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The Roles Suppressor of Cytokine Signaling 7 (SOCS7) Gene in *Bombyx mori* (Silkworm) against *Bombyx mori* Nucleopolyhedrosis Virus (BmNPV) infection: A Review

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Abstract

Bombyx mori silkworm belongs to the family of Bombycidae and the order Lepidoptera which are known to have originated and domesticated in China about 5,000 years ago. Silkworm is also a good model organism for production of recombinant proteins and the study of insect immunology. However, its populations are severely threatened by BmNPV, a virus that causes high mortality rates and reduced silk yield. B. mori nucleopolyhedrovirus (BmNPV) is a primary silkworm pathogen, and always causes serious economic losses. The paper review, the current understanding of silkworm suppressor of cytokine signal 7 (SOCS7) and its role in antiviral immunity against BmNPV infection, highlighting the insights gained from the silkworm infection model and functional analysis of SOCS7.

Keywords: *Bombyx mori, B. mori nucleopolyhedrovirus (BmNPV), silkworm, SOCS7*

Introduction

The silkworm, *Bombyx mori*, is an economically important insect primarily cultivated for silk production. There are several types of silkworm diseases, and they cause great economic losses to the sericulture industry. Among them, *B. mori* nucleopolyhedrovirus (*BmNPV*) disease is the most serious (Jiang and Xia, 2014; Xu *et al.*, 2015). Silkworm is also a good model organism for production of recombinant proteins and the study of insect immunology (Shao *et al.*, 2012). However, its populations are severely threatened by BmNPV, a virus that causes high mortality rates and reduced silk yield. *B. mori* nucleopolyhedrovirus (*BmNPV*) is a primary silkworm pathogen, and always causes serious economic losses (Jiang *et al.*, 2012). It is well known that there are two distinct forms of virion in the life cycle of *BmNPV*: the occlusion-derived virus (ODV) and the budded virion (BV) (Liu *et al.*, 2008). Initially, BmNPV infect silkworm larval mid-gut cells by ODV, and then infect the larger part of the larva by BVs (Sajjan and Hinchigeri, 2016). Silkworms are susceptible to infection by the *Bombyx mori nucleopolyhedrovirus* (*BmNPV*), which causes significant mortality and economic losses in sericulture (Chen *et al.*, 2018). Recent studies have shown that SOCS7 plays a crucial role in regulating antiviral immunity in silkworms, and its functional analysis has provided valuable insights into the molecular mechanisms underlying this process (Lie *et al*., 2020).

Bombyx mori (Silkworm)

Bombyx mori silkworm (hereafter called silkworm) belongs to the family of Bombycidae and the order Lepidoptera which are known to have originated and domesticated in China about 5,000 years ago (Lu *et al*., 2018). For the past few decades, silkworms have been widely reared in China, Japan, India, and other countries due to their numerous advantages, such as their low cost, convenience, and no ethical issues. The original purpose for rearing silkworms was to obtain silkworm silk. Silkworm production over centuries ago enriched mankind, encouraged art and culture, and was one of the primary forms of globalization during the Silk Road period (Goldsmith *et al*., 2005). As one of the important economic resources, silkworm silk has been widely used in the traditional textile industries for several years due to its essential properties, such as its pearly luster, excellent biocompatibility, large-scale production, and mechanical performance (Hu *et al*., 2017). Recently, numerous novel and essential applications of silks have been explored, such as drug delivery (Tsioris *et al*., 2012), tissue engineering (Kasoju and Bora, 2012), and so on. In addition, silkworm chrysalis and excrement also have medical values in traditional Chinese medicine (Xia *et al*., 2014; Qi *et al*., 2017). The silkworm chrysalis is high in protein and other minerals, making it an excellent source of nutrients for humans and feed additives for animals (Zhou *et al*., 2022). In addition, due to their important biological role, silkworms have also been used as model organisms for studying environmental toxicology, food safety, drug research, and human disease research (Xia *et al*., 2014; Qi *et al*., 2017; Andoh *et al*., 2021).

Bombyx mori Nucleopolyhedrovirus (BmNPV)

Bombyx mori nucleopolyhedrovirus (BmNPV) belongs to Baculoviridae, and its genome size is about 128 kb (Lacey *et al*., 2015; van Oers *et al*., 2015; Jiang, 2021). So far, there are two different BmNPV types identified, including budded virus (BV) and occlusion body-derived virus (ODV) (Blissard and Theilmann, 2018; Baci *et al*., 2022). ODVs mainly infect *B. mori* by oral ingestion and spread the infection from host to host. They pass through the peritrophic membrane to utilize the host to replicate and produce; meanwhile, the BV particles spread between cells and tissues of the infected host, causing systemic infection and resulting in the host's death (Jiang *et al*., 2012). Figure 1 shows the schematic diagram of BmNPV infection and replication within a host. These two types of BmNPV make it challenging to eradicate BmNPV, causing significant loss to sericulture and causing losses to enterprises that rely on the stable development of sericulture. Cocoon losses caused by BmNPV in sericulture production account for more than 60% of all silkworm diseases.

BmNPV is primarily transmitted through horizontal transmission, where infected larvae shed the virus in their feces, contaminating the environment. Vertical transmission, although less common, can occur when infected females pass the virus to their offspring through eggs. Environmental factors, such as temperature and humidity, significantly influence the virus's stability and transmission rates, complicating control measures (Shi *et al*. 2021). The impact of BmNPV on silkworm populations is profound, affecting various physiological processes: BmNPV infection disrupts normal growth and development, leading to stunted growth and reduced pupation rates. Infected larvae often display abnormal behaviors, such as reduced feeding and increased lethargy, which further exacerbate growth issues (Shi, X., *et al.*, 2021).

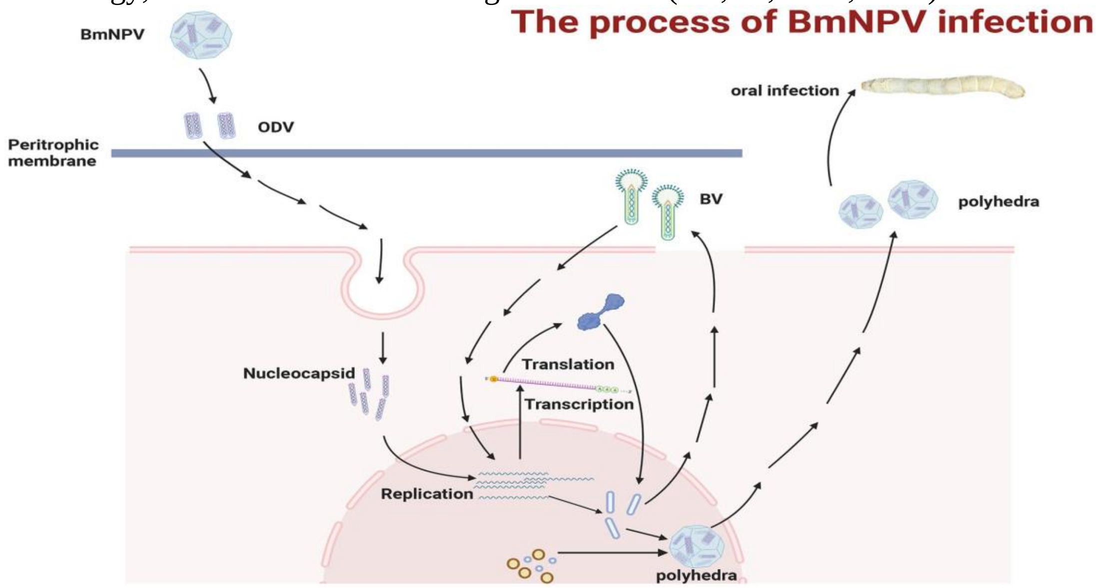

Figure 1: The process of infection with BmNPV in silkworms (Fan *et al*., 2023).

Silkworm Infection Model

The silkworm infection model is a valuable tool for studying host-pathogen interactions and bacterial virulence. *Bombyx mori*, the domesticated silkworm, is susceptible to various pathogens, including bacteria, viruses, and fungi. Infection models using silkworms have been established for several human pathogens, including *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and Candida albicans (Kaito *et al.*, 2011). The silkworm's relatively simple immune system and short lifespan make it an ideal model for studying infection dynamics and testing antimicrobial agents (Khan *et al* 2017). Additionally, silkworms are easy to rear and manipulate, allowing for high-throughput screening of pathogens and host responses (Lee *et al.*, 2018). The silkworm infection model has contributed significantly to our understanding of bacterial virulence mechanisms and has potential applications in developing novel therapeutics.

Cloning and Expression of SOCS7

SOCS7 has been cloned from silkworms and its expression patterns have been analyzed in response to *BmNPV* infection (Wang *et al*. 2020). The results show that SOCS7 is up regulated in response to *BmNPV* infection, suggesting its involvement in antiviral immunity. The SOCS7 gene was cloned from silkworms using a combination of molecular biology techniques, including PCR, DNA library construction, and DNA sequencing (Wang *et al*., 2020). The cloned SOCS7 gene was found to encode a protein of 498 amino acids, with a molecular weight of approximately 55 kDa

(Zhang *et al*., 2019).The expression of SOCS7 in silkworms was analyzed using various techniques, including RT-PCR, Western blotting, and immunohistochemistry (Li *et al.,* 2018; Chen *et al.*, 2017). The results showed that SOCS7 is constitutively expressed in various tissues, including the hemocytes, fat body, and integument (Wang *et al.,* 2020). However, its expression was significantly upregulated in response to *BmNPV* infection, suggesting its involvement in antiviral immunity (Wang *et al.*, 2020). Recombinant SOCS7 protein was expressed in Escherichia coli (*E. coli*) using a prokaryotic expression system (Zhang *et al.*, 2019). The recombinant protein was purified using affinity chromatography and characterized using Western blotting and enzyme-linked immunosorbent assay (ELISA) (Li *et al*., 2018). Functional analysis of SOCS7 has revealed its role in regulating cytokine signaling pathways, including the JAK/STAT pathway (Li *et al.*, 2018). SOCS7 has also been shown to interact with other immune-related genes, such as Toll and IMD (Wang *et al*., 2020).

Conclusion

BmNPV poses a significant threat to silkworm populations, with profound implications for the sericulture industry whereas SOCS7 plays a crucial role in antiviral immunity in silkworms. Further studies on SOCS7 will provide valuable insights into the development of novel strategies to combat *BmNPV* infection and improve silkworm resistance, continued research into the virus's biology, transmission dynamics, and host responses is essential for developing effective management strategies. By integrating scientific knowledge with practical applications, the sericulture industry can work towards mitigating the impact of *BmNPV* and ensuring the sustainability of silk production.

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