

## Advances in Animal Disease Resistance Research: Discoveries of Genetic Markers for Disease Resistance in Cattle through GWAS

Jue Huang ✉, Xiaofang Lin

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

✉ Corresponding author email: [348601583@qq.com](mailto:348601583@qq.com)

Bioscience Evidence, 2024, Vol.14, No.1 doi: [10.5376/be.2024.14.0004](https://doi.org/10.5376/be.2024.14.0004)

Received: 05 Jan., 2024

Accepted: 08 Feb., 2024

Published: 20 Feb., 2024

**Copyright** © 2024 Huang and Lin, This is an open access article published under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

### Preferred citation for this article:

Huang J., and Lin X.F., 2024, Advances in animal disease resistance research: discoveries of genetic markers for disease resistance in cattle through GWAS, Bioscience Evidence, 14(1): 24-31 (doi: [10.5376/be.2024.14.0004](https://doi.org/10.5376/be.2024.14.0004))

**Abstract** This study summarizes the recent advancements in the application of GWAS technology in animal disease resistance research, emphasizing the importance and value of such studies. Initially, the genetic basis of animal disease resistance is introduced, with a focus on the relationship between the host immune system and disease resistance, as well as the genetic foundations of disease resistance. Subsequently, the principles, advantages, and historical development of GWAS technology in animal disease resistance research are elucidated. Following this, the application of GWAS technology in the discovery of genetic markers for disease resistance in cattle is discussed, including the research background, design methods, identified genetic markers for disease resistance, and their functional analysis. Finally, the significance of continued attention and support for animal disease resistance research is underscored, advocating for enhanced functional analysis of disease resistance-related genes, improved research data quality and sample sizes to advance animal disease resistance breeding.

**Keywords** GWAS technology; Animal disease resistance; Genetic markers; Cattle; Immune system

Animal diseases have always been one of the significant challenges faced by the livestock breeding industry. During the breeding process, various pathogens such as bacteria, viruses, parasites, and fungi can cause animals to contract various diseases, severely affecting the economic benefits of the breeding industry and animal welfare (Liu et al., 2023). To reduce the adverse effects of diseases on the breeding industry and improve the health level and immunity of animals, scientists have been striving to find methods to enhance animals' disease resistance.

Disease resistance, as a complex trait, is influenced by both genetic and environmental factors. Over the past few decades, through traditional genetics methods and molecular biology techniques, people have gained a preliminary understanding of the genetic basis of animal disease resistance (Bishop and Woolliams, 2014). However, with the rapid development of genomics and bio-informatics technologies, especially the application of genome-wide association studies (GWAS) technology, our understanding of animal disease resistance is undergoing revolutionary changes.

GWAS technology, as a genetic association study method based on large-scale single nucleotide polymorphisms (SNP), has achieved many successes in humans and model organisms. With GWAS technology, researchers can identify genetic variations related to complex traits across the entire genome (Li and Ritchie, 2021). In the study of animal disease resistance, GWAS technology provides researchers with a new perspective, allowing them to understand the genetic mechanisms of animal disease resistance more comprehensively and deeply.

This study aims to review the new progress in research on animal disease resistance, especially focusing on the discovery of genetic markers for cattle disease resistance using GWAS technology. This study hopes to provide new ideas and methods for the research of animal disease resistance, promote the healthy development of the livestock breeding industry, and provide humans with safer and more sustainable animal products.

## **1 The Genetic Basis of Animal Disease Resistance**

### **1.1 The genetic basis of resistance**

Resistance, as the ability of animals to counteract pathogen invasion, has a diverse genetic basis across different species (Ridha, 2023). Genetic diversity refers to the variety of genotypes and phenotypes present in animal populations, where some genotypes are resistant to diseases, while others are susceptible. This diversity provides a basis for natural selection within animal populations, allowing individuals with disease-resistant genotypes to have a better chance of surviving and reproducing under disease pressure, thereby promoting the transmission and accumulation of resistance genes.

### **1.2 The relationship between the host immune system and disease resistance**

The host immune system is an essential defense against pathogen invasion in animals, divided into innate and adaptive immunity. Innate immunity provides basic disease protection through nonspecific mechanisms, such as the phagocytic action of macrophages and the activity of natural killer cells. These mechanisms enable the host to quickly and effectively counter various types of pathogens. Adaptive immunity, on the other hand, offers more targeted disease protection through specific antigen recognition and immune memory mechanisms. Once exposed to a specific pathogen, the adaptive immune system produces specific antibodies or cell-mediated immune responses, enhancing resistance to that pathogen and forming immune memory, allowing for a quicker response upon re-exposure.

### **1.3 The association between immune genes and disease resistance**

Immune genes, which encode proteins related to the immune system, are closely associated with an animal's disease resistance due to their expression and functional variations. For example, in humans, the HLA gene family is an important component of the immune system, with different HLA genotypes associated with susceptibility or resistance to specific diseases. This association indicates that polymorphisms in immune genes play a key role in animal disease resistance. By regulating the degree and manner of the immune system's response, the polymorphism in immune genes affects the host's ability to resist various pathogens, thereby influencing the level of disease resistance in the entire population. Therefore, research on immune genes not only helps understand the mechanisms of disease resistance in animals but also provides an important genetic basis for breeding for disease resistance.

## **2 Application of GWAS Technology in the Study of Animal Disease Resistance**

### **2.1 Principles and advantages of GWAS technology**

Genome-wide association studies (GWAS) are a technique for exploring the relationship between genes and traits by comparing large-scale genotype and phenotype data. The principle behind GWAS is to identify genetic markers associated with specific traits by finding association signals between genotypes and phenotypes (Uffelmann et al., 2021). A key advantage of GWAS technology is its ability to comprehensively screen the genome for disease-related variations without relying on prior hypotheses.

The core of GWAS technology involves the analysis of large-scale single nucleotide polymorphisms (SNPs). Researchers first genotype the subjects to obtain individual genotype data at millions of SNP sites. Relevant phenotype data, such as the occurrence of a disease or its severity, are also collected. Statistical methods are then used to perform association analyses between these genotype and phenotype data, identifying SNP sites related to the traits of interest.

Another advantage of GWAS technology is its high throughput and comprehensiveness. Traditional genetics research often requires hypothesis-driven analyses targeting specific genes or pathways, whereas GWAS can comprehensively screen for trait-related variations across the entire genome without prior hypotheses. This makes GWAS a powerful tool for discovering new genes related to diseases (Figure 1).

### **2.2 The history and development of GWAS in animal genetics research**

GWAS technology was initially applied in human genetics. With the advancement of sequencing technology and the increase in data volume, it has also been widely applied in animal genetics research. Through GWAS,

researchers can rapidly identify genetic variations associated with animal disease resistance, laying the foundation for further functional studies and breeding applications.

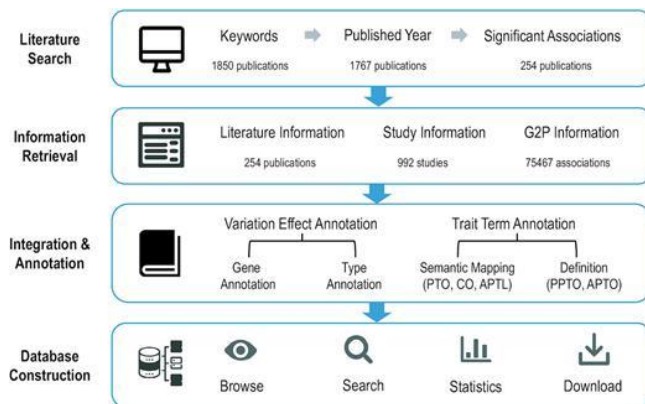


Figure 1 Data curation process adopted by GWAS Atlas (Tian et al., 2020)

The application history of GWAS in animal genetics research is relatively short but has progressed rapidly. With the continuous development of sequencing technology and the accumulation of data, GWAS has achieved a series of important results in livestock such as pigs, chickens, and cattle, as well as in experimental animals like mice.

The development of GWAS has also propelled progress in animal genetics research. Through GWAS technology, researchers can gain a more comprehensive understanding of the structure and function of animal genomes. It has revealed many genes and pathways related to disease resistance, providing important information for further functional studies and breeding applications.

### 3 Background and Significance of Research on Cattle Disease Resistance

#### 3.1 The threat of cattle diseases to the livestock industry

In the livestock industry, cattle diseases have always been a severe problem, causing significant economic losses (Andrews et al., 2008). Diseases can lead to decreased productivity, disease spread, and even death among cattle, posing a serious threat to the stability and development of the breeding industry. Some common cattle diseases include mastitis, rumen acidosis, pneumonia, etc. Therefore, improving cattle's disease resistance has become one of the keys to the development of the livestock industry.

#### 3.2 Genetic markers for cattle disease resistance discovered

In recent years, with the development of genetics and molecular biology technologies, an increasing number of genetic markers for cattle disease resistance have been discovered. These markers are usually gene polymorphism sites or genomic regions significantly associated with cattle's disease resistance performance. For example, single nucleotide polymorphisms (SNPs) related to resistance genes have been identified as genetic markers for cattle disease resistance. These markers can help breeders select cattle with stronger disease resistance, thereby reducing the incidence of diseases and improving breeding efficiency.

#### 3.3 Analysis of disease resistance genes and their relevance to diseases

For the discovered genetic markers of cattle disease resistance, researchers have conducted in-depth analyses to reveal the association between these markers and diseases. By performing functional analysis and expression regulation studies on these markers, a deeper understanding of the molecular mechanisms of cattle disease resistance can be achieved. At the same time, markers related to specific diseases have been identified, providing strong support for breeding against particular diseases. For instance, gene loci related to mastitis resistance have been discovered and proven to be significantly associated with resistance to mastitis, offering new insights into the control and prevention of mastitis.

In this research field, a thorough investigation of the functions and expression regulation mechanisms of disease resistance genes is crucial for uncovering the genetic mechanisms of cattle's disease resistance. By continuously

exploring and analyzing the genetic markers of cattle disease resistance, more precise and effective breeding strategies can be provided for the breeding industry. This, in turn, can enhance the disease resistance of cattle, reduce the incidence of diseases, and promote the healthy development of the livestock industry.

## 4 Application of GWAS in Livestock and Poultry Animals

### 4.1 Application of GWAS in cattle disease resistance research

Cattle are among the most important livestock animals, and their disease resistance is of great significance to the breeding industry. In recent years, with the development and widespread application of GWAS technology, significant progress has been made in the study of cattle disease resistance. The application of GWAS in cattle disease resistance research mainly includes two aspects: first, discovering genetic markers related to disease resistance; second, analyzing the functional relationship between these markers and disease resistance.

In cattle disease resistance research, researchers collect genotype and phenotype data from large cattle populations and use GWAS technology to analyze these data, identifying genetic markers associated with disease resistance. For example, in the study of common diseases such as mastitis, GWAS technology has been widely applied (Kurz et al., 2019). By comparing the genotype data of the diseased population and the control group, significant associations can be found between single nucleotide polymorphisms (SNPs) at certain gene loci and susceptibility to mastitis (Figure 2). These associated SNPs become potential genetic markers for disease resistance.

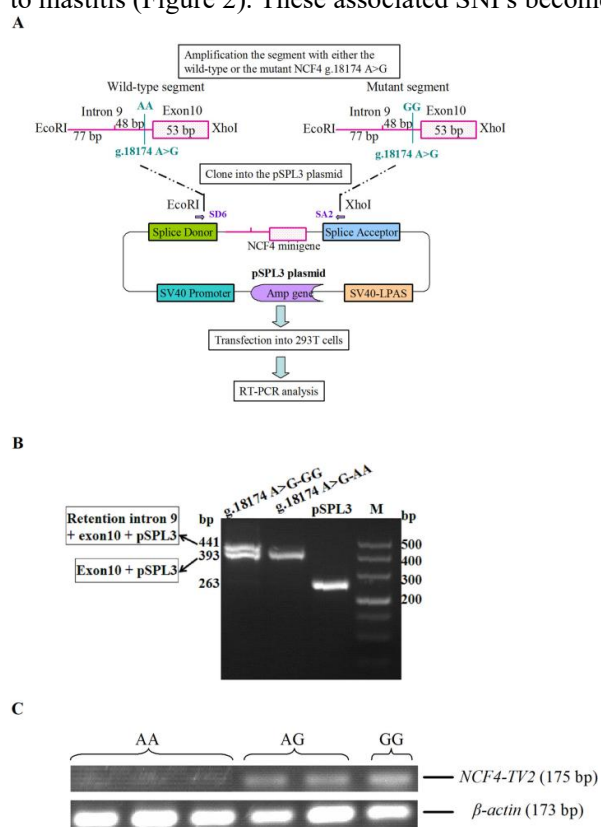


Figure 2 SNP g.18174 A>G induces aberrant NCF4-TV splicing (Ju et al., 2015)

Note: A: Schematic representation of the NCF4 mini-genes used in the functional splicing assay. The wild-type and mutant fragments contained 125 bp of intron 9 and 53 bp of exon 10; fragments harboring the A or G allele were separately cloned into the EcoRI and XhoI cloning sites of the pSPL3 vector; B: RT-PCR analysis of the NCF4 spliced transcripts on a 2% agarose gel. RT-PCR products were amplified from the total RNA of 293T cells transfected with the wild-type and mutant (g.18174 A>G) NCF4 mini-gene constructs. The size of the RT-PCR product (441 bp) corresponded to the amplified portion of intron 9 (77 bp), the retained portion of intron 9 (48 bp), the amplification of exon 10 (53 bp), and the pSPL3 control plasmid (263 bp). The size of the RT-PCR product (393 bp) corresponded to the amplified portion of intron 9 (77 bp), the amplification of exon 10 (53 bp), and the pSPL3 control plasmid (263 bp); C: Electrophoresis of RT-PCR products showing the presence and abundance of NCF4-TV transcript in bovine mammary samples with three NCF4 SNP g.18174 A>G genotypes. Expression of the NCF4-TV transcript is highest in mammary samples from GG animals, followed by those from AG and AA individuals

Beyond identifying genetic markers related to disease resistance, GWAS also facilitates the elucidation of the functional relationship between these markers and disease resistance. Through bioinformatics analysis and experimental validation, researchers can determine the functions and regulatory mechanisms of genes at these marker locations. For example, some markers may be located on immune-related genes, playing roles in regulating immune responses, thereby affecting the cattle's disease resistance capabilities. This functional analysis aids in deepening the understanding of the genetic mechanisms behind cattle's disease resistance, providing a scientific basis for further breeding strategies.

#### **4.2 Application of GWAS in pig disease resistance research**

Pigs are one of the vital livestock animals, and their disease resistance is crucial for the sustainable development of the breeding industry. In recent years, the application of GWAS technology in pig disease resistance research has matured, providing significant scientific support for the genetic mechanism analysis and breeding of pig disease resistance.

In pig disease resistance research, GWAS technology has been widely applied in the genetic analysis of various common diseases. For instance, diseases such as porcine circovirus (McKnite et al., 2014) and porcine reproductive and respiratory syndrome virus (PRRSV) (Walker et al., 2019) are significant afflictions in the pig breeding industry. By performing GWAS analysis on genotype and phenotype data from large pig populations, researchers can identify genetic markers associated with resistance to these diseases.

Besides identifying genetic markers related to disease resistance, GWAS also reveals the complex genetic mechanisms of disease resistance. Pig disease resistance is often influenced by multiple genes, and interactions among genes can also significantly impact resistance. GWAS analysis helps identify candidate genes related to disease resistance, further exploring their interactions and regulatory networks in the disease resistance process, aiding in unveiling the genetic mechanisms of pig disease resistance.

#### **4.3 Application of GWAS in chicken disease resistance research**

Chickens are important poultry animals, and their disease resistance is significant for the breeding industry. With the continuous development of GWAS technology, chicken disease resistance research has made notable progress. The application of GWAS technology in chicken disease resistance research mainly focuses on identifying genetic markers related to disease resistance and revealing their functions.

In chicken disease resistance research, researchers have identified a series of genetic markers related to disease resistance through GWAS analysis of genotype and phenotype data from large chicken populations (Deng et al., 2022). These markers can help breeders select individuals with better disease resistance for breeding, thereby improving the disease resistance capability of the entire chicken population.

Moreover, GWAS also reveals the genetic mechanisms behind chicken disease resistance. Through functional analysis and bioinformatics, researchers can determine the functions and regulatory mechanisms of genes related to disease resistance, further understanding the genetic basis of chicken disease resistance. This provides an important scientific basis for conducting precision breeding and enhancing chicken disease resistance.

### **5 Future Prospects in Animal Disease Resistance Research**

#### **5.1 The ongoing role of GWAS technology in animal disease resistance research**

As the fields of genetics and bioinformatics continue to evolve, GWAS technology will maintain its crucial role in research on animal disease resistance. GWAS can identify genetic markers associated with disease resistance, further unveiling the genetic underpinnings of animal disease resistance. By conducting in-depth studies on these markers, a better understanding of disease resistance mechanisms can be achieved, providing more genetic resources and strategies for livestock and poultry breeding. The continuous optimization and improvement of GWAS technology will make it more precise and efficient in animal disease resistance research. With the expansion of sample sizes, advancements in data analysis methods, and progress in genome sequencing technologies, GWAS will be able to analyze the genetic mechanisms of animal disease resistance more

comprehensively. This will offer more reliable disease resistance breeding strategies for the livestock industry (Figure 3).

No.	Trait	Chip	Animal	Method	Significant level	Result
1	Milk yield	50K	62,343 Holstein Friesian cows sired by 798 sires	Mixed linear models	$P < 0.001$	Identified 362 significant SNPs
2	Milk yield	50K	787 Holstein bulls	Single and Multiple trait regression analysis	$P < 0.001$	Identified 169 significant SNPs
3	Milk yield	50K	2,093 Chinese Holstein from the Holstein cattle farms in Bei**g, China	Single locus regression analysis	Bonferroni $P < 0.05$ level	Identified 105 significant SNPs including two SNPs located close to the <i>DGAT1</i> gene (160bp apart) and within the <i>GHR</i> gene, respectively
4	Milk yield	50K	1,039 bulls with pedigree information from Danish Jersey cattle	Regression analysis	Bonferroni correction $P < 1.5e^{-5}$	Identified 98 significant SNPs
5	Milk quality traits	50K	780 Holstein sons of 142 sires	Bayesian analysis (BayesA)	$P < 0.001$	Identified 73-461 significant SNPs (depending on trait)
6	Milk quality traits	50K	3,356 Japanese Black cattle from Yamagata Prefecture	GRAMMAR-CG method	Bonferroni correction $P < 1.28e^{-6}$ (5%); $P < 2.57e^{-7}$ (1%)	Identified 32 significant SNPs mainly in region of 49-55 Mb on BTA19 containing <i>FASN</i> gene
7	Milk quality traits	50K	1,905 Dutch Holstein Friesian cows from 398 commercial farms throughout the Netherlands	Two step single SNP association analysis using general linear model and animal model	$FDR < 0.05$	Identified 54 significant regions mainly on BTA14, 19, and 26 containing <i>ABCG2</i> , <i>PPARG-C1A</i> , <i>ACSS2</i> , <i>DGAT1</i> , <i>ACLY</i> , <i>SREBF1</i> , <i>STAT5A</i> , <i>GH</i> , <i>FASN</i> , <i>SCD1</i> and <i>AGPAT2</i>
8	Milk quality traits	50K	1,912 Holstein-Friesian cows from 398 commercial herds throughout the Netherlands	General linear model	$FDR < 0.01$	Identified several important regions mainly on BTA5, 6, 11 and 14
9	Fertility trait	10K	10 low-fertility and 10 high-fertility bulls of Pure Holstein	Regression analysis	$P < 0.01$	Identified 97 significant SNPs including one SNP in Integrin beta 5 gene
10	Fertility trait	50K	267 Holstein cows	Generalized linear mixed model	$P < 0.05$	Identified 27 significant SNPs
11	Fertility trait	50K	2,531 Danish and Swedish Holstein bulls	Mixed model analysis	Bonferroni correction $P < 2.16e^{-6}$ (BTA1); $P < 7.41e^{-5}$ (BTA28)	Identified 74 significant SNPs mainly on BTA 3, 5, 10, 13, 19, 20, and 24
12	Fertility trait	50K	2,062 Danish and Swedish Holstein bulls	Mixed model analysis	Bonferroni correction $P < 2.16e^{-6}$ (BTA1); $P < 7.41e^{-5}$ (BTA28)	Identified several important regions on BTA4, 6, 12, 18, 20, and 25
13	Growth trait	50K	150 sires representing 7 breeds including Angus, Charolais, Gelbvieh, Hereford, Limousin, Red Angus and Simmental	ANOVA test	$FDR < 0.01$	Identified 231 significant SNPs
14	Growth trait	10K; 50K	852 sires from 7 different pure breeds including Angus, Murray Grey, Shorthorn, Hereford, Brahman, Santa Gertrudis and Belmont Red	Regression analysis	$P < 0.001$	Identified 75 significant SNPs mainly on BTA3, 5, 7, and 8
15	Meat quality and carcass traits	50K	940 Beef cattle	Regression analysis	$P < 0.001$	Identified 87 significant SNPs for meat quality traits and 127 significant SNPs for carcass traits
16	Classical bovine spongiform encephalopathy (BSE)	50K	Holstein cows including 143 BSE affected (case) and 173 unaffected (control) collected in Southern England	Chi square test	$P < 5e^{-5}$	Identified one SNP on chromosome 1 at 25.15 Mb and another locus on chromosome 14
17	Bovine Tuberculosis (TB)	50K	14,013 Irish Holstein-Friesian cows	Regression analysis	Bonferroni correction $P < 1.21e^{-6}$	Identified 3 significant SNPs in a 65kb genomic region on BTA 22 containing <i>SLC6A6</i> gene
18	Bovine Paratuberculosis	50K	Italian and American Holstein cows including Group A with 590 cases vs 600 controls and Group B with 590 cases vs 117 controls	GRAMMAR-CG method	$P < 5e^{-5}$	Identified 6 significant SNPs on BTA 1, 12 and 15 and several other significant SNPs on BTA 1, 6, 7, 13, 16, 21, 23 and 25
19	Dominant White Phenotype and Bilateral Deafness	770K	Seven white and 79 spotted German Fleckvieh	General Linear Model (GLM)	$-\log_{10}P_{adj} = 254.4$ ; $-\log_{10}P_{Bonferroni-adjusted} = 248.6$	Identified a most significant region on BTA 22 containing <i>MTF</i> gene
20	Androstenedione	60K	987 pigs divergent for androstenedione concentration from a commercial Duroc-based sire line	QFAM test	$FDR$ of $q$ -value $\leq 0.05$	Identified 37 significant SNPs mainly on SSC1 and SSC8
21	skatole levels	60K	891 pigs from a composite Duroc sire line	QFAM test	$FDR$ of $q$ -value $\leq 0.05$	Identified 16 significant SNPs on SSC8: 0-6Mb
22	Boar taint and related sex steroids	60K	1,251 purebred Norwegian Landrace and 918 purebred Duroc male pigs	ANOVA test	$P < 0.05$	Identified g 28 regions related to boar taint
23	Boar taint and fertility traits	60K	1,533 purebred Landrace and 1,027 purebred Duroc male pigs	ANOVA test	$P < 0.05$	Identified 34 significant regions mainly on SSC1, 2, 3, 4, 7, 13, 14 and 15
24	Knobbed acrosome defect	60K	14 Finnish Yorkshire boars affected with KAD and 21 controls	Chi square test	Permutation correction $P < 0.0002$	Identified a significant 0.7 Mb region on SSC15 containing <i>STK17D</i> and <i>PHEW2</i> genes
25	Body Composition and Structural Soundness Traits	60K	412 Large White line pigs and 406 pigs from a Large White x Landrace cross	Bayes C	Bootstrap correction 0.001 $< P < 0.002$	Identified several important genes including <i>MC4R</i> , <i>IGF2</i> , <i>CHCHD3</i> , <i>EMMP2</i> and <i>HMOX4</i>
26	Fat area	60K	150 crossbred pigs [Pietrain x (German Large White x German Landrace)]	ANOVA test	$P < 1.0e^{-5}$	Identified 663 important genes
27	Brown coat colour	60K	Brown pigs (n = 121) vs non-brown-coated pigs (n = 745)	Chi square test	Permutation test	Identified <i>TYRP1</i> gene
33	Inherited Rickets	50K	Corriedale sheep including 17 affected and 3 carriers	IBD analysis	$P < 0.05$	Identified a 6Mb region on Chr6 including <i>DMP1</i> gene
34	Degenerative myelopathy (DM)	50K	Pembroke Welsh corgi including 38 DM-affected cases and 17 controls	Chi square test	$P < 0.01$	Identified a region of 28.91-29.67 Mb on CFA31 including <i>SOD1</i> gene
35	Canine atopic dermatitis (cAD)	20K	48 Golden Retrievers including 25 with atopic dermatitis and 23 healthy controls	Chi square test	$P < 0.001$	Identified 35 significant SNPs
36	Arrhythmogenic right ventricular cardiomyopathy (ARVC)	50K	65 ARVC-affected boxer dogs vs 100 controls	Chi square test	$P < 0.05$	Identified a region of CFA17: 32,256,760-32,398,077bp containing <i>STRN</i> gene
37	Intervertebral Disc Calcification	20K	Dachshund dogs including 48 cases and 46 controls	Chi square test	Permutation test using 100,000 permutations	Identified a region of CFA12: 36.8-38.6Mb with 36 significant SNPs
38	Fatness	3K	720 birds from two populations including $F_2$ Broiler x Fayoumi and $F_2$ Broiler x Leghorn	One-way ANOVA test	$P < 0.01$	Identified 39 significant SNPs mainly on GGA1, 2, 3, 4, 7, 8, 10, 12, 15 and 27
39	Body weight	60K	278 individuals from $F_2$ population crossed by Silky Fowl x White Plymouth Rock	Linear regression analyses	Bonferroni correction $P < 1.92e^{-6}$ (significant); $P < 3.85e^{-5}$ (suggestive)	Identified 9 significant SNPs on GGA4: 71.6-80.2 Mb including <i>LDB2</i> gene
40	Growth traits	60K	486 birds from $F_2$ population crossed by WRR x XH	Generalized least square analysis	Bonferroni correction $P < 4.08e^{-8}$ (highly significant); $P < 2.04e^{-6}$ (significant); $P < 4.08e^{-5}$ (suggestive)	Identified 68 significant SNPs and 23 genes for 18 growth traits
41	Egg production and quality	60K	385 White leghorn and 361 brown egg dwarf layers	Fisher's combined probability method	Bonferroni correction $P < 1.5e^{-6}$	Identified 8 significant SNPs and two genes including <i>GRE14</i> and <i>GALNT1</i>

Figure 3 Summary of reported GWAS on domestic animals (Zhang et al., 2012)

## 5.2 Prospects for the application of disease resistance genetic markers in livestock and poultry breeding

The application of disease resistance genetic markers holds broad prospects in livestock and poultry breeding. Using identified disease resistance genetic markers, selective breeding can quickly enhance the disease resistance of livestock and poultry. By breeding individuals with favorable genetic markers, it's possible to reduce disease incidence while maintaining other desirable traits, thus improving breeding efficiency (Kabir and Islam, 2021). The application of disease resistance genetic markers can also help overcome some challenges encountered in traditional breeding methods, such as genetic degeneration and loss of genetic diversity resulting from long-term selection. Targeted selection of disease resistance genetic markers can more effectively improve the overall health level of livestock and poultry, reduce breeding risks, and enhance the sustainable development of the breeding industry.

## 5.3 Application of disease resistance genetic markers in livestock and poultry health management

Beyond their use in breeding, disease resistance genetic markers can also play a crucial role in livestock and poultry health management. Molecular diagnostic techniques based on disease resistance genetic markers can help breeders timely detect the disease resistance levels of livestock and poultry, guiding health management and disease prevention efforts (Gavora, 2019). Monitoring and managing individuals at higher risk of disease can effectively reduce disease transmission and occurrence, ensuring the stable operation of the breeding industry. Disease resistance genetic markers can also offer new ideas and methods for disease prevention and treatment. By studying the association between disease resistance genetic markers and disease mechanisms, new vaccines and drugs can be developed, enhancing livestock and poultry's resistance to specific pathogens and further improving the production efficiency and economic benefits of the breeding industry.

In the future prospects of animal disease resistance research, the ongoing role of GWAS technology and the application prospects of disease resistance genetic markers in livestock and poultry breeding and health management will become significant driving forces for the development of the breeding industry. By fully leveraging the advantages of genetics and bioinformatics, strengthening interdisciplinary collaboration, and continuously optimizing technical methods and application strategies, it is hoped that more scientific and efficient solutions for the study and breeding of disease resistance in livestock and poultry can be provided, pushing the breeding industry towards a healthier and more sustainable development path.

## 6 Conclusion

GWAS technology, as a powerful genomics tool, plays a crucial role in the research of animal disease resistance. By analyzing vast amounts of genotype and phenotype data, GWAS can identify genetic markers related to animal disease resistance, offering new approaches and methods for breeding for disease resistance.

The significance and value of research on animal disease resistance are clear. Diseases are one of the major obstacles in the livestock industry, not only directly affecting the economic benefits of the industry but also posing potential threats to human health. Therefore, improving animals' disease resistance capabilities not only helps to enhance the productivity of the breeding industry but also ensures food safety and human health (Song and Yu, 2016).

Despite the significant progress made by GWAS technology in the study of animal disease resistance, there are still many challenges and unknowns (Ghosh et al., 2018). For example, since animal disease resistance is influenced by a variety of factors, including environment and breeding management, relying solely on genomic data may not fully explain the complexity of disease resistance. GWAS studies often face issues such as insufficient sample sizes and low-quality genotype data, which can affect the reliability and stability of the results.

Therefore, this study calls for continued attention and support for research on animal disease resistance. On the one hand, there is a need to strengthen the functional analysis of genes related to animal disease resistance, delving into their roles in immune regulation and disease resistance mechanisms. On the other hand, it is necessary to improve the data quality and sample sizes of disease resistance research, optimize research designs and analysis methods, to ensure the accuracy and reliability of the results. Only by doing so can GWAS

technology be better utilized to provide more effective scientific bases for breeding for disease resistance in animals, promoting the healthy and sustainable development of the breeding industry.

## References

- Andrews A.H., Blowey R.W., Boyd H., and Eddy R.G., Eds., 2008, *Bovine medicine: diseases and husbandry of cattle*, John Wiley & Sons.
- Bishop S.C., and Woolliams J.A., 2014, Genomics and disease resistance studies in livestock, *Livestock science*, 166: 190-198.  
<https://doi.org/10.1016/j.livsci.2014.04.034>  
PMid:26339300 PMCID:PMC4547482
- Deng Y.Y., Liu X., Wang T., He C.Q., Guo S.C., and Qu X.Y., 2022, Research progress of genome-wide association study (GWAS) in gene mapping of important economic traits in chicken, *China Poultry*, 44(9): 80-86.
- Gavara J.S., 2019, Genetic control of disease and disease resistance in poultry, In: *Manipulation of the Avian Genome*, CRC Press, pp. 231-241.  
<https://doi.org/10.1201/9780203748282-15>
- Ghosh M., Sharma N., Singh A.K., Gera M., Pulicherla K.K., and Jeong D.K., 2018, Transformation of animal genomics by next-generation sequencing technologies: a decade of challenges and their impact on genetic architecture, *Critical reviews in biotechnology*, 38(8): 1157-1175.  
<https://doi.org/10.1080/07388551.2018.1451819>  
PMid:29631431
- Ju Z.H., Wang C.F., Wang X.G., Yang C.H., Sun Y., Jiang Q., Wang F., Li M.J., Zhong J.F., and Huang J.M., 2015, Role of an SNP in alternative splicing of bovine NCF4 and mastitis susceptibility, *PLoS one*, 10(11): e0143705.  
<https://doi.org/10.1371/journal.pone.0143705>  
PMid:26600390 PMCID:PMC4658021
- Kabir S.L., and Islam S.S., 2021, Biotechnological applications in poultry farming, *Sustainable Agriculture Reviews 54: Animal Biotechnology for Livestock Production 1*: 233-271.  
[https://doi.org/10.1007/978-3-030-76529-3\\_8](https://doi.org/10.1007/978-3-030-76529-3_8)
- Kurz J.P., Yang Z., Weiss R.B., Wilson D.J., Rood K.A., Liu G.E., and Wang Z., 2019, A genome-wide association study for mastitis resistance in phenotypically well-characterized Holstein dairy cattle using a selective genotyping approach, *Immunogenetics*, 71(1): 35-47.  
<https://doi.org/10.1007/s00251-018-1088-9>  
PMid:30269158
- Li B., and Ritchie M.D., 2021, From GWAS to gene: transcriptome-wide association studies and other methods to functionally understand GWAS discoveries, *Frontiers in genetics*, 12: 713230.  
<https://doi.org/10.3389/fgene.2021.713230>  
PMid:34659337 PMCID:PMC8515949
- Liu Q., Zhang K., Guo Z.T., Wang L., Han S.W., Li D.P., Li J.X., Zhang J.Y., and Wang X.Z., 2023, Trained immunity: modern immune control strategies for infectious diseases of animals, *Chinese Journal of Veterinary Science*, 43(6): 1342-1349.
- McKnight A.M., Bundy J.W., Mural T.W., Tart J.K., Johnson T.P., Jobman E.E., Barnes S.Y., Qiu J.K., Peterson D.A., Harris S.P., Rothschild M.F., Galeota J.A., Johnson R.K., Kachman S.D., and Ciobanu D.C., 2014, Genomic analysis of the differential response to experimental infection with porcine circovirus 2b, *Animal genetics*, 45(2): 205-214.  
<https://doi.org/10.1111/age.12125>  
PMid:24444103
- Ridha S.N., 2023, Investigating the genetic basis of disease resistance in animal populations, *World Journal of Advanced Research and Reviews*, 18(1): 073-079.  
<https://doi.org/10.30574/wjarr.2023.18.1.0443>
- Song M.Y., and Yu Y., 2016, The main research fields and progress of livestock epigenetics, *China Animal Husbandry & Veterinary Medicine*, 43(10): 2701-2709.
- Tian D.M., Wang P., Tang B.X., Teng X.F., Li C.P., Liu X.N., Zou D., Song S.H., and Zhang Z., 2020, GWAS Atlas: a curated resource of genome-wide variant-trait associations in plants and animals, *Nucleic Acids Research*, 48(D1): D927-D932.  
<https://doi.org/10.1093/nar/gkz828>  
PMid:31566222 PMCID:PMC6943065
- Uffelmann E., Huang Q.Q., Munung N.S., De Vries J., Okada Y., Martin A.R., Martin H.C., Lappalainen T., and Posthuma D., 2021, Genome-wide association studies, *Nature Reviews Methods Primers*, 1(1): 59.  
<https://doi.org/10.1038/s43586-021-00056-9>
- Walker L.R., Jobman E.E., Sutton K.M., Wittler J.N., Johnson R.K., and Ciobanu D.C., 2019, Genome-wide association analysis for porcine reproductive and respiratory syndrome virus susceptibility traits in two genetic populations of pigs, *Journal of animal science*, 97(8): 3253-3261.  
<https://doi.org/10.1093/jas/skz184>  
PMid:31150538 PMCID:PMC6667235
- Zhang H., Wang Z.P., Wang S.Z., and Li H., 2012, Progress of genome wide association study in domestic animals, *Journal of animal science and biotechnology*, 3(26): 1-10.  
<https://doi.org/10.1186/2049-1891-3-26>