International Journal of Molecular Zoology 2024, Vol.14, No.1, 22-30
http://animalscipublisher.com/index.php/ijmz

Research Article Open Access

# Review of Porcine Disease Resistance Genetic Basis Research Based on GWAS

Xiao Zhu ✉ Xiaofang Lin
Hainan Institute of Tropical Agricultural Resources, Tropical Animal Center, Sanya, 572025, China
✉ Corresponding author email: 875931598@qq.com
International Journal of Molecular Zoology, 2024, Vol.14, No.1 doi: 10.5376/ijmz.2024.14.0004
Received: 04 Jan., 2024
Accepted: 13 Feb., 2024
Published: 25 Feb., 2024

**Preferred citation for this article**:
Zhu X., and Lin X.F., 2024, Review of porcine disease resistance genetic basis research based on GWAS, International Journal of Molecular Zoology, 14(1): 22-30 (doi: 10.5376/ijmz.2024.14.0004)

**Abstract** This study reviews the latest progress in research on the genetic basis of porcine disease resistance based on GWAS. This study first introduces the importance and challenges of porcine disease resistance to the breeding industry, as well as the history and current status of research on porcine disease resistance; Then elaborates on the role and advantages of GWAS technology in research on the genetic basis of disease resistance, including its characteristics of high-throughput, high-resolution and comprehensive detection of genetic variation; Furthermore, it focuses on the important results achieved by GWAS-based research in discovering genetic variations related to porcine disease resistance, and the impact of these variations on disease resistance. Potential influencing mechanisms of sex. This study also explores the limitations of GWAS in porcine disease resistance research, and looks at the direction and potential contributions of future research, with a view to providing more effective strategies and means for pig health management and the sustainable development of the breeding industry.
**Keywords** Porcine disease resistance; GWAS; Genetic basis; Genetic variation; Breeding industry

The importance of porcine disease resistance is self-evident, as it directly affects the stable development of the breeding industry. Pigs are one of the most important domestic animals for humans. They not only provide humans with abundant meat food, but are also an important model for experimental animals and biomedical research (Reiner, 2009). However, disease problems in pigs have always been an important problem plaguing the breeding industry. Diseases not only lead to reduced breeding efficiency, but also adversely affect animal welfare and the environment, and even pose a potential threat to human health. Over the past few decades, the livestock industry has been grappling with the challenge of disease by controlling the spread of disease through improved farming management, vaccinations and drug treatments. However, with the continuous expansion of breeding scale and increasing environmental pressure, disease problems are still very prominent. Therefore, studying porcine disease resistance has become one of the important issues facing the current breeding industry (Yang, 2004).

Past research has yielded some important discoveries about disease resistance in pigs, but its genetic basis is relatively poorly understood. In recent years, the rapid development of genomics technology has provided new opportunities for research on porcine disease resistance. Among them, research strategies based on genome -wide association study (GWAS) have attracted particular attention. As a high-throughput genetic analysis method, GWAS can simultaneously detect thousands of single nucleotide polymorphisms (SNPs) across the entire genome, thereby revealing the association between genotype and phenotype.

In the study of swine disease resistance, GWAS can be used to discover genetic variations related to disease resistance, thereby helping people to deeply understand the genetic basis of disease resistance (Niu et al., 2023). Compared with traditional genetic analysis methods, GWAS has higher resolution and wider coverage, and can discover genetic variants that have a small but statistically significant impact on disease resistance. GWAS can also provide more in-depth bioinformatics analysis, helping researchers understand the impact of these genetic variations on gene function and their mechanisms of action in disease resistance.

This study aims to review and summarize the latest progress in GWAS-based research on the genetic basis of disease resistance in pigs, explore the application advantages and limitations of GWAS in revealing the genetic

basis of disease resistance, and look forward to the direction and potential contributions of future research. By in-depth understanding of the genetic basis of disease resistance, this study can provide more effective strategies and means for pig health management and sustainable development of the breeding industry.

## 1 Genetic Basis of Pig Diseases

### 1.1 Diseases affecting pig health

Pigs are one of the most important agricultural livestock in the world and are widely raised for meat production. However, their health status is threatened by various diseases, which seriously affect the growth and development, production efficiency and stable development of the breeding industry of pigs. Among these diseases, swine fever, foot-and-mouth disease, porcine reproductive and respiratory syndrome virus (PRRSV), swine influenza, etc. are the most serious and common (Carr et al., 2018).

Swine fever is a highly contagious disease caused by swine fever virus and is mainly spread through contact infection or respiratory tract. After swine fever virus infection, the infection rate within the pig herd is extremely high, and the mortality rate is high, causing serious economic losses to the pig industry. Foot-and-mouth disease is also a highly contagious disease caused by the foot-and-mouth disease virus. It is characterized by causing foot-and-mouth disease lesions in pigs, including oral and hoof ulcers, which seriously affects the pigs' ability to eat and move, and even leads to large-scale deaths of pig herds. Porcine reproductive and respiratory syndrome virus (PRRSV) is a viral disease that seriously affects pig production performance and disease resistance (Figure 1). The virus mainly infects the immune system and respiratory system of pigs, causing frequent abortions, reduced sow productivity, pneumonia and other symptoms within the pig herd, seriously affecting the sustainable development of the pig industry. Swine flu is an acute respiratory infectious disease caused by influenza A virus infection. Its symptoms include high fever, difficulty breathing, cough, etc. Swine influenza not only affects the growth and development of pigs, but may also cause large-scale infections within pig herds, causing serious economic losses to the pig industry.

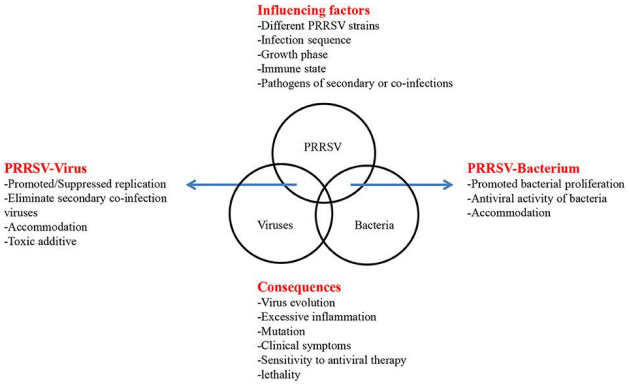


Figure 1 Influencing factors and consequences of PRRSV co-infection (Zhao et al., 2021)

The health of pigs is threatened by various diseases such as swine fever, foot-and-mouth disease, PRRSV, and swine flu. These diseases not only cause large-scale deaths and economic losses within the pig herd, but also seriously affect the stable development of the pig industry. Therefore, studying the genetic basis of disease resistance in pigs is crucial to improving pig health and the development of the breeding industry.

### 1.2 Overview of the genetic basis of disease resistance in pigs

Disease resistance in pigs is a complex genetic trait affected by multiple genes. These genes can affect the pig's immune system function, pathogen recognition and clearance capabilities, etc., thus determining the pig's infection and resistance levels to different diseases. Under the influence of genetic factors, disease resistance shows obvious differences between different strains and individuals, which reflects the importance of genetic background on disease resistance.

Studies have shown that immune-related genes are one of the important regulators of porcine disease resistance. For example, major histocompatibility complex (MHC) class genes play a key role in the immune response, and the proteins they encode are involved in the process of antigen presentation and recognition, thus affecting the pig's resistance to pathogens (Radwan et al., 2020). Pathogen receptor gene families, such as Toll-like receptor (TLR) family genes, also play an important role in disease resistance. The receptors encoded by these genes can recognize the specific molecular structure of pathogens and initiate corresponding immune responses, thus playing an important role in regulating porcine disease resistance. In addition to immune-related genes, some other genes have also been found to be closely related to disease resistance in pigs. For example, variations in some genes that regulate apoptosis (programmed cell death) and genes that regulate inflammatory responses may affect pigs' ability to clear pathogens, thereby affecting their disease resistance. The study also found that genes related to antioxidant capacity, cell signaling, etc. are also related to porcine disease resistance.

The genetic basis of porcine disease resistance is a complex system of multi-gene regulation. Interactions and polymorphisms between different genes lead to the existence of rich disease resistance phenotypes in pig herds. In-depth study of the genetic basis of pigs and the discovery of key genes and genetic variations related to disease resistance are of great significance for the selection of pig breeds with strong disease resistance and excellent production performance.

### 1.3 The mechanism of influence of genetic variation on disease resistance

SNPs present in the genome that determine an individual's level of infection and resistance to a specific disease. Studies have shown that porcine disease resistance is related to genetic variations in multiple genes involved in the regulation of the immune system, pathogen recognition and clearance, etc. By analyzing genetic variation in pigs, key genes and SNPs related to disease resistance can be discovered, providing important information for the selection of disease-resistant pig breeds.

Studies have shown that immune-related genes (such as MHC genes), pathogen receptor genes (such as TLR family genes), and cytokine and chemokine genes play an important role in disease resistance in pigs. Different alleles or SNPs of these genes will affect the pig's ability to recognize and eliminate pathogens, thereby affecting its disease resistance. The study also found that some genes related to apoptosis, inflammatory response, etc. are also closely related to porcine disease resistance.

Porcine disease resistance is regulated by complex genetic factors, among which genetic variation plays a key role in the formation of individual disease resistance. In-depth study of the genetic basis of pigs is of great significance for breeding pig breeds with high disease resistance and improving breeding efficiency.

## 2 Application of GWAS in Porcine Disease Resistance Research

### 2.1 Basic principles and methods of GWAS

GWAS (Genome-wide association analysis) is a powerful method designed to unravel the correlation between genetic variation and complex traits. The basic principle is to discover genetic variations related to target traits by comparing genotypic differences between individuals with specific traits and normal control individuals in large-scale samples (Cano-Gamez and Trynka, 2020). The GWAS method includes multiple key steps, including sample recruitment, genotype determination, and data analysis.

Sample recruitment for GWAS is the first step in research, and a sufficient number and diversity of samples need to be collected to ensure the reliability and representativeness of the results. These samples typically include individuals with the target trait and normal control individuals to allow for comparative analysis. Genotype determination is one of the key steps in GWAS (Buniello et al., 2019). Researchers used modern high-throughput sequencing technology to conduct genome-wide analysis of the DNA in the samples to determine the SNP distribution of each individual across the entire genome (Figure 2). These SNPs serve as markers of genetic variation for subsequent association analysis. Data analysis is one of the core steps of GWAS. At this stage, researchers conduct association analysis between the collected SNP data and the target traits to determine which SNPs are significantly associated with the target traits. Usually, statistical methods such as linear regression or

logistic regression are used to evaluate the degree of association between SNPs and traits and correct for other potential influencing factors, such as race, gender, etc. By performing association analysis of SNPs across the entire genome, researchers can identify genetic variants associated with target traits, thereby revealing their underlying mechanisms in the occurrence and expression of the trait. These findings not only help to understand the genetic basis of complex traits, but also provide important guidance for disease prevention, diagnosis and treatment.

| Trait | Chr | Range of SNP (Mb) | Number of SNP | Top SNP position (bp) | n_miss | Allele | Allele frequency | Candidate gene | P |
|---|---|---|---|---|---|---|---|---|---|
| FI_L12 | 1 | 91.98–92.02 | 1 | 92,003,527 | 22 | A/T | 0.028 | | 1.88E-08 |
| FI_L12 | 1 | 94.76–94.80 | 1 | 94,779,648 | 22 | A/T | 0.012 | | 9.18E-08 |
| FI_L12 | 1 | 193.57–193.61 | 1 | 193,593,040 | 22 | A/G | 0.021 | | 2.10E-07 |
| FI_L12 | 5 | 60.57–60.61 | 1 | 60,589,650 | 23 | T/G | 0.045 | ETV6 | 2.02E-07 |
| FI_L12 | 11 | 22.40–22.44 | 1 | 22,424,991 | 19 | G/A | 0.042 | | 1.45E-07 |
| FI_L12 | 12 | 24.86–24.90 | 1 | 24,879,958 | 13 | G/T | 0.027 | HOXB7/HOXB8/HOXB9/ MIR196A-1 | 2.04E-11 |
| FI_L12 | 14 | 4.88–4.92 | 1 | 4,904,707 | 10 | C/A | 0.011 | | 2.73E-09 |
| FI_L12 | 14 | 97.23–97.27 | 2 | 97,251,403 | 19 | A/G | 0.026 | | 6.52E-08 |
| FI_L23 | 7 | 46.65–46.69 | 1 | 46,665,496 | 6 | G/A | 0.017 | GSTA4/RF00100/ICK | 2.24E-09 |
| FI_L34 | 2 | 135.91–135.95 | 1 | 135,932,694 | 5 | C/A | 0.022 | | 8.09E-10 |
| FI_L34 | 5 | 55.26–55.30 | 1 | 55,275,110 | 7 | T/A | 0.013 | | 6.38E-15 |
| FI_L34 | 10 | 65.05–65.09 | 1 | 65,071,338 | 2 | C/A | 0.017 | FBH1 | 3.87E-10 |
| FI_L34 | 11 | 9.67–9.71 | 1 | 9,688,680 | 8 | T/C | 0.022 | | 2.35E-08 |
| FI_L34 | 11 | 45.04–45.08 | 1 | 45,058,333 | 5 | G/T | 0.03 | BORA/DIS3/PIBF1 | 5.34E-08 |
| FI_L34 | 14 | 59.76–59.80 | 1 | 59,780,380 | 9 | C/T | 0.022 | | 1.83E-08 |
| FI_L34 | 16 | 60.14–60.18 | 1 | 60,161,199 | 9 | C/T | 0.022 | | 2.30E-08 |
| FI_L34 | 17 | 63.80–63.84 | 1 | 63,824,477 | 6 | C/T | 0.017 | | 3.25E-11 |
| FI_Y12 | 1 | 162.16–162.20 | 2 | 162,179,241 | 6 | C/T | 0.016 | ALPK2 | 1.91E-08 |
| FI_Y12 | 1 | 162.20–162.24 | 3 | 162,222,395 | 0 | A/G | 0.016 | ALPK2 | 2.22E-08 |
| FI_Y12 | 1 | 162.36–162.40 | 1 | 162,375,129 | 0 | G/A | 0.016 | NEDD4L | 2.22E-08 |
| FI_Y12 | 1 | 162.39–162.43 | 2 | 162,406,916 | 18 | G/A | 0.015 | RF00100 | 2.61E-08 |
| FI_Y12 | 1 | 162.44–162.48 | 1 | 162,458,116 | 4 | G/A | 0.016 | | 2.45E-08 |
| FI_Y12 | 1 | 162.51–162.55 | 1 | 162,528,642 | 1 | T/G | 0.016 | | 2.29E-08 |
| FI_Y12 | 1 | 162.55–162.59 | 1 | 162,569,732 | 17 | G/A | 0.015 | | 2.12E-08 |
| FI_Y12 | 1 | 162.90–162.94 | 1 | 162,919,642 | 1 | T/C | 0.016 | ATP8B1 | 2.23E-08 |
| **FI_Y12** | **2** | **136.11–136.15** | **1** | **136,127,645** | **1** | **A/G** | **0.012** | | **6.04E-11** |
| FI_Y12 | 3 | 106.83–106.87 | 3 | 106,849,597 | 10 | G/A | 0.011 | TTC27 | 1.89E-11 |
| FI_Y12 | 3 | 107.26–107.30 | 4 | 107,281,336 | 0 | G/A | 0.011 | BIRC6 | 2.13E-11 |
| FI_Y12 | 3 | 109.38–109.42 | 3 | 109,400,403 | 2 | T/C | 0.012 | | 2.00E-11 |
| FI_Y12 | 4 | 111.53–111.57 | 1 | 111,553,999 | 12 | C/T | 0.013 | | 1.09E-09 |
| FI_Y12 | 4 | 38.34–38.38 | 1 | 38,362,147 | 23 | T/G | 0.013 | KCNS2 | 3.68E-08 |
| **FI_Y12** | **5** | **103.41–103.45** | **1** | **103,426,443** | **9** | **A/C** | **0.013** | | **5.22E-16** |
| FI_Y12 | 5 | 55.47–55.51 | 1 | 55,486,024 | 13 | A/C | 0.013 | RF00026 | 1.11E-09 |
| **FI_Y12** | **6** | **27.78–27.82** | **4 (including 27,811,226)** | **27,804,546** | **0** | **T/C** | **0.022** | **HSF4/B3GNT9/TRADD/ NOL3/KIAA0895L/ C16orf70** | **2.56E-08** |
| FI_Y12 | 7 | 2.04–2.08 | 9 | 2,061,622 | 0 | A/G | 0.012 | SLC22A23 | 3.32E-10 |
| FI_Y12 | 7 | 2.14–2.18 | 3 | 2,161,296 | 3 | T/A | 0.016 | | 6.46E-11 |
| FI_Y12 | 7 | 2.20–2.24 | 1 | 2,216,046 | 4 | G/A | 0.02 | | 6.08E-08 |
| FI_Y12 | 7 | 2.20–2.24 | 13 | 2,221,168 | 0 | G/A | 0.014 | PXDC1 | 9.60E-09 |
| FI_Y12 | 7 | 2.27–2.31 | 4 | 2,289,143 | 18 | G/C | 0.024 | FAM50B | 1.55E-07 |
| FI_Y12 | 7 | 2.54–2.58 | 1 | 2,557,543 | 3 | T/C | 0.014 | | 9.93E-09 |
| FI_Y12 | 7 | 2.72–2.76 | 1 | 2,737,334 | 2 | A/G | 0.014 | | 9.94E-09 |
| FI_Y12 | 7 | 2.77–2.81 | 2 | 2,790,067 | 21 | G/A | 0.015 | | 1.33E-08 |
| FI_Y12 | 7 | 2.93–2.97 | 2 | 2,946,286 | 7 | C/A | 0.014 | CDYL | 1.12E-08 |
| FI_Y12 | 7 | 2.96–3.00 | 2 | 2,984,884 | 6 | G/A | 0.014 | PPP1R3G/RPP40 | 1.07E-08 |
| FI_Y12 | 7 | 3.09–3.13 | 1 | 3,113,873 | 1 | A/G | 0.014 | | 9.62E-09 |
| FI_Y12 | 7 | 3.25–3.29 | 2 | 3,273,858 | 5 | G/A | 0.014 | FARS2 | 9.82E-09 |
| FI_Y12 | 7 | 3.34–3.38 | 1 | 3,358,876 | 2 | G/T | 0.014 | FARS2 | 2.36E-08 |
| FI_Y12 | 7 | 4.34–4.38 | 1 | 4,362,436 | 0 | C/G | 0.016 | | 7.90E-08 |
| FI_Y12 | 7 | 4.44–4.48 | 3 | 4,463,468 | 12 | T/C | 0.025 | | 7.57E-08 |
| FI_Y12 | 7 | 4.83–4.87 | 1 | 4,847,230 | 1 | T/A | 0.016 | DSP | 8.17E-08 |
| FI_Y12 | 7 | 126.22–126.26 | 1 | 126,240,205 | 0 | A/G | 0.012 | | 7.36E-10 |
| FI_Y12 | 7 | 133.35–133.39 | 1 | 133,368,593 | 0 | A/G | 0.498 | | 3.00E-20 |
| FI_Y12 | 8 | 144.75–144.79 | 1 | 144,770,928 | 21 | T/C | 0.018 | | 9.09E-08 |
| **FI_Y12** | **10** | **3.59–3.63** | **2** | **3,609,429** | **24** | **C/T** | **0.031** | | **3.40E-12** |
| FI_Y12 | 10 | 43.64–43.68 | 1 | 43,663,373 | 17 | C/A | 0.017 | ST8SIA6 | 4.56E-08 |
| FI_Y12 | 11 | 73.33–73.37 | 1 | 73,353,457 | 9 | C/A | 0.017 | | 1.26E-07 |
| FI_Y12 | 12 | 2.80–2.84 | 1 | 2,824,213 | 15 | A/G | 0.026 | RBFOX3 | 4.59E-08 |
| FI_Y12 | 13 | 209.06–209.10 | 3 | 209,081,546 | 1 | A/C | 0.011 | | 5.01E-11 |
| FI_Y12 | 14 | 15.45–15.49 | 2 | 15,472,751 | 1 | A/G | 0.018 | GLRA3 | 1.14E-09 |
| **FI_Y12** | **14** | **15.18–15.22** | **1** | **15,199,253** | **3** | **A/T** | **0.024** | | **8.60E-09** |
| FI_Y12 | 15 | 4.07–4.11 | 2 | 4,094,589 | 0 | A/G | 0.026 | ORC4 | 5.84E-09 |
| FI_Y12 | 15 | 4.10–4.14 | 1 | 4,121,092 | 4 | A/G | 0.02 | | 2.40E-07 |
| FI_Y12 | 15 | 4.47–4.51 | 1 | 4,487,592 | 24 | C/G | 0.02 | | 2.49E-08 |
| FI_Y12 | 15 | 4.88–4.92 | 1 | 4,895,899 | 0 | T/A | 0.022 | | 6.28E-08 |
| FI_Y12 | 15 | 5.22–5.26 | 6 | 5,235,766 | 6 | G/A | 0.023 | | 7.35E-08 |
| FI_Y12 | 15 | 134.32–134.36 | 1 | 134,340,038 | 21 | C/A | 0.013 | | 2.74E-10 |
| **FI_Y12** | **15** | **150.28–150.32** | **1** | **150,297,519** | **6** | **T/C** | **0.019** | | **4.32E-13** |
| FI_Y12 | 16 | 65.60–65.64 | 1 | 65,618,538 | 14 | A/G | 0.023 | LSM11/THG1L | 2.26E-07 |
| FI_Y12 | 17 | 16.52–16.56 | 3 | 16,543,976 | 20 | G/T | 0.015 | | 3.76E-09 |
| FI_Y12 | 17 | 63.20–63.24 | 1 | 63,224,611 | 18 | T/G | 0.058 | | 6.51E-08 |
| FI_Y12 | 18 | 0.05–0.09 | 1 | 65,826 | 2 | C/T | 0.038 | | 1.92E-07 |
| FI_Y23 | 4 | 81.79–81.83 | 1 | 81,813,944 | 18 | T/G | 0.011 | NME7 | 6.99E-10 |
| FI_Y23 | 4 | 73.90–73.94 | 1 | 73,919,093 | 14 | A/C | 0.011 | TOX | 3.35E-08 |
| FI_Y23 | 4 | 127.80–127.84 | 1 | 127,815,487 | 9 | C/A | 0.013 | | 1.51E-07 |
| FI_Y23 | 6 | 114.17–114.21 | 1 | 114,189,381 | 23 | T/C | 0.011 | | 1.38E-07 |
| FI_Y23 | 7 | 46.65–46.69 | 1 | 46,665,504 | 22 | G/T | 0.014 | GSTA4/RF00100/ICK | 8.67E-10 |
| FI_Y23 | 9 | 46.50–46.54 | 1 | 46,524,685 | 16 | G/T | 0.018 | CBL/MCAM/RNF26 | 8.49E-08 |
| FI_Y23 | 11 | 65.25–65.29 | 1 | 65,267,206 | 8 | C/A | 0.011 | DNAJC3 | 5.23E-09 |
| FI_Y23 | 15 | 123.50–123.54 | 1 | 123,522,220 | 18 | G/A | 0.044 | EPHA4 | 3.29E-09 |
| FI_Y34 | 2 | 62.61–62.65 | 1 | 62,633,629 | 3 | T/C | 0.498 | SLC1A6/LOC100736663/ LOC100523890 | 1.00E-07 |
| FI_Y34 | 7 | 133.40–133.44 | 5 | 133,416,643 | 1 | T/C | 0.498 | | 9.88E-08 |
| FI_Y34 | 9 | 33.26–33.30 | 1 | 33,275,594 | 3 | T/C | 0.041 | MMP20 | 3.58E-08 |
| FI_Y34 | 11 | 0.60–0.64 | 1 | 616,632 | 20 | C/A | 0.013 | ZMYM5 | 1.89E-08 |
| FI_Y34 | 15 | 35.81–35.85 | 1 | 35,828,705 | 1 | G/A | 0.498 | | 9.89E-08 |

*Chr, chromosome; range of SNP, range of significant chromosome region; number of SNP, number of SNP involved; n_miss, number of missing values of the SNP; alleles, alleles of top SNP.*
*The bolded text shown that the common SNPs detected in both GBS data and imputed WGS data.*

Figure 2 The GWAS results at genome significant level for FI of different parities using GBS data in pigs (Wu et al., 2019)

As a high-throughput genetic analysis method, GWAS has important application prospects in revealing the correlation between genetic variation and complex traits. Through the step-by-step steps of sample recruitment, genotyping, and data analysis, GWAS provides researchers with a powerful tool to study the genetic basis of complex traits.

### 2.2 Application cases of GWAS in research on the genetic basis of disease resistance in pigs

In recent years, GWAS has been widely used in research on the genetic basis of porcine disease resistance, providing new perspectives and methods for disease prevention and control and breeding and selection. Take swine fever as an example. This is an acute infectious disease caused by swine fever virus, which poses a serious threat to pig production. Through GWAS technology, researchers conducted genotype analysis on large-scale pig herds and discovered some genetic variations related to swine fever resistance (Kumar et al., 2023). These variants may be located in immune-related genes, such as those encoding specific immune cell surface receptors or immune regulatory factors. Through these correlation studies, researchers can initially determine which genes are associated with resistance in pigs. In addition to swine fever, GWAS has also played an important role in the study of other important diseases such as Streptococcus suis arthritis. Streptococcal arthritis of suis is a disease caused by Streptococcus bacteria that often causes arthritis and other serious health problems in pigs. Through GWAS technology, researchers discovered some genes and SNPs related to pig resistance to streptococcal infection (Figure 3). These genes may be closely related to the pig's immune system function or other related biological processes, thereby affecting the pig's infection and resistance to streptococci. GWAS also plays an important role in the study of diseases such as porcine circovirus (McKnite et al., 2014). Porcine circovirus is a virus that causes infectious diarrhea in pigs, seriously affecting the growth and production performance of pigs. Through GWAS analysis, the researchers discovered some genes and SNPs associated with pig resistance to viral infection. These findings provide important theoretical basis for further revealing disease resistance mechanisms and breeding selection.

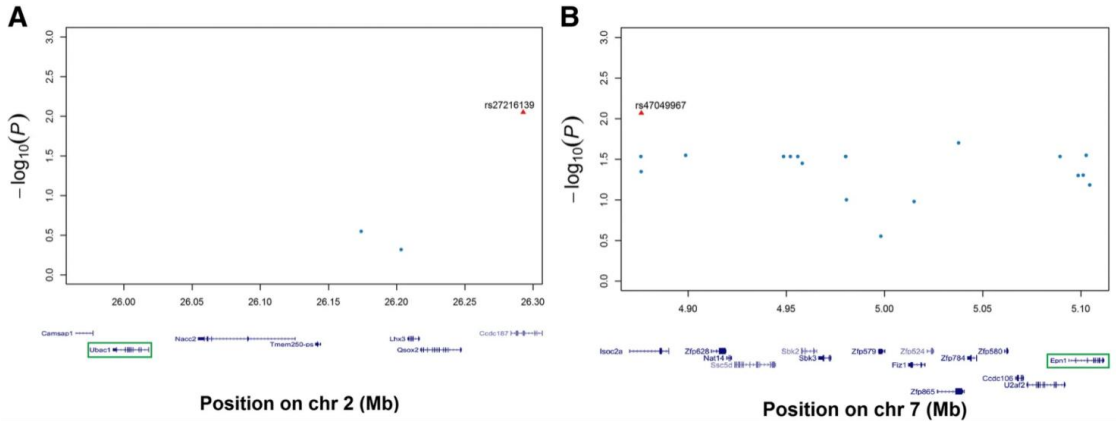


Figure 3 Enlarged Manhattan plots of interest SNPs and related DEGs (Ma et al., 2018)

The application cases of GWAS in the study of the genetic basis of porcine disease resistance are rich and diverse, providing researchers with important clues to deeply understand the genetic basis of porcine disease resistance. These research results provide new ideas and strategies for future disease prevention and control and breeding and selection.

### 2.3 Limitations and challenges of GWAS in identifying genetic genes for disease resistance in pigs

Although GWAS has achieved certain results in the study of porcine disease resistance genetic genes, there are still some limitations and challenges. First, since GWAS is a correlational study, the associations found do not represent causal relationships and require further functional studies to verify. Secondly, due to the relatively low genetic diversity of pig populations, GWAS has certain limitations in identifying genes related to disease resistance and may miss some important variations. The pathogenesis of pig diseases is complex and affected by environmental factors, which also increases the difficulty of GWAS research.

As a high-throughput genetic research method, GWAS has played an important role in the identification of porcine disease resistance genetic genes, but its limitations and challenges also require in depth research and solutions to better understand porcine disease resistance. genetic basis and provide more effective strategies and methods for disease prevention and control and breeding and selection.

## 3 Identification and Functional Study of Porcine Disease Resistance Genetic Genes

### 3.1 Prominent disease resistance-related genes and SNPs

Studies have shown that porcine disease resistance is related to the complex interactions of multiple genes, among which some genes and single nucleotide polymorphisms (SNPs) are particularly prominent (Geraci et al., 2019). For example, studies on swine fever resistance have found that some specific alleles in the SLA class I and class II gene families are closely related to disease resistance. Regarding resistance to Streptococcus suis infection, studies have found that some SNPs in the Toll-like receptor (TLR) gene family are closely related to disease resistance.

The study also found that genes IGF2, PIGF, SLA, CD163, etc. are also considered to be key factors in resistance to heat and respiratory diseases in pigs. The identification of these genes and SNPs provides important clues for further research on the molecular mechanisms of disease resistance.

### 3.2 Gene functions and their mechanisms in disease resistance

For prominent disease resistance-related genes and SNPs, researchers are in-depth exploration of their exact mechanisms of action in disease resistance. Through bioinformatics, molecular biology and other technical means, scientists have gradually revealed the functions of these genes in immune regulation, pathogen recognition, inflammatory response and other aspects.

For example, for the SLA gene, studies have found that the molecule it encodes plays an important role in pathogen recognition and antigen presentation. The TLR gene family is involved in the immune signaling process after pathogen recognition. These functional studies will help people gain a deeper understanding of the molecular mechanisms of porcine disease resistance and provide a theoretical basis for breeding disease-resistant pigs.

### 3.3 Application of gene editing and other technologies in the study of disease resistance gene functions

With the development of gene editing technologies, such as the widespread application of tools such as CRISPR/Cas9, researchers have begun to explore the application of these technologies in the functional study of disease resistance genes. By targeting specific gene edits or modifications, scientists can simulate the effects of different genotypes and gain a clearer understanding of the gene's role in disease resistance.

The application of gene editing technology can not only verify candidate genes previously discovered in GWAS and other studies, but also enable in-depth exploration of the specific functions of these genes in disease resistance. Gene editing also provides new methods and ideas for disease resistance breeding, such as improving pig resistance to specific pathogens through precise gene editing.

The identification and functional study of disease resistance-related genes provide important scientific support for researchers to deeply understand the immune mechanism of pigs, improve the disease resistance of pigs, and breed disease-resistant pigs. In the future, with the continuous development of technology and in-depth research, people are expected to make better use of gene editing and other technologies to solve challenges in the field of porcine disease resistance and make greater contributions to the sustainable development of the breeding industry.

## 4 Application Prospects of GWAS Research in Improving Porcine Disease Resistance

### 4.1 The importance and achievements of GWAS in research on the genetic basis of disease resistance in pigs

GWAS (Genome-wide association analysis), as a high-throughput genome analysis method, has shown great potential in the study of disease resistance in pigs. Through GWAS, researchers are able to comprehensively assess genetic variation in large-scale pig populations and identify genotypes and single nucleotide polymorphisms (SNPs) associated with specific disease resistance. This approach has led to a number of important achievements, most notably a deeper understanding of the genetic basis of disease resistance in pigs. Through GWAS, scientists have identified multiple genes related to porcine disease resistance, providing a strong theoretical basis for further disease control and genetic improvement (Korte and Farlow, 2013).

### 4.2 The practical application prospects of GWAS research in improving porcine disease resistance

The practical application prospect of GWAS lies in the use of identified disease resistance genes for the selection and improvement of pig populations. Through genetic marker-assisted selection (MAS) based on GWAS, the pig breeding industry can more accurately select breeds with good disease resistance. GWAS also provides important targets for gene editing and transgenic technologies, allowing researchers to directly adjust the genetic background of pigs and enhance their disease resistance through genome editing and other means. These practical application prospects will greatly promote the improvement of porcine disease resistance, increase breeding efficiency, and reduce losses.

### 4.3 Possible future contributions of porcine disease resistance research

Although GWAS has achieved impressive results, porcine disease resistance research still faces a series of challenges and unknowns. In the future, researchers need to delve deeper into the functional mechanisms of disease resistance-related genes in order to better utilize these genes for selection and improvement. At the same time, with the continuous development of technology, a new generation of genomics methods and tools will continue to emerge, providing more possibilities for research on porcine disease resistance. Therefore, the possible contribution of future research on porcine disease resistance is to deeply explore gene functions, continuously innovate technological methods, and apply research results to actual breeding production, injecting new vitality into the healthy development of the pig industry.

Through GWAS studies, researchers can better understand the genetic basis of porcine disease resistance, predict and improve disease-resistant pig breeds, and provide technical support and theoretical guidance for the sustainable development of the breeding industry.

## 5 Conclusion

The core focus of the research is to reveal the genetic basis of disease resistance in pigs through GWAS technology. The application of GWAS in this field provides researchers with the opportunity to deeply understand porcine disease resistance, thereby providing more effective disease management strategies for the breeding industry (Bai et al., 2021). Through the analysis of large-scale genotypic and phenotypic data, this study can identify candidate genes and SNPs related to disease resistance, and further study their functions and mechanisms of action.

The value and significance of GWAS in studying porcine disease resistance cannot be ignored. GWAS can help researchers understand the genetic basis of porcine disease resistance and reveal genetic differences between different breeds or individuals, thereby providing a basis for selective breeding (Uemoto et al., 2021). GWAS can discover new disease-resistant candidate genes and provide new targets and strategies for improving disease resistance. GWAS can also help people understand the complexity and diversity of disease resistance and provide guidance for further research.

In future research, people need to further improve GWAS technology and combine it with other bioinformatics and functional genomics methods to deeply explore the genetic basis of disease resistance (Li and Ritchie, 2021). At the same time, researchers also need to strengthen functional research on disease resistance-related genes, reveal their specific mechanisms of action in disease prevention and control, and provide more effective means for disease prevention and treatment.

The application of GWAS in porcine disease resistance research provides important tools and methods for people to deeply understand the genetic basis of disease resistance. Through GWAS technology, researchers can discover new disease-resistant genes and SNPs and reveal their mechanisms of action in disease resistance, thus making greater contributions to pig health management and the sustainable development of the breeding industry. In future studies, researchers will continue to deeply explore the potential of GWAS in disease resistance research, and strengthen gene function research to provide more scientific and accurate solutions for disease prevention and control.

## References

Bai X.C., Yang T.F., Putz A.M., Wang Z.Q., Li C.X., Fortin F., Harding J.C.S., Dyck M.K., Canada P., Dekkers J.C.M., Field C.J., and Plastow G.S., 2021, Investigating the genetic architecture of disease resilience in pigs by genome-wide association studies of complete blood count traits collected from a natural disease challenge model, BMC genomics, 22: 1-15.
https://doi.org/10.1186/s12864-021-07835-4
PMid:34256695 PMCid:PMC8278769

Buniello A., MacArthur J.A.L., Cerezo M., Harris L.W., Hayhurst J., Malangone C., McMahon A., Morales J., Mountjoy E., Sollis E., Suveges D., Vrousgou O., Whetzel P.L., Amode R., Guillen J.A., Riat H.S., Trevanion S.J., Hall P., Junkins H., Flicek P., Burdett T., Hindorff L.A., Cunningham F., and Parkinson H., 2019, The NHGRI-EBI GWAS Catalog of published genome-wide association studies, targeted arrays and summary statistics

Cano-Gamez E., and Trynka G., 2020, From GWAS to function: using functional genomics to identify the mechanisms underlying complex diseases, Frontiers in genetics, 11: 424.
https://doi.org/10.3389/fgene.2020.00424
PMid:32477401 PMCid:PMC7237642

Carr J., Chen S.P., Connor J.F., Kirkwood R., and Segalés J., 2018, Pig health, CRC Press.
https://doi.org/10.1201/9781315157061

Geraci C., Varzandi A.R., Schiavo G., Bovo S., Ribani A., Utzeri V.J., Galimberti G., Buttazzoni L., Ovilo C., Gallo M., Dall'Olio S., and Fontanesi L., 2019, Genetic markers associated with resistance to infectious diseases have no effects on production traits and haematological parameters in Italian Large White pigs, Livestock Science, 223: 32-38.
https://doi.org/10.1016/j.livsci.2019.03.003

Korte A., and Farlow A., 2013, The advantages and limitations of trait analysis with GWAS: a review, Plant methods, 9(1): 1-9.
https://doi.org/10.1186/1746-4811-9-29
PMid:23876160 PMCid:PMC3750305

Kumar S., Bhushan B., Kumar A., Panigrahi M., Bharati J., Kumari S., Kaiho K., Banik S., Karthikeyan A., Chaudhary R., Gaur G.K., and Dutt T., 2023, Elucidation of novel SNPs affecting immune response to classical swine fever vaccination in pigs using immunogenomics approach, Veterinary Research Communications, 1-13.
https://doi.org/10.1007/s11259-023-10262-3
PMid:38017322

Li B.L., 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

Ma Z., Zhu H.D., Su Y.Q., Meng Y., Lin H.X., He K.W., and Fan H.J., 2018, Screening of Streptococcus Suis serotype 2 resistance genes with GWAS and transcriptomic microarray analysis, BMC genomics, 19(1): 1-11.
https://doi.org/10.1186/s12864-018-5339-9
PMid:30541452 PMCid:PMC6292034

McKnite A.M., Bundy J.W., Moural 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

Niu AR, Zhang X., Yang YT, Yan ZC, Gong HZ, Ding RN, and Ma L., 2023, Progresses in research on genome-wide association studies in pig breeding, Animal Husbandry & Veterinary Medicine, 55(5): 139-147.

Radwan J., Babik W., Kaufman J., Lenz T.L., and Winternitz J., 2020, Advances in the evolutionary understanding of MHC polymorphism, Trends in Genetics, 36(4): 298-311.
https://doi.org/10.1016/j.tig.2020.01.008
PMid:32044115

Reiner G., 2009, Investigations on genetic disease resistance in swine—a contribution to the reduction of pain, suffering and damage in farm animals, Applied Animal Behaviour Science, 118(3-4): 217-221.
https://doi.org/10.1016/j.applanim.2009.02.011

Uemoto Y., Ichinoseki K., Matsumoto T., Oka N., Takamori H., Kadowaki H., Kojima-Shibata C., Suzuki E., Okamura T., Aso H., Kitazawa H., Satoh M., Uenish H., and Suzuki K., 2021, Genome-wide association studies for production, respiratory disease, and immune-related traits in Landrace pigs, Scientific reports, 11(1) : 15823.
https://doi.org/10.1038/s41598-021-95339-2
PMid:34349215 PMCid:PMC8338966

Wu P.X., Wang K., Zhou J., Chen D.J., Yang Q., Yang X.D., Liu Y.H., Feng B., Jiang A.A., Shen L.Y., Xiao W.H., Jiang Y.Z., Zhu L., Zeng Y.S., XuX., Li X.W., and Tang G.Q., 2019, GWAS on imputed whole-genome resequencing from genotyping-by-sequencing data for farrowing interval of different parities in pigs, Frontiers in Genetics, 10: 1012.
https://doi.org/10.3389/fgene.2019.01012
PMid:31681435 PMCid:PMC6813215

Yang HC, 2004, Epidemic feature and restraint measures of innune inhibition diseases in pigs, China Animal Husbandry & Veterinary Medicine, 31(5): 41-43.

Zhao D.S., Yang B., Yuan X.G., Shen C.C., Zhang D.J., Shi X.J., Zhang T., Cui H.M., Yang J.K., Chen X.H., Hao Y., Zheng H.X., Zhang K.S., and Liu X.T., 2021, Advanced research in porcine reproductive and respiratory syndrome virus co-infection with other pathogens in swine, Frontiers in Veterinary Science, 8: 699561.
https://doi.org/10.3389/fvets.2021.699561
PMid:34513970 PMCid:PMC8426627