



Research Article

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Research on Insect Pathogen Resistance Based on GWAS: Methods, Challenges, and Prospects

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Abstract This study reviews the application of genome-wide association studies (GWAS) in the field of insect pathogen resistance, and discusses the main methods, challenges, and future development prospects of this research direction. This study introduces the basic principles of GWAS and its application in revealing the genetic basis of insect resistance to pathogens. By analyzing genetic variations in the insect genome, GWAS helps scientists identify key genes and functional regions related to resistance. This study discusses the main challenges encountered in conducting GWAS research, including sample size limitations, genetic diversity, environmental factors, and difficulties in detecting rare variations. It also explores issues such as data sharing and privacy protection. This study looks forward to the potential of utilizing GWAS results to improve insect resistance strategies, including the application of gene editing techniques such as CRISPR-Cas9 in insect resistance improvement, and emphasizes the importance of interdisciplinary collaboration in solving complex scientific problems. This study aims to provide a comprehensive perspective for the research and management of insect pathogen resistance, promoting scientific progress and technological innovation in related fields.

Keywords Genome-wide association studies; Insect resistance; Gene editing technology; Interdisciplinary cooperation; Pathogen control

Insects, as one of the most diverse and widely distributed biomes on Earth, are closely linked to human life. They play a variety of roles in natural ecosystems, both as beneficial and harmful insects, the latter being particularly known for their enormous damage to agricultural crops. Insect pathogens, including viruses, bacteria, fungi and parasites, pose a major threat to agriculture and forestry and can cause significant reductions in crop yields, thus challenging global food security. Some insects are also capable of transmitting deadly diseases to humans, such as mosquito-borne malaria and dengue fever, further highlighting the importance of controlling the spread of insect pathogens (Pan et al., 2023).

In this context, understanding the mechanisms of insect resistance to these pathogens has become particularly important. This can not only help develop more effective pest management strategies and reduce the use of pesticides, but also provide new ideas for the prevention and control of infectious diseases. In recent years, genome-wide association studies (GWAS) have been widely used as a powerful genetic research tool in the study of insect pathogen resistance. By analyzing the association between genetic variants in the insect genome and resistance phenotypes, GWAS can help scientists to reveal the genetic basis of insect resistance and thus its complex genetic mechanisms.

The application of GWAS has greatly contributed to the understanding of the genetic basis of insect resistance. Compared with traditional genetic analysis methods, GWAS is able to provide a rapid and comprehensive scan of the entire genome without relying on a priori genetic information. This means that GWAS can efficiently identify key genetic variants even for resistance traits that have complex genetic backgrounds and are associated with multiple genes. This ability is critical for resolving the complexity of insect pathogen resistance, especially in the current context of global change and rapidly changing agricultural practices.

Although GWAS shows great potential for insect resistance research, its application faces a number of challenges, including the huge amount of data, computational complexity, and difficulties in interpreting the results. How to translate the genetic information discovered by GWAS into practical pest management strategies is also an important direction of current research (Li et al., 2022).

The aim of this study was to overview GWAS-based insect pathogen resistance research, analyze its methodology, challenges and future prospects, introduce the basic principles of GWAS technology and its application in insect resistance research, and discuss in detail the progress of research on the genetic basis of insect resistance, including the key genes and functional regions discovered through GWAS technology. This study explores the major challenges encountered in the implementation of GWAS research, such as the effects of sample size, genetic diversity and environmental factors, etc. It will also demonstrate the application and achievements of GWAS technology in revealing insect resistance mechanisms through several specific research cases. This study will discuss the potential applications and perspectives of GWAS technology in future entomopathogen resistance studies, and how complex problems in entomopathogen resistance studies can be solved through interdisciplinary collaborations.

1 Application of GWAS Technical Methods

1.1 The role of GWAS in insect pathogen resistance research

Genome-wide association studies (GWAS) is a scientific method used to study the association between genetic variation and complex traits, and has been widely used in insect pathogen resistance research in recent years. The basic principle of GWAS is to search for genetic markers associated with specific traits by scanning genome-wide genetic variation in a large number of individuals. Genetic markers associated with specific traits. This approach can reveal the genetic basis behind traits and provide new ideas for understanding the mechanisms of insect resistance to pathogens.

The GWAS technique is based on the premise that differences in traits can to some extent be explained by genetic variation in the genome. These variations usually refer to single nucleotide polymorphisms (SNPs), which are the most common genetic markers in the genome. By comparing the distribution of SNPs in populations of individuals with different traits (e.g., disease resistance versus disease susceptibility), it is possible to identify genetic loci that are significantly associated with a particular trait. GWAS studies usually require a large number of samples in order to ensure the reliability of the statistical results (Liu et al., 2023).

The basic steps in conducting a GWAS study include: sample collection, DNA extraction, genotyping, statistical analysis, and validation of candidate loci. Each step requires precise technical support and strict quality control to ensure the accuracy and reliability of the data.

1.2 Special considerations and applicability of GWAS technology in insect research

Insects, as research objects, have their own special characteristics when applying GWAS technology. There are many kinds of insects, and the genetic backgrounds of different kinds vary greatly, which requires representativeness and comparability when choosing research objects. Insects have a short life cycle and fast reproduction rate, which facilitates the rapid acquisition of a large amount of genetic material, but also requires researchers to be able to effectively manage and maintain the experimental population. The small size of insects and the limited amount of DNA extracted require the use of highly sensitive genotyping techniques.

The application of GWAS techniques in insect resistance research also requires consideration of the impact of environmental factors. Insect resistance traits are often affected by a combination of multiple genetic and environmental factors, which requires the use of appropriate models to control these confounding factors when performing GWAS analysis to ensure the accuracy of the research results.

1.3 Data processing and statistical analysis methods

In genome-wide association studies (GWAS), data processing and statistical analysis are crucial steps that ensure the accuracy and reliability of the study results. This process involves a complex transformation from quality control of raw data to final association analysis aimed at identifying statistically significant correlations between insect pathogen resistance and specific genetic markers.

Overall, data processing and statistical analysis play a central role in GWAS, involving not only the initial stages of study design, but also every detail of data analysis and interpretation of results. Through these fine steps, researchers are able to mine meaningful information from massive amounts of genetic data to provide a scientific basis for understanding pathogen resistance in insects.

2 Genetic Basis of Insect Resistance

2.1 Genetic mechanisms of insect resistance to major pathogens

As the most diverse group of organisms on earth, the diversity and complexity of resistance mechanisms in insects have been the focus of scientific research. Insects are capable of resisting a wide range of pathogens, including viruses, bacteria, fungi and parasites, and this ability is based on their complex genetic and molecular mechanisms. In recent years, genome-wide association studies (GWAS) have provided powerful tools for resolving these resistance mechanisms, revealing many key genes and functional regions, and these findings have opened up new horizons for understanding the genetic basis of insect resistance (Wang et al., 2022).

The ability of insects to defend themselves against pathogen attacks is largely dependent on the effective response of their immune system. For different types of pathogens, insects exhibit different resistance strategies. For example, against viruses, the RNA interference (RNAi) machinery in insects is activated to prevent viral replication by specifically degrading viral RNA. In contrast, when confronted with bacteria and fungi, insects initiate an immune response that produces antimicrobial peptides to directly kill or inhibit the growth of these microorganisms. Insects are also able to limit parasite infestation through, for example, physical isolation.

2.2 Key genes and functional regions identified in GWAS studies

Through GWAS analysis, scientists have successfully identified several key genes and functional regions associated with insect pathogen resistance. For example, in studies against certain viruses, GWAS has helped identify several key genes associated with the RNAi pathway, such as Dicer-2 and Argonaute-2, which play important roles in the recognition and cleavage of viral RNA.

In terms of viral resistance, GWAS studies have revealed several genes associated with the RNA interference (RNAi) pathway, such as Dicer-2 and Argonaute-2, which play key roles in the recognition and degradation of viral RNA, one of the major defense mechanisms against viral infestation in insects. This mechanism protects insects from viral infection by specifically cleaving the genetic material of viruses and blocking their replication and spread.

For bacterial and fungal resistance, GWAS studies have similarly identified key components of insect immune signaling pathways, particularly some components of the Toll and Imd signaling pathways. These pathways play a central role in activating the insect's natural immune response, including defense mechanisms such as recognition of pathogens, activation of immune cells, and production of antimicrobial peptides. Through these mechanisms, insects are able to effectively defend themselves against bacterial and fungal attacks.

In the face of bacterial attack, some key components of signaling pathways, such as those of the Toll and Imd signaling pathways, have also been pointed out by the GWAS study to be closely related to the anti-bacterial capacity of insects. These findings not only deepen the understanding of insect immune mechanisms, but also offer the possibility of developing novel biopesticides or improving insect resistance.

2.3 Association of resistance with physiological and behavioral characteristics of insects

Pathogen resistance in insects is not only limited to its genetic basis, but is also strongly influenced by its physiological and behavioral characteristics. These traits are closely related to insect resistance, and together they constitute a complex set of defense mechanisms that enable insects to display amazing adaptability and resistance in the face of pathogen attack.

From a physiological point of view, an insect's immune system is its first line of defense against pathogens. Immune cells and antimicrobial peptides in insects are able to respond rapidly to pathogen invasion and directly kill or inhibit pathogen growth. The metabolic pathways of insects are also closely linked to their resistance capabilities. For example, insects are able to resist or eliminate toxins from their bodies by metabolizing specific compounds that may be inhibitory to certain pathogens. Detoxification enzyme systems in insects, such as cytochrome P450 enzymes, are also able to help insects detoxify, thereby enhancing their resistance to various pathogens in the environment (Figure 1).

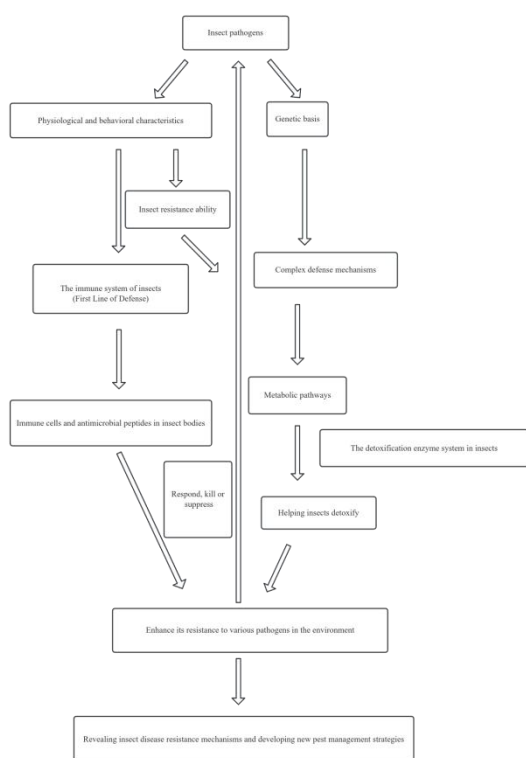


Figure 1 Correlation between resistance and insect physiological and behavioral characteristics

Insect resistance is a complex trait with multiple levels and dimensions, in which physiological and behavioral traits are adapted and optimized to provide insects with additional means of defense. These adaptive behaviors and physiological responses are not only part of an insect's survival strategy, but also important mechanisms developed during its evolution to counteract environmental stresses, especially pathogen threats. An in-depth understanding of the physiological and behavioral characteristics of insects and their association with resistance is important for unraveling the mechanisms of insect disease resistance and even for developing novel pest management strategies.

3 Challenges and Limitations

3.1 Impact of sample size, genetic diversity and environmental factors on GWAS accuracy

Genome-wide association studies (GWAS), as a powerful genetic research tool, have made a series of breakthroughs in the field of insect pathogen resistance. However, this research method still faces a series of

challenges and limitations, including the effects of sample size, genetic diversity, environmental factors, and the difficulties of detecting rare variants and complex traits, as well as issues of data sharing and privacy protection.

First, sample size is one of the important determinants of GWAS accuracy. A sufficiently large sample size can improve the statistical efficacy of a study, allowing even small genetic effects to be detected. However, in entomopathogen resistance studies, obtaining large numbers of high-quality samples is often difficult, especially for rare or geographically diverse insect species. Genetic diversity also affects the results of GWAS. Highly diverse genetic backgrounds may mask or obscure important genetic signals, making it difficult to analyze the genetic basis of traits.

The influence of environmental factors should not be ignored. Insects live in extremely complex environments, and environmental variables such as temperature, humidity, and food sources may affect their resistance to pathogens. Even under the same genetic background, different environmental conditions may lead to significant differences in insect resistance. Failure to adequately control these environmental factors in GWAS studies may lead to an increase in false positive results and affect the accuracy of the study.

3.2 Difficulties in detecting rare variants and complex traits

A major challenge in genome-wide association studies (GWAS) is the detection of rare variants and complex traits. These two problems center on the fact that, on the one hand, rare variants are difficult to be effectively detected in conventional GWAS sample sizes due to their extremely low frequency in populations; on the other hand, complex traits are usually the result of multiple genes as well as environmental factors, which makes it particularly difficult to accurately identify all the relevant genetic factors (Du et al., 2021).

Rare variants, despite their low frequency, may in some cases have a decisive impact on pathogen resistance in insects. For example, a rare variant may make an insect highly resistant to a specific pathogen, but because the frequency of such variants in a population is extremely low, it is difficult for conventional GWAS designs to be statistically efficacious enough to detect these rare variants that are significantly correlated with traits. Detection of rare variants is also affected by sample selection and genotype quality control criteria, which further increases the difficulty of detection.

For the detection of complex traits, the complexity of the polygenic genetic mechanisms and gene-environment interactions underlying the trait are involved. Insect resistance traits are often not simple genetic traits determined by a single gene, but are the result of the interaction of multiple genes under specific environmental conditions. In this case, even if GWAS are able to identify some genetic markers associated with the trait, it is difficult to fully explain the genetic variation in the trait, especially when the trait is strongly influenced by the environment. Interactions between genes (phenotypically non-additive effects) and between genes and the environment also pose challenges in identifying relevant genetic factors.

3.3 Challenges of data sharing and privacy protection

Data sharing is an important aspect of accelerating scientific discovery and technological advancement when conducting genome-wide association studies (GWAS). By sharing data, researchers can validate the results of other studies, discover new research directions, or improve statistical validity through meta-analysis. However, the process of data sharing also faces the challenge of privacy protection, and although individual privacy issues may not be as prominent in insect research as in human research, a range of privacy and sensitive information protection issues are still involved.

In order to address these challenges, it is crucial to develop sound data management and sharing policies. For example, the legality and legitimacy of the purpose of data use can be ensured through the establishment of a data access committee (DAC) to scrutinize data access requests. De-identify or anonymize data through technical means to reduce the risk of exposing sensitive information. The establishment of clear data use agreements and

copyright notices can protect the interests of data providers to a certain extent and promote the construction of a healthy sharing ecology for scientific data. Data sharing and privacy protection is also an issue that needs to be emphasized in insect GWAS research. Through the formulation of reasonable policies and the application of technical means, the value of data sharing can be maximized, while protecting the interests of all parties involved in the research, and promoting the healthy development of entomological research and related application fields.

4 Research Case Studies

4.1 Insect resistance to agricultural pest pathogens

The research team of Leeuwen et al. (2020) in 2020 carried out the interpretation of saliency and molecular diagnostics in the management of resistance to agricultural pests in the current agriculture, where insecticide options against agricultural pests are diminishing due to environmental and health concerns, and insecticide-resistant pests are becoming increasingly difficult to control. Rational decisions on insecticide use are needed to ensure effective resistance management. However, monitoring programs that can inform about pest susceptibility and resistance are currently not widely available in agriculture.

Sparks et al. (2020) team used insecticides, biological agents, and nematicides: an update of the IRAC classification of modes of action-tools for resistance management. Insecticide resistance is an important issue and the IRAC mode of action classification update provides the latest information for implementing effective resistance management strategies.

Pests and pathogens are common problems in agricultural production and they pose a significant threat to crop growth and yield. However, some insect populations exhibit resistance to these pest pathogens, which provides an important biological control method for agricultural production. By studying and analyzing these resistant insect populations, the principles of their resistance mechanisms can be revealed, thus providing a theoretical basis for the development of more effective control strategies.

4.2 Role of rare genetic variation in insect resistance

The team of Nam et al. (2019) tested whether copy number variation was responsible for increased levels of insect resistance in two populations of fall stickleback (*Spodoptera frugiperda*) in different geographic locations and different host plants.

Mckenzie (2000) conducted experiments on the nature or variation of resistance and genetic analysis of insecticide resistance phenotypes in insects, and discussed the genetic basis of resistance evolution as dependent on the manner in which phenotypes and their underlying genotypic variation are directed during selection responses. A polygenic response is favored if selection acts within the distribution of susceptible phenotypes, and a monogenic response is predicted if selection screens for rare mutations whose phenotypes lie outside that susceptibility distribution.

Insect populations are rich in genetic variation, some of which may be closely associated with their resistance phenotypes. Rare genetic variation, an important form of genetic variation, plays an important role in insect resistance. Through the study of these rare genetic variants, a deeper understanding of the genetic basis of insect resistance and its evolutionary mechanism can be achieved.

4.3 Utilizing GWAS results to improve resistance strategies

Chen et al. (2021) conducted cotton disease and insect resistance: this study identified loci significantly associated with yellow wilt resistance by GWAS and found that two non-specific lipid transfer protein genes (GhnsLTPsA10) were highly expressed under yellow wilt pathogen stress. The expression of these genes was significantly increased in roots against the yellow wilt pathogen, but significantly decreased in leaves under insect attack.

Siddiqui et al. (2023) conducted Resistance mechanisms and control strategies: this study discussed resistance mechanisms in invasive species including behavioral, biochemical, physiological, genetic and metabolic

approaches that can lead to the development of resistance by sustained overexpression of detoxifying enzymes to deal with toxic chemicals.

The team of Monnot et al. (2021) conducted GWAS for plant virus resistance, analyzed general and specific issues in applying GWAS in plant virus resistance studies, explored the key steps from the assembly of diversity panels to the analysis of GWAS results, and demonstrated a variety of GWAS methods for various types of viruses based on 48 published articles (Figure 2).

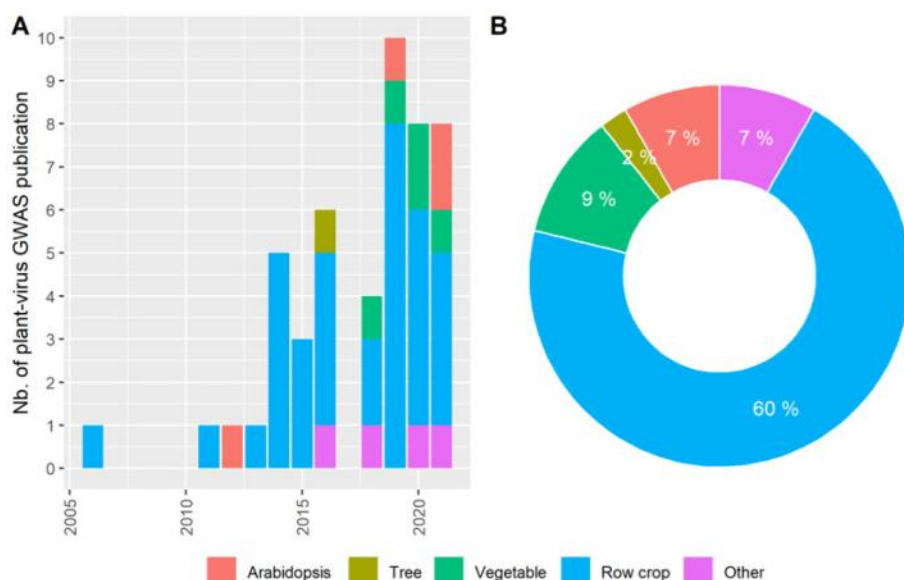


Figure 2 Overview of the publications of plant–virus GWAS (Monnot et al., 2021)

Note: A: Number of plant-virus GWAS articles published each year; B: Proportion of plant-virus GWAS articles regarding the crop type; Other: contains publications on peanut, cassava, and yam

Genomic association analysis (GWAS) is an effective genetic research method that has been widely used in insect resistance research. Through GWAS technology, key genes or gene regions associated with insect resistance can be identified, providing important genetic information for improving resistance strategies. Using advanced technological tools such as genetic variation and genomic association analysis, resistant varieties can be screened and bred more precisely, providing sustainable solutions for agricultural production. In the future, it is necessary to further strengthen the related research, to deeply explore the genetic diversity of insect resistance, to continuously improve the resistance improvement strategy, and to contribute more scientific power to realize the efficient, green and sustainable development of agriculture.

5 Resistance Management and Application Prospects

5.1 Application of GWAS findings to resistance management and pathogen control strategies

The application of genome-wide association studies (GWAS) in the field of insect pathogen resistance provides new ideas and methods for resistance management and pathogen control strategies. With the development of gene editing technologies, especially the CRISPR-Cas9 system, powerful tools for improving insect resistance are now available, along with new challenges for genetic resource conservation and biodiversity maintenance.

The GWAS study provides a scientific basis for effective management of resistant pests by revealing the association between insect resistance and specific genetic variants. These findings can guide the development of pathogen control strategies, such as enhancing natural resistance to pathogens by breeding or screening insect populations carrying specific resistance genes. The GWAS results can also help agricultural scientists and pest management experts to identify risk factors for possible resistance decay in pest populations, so that they can adjust and optimize pest control programs in a timely manner to prolong the effectiveness of resistance traits.

5.2 Potential of gene editing technologies in insect resistance improvement

Gene editing technology, especially the CRISPR-Cas9 system, has triggered revolutionary changes in the field of biological sciences in recent years, and insect resistance improvement is precisely one of the areas in which it has exerted great potential. By precisely introducing specific modifications into the insect genome, this technology not only enhances the resistance of insects to known pathogens, but also has the potential to confer resistance to new ones.

Gene editing technology allows scientists to directly target resistance-related genes that have already been identified through GWAS studies. For example, if a specific variant in a gene is associated with increased resistance to a particular pathogen, with CRISPR-Cas9, scientists can introduce that variant into a population of non-resistant insects, thereby enhancing their resistance. The precision and efficiency of this method far exceeds that of traditional breeding techniques, offering the possibility of rapidly generating new resistant insect varieties.

The application of gene editing technology also faces the challenges of ethical and ecological risk assessment. In practical application, the possible ecological impacts of editing insect genomes need to be carefully considered to ensure that they do not cause irreversible negative impacts on natural ecosystems. With the development and application of the technology, it is also necessary to establish corresponding laws and regulations and ethical guidelines to ensure the responsibility and sustainability of scientific research and application.

In summary, gene editing technology shows great application prospects in insect resistance improvement, which can not only provide new resistant insect species, but also deepen the understanding of insect immune mechanisms. With deeper research and technological advances, it is expected to play a greater role in areas such as pest management and agricultural production.

5.3 Importance of genetic resources conservation and biodiversity maintenance

Genetic resource conservation and biodiversity maintenance is one of the global challenges currently facing the world, and plays a crucial role in maintaining the health and stability of ecosystems and guaranteeing the sustainable development of human societies. This topic is particularly important in the field of research and application of insect pathogen resistance, because the genetic diversity of insects, as a key component of ecosystems, has a direct impact on agricultural production, pathogen transmission, and the effectiveness of biocontrol strategies (Yang et al., 2022).

Conservation of genetic resources is the basis for achieving resistance persistence and diversity in insect populations. Genetic diversity of insect populations is an important safeguard for their adaptation to environmental changes and resistance to pathogens. Loss of genetic diversity will make insect populations more susceptible to pathogens, reducing ecosystem stability and the sustainability of agricultural production. Conserving insect genetic resources and maintaining genetic diversity within them is an effective way to prevent the spread of diseases and increase crop yields.

With the increasing impact of global warming and human activities, the living environment of insects is seriously threatened. The conservation of genetic resources and the maintenance of biodiversity are not only responsible for the current ecosystem, but also for future generations. Through the implementation of scientific conservation measures and the promotion of sustainable agricultural practices, it is possible to reduce the negative impacts on biodiversity and to protect and restore the natural habitats of insects and other organisms.

In summary, genetic resource conservation and biodiversity maintenance are key to ensuring the sustainability of entomopathogen resistance research and applications. By strengthening research and practice in these areas, a solid foundation can be provided for future ecosystem stabilization, agricultural production safety and the effectiveness of biological control strategies.

6 Conclusion

Genome-wide association studies (GWAS) have made remarkable achievements in the field of insect pathogen resistance research, but they also face a series of challenges. By precisely correlating genetic variation with insect resistance traits, GWAS has revealed the genetic basis of resistance formation and provided possible ways to improve pest management strategies. However, limitations in sample size, genetic diversity considerations, complexity of environmental factors, difficulties in detecting rare variants, and data sharing and privacy protection are challenges that need to be addressed in current research.

GWAS has revealed several key genes and genetic markers associated with insect resistance through association analysis, which provides new perspectives for understanding the mechanisms of insect resistance to pathogens. These research results not only enrich the basic knowledge about insect immune responses, but also provide a scientific basis for breeding pathogen-resistant insect species and developing novel biopesticides. In addition, the application of GWAS has promoted the cross-fertilization of genetics, molecular biology, ecology and other multidisciplinary fields, and promoted the in-depth development of entomological research.

Future research will continue to deepen the understanding of the genetic basis of insect resistance, and the application of new technologies and methods will play a key role in this process. For example, gene editing technologies (e.g., CRISPR-Cas9) will make it possible to target specific resistance genes for precise modifications, providing new strategies for insect resistance improvement. In addition, with the development of bioinformatics and systems biology, technologies such as big data analysis and machine learning will be widely used in the processing and parsing of GWAS data to improve the efficiency and accuracy of research. In terms of research methodology, multi-omics integrated analysis (e.g., transcriptomics, proteomics combined with GWAS) will help to deeply understand the complex mechanisms of insect resistance from multiple levels.

In the face of the complex scientific problem of insect pathogen resistance, interdisciplinary cooperation is particularly important. By collaborating, experts from multiple disciplines, such as genetics, molecular biology, ecology, computational biology, etc., can share knowledge, technology, and resources to explore more comprehensively and in depth the formation mechanisms and management strategies of insect resistance. In addition, interdisciplinary cooperation can help to balance the relationship between scientific research, social ethics and ecological protection, and ensure that scientific progress is balanced with the maintenance of biodiversity and the sustainable development of the ecological environment.

In conclusion, interdisciplinary collaboration provides a broad perspective for the study of entomopathogen resistance, enabling scientists to synthesize the latest research results and technological tools from different fields, and to jointly face the challenges in scientific research and practical applications. In the future, this mode of collaboration will continue to play a key role in promoting the progress of entomopathogen resistance research and related application fields.

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