

GENERAL ARTICLE

Insect Epigenetics: Vital Information for Next-Gen Pest Management

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Abstract

Epigenetics is transforming our understanding of insect biology by revealing how gene activity can be regulated without altering the underlying DNA sequence. Through mechanisms such as DNA methylation, histone modifications, and non-coding RNAs, insects rapidly respond to environmental cues, influencing development, behaviour, insecticide resistance, stress adaptation, and interactions with symbionts and pathogens. Unlike permanent genetic mutations, epigenetic modifications are reversible and, in some cases, can be inherited across generations, enabling pest populations to adapt rapidly to changing environments and management practices. Recent discoveries have demonstrated that epigenetic regulation contributes to xenobiotic detoxification, climate resilience, diapause, migration, and host-microbe interactions, highlighting its significance in pest ecology. Advances in RNA interference, CRISPR/dCas9-mediated epigenome editing, epigenetic priming, and small-molecule inhibitors offer exciting opportunities to exploit these mechanisms for sustainable pest control. Although technical and ecological challenges remain, integrating epigenetic knowledge into integrated pest management promises innovative, precise, and environmentally friendly strategies for managing insect pests in the era of climate change and emerging insecticide resistance.

Keywords: DNA methylation; Transgenerational resistance; non-coding RNA; Epi-transcriptomics; Stress memory; dCas9

Introduction

Every insecticide spray, every resistant pest population, every characteristic and miraculous behaviour of insects is being explained nowadays purely through the lens of genetic information: mutations, gene amplifications, inherited alleles. But a quieter layer of biology has been steering these same outcomes all along. It doesn't change a single letter of the genetic code, yet it decides which genes speak, when they speak, and how loudly. In very simple terms, DNA is hardware, and epigenetics is software for a living organism. This is epigenetic, and for anyone working on insect pest management today, it is no longer a curiosity

confined to textbooks. It is becoming a working part of the toolkit for next-generation insect pest management.

Epigenetics: Language Beyond DNA

The word epigenetics was coined in the 1940s by embryologist Conrad Waddington, who imagined development as a ball rolling down a landscape of branching valleys, in the sense that genes provide the terrain and the environment nudges the ball's path (Waddington, 1942). Decades of molecular biology later, the definition has sharpened considerably; epigenetics is now understood as the study of mitotically and, in some cases, meiotically heritable changes in gene

function that occur without any change to the underlying DNA sequence.

What makes this field interesting for pest management is the question of inheritance. Not all epigenetic changes are passed on. Some of it is intragenerational: a single cell responds to a stimulus, and that response is faithfully copied every time the cell divides, which is essentially how one genome gives rise to hundreds of different cell types in a developing insect. Some of it is intergenerational: a parent's environment reprograms its germ cells, so the very next generation carries the mark. And a rarer category, transgenerational inheritance, means the change persists even in individuals who were never directly exposed to the triggering stimulus. It is this last category that has excited and worried entomologists the most, because it implies that a single stress event, such as one round of insecticide spraying, could leave a signature that outlives the exposed generation.

Insect Epigenetics and Underlying Mechanisms

Three molecular systems do most of the epigenomic framework; among them, DNA methylation the addition of a methyl group to cytosine bases is the best studied. Interestingly, insects methylate a much smaller fraction of their genome than vertebrates, and the marks are typically enriched within gene bodies rather than at promoters, the reverse of the canonical vertebrate pattern. However, this is a broad trend rather than a fixed rule, and methylation levels and patterns vary substantially across insect orders, ranging from near-total absence in dipterans such as *Drosophila* to appreciable gene-body methylation in Hymenoptera and other lineages that retain a functional Dnmt3 (Field et al., 2004; Provataris et al., 2018). Apart from these methylation marks,

the enzymes that write these marks, DNMT1 and DNMT3, are essential for reproduction and development in several insects investigated.

Histone modification is the second major system. DNA in the nucleus is spooled around histone proteins, and chemical tags, acetyl groups being the best known, determine how tightly that spool is packed. Loosely packed chromatin is accessible to transcription machinery; tightly packed chromatin is silent. Enzymes called histone acetyltransferases and deacetylases add and remove these tags respectively, and their balance has been shown to govern the timing of metamorphosis in moths and beetles (Mukherjee *et al.*, 2012).

The third system, non-coding RNA, encompasses several classes of small RNAs that regulate gene expression through mechanistically distinct routes. Small interfering RNAs (siRNAs) and microRNAs (miRNAs) act primarily at the post-transcriptional level: loaded into Argonaute proteins within the RNA-induced silencing complex (RISC), they base-pair with complementary messenger RNA to trigger its cleavage or translational repression, without directly altering chromatin state. PIWI-interacting RNAs (piRNAs), by contrast, function predominantly in the germline, where PIWI-clade Argonautes use them to silence transposable elements; alongside transcript cleavage, piRNA-PIWI complexes can be recruited to nascent transcripts at target loci to deposit repressive histone marks such as H3K9 methylation and promote heterochromatin formation - a chromatin-associated, transcriptional silencing role that siRNAs and miRNAs generally lack. Together, these pathways make non-coding RNA a genuinely two-tiered regulatory layer, both of which are now recognised as central to antiviral defence, silencing of mobile genetic elements in the

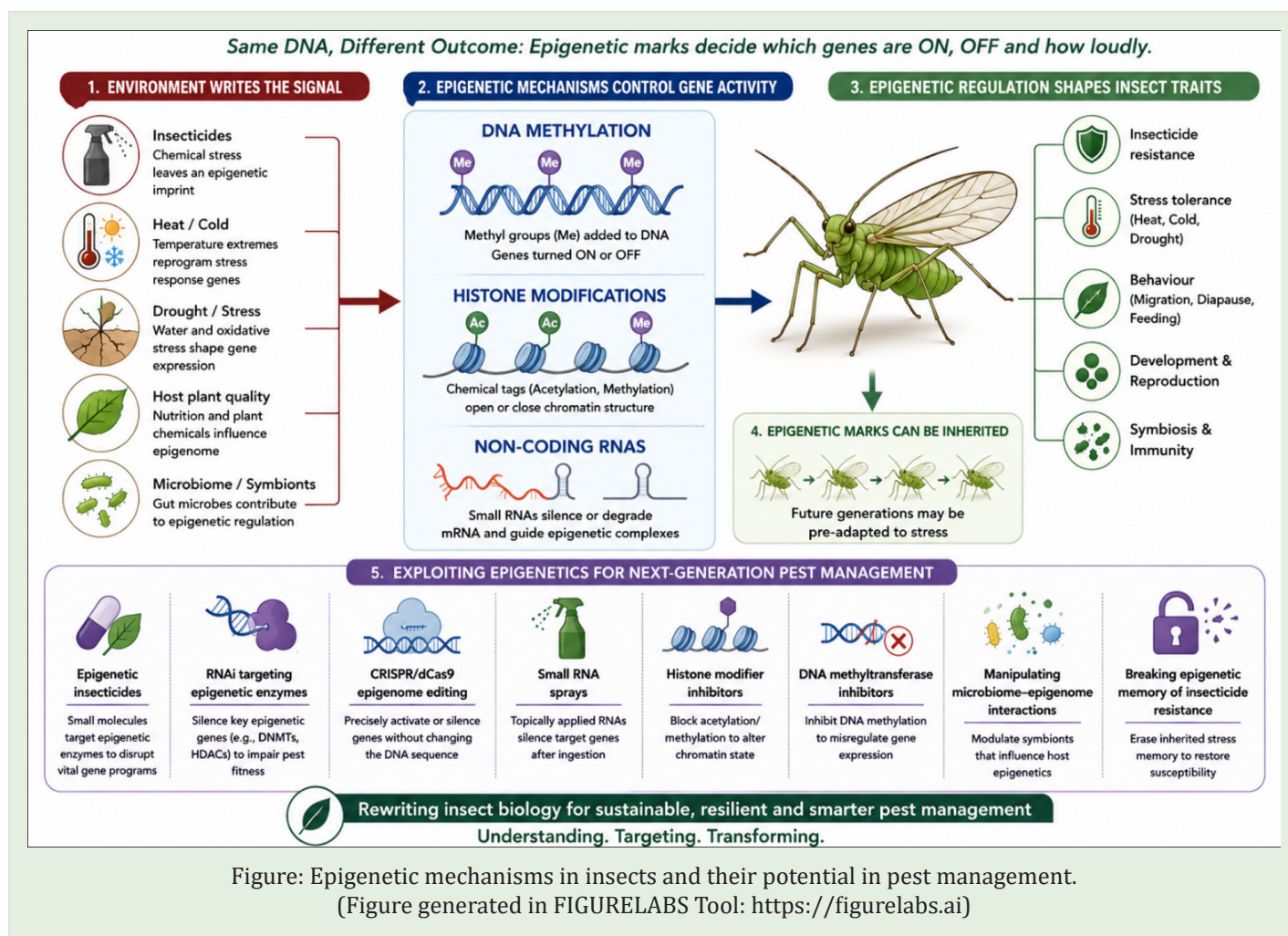


Figure: Epigenetic mechanisms in insects and their potential in pest management.
(Figure generated in FIGURELABS Tool: <https://figurelabs.ai>)

germline, and xenobiotic degradation (de Vanssay et al., 2013).

Insect Epigenome-Regulated Mechanisms: Refining Present Control Methods

Insect Physiology and Development

Development and reproduction in insects are epigenetically gated at several checkpoints. The transcriptional co-activator CREB-binding protein (CBP) also called as Nejire, which carries histone acetyltransferase activity, sits at the centre of a network with hundreds of interacting partners governing hormone signalling, metamorphosis, and circadian rhythm across insect orders (Hung et al., 2007). Because many downstream physiological outcomes converge on a small set of epigenetic regulators, these nodes are attractive candidates for targeted disruption.

Insect Behaviour

Two of the most dramatic insect behaviours are diapause and long-distance migration; both carry a possible epigenetic signature. In the parasitoid wasp *Nasonia vitripennis*, DNA methylation tracks the photoperiodic timer that guides the insect when to enter and exit dormancy, echoing the well-established role of epigenetic regulation in circadian clocks more broadly (Pegoraro et al., 2016). In the monarch butterfly, the same set of migratory genes is present in every generation, but it is switched on or off depending on the season, producing the reversal in flight direction seen between the outbound autumn migration and the return journey in spring, hypothesised to a possible epigenetics regulation, though not fully evident (Zhu et al., 2009). Much more concrete

evidence in insect behaviour is the migratory locust *Locusta migratoria*; epigenetic regulation has been experimentally linked to behavioural phase change. Knockdown of DNA methyltransferase 3 (Dnmt3) altered locomotor activity associated with the transition between solitary and gregarious phases and produced substantial changes in brain gene expression, implicating DNA methylation in the regulation of phase-related behaviour (Hou et al., 2020). More recently, chromatin accessibility was shown to regulate promoter usage of the dopamine-synthesis gene *henna* in response to population density, providing a mechanistic link between chromatin remodelling and gregarious behaviour (Li et al., 2025). Because gregarious locusts form migratory swarms, these findings demonstrate how epigenetic regulation can contribute to the behavioural plasticity underlying swarm formation and migration.

Drivers of Insecticide Resistance

Insecticide resistance costs the world tens of billions of dollars annually, and for decades the story was almost entirely genetic with target-site mutations, detoxifying enzyme amplification. The first evidence linking epigenetic modification to insecticide resistance came from the peach-potato aphid, *Myzus persicae*, where loss of resistance in clonal lineages was accompanied by a simultaneous loss of DNA methylation at the amplified esterase gene (Field et al., 1989) demonstrated methylation is tightly associated with the transcriptional state of the gene, although the direct causal role was not established. Since then, the investigations have widened considerably. Recent studies describe how DNA methylation can silence or activate detoxification genes, how histone acetylation dynamically remodels chromatin around stress-responsive loci and, in whiteflies, how an RNA-level modification called m6A methylation on

the CYP4C64 detoxification gene transcript enhances its expression and boosts enzymatic breakdown of insecticide, adding an entirely new “epi-transcriptomic” layer to the resistance story (Yang et al., 2021). The sublethal effect on parental generations drives the resistance marks to change in methylation pattern in the resistance conferring CYP genes of intergenerational offspring (Brevik et al., 2021). Evidence for the inheritance of stress-associated epigenetic changes across generations is emerging in insects, but the extent to which such inheritance contributes directly to insecticide resistance remains species and context-dependent. Unless we understand these mechanisms, solely the classic insecticide resistance mechanisms can't manage xenobiotic resistance in insects (Mogilicherla and Roy, 2023).

Microbiome Interactions

Many sap-feeding pests, whiteflies and aphids depend on obligate bacterial symbionts for nutrients supply, and the relationship is regulated epigenetically from both sides. *Wolbachia* infection, for instance, reshapes genome-wide DNA methylation patterns in the mosquito *Aedes aegypti* (Ye et al., 2013), silencing some genes and de-repressing hundreds of others, in part by suppressing the host's own methyltransferase (Zhang et al., 2013). Because *Wolbachia*-based approaches are already deployed for vector control, understanding this epigenetic cross-talk is directly relevant to refining those programmes.

Insect Parasite Interaction

Entomopathogens manipulate the host's epigenome rather than its DNA sequence, hijacking histone acetylation and deacetylation to delay development or blunt immune gene expression, buying themselves time to establish infection. Recent studies in this area describe it as a two-way

epigenetic arms race: hosts fine-tune immune gene expression through methylation, histone marks and small RNAs to fight back, while pathogens counter by reprogramming those very same systems (Sharakhov and Sharakhova, 2015).

Climate Adaptation

Heat waves, cold snaps, drought, starvation, and other environmental extremes are becoming increasingly frequent under climate change, challenging insect survival across ecosystems. Traditionally, stress tolerance in insects was attributed to physiological acclimation and natural selection acting on genetic variation. However, recent research has revealed that insects can also develop “epigenetic stress memory”, enabling them to rapidly adjust gene expression without altering their DNA sequence. The epigenetic mechanisms modulate genes involved in heat shock proteins (HSPs), antioxidant defence, energy metabolism, osmotic regulation, and immunity. Studies in insects such as *Drosophila melanogaster*, *Tribolium castaneum*, aphids, and mosquitoes suggest that some of these epigenetic signatures can persist beyond the exposed individual and be inherited by subsequent generations, producing offspring that are better equipped to withstand similar environmental stresses. Such transgenerational plasticity allows pest populations to establish rapidly in new environments, survive extreme climatic events, and expand their geographical distribution.

Understanding these adaptive mechanisms opens new opportunities for sustainable pest management. Targeting the epigenetic machinery that governs stress tolerance could reduce the ability of pests to cope with heat, cold, and drought, making them more vulnerable to climatic extremes and increasing the efficacy of insecticides and biological control agents. Integrating epigenetic

insights into pest forecasting could also improve predictions of climate-driven pest outbreaks and invasions. As global temperatures continue to rise, deciphering insect epigenetic stress responses will be crucial for developing resilient and climate-smart integrated pest management strategies.

Approaches to Reframe these Epigenetic Mechanisms for Insect Pest Control

Unlike DNA sequence, epigenetic marks are, in principle, reversible, which is exactly what makes them attractive as management targets.

CRISPR-Cas9 has added a second layer of precision. Beyond making outright gene deletions, a catalytically “dead” version of the Cas9 enzyme (dCas9) can be fused to activator or repressor domains and guided to a specific locus, switching a gene on or off without cutting the DNA at all, a programmable epigenome editing (Brocken et al., 2018). This has already been demonstrated in flies, ants and butterflies, and offers a route to testing exactly which epigenetic marks are functionally responsible for a given pest phenotype, rather than merely correlated with it.

Epigenetic priming in plants, an adaptive strategy observed in plants, enhances the activation of induced defence mechanisms, fortifying plants against impending herbivore threats. RNA-directed DNA methylation (RdDM) is another approach to utilise these epigenetic mechanisms, making plants resistant to insects. So far, the proof of concept for these techniques has been performed in a few model plants (Reddy et al., 2025).

Finally, the use of small-molecule drugs that interfere chemically with the enzymes writing or erasing epigenetic marks includes 5-azacitidine and zebularine, which block DNA methylation, while compounds such as trichostatin A inhibit histone deacetylases. In the carpenter ant, one such

drug reversibly altered worker behaviour, and its effect could even be “rescued” by co-administering a second drug that targets an overlapping pathway (Simola et al., 2016).

Bottlenecks in Studying Epigenetics

Though these mechanisms sound fascinating, practical field deployment and accurate exploration are formidable challenges. Techniques such as bisulfite sequencing, methylation-sensitive amplification polymorphism, and chromatin immunoprecipitation remain expensive and technically demanding for routine use outside well-funded laboratories. Off-target effects are a genuine concern for both RNAi and CRISPR-based epigenome editing, and the ecological and ethical implications of deliberately manipulating heritable information in wild or semi-wild insect populations are only beginning to be discussed seriously. Most of the studies are from a handful of model species: *Drosophila*, *Tribolium*, *Apis mellifera*, and *Nasonia*, while economically important non-model pests remain comparatively understudied.

Road Ahead

Insecticide resistance research is increasingly treating epigenetic marks as a mechanism in their own right rather than a footnote to genetic mutation. RNAi and epigenome-editing platforms are converging on field-ready delivery systems and species like the whitefly, already central to virus transmission and resistance concerns in agriculture, are emerging as genuinely useful epigenetic models rather than side notes to *Drosophila*. Epigenetics will not replace conventional pest management, but as a layer of biology that governs resistance, behaviour, symbiosis and development.

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