evolution can overcome host resistance. Therefore, genetic approaches must be integrated with vaccination, biosecurity and management practices rather than used in isolation.

Future perspectives and integrated disease management

The future of livestock disease control lies in integrated strategies combining genetic improvement, vaccination, biosecurity, precision livestock farming and digital disease surveillance within a One Health framework (FAO, 2022) [5]. Climate-resilient and disease-tolerant livestock populations will be critical for ensuring food security and farmer resilience in the face of climate change and emerging diseases (Smith & Jones, 2024) [12].

Strengthening genetic resistance contributes to reduced drug use, improved animal welfare and lower environmental impact. Continued investment in research, capacity building and supportive policy frameworks will be essential to translate scientific advances into field-level impact.

Conclusion

Livestock diseases remain a major constraint to animal production, farmer livelihoods and public health. While conventional control measures such as vaccination and chemotherapy are indispensable, genetic resistance, tolerance and resilience offer sustainable, long-term complementary solutions. Advances in genomics, immune-genomics and gene-editing technologies have significantly enhanced our ability to breed healthier and more resilient livestock populations (Bishop, 2020; Hetzel & Thorley, 2023) [3, 6]. Integrating genetic improvement with sound veterinary practices, disease surveillance and One Health strategies will play a pivotal role in achieving sustainable, climate-resilient and economically viable livestock production systems.

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