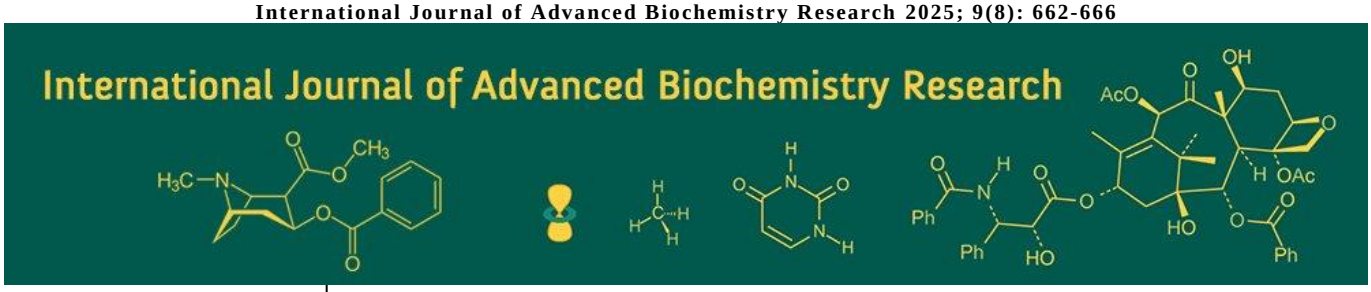


**ISSN Print:** 2617-4693
**ISSN Online:** 2617-4707
NAAS Rating (2025): 5.29
IJABR 2025; 9(8): 662-666
www.biochemjournal.com
Received: 15-05-2025
Accepted: 19-06-2025

**Ashrith S**
M.Sc. Scholar,
University of Agricultural Sciences, Bangalore, Karnataka, India

**Pavithra MR**
M.Sc. Scholar,
University of Agricultural Sciences, Bangalore, Karnataka, India

**Basangouda Jekinakatti**
M.Sc. Scholar,
University of Agricultural Sciences, Bangalore, Karnataka, India

**Shwetha GV**
M.Sc. Scholar,
University of Agricultural Sciences, Bangalore, Karnataka, India

**Nandha Kumar R**
M.Sc. Scholar, Tamil Nadu Agricultural University, Tamil Nadu, India

**Arun Kumar MR**
Ph.D. Scholar, University of Agricultural Sciences, Bangalore, Karnataka, India

**Suhas BV**
M.Sc. Scholar,
University of Agricultural Sciences, Dharwad, Karnataka, India

**Corresponding Author:**
**Ashrith S**
M.Sc. Scholar,
University of Agricultural Sciences, Bangalore, Karnataka, India

# Advances in molecular breeding and CRISPR-Cas9-mediated genome editing in silkworms: Applications and future prospects

**Ashrith S, Pavithra MR, Basangouda Jekinakatti, Shwetha GV, Nandha Kumar R, Arun Kumar MR and Suhas BV**

**DOI:** https://www.doi.org/10.33545/26174693.2025.v9.i8i.5284

**Abstract**
The domesticated silkworm (*Bombyx mori* L.) is a model species of great economic and biological significance. Traditional breeding has significantly enhanced silk yield and disease resistance; however, it remains time-consuming and lacks precision. Recent advancements in molecular breeding and genetic engineering—particularly the advent of gene editing technologies such as CRISPR-Cas9-have revolutionized silkworm research. These approaches enable precise manipulation of target genes, facilitating the development of transgenic silkworms with desirable traits, including enhanced silk productivity, resistance to viral pathogens such as nucleopolyhedrovirus (*Bm*NPV), and the ability to produce therapeutic and industrial recombinant proteins, such as human interferon, epidermal growth factor, and spider silk proteins. This review comprehensively discusses the progress in molecular breeding strategies (including marker-assisted selection and traditional transgenic), gene editing tools with a focus on CRISPR-Cas9, and future prospects for the genetic improvement of silkworms in both commercial sericulture and biotechnology applications.

**Keywords:** Silkworm, breeding, selection, gene editing

## 1. Introduction
The silkworm a domesticated insect has been an indispensable component of the sericulture industry for millennia. As the exclusive producer of commercial silk, it holds immense economic value, particularly in Asia. Beyond its role in silk production, silkworm serves as a powerful model organism for genetic, molecular, and physiological studies due to its fully sequenced genome, short life cycle and well established rearing protocols (Goldsmith *et al.*, 2005; Xia *et al.*, 2004) [7, 23].

Historically, genetic improvement of silkworms was achieved through conventional breeding approaches such as hybridization, mass selection and recurrent selection. These methods led to the development of strains with improved cocoon yield, disease resistance and adaptability to specific climatic conditions. However, traditional breeding is inherently time-consuming, labor-intensive and limited in precision. It also faces challenges in addressing emerging threats such as climate variability, pathogen resistance and demand for specialized silk traits (Maheswar, i 2023) [14].

The advent of molecular breeding tools including marker-assisted selection (MAS), quantitative trait loci (QTL) mapping and transcription profiling has significantly improved the resolution and efficiency of genetic improvement in silkworms (Yamamoto *et al.*, 2008) [25]. Furthermore, recent breakthroughs in genetic engineering and genome editing technologies, particularly the CRISPR-Cas-9 system have opened new avenues for precise gene manipulation. These tools enable targeted gene knockouts, insertions or replacements allowing researchers to dissect gene function and engineer desirable traits such as enhanced silk quality, pathogen resistance, thermal tolerance and recombinant protein expression.

As a result, silkworm biotechnology is transitioning from classical breeding paradigms to precision molecular breeding with implications for both industrial sericulture and biotechnological applications. This review provides an overview of molecular breeding strategies and highlights the transformative impact of gene editing technologies-especially CRISPR-Cas-9 on functional genomics and genetic improvement in *B. mori.*

## 2. Molecular breeding in silkworm

Molecular breeding refers to the use of DNA-based molecular markers and biotechnological tools to assist in the selection and propagation of desirable traits in organisms. In silkworm this approach complements traditional breeding by providing a more precise, efficient and faster method of identifying and incorporating beneficial genes related to traits such as high cocoon yield, disease resistance, thermotoleraent and improved silk quality (Tang *et al.*, 2024) [16].

### 2.1 Marker-assisted selection (MAS)

Marker-Assisted Selection (MAS) is a molecular breeding technique that utilizes specific DNA markers to track the inheritance of genes associated with desirable traits. In silkworms MAS has emerged as a powerful tool to accelerate the development of superior strains by enabling early and accurate selection at the molecular level rather than relying solely on observable traits.

#### 2.1.1 Molecular markers in silkworm

Various types of molecular markers have been applied in silkworm MAS including:

- **RAPD (Random Amplified Polymorphic DNA):** Useful for identifying genetic variation in populations, though less reproducible.
- **SSR (Simple Sequence Repeats or Microsatellites):** Highly polymorphic and co-dominant markers used for mapping QTLs, diversity analysis and strain identification (Jiang *et al.*, 2012) [9].
- **SNPs (Single Nucleotide Polymorphisms):** Abundant and stable markers suited for high-resolution mapping and genome-wide association studies (GWAS).

These markers have been employed to map Quantitative Trait Loci (QTLs) linked with economically significant traits such as cocoon weight, shell ratio, silk fineness, larval growth rate, thermotolereant and disease resistance.

#### 2.1.2 MAS applications in silkworm breeding

Several research efforts have successfully applied MAS to improve silkworm traits:

- **Cocoon and Silk Yield Traits:** QTL mapping using SSR and SNP markers has identified loci on chromosomes 2, 3, 11, and 18 associated with cocoon weight, shell percentage, and filament length (Maheswari *et al.*, 2023) [14].
- **Thermal Tolerance:** DNA markers linked to heat-shock protein genes (e.g., *hsp70*, *hsp90*) have been used to screen thermotolerant genotypes for summer rearing (Xiao *et al.*, 2017; Yamamoto *et al.*, 2008) [17, 25].
- **Disease Resistance:** QTLs related to resistance against *Bombyx mori nucleopolyhedrovirus* (*Bm*NPV) and *Beauveria bassiana* have been identified using SSR markers, enabling the selection of resistant lines (Lie *et al.*, 2010) [12].
- **Sex Determination and Hybrid Identification:** Markers such as W-chromosome specific sequences and strain-specific SSRs have been applied for gender determination in early larval stages and hybrid verification in seed production.

#### 2.1.3 Benefits of MAS in silkworm breeding

- Enables early selection of desirable genotypes before phenotypic traits are expressed.
- Reduces generation time and breeding cost.
- Increases precision and success rate of hybrid development.
- Facilitates introgression of specific traits into elite lines without disturbing other desirable attributes.

#### 2.1.4 Limitations and future prospects

Despite its advantages MAS requires initial investment in marker development and genotyping infrastructure. Moreover, traits governed by multiple genes or strongly influenced by the environment (e.g., cocoon quality under fluctuating temperature) may be harder to manage solely through markers. However, combining MAS with genomic selection and CRISPR-based validation offers a promising strategy for next-generation silkworm improvement.

#### 2.1.5 Genomic resources

The availability of high-quality genomic and transcriptomic resources has significantly accelerated molecular breeding and functional genomics research in the silkworm. The complete genome sequence of the silkworm was first published by Xia *et al.* (2004) [23], marking a major milestone in lepidopteran genetics. This genome revealed over 14, 000 protein-coding genes and provided a comprehensive view of metabolic and silk-producing pathways.

To further support research and breeding applications, specialized databases like SilkDB and KAIKObase have been developed:

- SilkDB (http://silkworm.genomics.org.cn): Offers genome annotations, gene expression profiles, and comparative genomics tools for gene discovery and marker development.
- KAIKObase (https://kaikobase.dna.affrc.go.jp/): A comprehensive database integrating genomic, EST, and BAC data, used extensively for gene mapping, mutant analysis, and trait association studies.

These resources have enabled advanced approaches such as Genome-Wide Association Studies (GWAS) and differential gene expression analysis, allowing researchers to identify candidate genes associated with key agronomic traits such as cocoon weight, thermal resistance and disease tolerance (Xia *et al.*, 2004) [23]. These genes can then be targeted through marker-assisted selection or genome editing for trait improvement.

## 3. Genetic engineering in silkworm

Genetic engineering in silkworm enables precise insertion and expression of foreign genes to improve desirable traits or introduce novel functionalities. This approach has become a cornerstone in silkworm biotechnology, contributing to both sericulture and recombinant protein production.

### 3.1 Transgenic silkworms

The development of transgenic silkworms primarily utilizes transposon-based vectors, such as piggyBac to stably integrate foreign genes into the silkworm genome. These vectors have high transformation efficiency and stable germ line transmission. Pioneering studies successfully produced transgenic silkworms expressing green fluorescent protein (GFP) as a reporter system (Tomita *et al.*, 2003) [18]. Subsequently, functional proteins such as antiviral peptides and enzymes have also been expressed.

### 3.2 Applications

Genetic engineering has expanded the functional potential of silkworms across several domains:

- **Production of Human Therapeutic Proteins:** Transgenic silkworms have been engineered to express recombinant human proteins such as collagen, antibodies, and interferons within their silk glands or hemolymph, offering a cost-effective platform for biopharmaceutical production (Tomita *et al.*, 2003) [18].
- **Enhanced Disease Resistance:** Introduction of genes encoding antiviral or antifungal peptides has significantly improved resistance against major silkworm pathogens such as *Bombyx mori nucleopolyhedrovirus* (*Bm*NPV) and *Beauveria bassiana*, helping stabilize cocoon yield (Gaudelli *et al.*, 2017) [6]
- **Functional Silk Biomaterials:** Through targeted gene expression in silk glands, transgenic silkworms have produced silk fibers embedded with bioactive molecules or engineered with enhanced tensile strength, elasticity, or biodegradability making them ideal for biomedical applications (Teule *et al.*, 2012) [17].

These advances position genetically modified silkworms as dual-purpose bioreactors for silk production and therapeutic protein synthesis, while also offering solutions to key challenges in commercial sericulture.

## 4. CRISPR-Cas9 and gene editing in silkworm

Recent advances in genome editing technologies have revolutionized functional genomics and breeding programs in *Bombyx mori*. Among these, the CRISPR-Cas9 system has emerged as the most versatile and efficient tool, enabling precise genetic modifications that are faster and more economical than traditional gene-editing platforms (Miao *et al.*, 2005) [21].

### 4.1 CRISPR-Cas9 System

The CRISPR-Cas9 (Clustered Regularly Interspaced Short Palindromic Repeats-CRISPR-associated protein 9) system is a bacterial adaptive immune mechanism repurposed for targeted genome editing. It uses a synthetic single-guide RNA (sgRNA) to direct the Cas9 endonuclease to specific genomic loci, creating double-stranded breaks (DSBs). These breaks are repaired by either non-homologous end joining (NHEJ) or homology-directed repair (HDR), allowing for targeted gene knockouts or insertions (Cong *et al.*, 2013; Doudna & Charpentier, 2014) [2, 4].
Its high efficiency, simplicity, and adaptability to multiplex editing have made CRISPR-Cas9 a tool of choice for gene function analysis and trait improvement in silkworms.

### 4.2 CRISPR-Cas9 in silkworm research

The application of CRISPR-Cas9 in *B. mori* has rapidly expanded since its first implementation, enabling targeted edits across a wide range of gene families:

- **Knockout of *BmNPV* Entry Receptors:** Disrupted genes encoding viral entry receptors such as Niemann-Pick C1 (BmNPC1), leading to reduced viral replication and improved resistance against *Bombyx mori nucleopolyhedrovirus* (*BmNPV*) (Jiang *et al.*, 2012. Gundi *et al.*, 2023) [9, 8]
- **Silk Protein Genes:** Used CRISPR-Cas9 to target *fibroin heavy chain* (*FibH*) and *sericin* genes, altering silk fiber properties and enabling the creation of functional silk biomaterials Anzalone *et al.* (2019) [1].
- **Sex Determination Genes:** Targeted *Masc* gene, a key male sex-determination factor, leading to sex reversal and providing insights for gender-specific breeding and sterile line development.
- **BmNPV-Resistant Silkworms:** Dong *et al.* (2020) [3] generated BmNPV-resistant lines by editing multiple antiviral target genes, showcasing the potential for durable and inheritable viral resistance.
- **Pigmentation and Morphological Traits:** CRISPR has also been used to manipulate visible traits (e.g., melanin synthesis genes like *yellow*, *ebony*) for genetic tracking and functional validation (Tang *et al.*, 2024) [16].

These applications demonstrate the utility of CRISPR-Cas9 not only in trait enhancement but also as a research tool for functional genomics and synthetic biology in lepidopterans.

### 4.3 Other gene editing tools

Before CRISPR, earlier programmable nucleases were used in silkworms but had notable limitations:

- TALENs (Transcription Activator-Like Effector Nucleases) and ZFNs (Zinc Finger Nucleases) enabled site-specific gene editing but required complex protein engineering for each target site. Their application in silkworms included gene knockouts and transgenic model development (Yamamoto, *et al.*, 2018) [26] but adoption remained limited due to high technical demands.
- Base Editing and Prime Editing: These are the next-generation tools for precise genome modifications without causing double-stranded breaks:
    - Base Editors enable direct conversion of specific base pairs (e.g., C-G to T-A), ideal for correcting point mutations.
    - Prime Editors expand this capability by inserting or replacing short DNA sequences without inducing DSBs.

Although not yet widely used in *B. mori*, these advanced systems are being explored for applications requiring high-fidelity editing, such as the creation of designer silkworms and functional gene validation with minimal off-target effects.

## 5. Challenges and ethical considerations

While gene editing holds promise, there are concerns regarding:

- Off-target effects (Yang *et al.*, 2021) [27]
- Regulatory frameworks for genetically modified organisms (GMOs)
- Public perception and ecological risks

Efforts are being made to improve specificity and assess long-term environmental impacts before commercial deployment.

## 6. Future prospects

The integration of CRISPR-Cas9 and emerging genome editing tools into silkworm research represents a paradigm shift in both basic and applied sciences. These technologies not only expedite the understanding of gene function but

also open up vast possibilities for industrial, agricultural, and biomedical applications. Several promising future directions include:

### 6.1 Designing climate-resilient silkworm

With climate change threatening traditional sericulture, there is a pressing need to develop silkworm strains that can withstand thermal stress, fluctuating humidity and oxidative damage. Genome editing can be harnessed to target heat-shock proteins, antioxidant enzymes, and stress-responsive transcription factors to enhance thermotolerance and survivability under extreme climatic conditions. CRISPR-based functional validation of these stress-related genes can accelerate the breeding of resilient silkworms tailored for tropical and subtropical regions (Xia *et al.*, 2004; Xia *et al.*, 2014) [23, 22].

### 6.2 Biomanufacturing of vaccines and enzymes

Transgenic and genome-edited silkworms offer a cost-effective platform for biopharmaceutical production. The silkworm silk gland and hemolymph are excellent biofactories for producing:

- Therapeutic proteins (e.g., collagen, monoclonal antibodies)
- Vaccines (e.g., virus-like particles)
- Industrial enzymes (e.g., proteases, cellulases)

The CRISPR system allows precise gene integration under tissue-specific promoters, improving expression efficiency and product quality (Tomita *et al.*, 2013). This holds tremendous potential for low-cost, scalable production of biopharmaceuticals, especially in developing countries.

### 6.3 Integration with AI and genomic selection

The convergence of genomic tools with artificial intelligence (AI) and machine learning offers new pathways for precision breeding. AI can process multi-omics data (genomics, transcriptomics, proteomics) to predict gene function, identify elite genotypes, and model gene-environment interactions. When combined with CRISPR, this can lead to predictive gene editing, enabling breeders to forecast and achieve specific phenotypic outcomes more accurately and rapidly.

### 6.4 Gene drives for pest and disease vector control

Gene drive systems powered by CRISPR have been proposed as a revolutionary tool to control insect pests and vectors by promoting the inheritance of targeted traits (e.g., sterility, pathogen resistance) through natural populations. In Lepidoptera, including wild silkworms and pest moths, gene drives could:

- Prevent mating between wild and commercial silkworms
- Control invasive pests in sericulture farms
- Reduce the spread of viral and fungal pathogens

Although still at a theoretical and experimental stage, gene drives hold transformative potential for sustainable pest control in sericulture ecosystems (Esvelt *et al.*, 2014) [5].

### 6.5 Multi-omics integration for synthetic biology

The integration of CRISPR-based editing, synthetic promoters, and multi-omics approaches (including epigenomics and metabolomics) will enable the design of custom silkworm strains. These could produce specialty silks (e.g., spider silk-like fibers), exhibit biocontrol traits, or serve as biosensors in agriculture and environmental monitoring.

### 6.6 Collaborative imperative

To realize these prospects, interdisciplinary collaboration is crucial. Progress will require:

- Molecular biologists to identify and edit target genes
- Bioinformaticians to manage and interpret large-scale genomic data
- Biotechnologists to scale and commercialize edited silkworm lines
- Ethicists and policymakers to develop regulatory frameworks that balance innovation with biosafety

Public-private partnerships, funding for CRISPR-related silkworm research, and open-access genomic platforms will further catalyze innovation in this field.

## 7. Conclusion

Molecular breeding and genome editing have ushered in a new era in silkworm research and sericulture improvement. Marker-assisted selection, QTL mapping, and transcriptome analyses have facilitated the identification of genes linked to vital traits like cocoon yield, disease resistance, and stress tolerance. The advent of CRISPR-Cas9 has revolutionized functional genomics in silkworms by enabling precise gene knockouts and insertions with remarkable efficiency. These tools have allowed the development of transgenic silkworms for producing pharmaceutical proteins, novel silk biomaterials, and *Bm*NPV-resistant lines.

CRISPR-based systems, including base editing and gene drives, hold potential for even more refined applications such as climate-resilient strains and sustainable pest control. The integration of AI with genomics can further accelerate precision breeding. However, challenges remain in terms of biosafety regulations, public acceptance, and ecological risk assessments. Moving forward, multidisciplinary collaboration and ethical governance will be essential to harness the full potential of genetic engineering in sericulture. These innovations not only promise to enhance silk production but also broaden the utility of silkworms as biofactories for future biotechnological applications.

## 8. Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Mode (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

## 9. Competing Interests

Authors have declared that no competing interests exist.

## References

1. Anzalone AV, Randolph PB, Davis JR, Sousa AA, Koblan LW, Levy JM, *et al.* Search-and-replace genome editing without double-strand breaks or donor DNA. Nature. 2019 Dec;576(7785):149-157.
2. Cong L, Ran FA, Cox D, Lin S, Barretto R, Habib N, *et al.* Multiplex genome engineering using CRISPR/Cas systems. Science. 2013 Feb 15;339(6121):819-823.
3. Dong Z, Qin Q, Hu Z, Zhang X, Miao J, Huang L, *et al.* CRISPR/Cas12a mediated genome editing enhances *Bombyx mori* resistance to BmNPV. Front Bioeng

Biotechnol. 2020 Jul 15;8:841. doi: 10.3389/fbioe.2020.00841. PMID: 32760714; PMCID: PMC7373793.
4. Doudna JA, Charpentier E. The new frontier of genome engineering with CRISPR-Cas9. Science. 2014 Nov 28;346(6213):1258096. doi: 10.1126/science.1258096. PMID: 25430774.
5. Esvelt KM, Smidler AL, Catteruccia F, Church GM. Concerning RNA-guided gene drives for the alteration of wild populations. Elife. 2014 Jul 17;3:e03401. doi: 10.7554/eLife.03401. PMID: 25035423; PMCID: PMC4117217.
6. Gaudelli NM, Komor AC, Rees HA, Packer MS, Badran AH, Bryson DI, *et al.* Programmable base editing of A•T to G•C in genomic DNA without DNA cleavage. Nature. 2017 Nov 23;551(7681):464-471.
7. Goldsmith MR, Shimada T, Abe H. The genetics and genomics of the silkworm, *Bombyx mori*. Annu Rev Entomol. 2005;50:71-100. doi: 10.1146/annurev.ento.50.071803.130456. PMID: 15355234.
8. Gundi R, Vanitha C, Tulsi KN, Velusamy L, Ramesha A, Ponnuvel KM, *et al.* Molecular marker assisted breeding and development of bidensovirus resistant and thermo tolerant silkworm (*Bombyx mori*) hybrids suitable for tropical climatic conditions. Agricultural Research. 2023;12(4):428-438.
9. Jiang L, Wang G, Cheng T, Yang Q, Jin S, Lu G, *et al.* Resistance to *Bombyx mori* nucleopolyhedrovirus via overexpression of an endogenous antiviral gene in transgenic silkworms. Arch Virol. 2012 Jul;157(7):1323-1328. doi: 10.1007/s00705-012-1309-8. PMID: 22527866.
10. KAIKObase. Available from: https://kaikobase.dna.affrc.go.jp/
11. Yu L, Cao Y, Ge S, Xu A, Qian H, Li G. Identification of key genes involved in resistance to early stage of BmNPV infection in silkworms. Viruses. 2022 Oct 29;14(11):2405. doi: 10.3390/v14112405. PMID: 36366503; PMCID: PMC9694779.
12. Lie Z, Cheng L, Fang-yin D, Shou-min F. Mapping of major quantitative trait loci for economic traits of silkworm cocoon. Genet Mol Res. 2010;9(1):78-88. doi: 10.4238/vol9-1gmr676. PMID: 20092037.
13. Chen S, Hou C, Bi H, Wang Y, Xu J, Li M, *et al.* Transgenic CRISPR/Cas9-mediated viral gene targeting for antiviral therapy of *Bombyx mori* nucleopolyhedrovirus. J Virol. 2017 Jul 28;91(18):e00379-17. doi: 10.1128/JVI.00379-17. PMID: 28747501.
14. Maheswari M, Tulsi Naik, Sur Chaudhuri R, Lokesh G, Sreenivasa BT. Marker-assisted selection of bivoltine silkworm genetic resources for thermotolerance. Current Journal of Applied Science and Technology. 2023;42(22):17-33.
15. SilkDB. Available from: http://silkworm.genomics.org.cn/
16. Tang YH, Zhang X, Dai ZC, Li H, Yang Y, Zhao TJ, *et al.* CRISPR-Cas13-mediated RNA editing in the silkworm *Bombyx mori*. Zool Res. 2024 Nov 18;45(6):1249-1260. doi: 10.24272/j.issn.2095-8137.2024.105. PMID: 39397244; PMCID: PMC11668950.
17. Teule F, Miao YG, Sohn BH, Kim YS, Hull JJ, Fraser MJ Jr, *et al.* Silkworms transformed with chimeric silkworm/spider silk genes spin composite silk fibers with improved mechanical properties. Proc Natl Acad Sci U S A. 2012 Jan 17;109(3):923-928. doi: 10.1073/pnas.1109420109. PMID: 22215590; PMCID: PMC3271896.
18. Tomita M, Munetsuna H, Sato T, Adachi T, Hino R, Hayashi M, *et al.* Transgenic silkworms produce recombinant human type III procollagen in cocoons. Nat Biotechnol. 2003 Jan;21(1):52-56. doi: 10.1038/nbt771. PMID: 12483223.
19. Tomita M. Transgenic silkworms that weave recombinant proteins into silk cocoons. Biotechnol Lett. 2011 Apr;33(4):645-654. doi: 10.1007/s10529-010-0498-z. PMID: 21184136.
20. Tamura T, Sezutsu H, Kobayashi I, Kojima K, Kanda T, Uchino K. Production of recombinant proteins in transgenic silkworms. Nat Biotechnol. 2000 Jan;18(1):81-84. doi: 10.1038/71978. PMID: 10625398.
21. Miao X, Xu S, Li M, Li M, Huang J, Dai F, *et al.* Simple sequence repeat-based consensus linkage map of *Bombyx mori*. Proc Natl Acad Sci U S A. 2005 Nov 8;102(45):16303-16308. doi: 10.1073/pnas.0507794102. PMID: 16260754; PMCID: PMC1283455.
22. Xia Q, Li S, Feng Q. Advances in silkworm studies accelerated by the genome sequencing of *Bombyx mori*. Annu Rev Entomol. 2014;59:513-536. doi: 10.1146/annurev-ento-011613-161940. PMID: 24160415.
23. Xia Q, Zhou Z, Lu C, Cheng D, Dai F, Li B, *et al.*; Biology Analysis Group. A draft sequence for the genome of the domesticated silkworm (*Bombyx mori*). Science. 2004 Dec 10;306(5703):1937-1940. doi: 10.1126/science.1102210. PMID: 15591204.
24. Xiao W, Chen P, Xiao J, Wang L, Liu T, Wu Y, *et al.* Comparative transcriptome profiling of a thermal resistant vs. sensitive silkworm strain in response to high temperature under stressful humidity condition. PLoS One. 2017 May 18;12(5):e0177641. doi: 10.1371/journal.pone.0177641. PMID: 28542312; PMCID: PMC5436693.
25. Yamamoto K, Nohata J, Kadono-Okuda K, Narukawa J, Sasanuma M, Sasanuma S, *et al.* A BAC-based integrated linkage map of the silkworm *Bombyx mori*. Genome Biol. 2008 Jan 28;9(1):R21. doi: 10.1186/gb-2008-9-1-r21. PMID: 18226216; PMCID: PMC2395255.
26. Yamamoto K, Higashiura A, Hirowatari A, *et al.* Characterisation of a diazinon-metabolising glutathione S-transferase in the silkworm *Bombyx mori* by X-ray crystallography and genome editing analysis. Sci Rep. 2018 Nov 13;8:16835. doi: 10.1038/s41598-018-35207-8. PMID: 30425277; PMCID: PMC6237302.
27. Yang X, Zhang X, Liu Y, Yang D, Liu Z, Chen K, *et al.* Transgenic genome editing-derived antiviral therapy to nucleopolyhedrovirus infection in the industrial strain of the silkworm. Insect Biochem Mol Biol. 2021 Dec;139:103672. doi: 10.1016/j.ibmb.2021.103672. PMID: 34506871.