

GENERAL ARTICLE

Genomic Insights into Insecticide Resistance in the Fall Armyworm and Implications for Pest Management

Ranjitha S. M.*, Suresh M. Nebapure, Rajna S. and Preeti Sharma

ICAR-Indian Agricultural Research Institute, New Delhi-110012, India

* ranjithasm6@gmail.com; ORCID ID [0009-0002-3200-9547](https://orcid.org/0009-0002-3200-9547)

Abstract

The fall armyworm, *Spodoptera frugiperda* (J.E. Smith) is a highly invasive and destructive agricultural pest that threatens global food security because of its broad host range, high reproductive capacity, and remarkable adaptability. Since its introduction into Africa and Asia, it has spread rapidly and now infests more than 350 plant species, including maize, cotton, rice, sorghum, and wheat. Although insecticides remain the primary means of control, their effectiveness has declined owing to the rapid evolution of insecticide resistance. Resistance mainly develops through two mechanisms: target-site resistance, where genetic mutations reduce insecticide binding, and metabolic resistance, in which detoxification enzymes such as cytochrome P450 monooxygenases, carboxylesterases, glutathione S-transferases, and ATP-binding cassette transporters detoxify or eliminate insecticides before they reach their target sites. Recent advances in whole-genome sequencing, comparative genomics, transcriptomics, RNA sequencing, single-nucleotide polymorphism (SNP) discovery, and molecular diagnostics have improved the identification of resistance-associated genes and markers and enabled population-level molecular surveillance. Integrating genomic knowledge with insecticide rotation and integrated pest management is essential for delaying resistance evolution and ensuring long-term suppression of fall armyworm populations.

Keywords: Insecticide resistance, genomics, target-site resistance, metabolic resistance, integrated pest management.

Introduction

The fall armyworm, *Spodoptera frugiperda* (J.E. Smith) (Lepidoptera: Noctuidae), has become one of the most serious invasive insect pests affecting agricultural production worldwide. Originally distributed in the Americas, it has expanded rapidly into Africa, Asia, and Oceania, where it now causes extensive damage to maize and numerous other economically important crops. Its remarkable invasive success is attributed to its long-distance migratory ability, high reproductive capacity, broad host range exceeding 350 plant species, and

adaptability to diverse agroecological conditions (Montezano et al., 2018). Since its first occurrence in Karnataka, India, in 2018, the pest has spread throughout nearly all major maize-growing regions, creating significant challenges for crop production and food security. The rapid establishment of fall armyworm populations, together with the increasing occurrence of insecticide resistance, has intensified concerns regarding its sustainable management (Mamahit and Kolondam, 2023).

Evidence of insecticide resistance in *S. frugiperda* was first documented in the United

States during the late 1970s, when field populations from Georgia and Alabama exhibited reduced susceptibility to synthetic pyrethroids. Subsequent studies reported resistance to additional insecticides, including carbaryl, methyl parathion, and trichlorfon (Young and McMillan, 1979). Since then, the pest has developed resistance to multiple insecticide groups, making chemical management increasingly difficult. By 2017, resistance had been recorded against 29 active ingredients representing six different modes of action across the Americas (Van den Berg and du Plessis, 2022). According to the Arthropod Pesticide Resistance Database (APRD, 2025), resistance has now been documented to 47 insecticidal active ingredients belonging to several chemical classes, with approximately 280 confirmed resistance cases reported globally.

Although insecticides remain indispensable for the management of fall armyworm, their field performance has gradually declined in many regions. Frequent and repeated application of the same insecticides imposes strong selection pressure on pest populations, enabling resistant individuals to survive treatments and pass resistance-associated traits to their offspring. As these resistant insects become more prevalent over successive generations, the effectiveness of insecticides decreases, resulting in repeated control failures and making the long-term management of fall armyworm increasingly challenging. Recent advances in genomics have expanded the study of insecticide resistance beyond conventional physiological and biochemical assays. In *S. frugiperda*, whole-genome sequencing has been used to detect resistance-associated variants in genes such as *ace-1*, the voltage-gated sodium channel (VGSC), ryanodine receptor (RyR), and ABCC2, demonstrating the value of genomic approaches for linking genetic variation with resistance phenotypes (Guan et al.,

2021). Furthermore, these genomic approaches provide candidate molecular markers that can be incorporated into rapid diagnostics, allowing resistance alleles to be tracked via targeted molecular surveillance before they become widespread in field populations (Mavridis et al., 2025).

How Does Insecticide Resistance Develop?

Insecticide resistance is an evolutionary process driven by natural selection within insect populations. Naturally occurring genetic variation means that a small proportion of individuals may carry genes that reduce their susceptibility to a particular insecticide. Following repeated exposure to the same insecticide, susceptible insects are eliminated, whereas resistant individuals survive and continue to reproduce. Their offspring inherit the resistance traits, gradually increasing the frequency of resistant genes in subsequent generations. As this process continues, resistant individuals become dominant within the population, leading to a progressive decline in the effectiveness of the insecticide (Fig. 1). Consequently, pest management becomes less reliable, and satisfactory control may no longer be achieved even when insecticides are applied at the recommended field rates (Panini et al., 2016).

Mechanism of resistance

Resistance is an adaptive phenomenon that results from physiological and biochemical modifications in insects, enabling them to survive insecticide exposure. These adaptations involve changes in both toxicokinetic and toxicodynamic processes. Toxicokinetic mechanisms influence the absorption, activation, metabolism, transport, and elimination of insecticides, thereby reducing the amount of toxic compound that reaches its target site and contributing to metabolic

resistance. In contrast, toxicodynamic mechanisms alter the interaction between the insecticide and its target through structural modifications, gene amplification, or target-site mutations, thereby contributing to target-site resistance and decreasing the insecticide's effectiveness (Kennedy & Tierney, 2012; Fig. 2).

How Does the Fall Armyworm Outsmart Insecticides?

FAW survives insecticide exposure mainly through **two remarkable defence strategies** (Fig. 3)

- **Changing the insecticide target (Target-site resistance)**
- **Detoxifying insecticides before they can act (Metabolic resistance)**

Together, these mechanisms greatly reduce the effectiveness of chemical control and complicate resistance management.

Changing the Lock: Target-Site Insensitivity

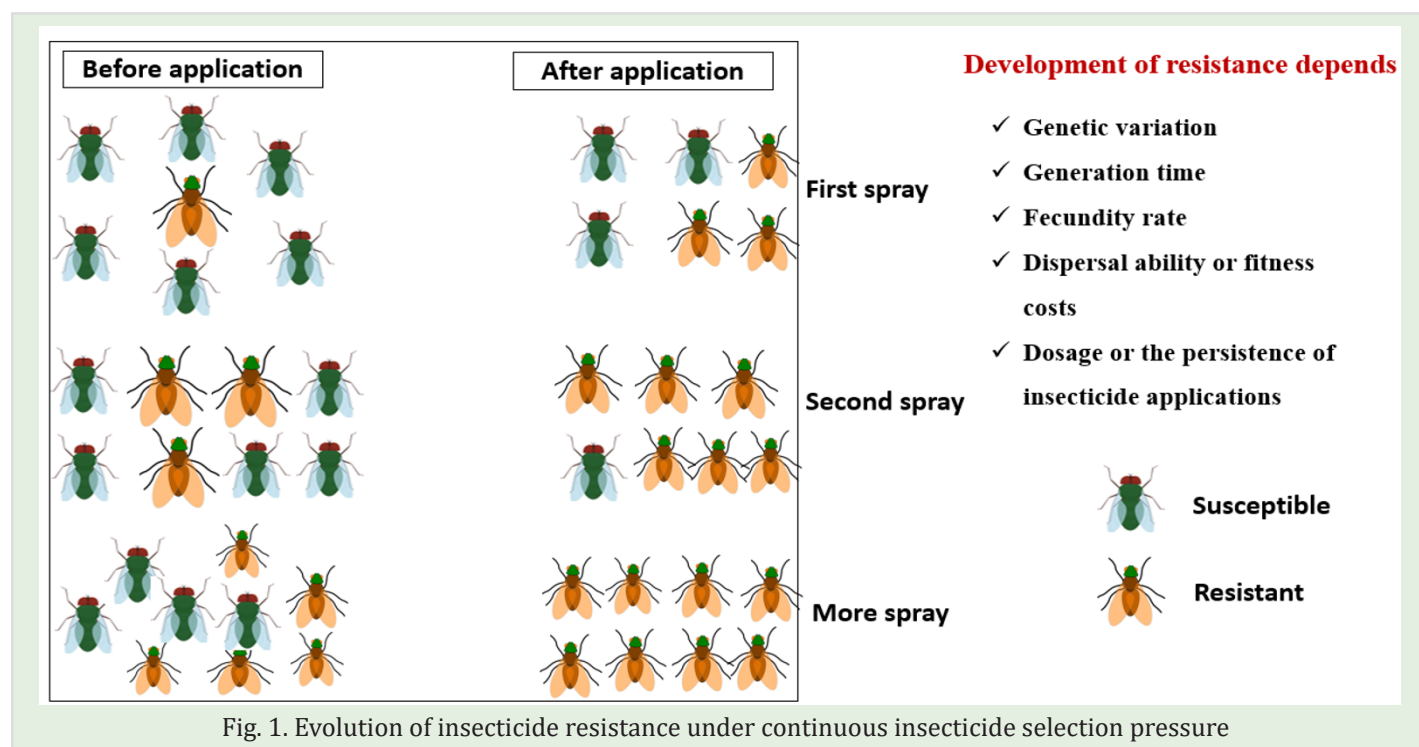
Target-site resistance results from alterations in insecticide target proteins caused

by genetic mutations or changes in target-gene expression, thereby decreasing the sensitivity of insects to these chemicals. A useful analogy is to imagine the insecticide as a key and the target protein as a lock. When mutations change the shape or properties of the lock, the key can no longer interact with it effectively, allowing the insect to survive. In *S. frugiperda*, resistance-associated variants have been documented in several target genes, although the strength of experimental evidence differs among targets.

Several important target proteins have been identified in *S. frugiperda*.

Acetylcholinesterase (AChE)

AChE is a serine hydrolase enzyme that terminates nerve impulse transmission by hydrolysing acetylcholine at cholinergic synapses. It contains a conserved **Ser-His-Glu catalytic triad** located within a deep active-site gorge, along with an anionic binding site that facilitates acetylcholine binding. AChE is the primary target of **organophosphate and carbamate insecticides**, which inhibit the enzyme and disrupt



normal nerve function. However, mutations in the **Ace-1** gene reduce the binding affinity of these insecticides, allowing normal nerve transmission to continue and thereby conferring resistance (Davir et al., 2010). In case *S. frugiperda* mutation of the *ace-1* gene revealed three amino acid substitutions in the acetylcholinesterase (AChE) gene (A201S, G227A, and F290V) were associated with organophosphate resistance (Carvalho et al., 2013).

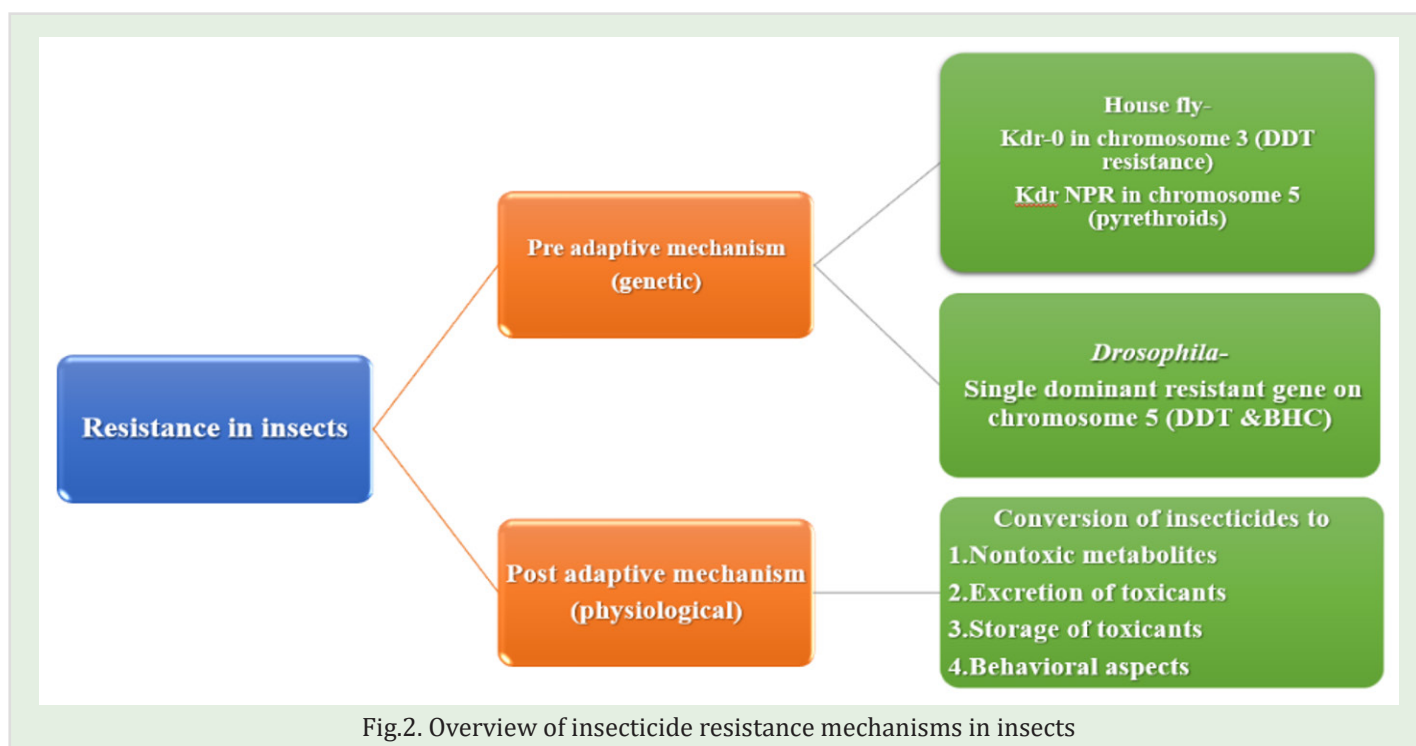
Voltage-gated sodium channel (VGSC)

VGSC consists of six transmembrane segments (S1–S6), where S1–S4 function as voltage sensors and S5–S6 form the sodium-conducting pore. Pyrethroids bind to a hydrophobic pocket between the S4–S5 linker and S5–S6 helices, disrupting normal channel function and causing prolonged nerve excitation. **Knockdown resistance (kdr)** mutations in the **VGSC** gene reduce pyrethroid binding, resulting in insecticide resistance (Field et al., 2017). There are six target VGSC gene mutations (M918T, I936V, F1020S, T929I, L932F, and L1014F) identified in

lambda-cyhalothrin resistant population (Wang et al., 2023a). Point mutations in VGSC (T929I, L932F, and L1014F) are associated with resistance to pyrethroid insecticide insecticides and Bt proteins in *S. frugiperda* (Guan et al., 2021).

Glutamate-gated chloride channel (GluCl)

A Cys-loop ligand-gated ion channel that acts as the molecular target of avermectins such as abamectin and emamectin benzoate. Binding of glutamate opens the chloride channel, whereas avermectins bind between adjacent transmembrane domains (M1 and M3), causing prolonged chloride influx, neuronal hyperpolarization, paralysis, and insect death (Ozoe et al., 2013). Alterations in GluCl can reduce insecticide sensitivity and contribute to resistance. Wang et al. (2023b) reported that the higher expression of SfGluCl gene in the head and nerve cord was significantly higher than that in other tissues. They found that the expression level of SfGluCl was significantly higher in eggs than in other developmental stages. Knockdown of the GluCl gene reduced FAW mortality by EB, suggesting its key role in EB effectiveness. Cai et al.



(2024) reported that, four target-site mutations—A309V, G314D, A309T, and G326E—were identified in the GluCl channel of the fall armyworm (FAW).

Ryanodine receptor (RyR)

RyR is a calcium-release channel located in the sarcoplasmic reticulum and is the primary target of diamide insecticides, including chlorantraniliprole and flubendiamide. Binding of diamides to the receptor disrupts calcium homeostasis, leading to continuous muscle contraction, paralysis, and ultimately insect death. Mutations such as **G4946E**, **I4790M**, and **I4734M** reduce diamide sensitivity and have been reported in resistant lepidopteran pests, including *S. frugiperda* (Zuo et al., 2020). The molecular studies, including PCR amplification and sequencing of a FAW RyR fragment, revealed the presence of an I4790M mutation in the C-terminal region, previously associated with target-site mutations in diamide-resistant lepidopteran pests (Boaventura et al., 2020)

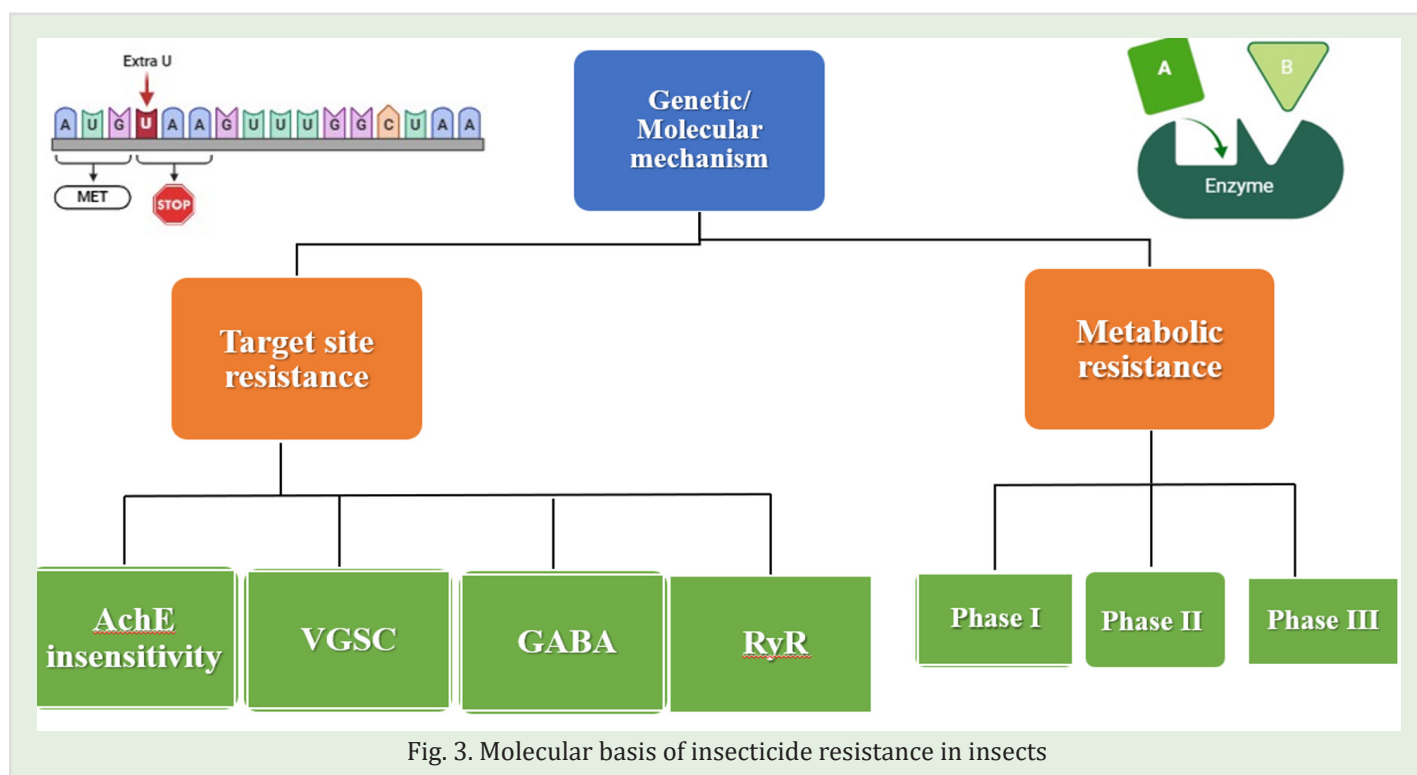
Chitin synthase A (CHSA)

CHSA gene encodes the enzyme responsible

for chitin biosynthesis, making it the target of benzoylurea insecticides such as lufenuron. The enzyme contains a catalytic domain and multiple transmembrane helices that facilitate chitin polymer synthesis and transport. Mutations in the **CHSA** gene, particularly **I1043L**, are associated with resistance to benzoylurea insecticides in several insect species. In *S. frugiperda*, however, no resistance-conferring mutation has been identified in **SfCHSA**. Nevertheless, the increased expression of **SfCHSA** after lufenuron exposure indicates that changes in gene regulation may contribute to reduced susceptibility (Lv et al., 2022).

Insect's Chemical Defence Factory: Detoxification mechanism

Metabolic resistance is characterized by increased detoxification of insecticides rather than alterations in their target proteins, limiting the amount of insecticide available to produce toxicity. This defence system functions much like a **chemical processing factory** and involves three major enzyme families.



Phase I: Cytochrome P450 Monooxygenases (CYPs): The First Line of Defence

Cytochrome P450 genes (CYP) represent one of the largest gene families, found in nearly all living organisms. CYPs catalyze a wide range of reactions, including hydroxylation, epoxidation, and oxidation. In insects, CYPs play a role in endogenous metabolism, such as ecdysteroid biosynthesis and hydrocarbon production, and are also involved in detoxifying xenobiotics. Cytochrome P450 enzymes chemically modify insecticides through oxidation, reducing their toxicity. The FAW genome contains an exceptionally large P450 gene family comprising **425 CYP genes**, including **283 species-specific genes**, reflecting its remarkable detoxification potential (Gui et al., 2022).

Carboxyl/Cholinesterases (CCEs): Breaking Down Insecticides

Insect carboxylesterases, also known as carboxyl/cholinesterases (CCEs), are involved in a variety of physiological processes in living things, including the detoxification of different xenobiotics and the metabolism of endogenous substances like hormones, pheromones, and neurotransmitters. They are essential for protection against a variety of allelochemicals found in plants and insecticides (Oakeshott et al., 2005). Carboxylesterases hydrolyse organophosphates, carbamates and pyrethroids before they reach their targets. Nearly **96 CCE genes** have been identified in *S. frugiperda*, and overexpression of members of the **CCE001** family has been strongly associated with metabolic resistance (Gouin et al., 2017).

Phase II: Glutathione S-transferases (GSTs): Neutralising Toxic Molecules

GSTs conjugate glutathione to suitable electrophilic compounds or metabolites, increasing their water solubility and facilitating elimination.

In insects, the Delta and Epsilon classes are particularly important for xenobiotic detoxification and have been repeatedly implicated in insecticide resistance. GSTs convert toxic metabolites into water-soluble compounds that can be safely removed from the insect body (Koirala et al., 2022). Transcriptomic studies have identified **31 GST genes**, many of which are induced after exposure to chlorantraniliprole and emamectin benzoate (Aioub et al., 2023).

Phase III: ABC Transporters: Pumping Out the Poison

ATP-binding cassette (ABC) transporters do not directly detoxify insecticides enzymatically. Instead, they use ATP to transport insecticides, their conjugates, and other metabolites across cellular membranes, thereby reducing intracellular accumulation and facilitating excretion. Mutations in ABCC2 and ABCC3 have also been associated with resistance to *Bacillus thuringiensis* (Bt) Cry toxins, illustrating that ABC proteins can also act as receptors or components of toxin-response pathways in addition to their transport functions (Franz et al., 2022).

Implication

- Reduced Effectiveness of Insecticides: Leading to control failures and increased pest numbers.
- Increased Use of Insecticides: higher doses and more frequent applications.
- Increased Costs and Economic Losses: Higher costs due to the need for additional insecticide applications.
- Environmental and Non-Target Impacts: Environmental contamination, affecting soil, water, and non-target organisms.
- Cross-Resistance and Multi-Resistance:

Resistance to a single insecticide may also reduce susceptibility to other insecticides within the same or even different chemical classes.

- **Challenges for Integrated Pest Management:** Resistance can reduce the number of effective chemical options available within IPM programmes, making coordination of biological, cultural, mechanical, physical, and chemical tactics more difficult.
- **Rapid Spread of Resistant Invasive Populations:** The high dispersal capacity of FAW can facilitate the movement of resistance alleles between regions, particularly when resistant individuals are introduced into newly invaded areas.

Integrated Resistant Management

- **Rotation of Insecticides:** Insecticides should be rotated according to their IRAC mode-of-action (MoA) groups rather than simply alternating products with different trade names. Sequential use of insecticides with the same MoA can impose similar selection pressure and favour resistant genotypes; rotation across effective MoA groups can reduce this pressure when implemented with appropriate label and resistance-management guidance
- **Use of Synergists:** Synergists that inhibit specific detoxification enzymes can restore susceptibility in some cases and can also help identify metabolic mechanisms, but their practical use depends on regulatory approval and demonstrated field relevance.
- **Negative Cross-Resistance:** Negative cross-resistance occurs when resistance to one compound is associated with increased susceptibility to another compound.

Where this relationship is experimentally demonstrated, it may provide an additional option for designing rotation strategies.

- **Integrated Pest Management (IPM):** Combining biological, cultural, mechanical, physical, and judicious chemical control methods to achieve sustainable pest management.
- **Biotechnological Approaches:** Gene-editing technologies such as CRISPR/Cas9 and RNA interference (RNAi) can help validate candidate resistance genes and may contribute to future diagnostic or control approaches.
- **Regular Monitoring:** Tracking resistance trends in pest populations to detect early signs and implement timely interventions.

Conclusion

The remarkable adaptability of the fall armyworm has enabled it to evolve resistance through two major mechanisms: **target-site resistance**, in which mutations reduce insecticide binding, and **metabolic resistance**, in which detoxification enzymes rapidly degrade insecticides before they reach their targets. Advances in genomics have greatly improved our understanding of these resistance mechanisms and provided valuable tools for monitoring resistant populations. Nevertheless, sustainable management requires these molecular insights to be translated into routine resistance monitoring and practical insecticide-resistance management. Looking ahead, genomic surveillance, molecular diagnostics, and integrated phenotypic monitoring will play an increasingly important role in detecting emerging resistance alleles, tracking their spread, and supporting evidence-based insecticide selection and IPM programmes. Such

a forward-looking approach can help preserve the effectiveness of existing insecticides, delay resistance evolution, and support long-term management of fall armyworm populations.

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