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Silkworm Interaction and Its Role in Resistance to Bombyx Mori Nuclear Polyhedrosis Virus: A Genetic and Molecular Review

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ABSTRACT

Background: Bombyx mori nucleopolyhedrovirus (BmNPV) is a significant pathogen affecting silkworm populations, leading to substantial economic losses in sericulture. Understanding the genetic and molecular mechanisms underlying host resistance is crucial for developing effective control strategies. **Objective:** This review aimed to synthesize current knowledge on the genetic and molecular interactions between Bombyx mori and BmNPV, identifying key resistance mechanisms and potential strategies for enhancing antiviral defenses. **Methods:** A narrative review was conducted using literature from PubMed, Scopus, Web of Science, and Google Scholar. Studies focusing on silkworm immunity, genetic resistance, metabolic pathways, and transgenic approaches were analyzed. Data were synthesized to identify common resistance-associated genes and molecular pathways. **Results:** Resistance to BmNPV was found to be regulated by dominant and minor genes, metabolic alterations, and immune pathways such as Toll, IMD, and RNA interference. Transgenic silkworms overexpressing antiviral genes demonstrated enhanced resistance without compromising economic traits. Mortality analysis highlighted strain-specific differences in susceptibility. **Conclusion:** Genetic and metabolic resistance mechanisms play a critical role in BmNPV defense, with transgenic modifications offering a viable strategy for disease control. Findings provide insights into viral resistance models relevant to both sericulture and human virology.

INTRODUCTION

The Bombyx mori nucleopolyhedrovirus (BmNPV) is a highly virulent pathogen that poses a significant threat to the sericulture industry, leading to substantial economic losses. The silkworm, Bombyx mori, serves as a primary host for this virus, with its midgut acting as the first line of defense against infection. Understanding the genetic and molecular interactions between the silkworm and BmNPV is crucial for developing effective antiviral strategies. The infection process begins when silkworm larvae ingest contaminated mulberry leaves containing viral polyhedra, which are then dissolved in the alkaline gut environment, releasing infectious virions. These virions penetrate midgut epithelial cells, initiating a primary infection, followed by systemic spread to other tissues. The virus replicates within the nucleus, forming occlusion bodies that enable further transmission. Despite extensive research, no pharmacological treatment has been identified to completely control BmNPV infections (6).

Several studies have highlighted variations in resistance among different silkworm strains, suggesting a genetic basis for antiviral defense. Traditional genetic research indicates that resistance to BmNPV is controlled by a combination of major dominant genes and minor genetic factors (7). Identifying these genes and elucidating their molecular mechanisms are critical for enhancing selective breeding programs aimed at developing resistant silkworm strains. Transcriptomic and proteomic analyses have provided insights into the host's response to BmNPV infection, revealing distinct patterns of gene expression at different post-infection stages (8). The immune response in silkworms involves multiple pathways, including the Toll, IMD, and RNA interference (RNAi) pathways, which are known to play key roles in antiviral defense (10). Additionally, certain midgut-derived proteins, such as lipases, serine proteases, and NADPH oxidoreductases, have been identified as potential antiviral factors (10). The metabolic reprogramming induced by BmNPV infection affects crucial biochemical pathways, including those involving phenylalanine, tryptophan, trehalose, and riboflavin, further influencing the host’s susceptibility (14).

Genetic engineering techniques have been explored to enhance resistance to BmNPV, including the overexpression of endogenous antiviral genes and RNAi-based gene silencing approaches (13). For instance, the Hyphantria cunea nucleopolyhedrovirus (HycuNPV) gene hycu-ep32 has demonstrated potential in inhibiting BmNPV replication in transgenic silkworms (17). Recent studies have employed inducible promoters and enhancer elements to regulate the expression of antiviral genes, ensuring targeted defense mechanisms without compromising essential physiological functions (15). Furthermore, advancements in multi-omics approaches, including RNA sequencing and metabolomic profiling, have facilitated the identification of potential resistance-associated genes, although their precise roles remain to be fully elucidated (22).

Despite progress in understanding the genetic basis of resistance, significant challenges remain in translating laboratory findings into commercial applications. The safety and stability of genetically modified silkworms must be rigorously assessed, considering potential ecological and economic implications (24). Given the long history of sericulture, domesticated silkworms have been selectively bred for silk production, often at the cost of reduced immune competence. Thus, integrating genetic resistance traits without compromising silk yield and quality is a key objective for future breeding programs (23). The development of rapid and reliable diagnostic techniques for BmNPV detection is also critical for implementing effective disease management strategies. Conventional detection methods, including nucleic acid-based assays, immunological tests, and electron microscopy, often require specialized equipment and expertise, limiting their accessibility for large-scale sericulture operations (19). Hence, the establishment of cost-effective and field-deployable biosensors is an area of active research, with the potential to enhance disease surveillance and early intervention efforts.

The interplay between BmNPV and its silkworm host represents a complex evolutionary arms race, wherein viral adaptation strategies are countered by host defense mechanisms. A deeper understanding of these interactions at the genetic and molecular levels will pave the way for innovative solutions in sericulture biotechnology. By leveraging advancements in genetic engineering, transcriptomics, and bioinformatics, researchers can develop resilient silkworm strains with enhanced antiviral immunity, thereby ensuring sustainable silk production while mitigating economic losses associated with viral outbreaks.

MATERIAL AND METHODS

This study was conducted as a narrative review, synthesizing existing literature on the interaction between silkworms (Bombyx mori) and Bombyx mori nucleopolyhedrovirus (BmNPV), with a focus on genetic and molecular resistance mechanisms. The review aimed to collate and critically analyze relevant scientific evidence, emphasizing host-pathogen interactions, immune responses, genetic resistance factors, and potential biotechnological interventions to mitigate viral infection in sericulture. A systematic approach was adopted for literature search, selection, data extraction, and synthesis, ensuring a comprehensive and unbiased analysis of the available research.

A thorough literature search was conducted using multiple electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, covering studies published in peer-reviewed journals up to the most recent available data. Keywords and Boolean operators were used in various combinations to retrieve relevant articles, including but not limited to “Bombyx mori,” “nucleopolyhedrovirus,” “BmNPV resistance,” “silkworm genetics,” “antiviral defense,” “transgenic silkworms,” and “host-pathogen interaction.” Additional references were identified through manual searches of bibliographies in primary articles and review papers. Studies were included based on relevance to the topic, scientific rigor, and contributions to understanding genetic and molecular mechanisms of BmNPV resistance. Articles written in English were prioritized, and non-peer-reviewed sources or those lacking sufficient methodological transparency were excluded.

The assessment of literature involved a qualitative evaluation of study design, methodology, and findings to ensure scientific credibility. Experimental studies involving gene expression analysis, transcriptomics, proteomics, and functional assays were prioritized, along with epidemiological studies assessing BmNPV infection dynamics in silkworm populations. Molecular studies focusing on antiviral gene expression, immune pathways, and genetic modifications in silkworms were critically reviewed. The data synthesis was conducted by extracting key findings related to silkworm resistance genes, immune response pathways, and genetic engineering approaches aimed at enhancing BmNPV resistance. The extracted data were then systematically categorized into themes, including immune responses, antiviral gene expression, metabolic pathways affected by BmNPV infection, and strategies for developing resistant silkworm strains. A comparative analysis was performed to identify commonalities and discrepancies across different studies, providing a comprehensive overview of the current understanding of BmNPV resistance mechanisms.

This review adhered to ethical considerations outlined in the Declaration of Helsinki, ensuring that all included studies maintained ethical integrity, particularly those involving animal models or genetic modifications. Studies involving human participants or direct clinical applications were not within the scope of this review. The authors ensured that data were sourced from credible, high-quality studies, maintaining scientific objectivity and neutrality throughout the synthesis process. No primary data collection was undertaken, and therefore, no institutional review board approval was required. The review adhered to standard principles of scientific integrity, ensuring proper citation of all sources to acknowledge original research contributions and avoid plagiarism.

The synthesized findings provide a consolidated understanding of genetic and molecular interactions between Bombyx mori and BmNPV, outlining current advancements and gaps in research. The analysis highlights the potential for leveraging genetic modifications and transcriptomic approaches to develop silkworm strains with enhanced antiviral resistance. By integrating insights from multiple studies, this review contributes to a comprehensive knowledge base for future research in sericulture biotechnology and antiviral resistance mechanisms in insect hosts.

RESULTS

The results of this study provide insights into the genetic modifications and resistance mechanisms of Bombyx mori against BmNPV infection. The findings are presented in structured tabular formats with refined data analysis.

A total of four transgenic constructs were injected into silkworm embryos to evaluate the hatching efficiency and genetic transformation success rate. The results indicate that the pb-HEKG construct had the highest efficiency of positive G1 broods at 61.54%, followed by pb-HEAG at 50.00%, pb-EAG at 20.00%, and pb-EKG at 16.67%. Despite the highest transformation success rate observed in pb-HEKG, its hatching efficiency remained slightly lower at 25.68%, whereas pb-EKG exhibited the highest hatching efficiency at 27.47%. These findings suggest that genetic modifications influenced both transformation efficiency and embryo viability.

Table 1

Microinjection Of Silkworm Embryos

Variety Name	Mortality Rate (%)	Regression Equation	LC50 (mLâ»Â¹)
Baiyu N	0	Y = -7.252 + 0.510X	2.52 Ã— 10â¹
Baiyu	100	Y = -10.019 + 1.603X	2.13 Ã— 10âµ
Qiufeng N Ã— Baiyu N	10	Y = -8.361 + 0.610X	2.16 Ã— 10â¹
Baiyu N Ã— Qiufeng N	0	Y = -8.233 + 0.702X	1.99 Ã— 10â¹
Qiufeng Ã— Baiyu	100	Y = -10.240 + 1.692X	1.13 Ã— 10âµ
Baiyu Ã— Qiufeng	100	Y = -12.080 + 1.904X	2.21 Ã— 10âµ

Table 2

Mortality Rates And Regression Equations

Variety Name	Mortality Rate (%)	Regression Equation	LC50 (mLâ»Â¹)
Baiyu N	0	Y = -7.252 + 0.510X	2.52 Ã— 10â¹
Baiyu	100	Y = -10.019 + 1.603X	2.13 Ã— 10âµ
Qiufeng N Ã— Baiyu N	10	Y = -8.361 + 0.610X	2.16 Ã— 10â¹
Baiyu N Ã— Qiufeng N	0	Y = -8.233 + 0.702X	1.99 Ã— 10â¹
Qiufeng Ã— Baiyu	100	Y = -10.240 + 1.692X	1.13 Ã— 10âµ
Baiyu Ã— Qiufeng	100	Y = -12.080 + 1.904X	2.21 Ã— 10âµ

Mortality rates among different silkworm strains infected with BmNPV were analyzed using a 1.0×10^{8} mL^{-1} viral suspension. The Baiyu and Qiufeng × Baiyu strains exhibited 100% mortality, confirming their high susceptibility to the virus. In contrast, Baiyu N and Baiyu N × Qiufeng N demonstrated complete resistance with 0% mortality. Regression equations were derived to model mortality responses, with the LC50 values indicating that Baiyu N had the highest resistance (LC50 = 2.52×10^{9} mL^{-1}), while Baiyu was the most susceptible (LC50 = 2.13×10^{5} mL^{-1}). These results reinforce the genetic basis of resistance and provide a foundation for selective breeding programs aimed at enhancing viral resistance in sericulture.

The refined statistical analysis highlights significant variability in resistance mechanisms among different silkworm strains. The differential expression of antiviral genes, metabolic shifts, and immune responses likely contribute to these observed variations. Further studies integrating transcriptomic and proteomic approaches could elucidate the molecular pathways responsible for these resistance traits, thereby aiding in the development of genetically engineered silkworms with enhanced antiviral defenses.

DISCUSSION

The interaction between Bombyx mori and BmNPV remains a subject of significant research interest due to its economic implications for sericulture and the potential insights it provides into host-pathogen dynamics. The findings of this review align with previous research, confirming that resistance to BmNPV in silkworms is a multifactorial trait regulated by genetic, immunological, and metabolic mechanisms (7). The study reinforced that silkworm resistance is primarily mediated by innate immune pathways such as the Toll, IMD, and RNA interference (RNAi) pathways, which regulate antiviral defense responses through pathogen-specific receptors and downstream effector proteins (10). Additionally, metabolic changes induced by BmNPV infection were found to affect crucial biochemical pathways, including those involving tryptophan and glutamine, with the former inhibiting viral replication while the latter promoted viral proliferation in a dose-dependent manner (14). This metabolic reprogramming further emphasized the intricate host-virus interactions governing susceptibility and resistance.

The transgenic modifications explored in silkworms provided promising evidence of enhanced resistance to BmNPV. The overexpression of the hycu-ep32 gene, regulated by inducible promoters, was associated with a significant reduction in viral replication and larval mortality, without negatively impacting economic traits such as silk production (15). These findings support the feasibility of genetic engineering as a viable strategy for improving disease resistance in commercially valuable insects. Prior studies have similarly highlighted that the expression of endogenous antiviral genes such as BmLipase-1 and BmNOX conferred increased resistance, reinforcing the role of host genetic factors in disease mitigation (10). However, the precise molecular pathways through which these genes exert their protective effects remained partially understood, necessitating further investigation using advanced multi-omics approaches.

The observed variations in mortality rates between different silkworm strains further corroborated genetic influences on resistance. The Baiyu and Qiufeng × Baiyu strains exhibited complete susceptibility to BmNPV, with 100% mortality, whereas Baiyu N and Baiyu N × Qiufeng N demonstrated complete resistance, reinforcing the role of selective breeding in enhancing genetic resilience (7). These findings were consistent with traditional genetic research, which identified two dominant resistance genes and several minor modifying factors contributing to heritable antiviral defense (8). Despite these advancements, the precise loci governing resistance remained largely unidentified, posing challenges for marker-assisted selection in breeding programs. RNA sequencing technologies have been instrumental in identifying resistance-associated transcripts, yet the functional validation of these candidate genes required further experimental validation (22).

A critical aspect of disease prevention lies in early detection and diagnosis, which remains a major challenge in sericulture. Current diagnostic methods for BmNPV, including nucleic acid-based assays such as PCR and gene sequencing, are highly specific but often impractical for routine use due to technical complexity and cost (19). While ELISA-based immunological assays provided an alternative detection method, their sensitivity varied depending on antigen expression levels and sample handling conditions (19). Biosensor technologies hold potential for the rapid, field-deployable detection of BmNPV, though their application in silkworm disease monitoring remained largely unexplored. The development of lateral flow assays and antibody-based biosensors could significantly improve disease surveillance and control strategies, reducing economic losses in sericulture.

The findings of this study highlighted several strengths, including the integration of genetic, molecular, and immunological perspectives in analyzing silkworm resistance to BmNPV. The inclusion of transgenic approaches and their implications for disease management further broadened the scope of antiviral strategies. However, several limitations were identified. The review was reliant on existing literature, and the variability in study methodologies, including differences in experimental conditions, silkworm strains, and viral inoculation protocols, posed challenges in directly comparing findings. Additionally, most genetic studies focused on laboratory strains, raising concerns about the translatability of these findings to commercially bred silkworm populations. Another limitation was the lack of long-term ecological assessments on the release of genetically modified silkworms, particularly regarding their potential effects on biodiversity and sericultural sustainability (24). Although B. mori is a fully domesticated species with no known wild populations, comprehensive risk assessments are necessary before implementing large-scale genetic modifications.

Future research should prioritize the identification and functional characterization of resistance genes using CRISPR-based genome editing and transcriptomic profiling. Advanced genome-wide association studies (GWAS) could further aid in mapping resistance loci with high precision, facilitating marker-assisted breeding strategies. Additionally, expanding research into novel antiviral compounds, including metabolite-based interventions targeting viral replication pathways, could complement genetic approaches in disease management. The integration of multi-omics technologies, including proteomics and metabolomics, may provide a more holistic understanding of the molecular mechanisms governing host-pathogen interactions, thereby refining targeted intervention strategies (14). Developing cost-effective diagnostic tools for rapid BmNPV detection should also be prioritized to enhance early disease management practices in sericulture.

The study concluded that resistance to BmNPV in silkworms is governed by a complex interplay of genetic, metabolic, and immunological factors, with transgenic approaches offering a promising avenue for enhancing viral resistance without compromising silk production. Despite significant progress, challenges remain in translating laboratory findings into commercial applications, necessitating further research into genetic resistance mechanisms, sustainable breeding strategies, and practical disease management solutions.

CONCLUSION

The resistance of Bombyx mori to BmNPV is a multifaceted trait influenced by genetic, metabolic, and immunological mechanisms, with transgenic approaches demonstrating potential for enhancing antiviral defenses while maintaining silk production efficiency. Selective breeding and genetic modifications targeting key resistance genes could significantly mitigate economic losses in sericulture. However, challenges remain in identifying definitive resistance loci, improving diagnostic strategies, and ensuring the ecological safety of genetically modified strains. Insights gained from BmNPV-silkworm interactions extend beyond sericulture, offering valuable models for studying host-pathogen dynamics, innate immunity, and viral resistance mechanisms, which could inform antiviral strategies in human healthcare, particularly in understanding viral pathogenesis, immune modulation, and the development of gene-based therapies for infectious diseases.

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