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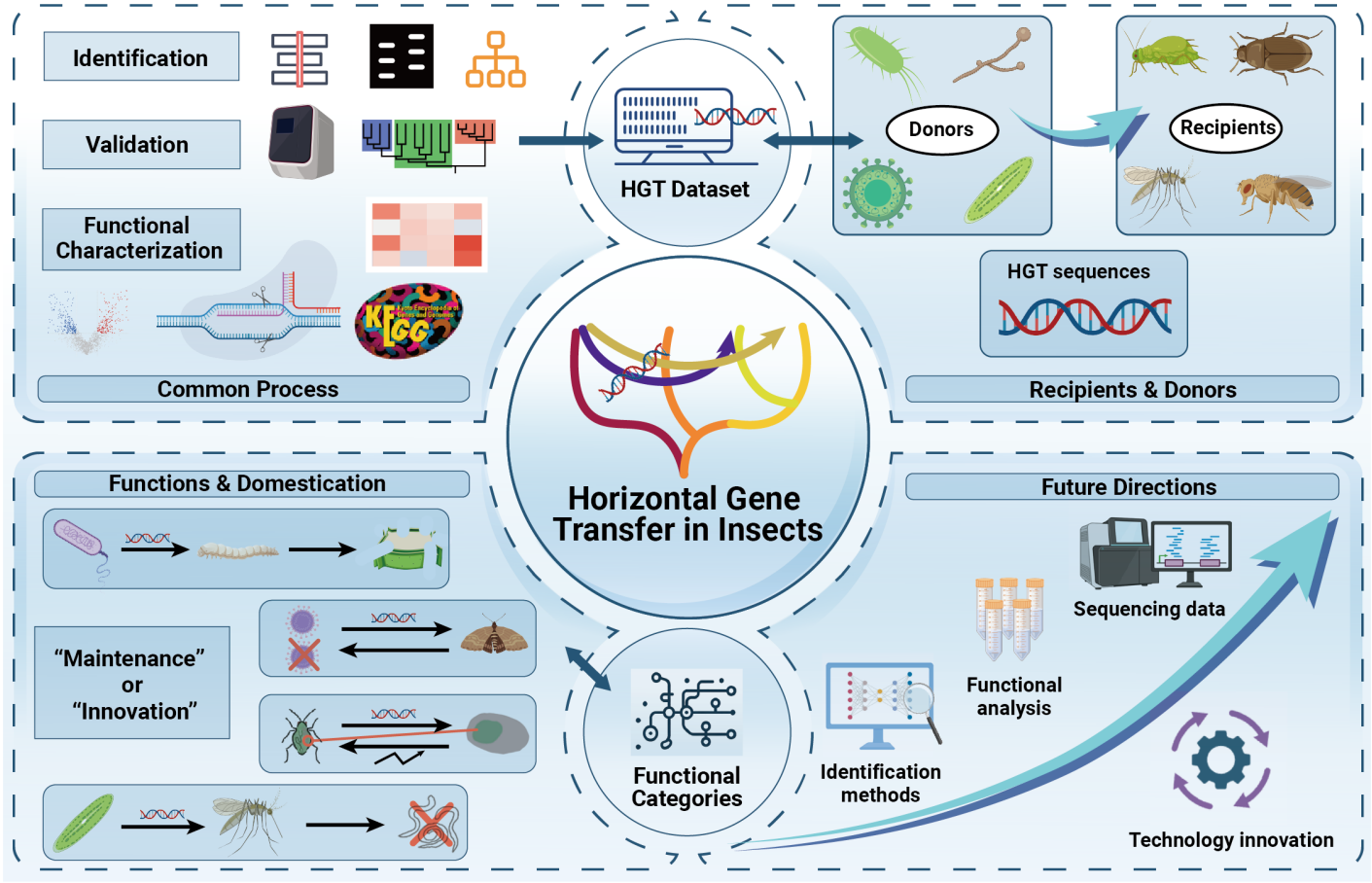
Dongwu Zhan,[1] Zening Wang,[1] Jixing Xia,[1] Yuange Duan,[1] Ling Ma,[1] Li Tian,[1] Wanzhi Cai,[1] and Hu Li[1,*]

*Correspondence: tigerleecau@hotmail.com

Received: December 3, 2025; Accepted: May 26, 2026; Published Online: May 29, 2026; https://doi.org/10.59717/j.xinn-life.2026.100223

GRAPHICAL ABSTRACT



PUBLIC SUMMARY

- Horizontal gene transfer (HGT) can drive evolutionary innovation via cross-species transfer of genes.
- Insect HGT are commonly analyzed through identification, validation, and functional exploration.
- We compiled 3336 insect HGT-origin peptides, identifying bacteria and fungi as the primary donor sources.
- HGT facilitate symbiosis and biosynthesis, undergoing domestication via maintenance or innovation.

REVIEW Animal Science

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Horizontal gene transfer in insects: Insights into origins, detection, and functional roles

Dongwu Zhan,[1] Zening Wang,[1] Jixing Xia,[1] Yuange Duan,[1] Ling Ma,[1] Li Tian,[1] Wanzhi Cai,[1] and Hu Li[1,*]

[1]State Key Laboratory of Agricultural and Forestry Biosecurity, College of Plant Protection, China Agricultural University, Beijing 100193, China

*Correspondence: tigerleecau@hotmail.com

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Citation: Zhan D., Wang Z., Xia J., et al. (2026). Horizontal gene transfer in insects: Insights into origins, detection, and functional roles. *The Innovation Life* **4**:100223.

Unlike vertical gene transfer, horizontal gene transfer (HGT) allows organisms to acquire genetic material from distantly related lineages, serving as a vital source of evolutionary innovation beyond conventional inheritance. Advances in meta-omics technologies have enabled the identification of thousands of horizontally transferred genes (HTGs) across diverse insect taxa, with mounting evidence supporting their recurrent integration and functional importance. This review synthesizes current understanding of insect HGT, focusing on four major themes: (1) Methodologies for detecting HGT have evolved from PCR-based assays to include parametric and phylogenetic approaches, often complemented by transcriptomic validation; (2) Donor sources span bacteria, fungi, viruses, plants, and metazoans, with bacterial endosymbionts being the predominant contributors, and Lepidoptera, Hemiptera, and Coleoptera emerging as the most frequent recipients; (3) Functional analyses indicate lineage-specific biases, with the majority of well-characterized HTGs involved in glycoside hydrolysis or symbiosis-related processes; (4) HTGs undergo domestication via either "maintenance"—preserving ancestral functions—or "innovation"—enabling novel traits. These dynamics are reflected in four recurrent adaptive patterns: ecological versatility, symbiotic synergy, adversary subversion, and weaponized innovation. Despite significant progress, challenges persist in refining detection pipelines, expanding taxonomic coverage, and strengthening functional validation. Collectively, these findings provide a conceptual framework for deciphering cross-kingdom genetic exchanges and their contributions to insect adaptation and diversification.

INTRODUCTION

Unlike vertical parent-offspring inheritance, horizontal (or lateral) gene transfer (HGT/LGT) involves the non-genealogical transmission of genetic material across species boundaries. Since its discovery in *Escherichia coli* in 1947,[1] HGT has been documented across all domains of life (Figure 1).[2–7] In prokaryotes, it is mediated by mechanisms like conjugation (as exemplified by *Agrobacterium*-plant interactions), transformation, transduction (generalized or specialized), cell fusion, and gene transfer agents.[6,8] Eukaryotes utilize these routes alongside specialized pathways such as intracellular or endosymbiotic gene transfer, introgression and DNA break-repair machinery, exemplified by the bdelloid rotifer *Adineta vaga*, which integrates foreign DNA during the repair of desiccation-induced DNA double-strand breaks.[2–4] While HGT broadly encompasses the movement of various genetic elements, in a narrower sense, it refers specifically to cross-species transfer, resulting in horizontally transferred genes (HTGs). Regardless of definition, eukaryotic HGT tends to be influenced by ecological and phylogenetic proximity,[6,9] but remains constrained by biological barriers, such as the nuclear envelope and the necessity for host regulatory integration, which often leads to the loss of transient sequences through drift or negative selection.[7,10]

In nature, HGT events exhibit a distinct domain-specific asymmetry: prokaryotes acquire foreign sequences far more frequently than eukaryotes.[7,10–12] Theoretical frameworks like Doolittle's "gene transfer ratchet",[11] and Huang's "weak-link model"[13], proposed that phagotrophic feeding or early developmental stages could serve as entry points for foreign DNA. Modern high-throughput sequencing has since confirmed HGT's significant role in eukaryotic adaptive evolution and ecological diversification.[10,13] The accumulating evidences of HGT reshaping modern evolutionary biology suggest that a "web of life" model may more accurately than the classical "tree of life" to represent the history of life diversification.[6]

Insects, which originated over 400 million years ago, now represent more than half of all described animal species, reflecting their extraordinary diversity and ecological importance.[14,15] Although functional HGTs are less frequent in insects than in non-metazoan lineages, numerous adaptive cases have been reported, with HTGs originated from bacteria, fungi, plants, and viruses have been shown to confer advantages in detoxification, defense, pigmentation, and metabolic innovation.[5,16–20] Studying HGT in insects can therefore help elucidate the mechanisms underlying their diversification, reveal the dynamic and innovative nature of insect genomes, and inform practical applications in beneficial insect conservation and pest management. To date, thousands of HTGs have been identified in insects across diverse studies,[5,7,18,21–23] but a systematic synthesis of these findings—particularly the construction of a unified dataset for future analysis—has been lacking. To address this knowledge gap, we conducted a systematic search of the NCBI PubMed database (https://pubmed.ncbi.nlm.nih.gov/) using the terms "insect AND HGT" "insect AND LGT", and "insect AND horizontal transfer gene", covering English-language articles published between January 2002 and December 2025. We focused specifically on natural interspecific HTGs (narrow-sense of HGT) in insects, distinguishing them from other genetic transfer phenomena. While mobile genetic elements (MGEs), intracellular transfers, and antibiotic resistance genes (ARGs) share mechanistic parallels with HTGs, such as the requirement for genomic integration, they represent fundamentally different evolutionary trajectories.[24–27] MGEs often prioritize self-propagation, intracellular transfers can follow different selective constraints other than cross-species leap, and ARGs are driven by recent anthropogenic selection.[24–27] By excluding these categories to isolate long-term, natural protein-coding HTGs, we identified 124 eligible publications from an initial set of 1,013, collectively reporting at least 4,029 inferred HTGs. In this article, HTGs were counted as individual gene instances based on distinct sequence records, therefore, orthologous genes identified in different species or multiple paralogs within a gene family were each counted as separate HTGs. Our analysis reveals a general upward trend in both the number of HGT studies and HTGs identified over time (Figure 2). Peaks in publications around 2012-2014 and 2020-2021 likely reflect progress in sequencing technologies, whereas the 2022 surge in HTG detection is primarily driven by the accumulation of insect genomic resources and the landmark large-scale integration provided by Li et al. (2022).[5] These technical advances, along with improved computational pipelines and reduced sequencing costs, have collectively accelerated the discovery of HGT in insects.

From the included studies, we compiled a curated set of 3336 annotated HTGs that had at least one of phylogenetic or experimental proofs (i.e., candidate HTGs reported in the literature proved by phylogenetic reconciliation or experimental results like PCR and have a protein annotation in public databases). Focusing on the above information, this review summarizes the common methodologies and workflows in HGT research, the donors and recipients of insect HTGs, as well as their functional roles and common patterns. Additionally, current challenges in insect HGT studies will be discussed alongside future research perspectives. This review tries to conceptually offer a more rounded insight into the mechanisms, sources, and functional roles of HGT of insect, shedding light on its implications for the evolution of genetic diversity and environmental adaptation.

TOOLS AND METHODS FOR INSECT HGT IDENTIFICATION AND ANALYSIS

HGT research generally proceeds through three key phases: identification, validation, and functional characterization (Figure 3). The identification phase

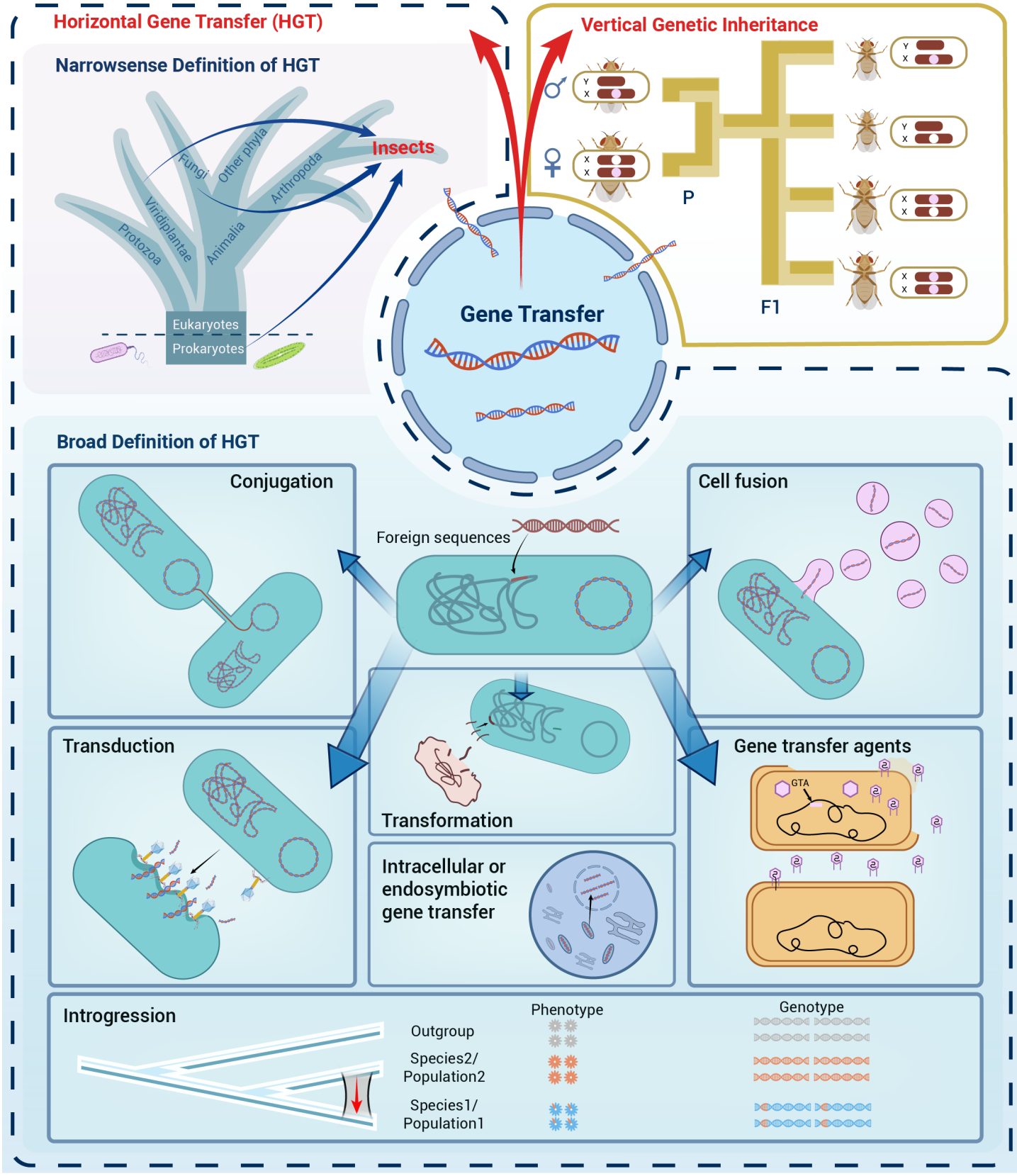

Figure 1. Illustration of gene transfer Gene transfer can be categorized into vertical and horizontal modes, with the latter defined in both narrow and broad senses.

focuses on detecting HGT sequences through parametric, experimental or phylogenetic approaches. Validation phase encompasses bioinformatic or experimental confirmation to exclude contaminant sequences, while validate the HGT donors. Functional characterization then integrates further evidence to elucidate the evolutionary dynamics and biological roles of the identified HGT sequences. Below we summarize key methodologies for each phase.

Identification of HGT sequences: From prokaryotes-specific to insects

The identification of horizontally transferred sequences centers on assessing their 'alienness', that is, the likelihood that a genomic element originated

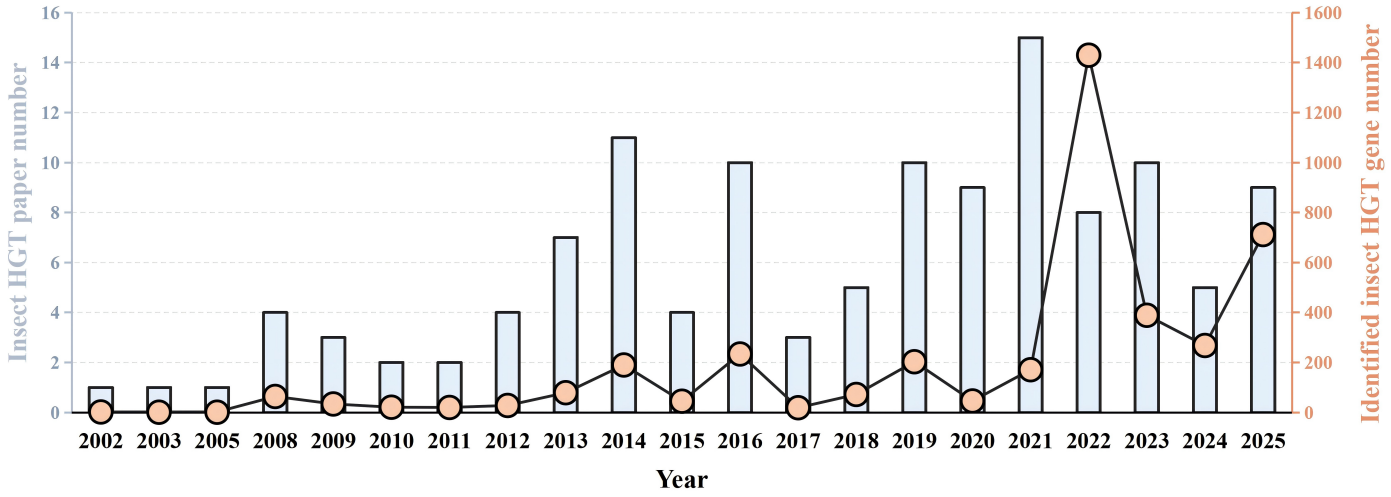

Figure 2. The number of published papers on insect HGT and their recorded HTGs since 2002 The bar chart illustrates annual publications on insect HTGs, while the line graph depicts newly identified HTG number per year. Eligible articles were required to be published in English and indexed in the NCBI PubMed database, focusing on insect HTGs, while excluding those addressing only MGEs, interspecies or intracellular gene transfer, and ARGs.

from a distinct lineage. Parametric approaches identify anomalies in sequence composition such as GC content, oligonucleotide frequency, codon usage, or structural characteristics.[28–31] For example, the metagenomic pipeline hgtseq implemented in Nextflow uses bwa and Kraken to measure rates and patterns of HGT loci,[28] and the software LocalHGT that utilizes k-mer matching to identify HGT-related segments from shotgun metagenomic data.[32] Notably, machine learning (ML) and deep learning (DL) methods have seen a significant rise in recent years, offering high-accuracy classification by capturing complex sequence dependencies.[33] Representative tools include DeepHGT, a DL tool employs deep residual networks to capture HGT-specific insertion patterns,[34] and Hgtident, an ML tool integrates feature selection with support vector machine modeling.[35] These tools excel at recognizing subtle compositional shifts that traditional statistical methods often overlook.

In contrast, phylogenetic approaches detect incongruence between gene trees and species trees.[36] These range from explicit topological reconciliation tests (e.g., Shimodaira–Hasegawa or subtree pruning)[30,37] such as MetaCHIP[38] and HGTree,[39] to implicit evolutionary distance comparisons, such as DLIGHT detecting HGT by quantifying gene-species distance discrepancies[40] and RecentHGT identifying HGT using an Expectation Maximization (EM) algorithm.[41] While effective for donor and transfer timing identification or high-throughput screening, these methods remain susceptible to false positives from paralogy, incomplete lineage sorting, unsampled donors or gene decay (explicit)[30,31,42,43] or may conflate sequence similarity with actual phylogenetic relatedness (implicit).[29,36,42,44] To mitigate these constraints, hybrid tools like ShadowCaster[31] that integrating support vector machines for compositional analysis with Bayesian phylogenetic inference for more robust and accurate results. However, all of the above mentioned HGT tools are developed for prokaryotes or eukaryotic genetic materials other than genes, and a comprehensive summary of popular HGT identification methods of this scope is provided in Table S1.

Regarding eukaryotic and insect HGT, although currently numerous tools have been developed for HGT detection, very few are specifically designed for or can be applied in eukaryotes. Many eukaryotic HGT identification methods are adapted from prokaryotic theories, which are summarized in Table 1. For insects, early HGT discoveries often arose serendipitously during sequence alignment or PCR-based screening, particularly in endosymbiont-to-host transfer contexts.[45–47] Currently, parametric tools such as SigHunt (using discrete interval accumulative scores)[48] and Batch Learning Self-Organising Map (BLSOM, clustering sequences by oligonucleotide frequency) are widely applied to insect HGT identification.[49] However, because eukaryotic HTGs are more complex than prokaryotic ones or other genetic materials, and often require additional rigorous contamination filtering to maintain accuracy, there are currently relatively few parametric tools available for eukaryotes.

In contrast, explicit and hybrid methods represent the most recent trend in insect HGT identification (Figure 3). Explicit tools such as RIATA-HGT,[50] T-REX,[51] AnGST[52] and RANGER-DTL[53] can infer HGT via gene tree-species tree reconciliation under selectable evolutionary models. Recent tools often integrate multiple robust indicators from sequence alignments. For example, *AvP* combines Aggregate Hit Support (*AHS*) and an F1 score to account for contamination and donor support,[54] while Gilbert and Maumus (2022) applied MMseq2 for last common ancestor inference in plant-derived insect genes. As for implicit phylogenetic tools, DarkHorse introduced the lineage probability index (*LPI*) based on BLAST bit scores for HGT inference,[55] while subsequent Wheeler's method[56] and HGTector[44] refined e-value cutoffs and hit-weight distributions. HGT-Finder further advanced this thought by introducing the transfer index (X, later modified to alien index (*AI*)), and outgroup percentage (*outg_pct*) as key metrics.[5,42,57] Recently, user-friendly pipelines have gained traction, such as the Alienness that provides a web-based platform for intuitive, visualization-supported detection with integrated contamination filtering.[58] Hybrid approaches are also evolving, for instance, HGTphyloDetect incorporated with phylogenetic implicit HGT candidates selection pipeline and explicit homolog analyses for phylogenetic verification that outperformed HGTector in various metrics (e.g., accuracy, sensitivity, specificity),[59] while preHGT developed combining parametric concepts of pseudo-pangenome construction with BLAST-based phylogenetic analyses.[29] Moreover, the possible future integration of *AvP* into Alienness[54] and expansion of HGTree to include additional eukaryotic datasets[39] will further enhance accessibility and functionality of insect HGT detection, which reflects a trend toward more integrated and user-friendly analytical frameworks of insect HGT identification.

Validation of insect HTGs

Following the initial identification of candidate HTGs, rigorous validation is essential to confirm genuine transfer events and exclude potential contamination. Most studies employ phylogenetic reconstruction, sometimes combined with taxonomic or homolog features inspection and experimental verification to establish robust evidence for HGT.[5,21,60,62–65] For this, a key phylogenetic criterion is whether candidate insect genes form a monophyletic clade within non-insect donor lineages, and such topology strongly supports horizontal acquisition. In contrast, singleton candidates nested within large outgroup clades are often artifacts or contaminants, as authentic insect HTGs typically occur as multiple copies or homologs and often evolve features resembling host genes, such as intron gain.[5] The bioinformatics validation processes can typically include aligning candidate genes and their homologs (identified via BLAST) using tools such as MAFFT,[66] followed by alignment trimming and phylogenetic analysis with RAxML,[67] FastTree,[68] or IQ-TREE,[69] and subsequent visualization in platforms such as iTOL.[70] For transcriptome-based candidates, additional BLASTN or TBLASTN searches against the recipient genome help verify genomic integration.[71] Genomic features can also be examined. Tools such as SignalP[72] can assess

Table 1. The representative HGT detection tools or methods that can be used in insect.

Tools or methods	Category	Year	Scope of identified HGT event	Criterion for HGT candidate	Main processes	Available source	References
SigHunt	Parametric	2013	Genetic sequence	Discrete interval accumulative score (DIAS) & 4-mer density	[1] Calculate genomic signatures; [2] Calculate 4-mer density and DIAS; [3] Establish putative genomic islands	https://github.com/J-Moravec/sighunt	Jaron et al.[48]
BLSOM	Parametric	2016	Genetic sequence	Batch-Learning Self-Organizing Map (BLSOM)	[1] Oligonucleotide composition calculation and multivariate analyses; [2] Unsupervised Mapping to BLSOM clusters; [3] HGT segments assignment and Strain-specific HGTs extraction	http://bioinfo.ie.niigata-u.ac.jp/?BLSOM	Nakao et al.[49]
RIATA-HGT	Phylogenetic explicit	2005	All	Incongruence between gene and species tree	Use the polynomial-time heuristic algorithm ComputeHGT for HGT events inference in gene trees	https://phylogenomics.rice.edu/html/commands/RIATAHGT.html	Nakhleh et al.[50]
AnGST	Phylogenetic explicit	2010	All	Phylogenetic algorithm reconciling differences between gene and reference species tree	Use the topology of reconciled gene family tree and account for its uncertainty to infer the gene transfer events and directions	https://github.com/almlab/angst/tree/master	David and Alm[52]
T-REX	Phylogenetic explicit	2012	All	Selectable models for tree building	[1] Phylogenetic tree reconstruction based on distance matrix; [2] Determine HGT scenario by reconciliation of species/gene trees	www.trex.uqam.ca	Boc et al.[51]
RANGER-DTL	Phylogenetic explicit	2018	All	Distance-dependent transfer costs & support values for DTL event	[1] Phylogenetic tree reconstruction based on distance matrix and improved algorithm; [2] Determine HGT scenario by DTL event values	http://compbio.engr.uconn.edu/software/RANGER-DTL/.	Bansal et al.[53]
AvP package	Phylogenetic explicit	2022	All	hgt_local_score, Aggregate Hit Support (AHS),and F1 score for optimal AI	[1] Prepare fasta file, similarity search and AI feature file;[2] Mafft-trim;[3] Calculate hgt_local_score, optimal AI and AHS, using best AI for filtering cutoff; [4] Analyze the topology	https://github.com/GDKO/AvP	Koutsovoulos et al.[54]
Gilbert and Maumus's method	Phylogenetic explicit	2022	All	>35% identity and ≥30% query coverage	[1] Use the taxonomy module of MMseq2 for the last common ancestor (LCA) inference with different modes;[2] Confirm high-confidence HGTs through phylogenetic evidence and comparison with previously reported plant-derived genes	https://academic.oup.com/gbe/article/14/10/evac141/6717574	Gilbert and Maumus[60]
DarkHorse	Phylogenetic implicit	2007	Sub-kingdom	lineage probability index (LPI) scores	[1] BLAST query and select non-self-candidate set; [2] Calculate lineage probabilities (based on top bit scores) and select the highest; [3] Recalculate the top-ranking matches' lineage probabilities	https://github.com/spodell/Darkhorse2	Podell and Gaasterland[55]
HGTector	Phylogenetic implicit	2014	Sub-kingdom	Cutoffs based on three groups' weight distributions (BLASTP hits normalized bit scores)	[1] BLASTP and normalize bit scores, define self, close and distal groups;[2] Categorize hits into three groups and compute weight;[3] Assign cutoffs according to weihgt distributions and test each gene	https://github.com/DittmarLab/HGTector	Zhu et al.[61]
Blast2hgt	Phylogenetic implicit	2018	Kingdom	Alien index (AI) and HGT index (*h*)	[1] BLAST query (can enlarge hits number if needed) and get e-value & bit score for each taxonomy group; [2] Calculate AI and h index; [3] Consider HGT candidate if h and AI lead to the same conclusion	https://github.com/waterml/blast2hgt	Li et al. [36]
Alienness	Phylogenetic implicit	2017	Kingdom	possible HGT: AI > 0 and < 70% identity; very likely HGT: AI > 30 and < 70% identity; contamination: ≥70% identity	[1] BLASTP;[2] Calculating AI;[3] Classify HGT according to AI values	https://alienness.sophia.inrae.fr/cgi/index.cgi	Rancurel et al.[58]

signal peptides, while other features, like functional domains, catalytic sites, polyA signals, and GC content, may provide additional evidence. Moreover, intron presence and length, which often converge toward host-like architectures, also serve as informative indicators of gene domestication.[5,73] However, structural features like signal peptides may reflect functional divergence rather than providing definitive evidence for HGT, as exemplified by the distinct signal peptide variations reported in *TvTLP*.[74] Consequently, such traits should be treated only as auxiliary indicators and must be integrated with rigorous phylogenetic and genomic analyses to reliably exclude contamination or endosymbiont-derived sequences.

Experimental validation is the cornerstone of confirming HTG authenticity, with recent studies providing detailed practical frameworks for this

Table 1. *(Continued)*

Tools or methods	Category	Year	Scope of identified HGT event	Criterion for HGT candidate	Main processes	Available source	References
HGT-Finder	Phylogenetic implicit	2015	Sub-kingdom	AI score > 0 & OUTGROUP percentage ≥ 80%	[1] BLASTP;[2] Filtering by AI (alien index) and outg_pct;[3] Multiple sequence alignment (mafft-trim), tree reconstruction, manually inspection	https://github.com/xingxingshen/HGTfinder	Y. Li et al.[5], Nguyen et al.[42], Shen et al.[57]
HGTphyloDetect	Hybrid	2023	Sub-kingdom	AI score & OUTGROUP percentage	Implicit part: Similar to HGT-Finder for HGT candidate inference, with default threshold of HGT: AI value = 45, out_pct = 0.90; Explicit part: Homolog identification, multiple sequence alignment (mafft-trim), tree reconstruction, manually detect gene flow	https://github.com/SysBioChalmers/HGTphyloDetect	Yuan et al.[59]
preHGT	Hybrid	2023	Sub-kingdom	Phylogenetic explicit & parametric algorithm with multiple parameters	[1] Use MMSeq2 and EMBOSS for pseudo-pangenome building; [2] Compositional and BLASTP scan; [3] Annotation of HGT candidates and reporting	https://github.com/Arcadia-Science/prehgt/tree/v1.0.0	Dutton and Reiter[29]

process.[5,19,20,74,75] To definitively rule out environmental contamination, PCR-based assays typically target upstream and downstream flanking regions, where Sanger sequencing of these regions can validate integration when at least one flank shows high sequence identity (e.g., ≥ 98%) to the reference genome. Furthermore, expression analysis via RNA-seq and qRT-PCR provides essential evidence of transcriptional activity. To ensure these signals originate from the insect rather than its diet or microbiome, qRT-PCR can be used to compare expression across treatment and controlled conditions (such as before and after RNAi knockdown), and thereby verifying that the HTG is a functional component of the host genome.[5,19,20,74,75] Finally, cross-referencing with previously reported HTGs or gene families offers an additional layer of verification, particularly in studies applying novel detection strategies.[5,22,60]

Incomplete lineage sorting (ILS) represents important evolutionary processes that can generate phylogenetic incongruence resembling HGT, particularly in insects with rapid radiations or complex population histories.[76,77] However, researches have found phylogenomic frameworks that explicitly model gene tree heterogeneity, such as quartet-based species tree estimation (e.g., ASTRAL) or coalescent-based likelihood approaches can help distinguish ILS from true HGT.[78,79] These methods are robust across eukaryotic systems as they effectively differentiate the localized, specific phylogenetic discordance characteristic of HGT or introgression from the more pervasive, genome-wide conflict typical of ILS.[78,79] Beyond methodological rigor, the reliability of HGT inference can be also strictly governed by genome assembly quality. Fragmented assemblies derived from short-read data often fail to resolve HGT events, particularly those situated in repetitive regions, leading to significant biases or false positives.[80] Consequently, high-contiguity assemblies, ideally facilitated by long-read sequencing technologies, are indispensable for providing the structural context necessary to validate genuine HGT events.

Structural and functional characterization of insect HTGs

As a later stage of HTG research, functional characterization can be broadly categorized into bioinformatics inference and experimental validation. Early studies, constrained by limited molecular tools, primarily relied on comparative bioinformatics to infer HTG functions through orthology analysis and functional annotation using databases such as GO and KEGG.[81–85] Concurrently, PCR-based detection of endosymbiont-to-host transfers allowed functional inference directly from donor gene annotations.[45–47] These foundational efforts mostly focused on assessing donor origins through phylogenetic anomalies, predicting protein domains (e.g., using Pfam/InterPro), and profiling expression via EST libraries or microarrays.

The advent of next-generation sequencing and protein structure prediction later significantly expanded the scope of functional studies. Evolutionary dynamics began to be systematically investigated through gene family evolution analysis (e.g., HMMscan-based clustering), synteny mapping, and selection pressure estimation (e.g., *dN*/*dS* ratios with EasyCodeML).[86–90] These approaches have revealed the involvement of insect HTGs in diverse essential gene families, including immunity or nutrient acquisition, and their conserved trends under positive selection.[2,65,91–93] More recently, transcriptome-wide profiling through RNA-seq and qRT-PCR has enabled precise spatiotemporal expression analysis of HTGs.[5,19,89] Furthermore, functional genetic techniques such as RNA interference (RNAi) and CRISPR-Cas-mediated knockout, coupled with multi-omics phenotyping tests like the insect fitness assays under gene suppression, have established causal links between HTGs and adaptive traits.[5,19,62,89] Recent studies further demonstrate that structure-based analyses provide critical functional insights into insect HTGs beyond sequence similarity alone. By combining AlphaFold-derived structural models with protein-protein docking, these works have revealed specific molecular interactions underlying HTG function, such as stable binding between HTG-encoded proteins and host respiratory chain components, chitin substrates, or transcription factors, thereby supporting roles in metabolism.[94,95] Structural analyses can also indicate that bacterium-derived HTGs retain conserved pore-forming toxin architectures, providing strong mechanistic support for their membrane-permeabilizing functions in insect hosts.[96]

RECIPIENTS AND DONORS OF THE INSECT HTGS

HGT has been identified across nearly all insect orders, with the majority of reported HTGs concentrated in Lepidoptera, Hemiptera, and Coleoptera.[5,7,23] A comprehensive survey by Li et al.[5] compiled 1410 HTGs across 218 representative insect species spanning all orders, revealing Lepidoptera as the order with the highest total number (613 HTGs, averaging ~16 per species), followed by Hemiptera (249 HTGs, ~13 per species). Notably, the tobacco whitefly *Bemisia tabaci* was reported to harbor the largest number of HTGs (170) among individual species.[5] By integrating data from hundreds of published insect HGT studies, we have expanded this inventory to at least 3,336 annotated HTGs distributed across diverse insect taxa via at least distinct 191 HGT events (Figure 4 and Tables S2-S5). Although Hemiptera is the most extensively studied order in insect HGT research (Figure 4), Lepidoptera continues to contain the highest absolute number of HTGs (1,301 out of 3,336) (Figure 4). Within Lepidoptera, studies have predominantly focused on some popular species such as *Bombyx mori* and *Papilio* species, while research in Hemiptera has largely centered on the suborder Sternorrhyncha, particularly aphids (Aphidinea) and whiteflies (Aleyrodoidea), with *Bemisia tabaci* again emerging as the species with the most HTGs (305). Table S2 summarizes representative insect HTGs, and detailed gene-level information is provided in Table S3, with corresponding annotated peptide sequence list and glossary available in Table S4 and Table S5.

Donors of insect HTGs include both prokaryotic and eukaryotic lineages that have contributed genetic material to insect genomes over evolutionary

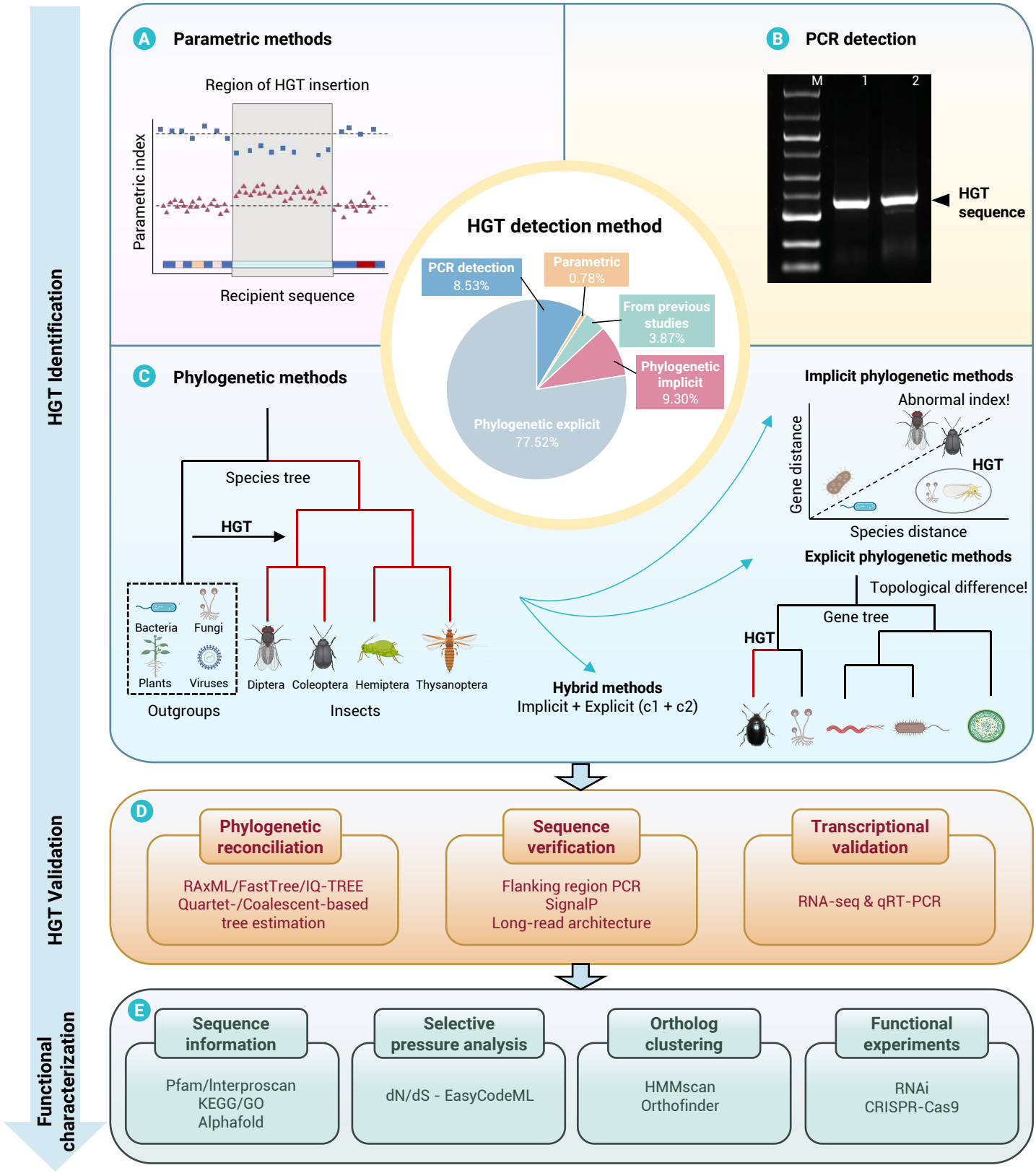

Figure 3. Methodological framework of insect HGT analyses HGT analyses can be generally divided into three parts: identification, validation and functional characterization. Among these, HGT identification methods contain (A) Parametric; (B) PCR detection and (C) Phylogenetic (implicit, explicit or hybrid). HGT validation (D) employs phylogenetic reconciliation, structural verification and transcriptional validation. Functional characterization (E) integrates sequence information, selective pressure, ortholog clustering and functional analysis.

time. Currently identified donor sources encompass intracellular symbionts, gut microbiota, and entomopathogens, spanning nearly all major biological kingdoms, including bacteria, fungi, viridiplantae, viruses, and other metazoa (Table S2 & Figure 4). Although precise donor identities or intermediate vectors (e.g., bacteriophages) often remain speculative and are challenging to trace definitively, donor-recipient ecological associations provide plausible

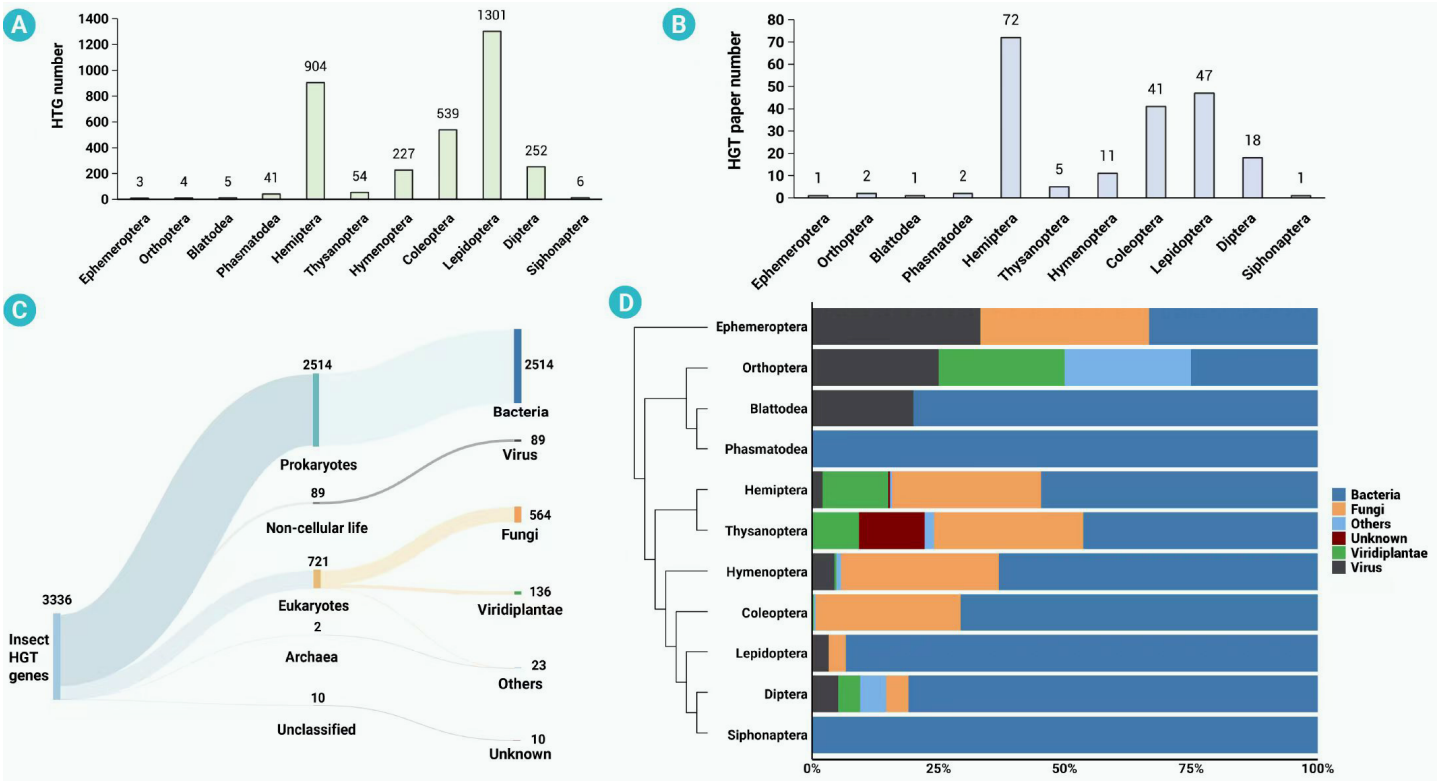

Figure 4. Donors, gene counts, and published paper counts in insect functional HGT analyses (A) the total currently-identified annotated-HTG quantities across insect orders; (B) the total currently-published insect HGT paper number across insect orders; (C) Sankey diagram depicting donor lineages and their corresponding numbers of insect HTGs; (D) stacked bar chart visualizing the percentage contributions of HTGs from different donor kingdoms across insect orders.

inference, as HGT events frequently occur between closely interacting organisms.[5,19,62,89] Consistent with the findings of numerous insect HGT studies,[5,7,22,23] our expanded dataset confirms bacteria as the dominant donor group (2,514 out of 3,336 HTGs), underscoring their intimate and persistent associations with insects. Fungi represent the second most frequent source (564 HTGs), followed by viridiplantae (136 HTGs) (Figure 4). In the following contents, we highlight representative insect HTGs originating from bacteria, fungi, and plants, along with notable examples from other donor lineages.

Insect HTGs from bacteria

As the most prevalent category of horizontally transferred genes (HTGs) in insects, bacterial-origin HTGs have been extensively documented and functionally characterized across diverse insect taxa, contributing to a wide range of adaptive traits.[5,7,21–23] In addition to the widely reported glycoside hydrolase (GH) families and uncharacterized propellin family genes, thousands of other bacterial-derived HTGs have been identified with varied functional roles. In Lepidoptera, the silkworm *Bombyx mori* serves as a key model system. Early studies have identified horizontally acquired bacterial genes such as the chitinase *BmChi-h* and kynureninase *BmKynu*, the latter of which associated with larval red body coloration.[97–99] Subsequent genome-wide surveys expanded this repertoire to 23 bacterial-origin genes, including GH31, GH32, *BmChi-h*, and *BmKynu*, highlighting their roles in sugar and amino acid metabolism.[44,82,85] Notably, the cysteine synthase gene (*cys* gene) family, acquired from bacteria and subsequently duplicated in lepidopterans, confers both cysteine synthase (CYS) and β-cyanoalanine synthase (CAS) activities, enabling detoxification of cyanogenic glucosides.[100–102] Other remarkable examples include megalysin-like toxin genes in ditrysian Lepidoptera, acquired from Gammaproteobacteria, which encode pain-inducing defense proteins through membrane permeabilization,[96] and a *Listeria*-derived HTG (*LOC105383139*) in the diamondback moth (*Plutella xylostella*) that may enhance male courtship behavior.[5]

In Diptera, several gall midge (Family Cecidomyiidae) species (*Contarinia nasturtii*, *Sitodiplosis mosellana*, *Mayetiola destructor*) were identified harbor toxin genes of bacterial origin that provide protection against parasitoid wasps.[9] The Hessian fly (*Mayetiola destructor*) also acquired a cluster of ten levanase genes, expressed during early larval feeding, likely enabling fructan utilization as energy reserve.[103] In Hemiptera, several bacterial-origin HTGs were found involved in feeding adaptation. Examples include genes encoding salivary proteins such as HESPs for salivary sheath formation in pentatomoid insects,[104] and horizontally acquired phospholipase C (PLC) genes in *Halyomorpha halys* associated with plant feeding.[105] Another Miridae species *Nesidiocoris tenuis* was found containing three bacterial-origin HGT regions (four HTGs), one linked to *Sodalis*-derived phenazine biosynthesis protein (*PhzF*), while others potentially from *Rickettsia*.[106] Moreover, in the whitefly *Bemisia tabaci*, bacterial-origin genes (*BtUCA*, *BtAtzF*) were found could coordinate nitrogen recycling and improve reproductive capacity under nutrient stress.[75]

In Coleoptera, a suite of bacterial-origin cell wall hydrolase (*cwh*) genes was identified across ladybird beetles, with infection and RNAi knockdown experiments confirming their role in antibacterial defense and suggesting contributions to carnivorous niche expansion.[89] The research team further found another bacterial-acquired genes, NADAR genes that underwent lineage-specific expansion across beetles to serve as critical immune effectors.[107] These genes are essential for maintaining intestinal epithelial integrity and host survival by orchestrating defense responses against bacterial pathogens.[107] Another case of horizontally-acquired defensive gene is the *PjDUF1* gene found in *Propylea japonica* that derived from its gut symbiont Acinetobacter.[95] This gene enhances insecticide tolerance, locomotion and predatory performance of beetles by promoting oxidative phosphorylation and ATP synthesis, facilitating a co-evolutionary feedback loop where the symbiont upregulates *PjDUF1* to improve host fitness and predatory performance.[95] Other Diptera and Hymenopteran examples include the bacterial-origin ribosome-inactivating protein (*RIP*) gene was reported in *Drosophila neotestacea-Spiroplasma* endosymbiotic system encoding toxin protecting against nematode parasitism.[108] Additionally, two parasitoid wasps, *Leptopilina heterotoma* (generalist parasitism) and *Leptopilina boulardi* (specialist parasitism), harbor two distinct HTGs: the non-metazoan-origin *Lar*, which actively suppresses host immunity by lysing host lymph glands, and the bacteria-derived *Warm*, which passively evades host immune responses by anchoring wasp eggs to host organs.[109] These examples illus-

trates alternative evolutionary strategies for host adaptation through horizontal acquisition of bacterial genes.[108,109]

Insect HTGs from Fungi

Current identified fungi-derived HGTs span most in Hemiptera and Diptera, with facilitate functions such as carotenoid biosynthesis, defensive adaptations, and metabolic regulation. Specifically in aphids, Moran and Jarvik (2010) first identified three carotenoid cyclase (*CarRP*) and four desaturase (*Tor*) genes of fungal origin in *Acyrthosiphon pisum*, later expanded by Nováková and Moran to additional six aphid species, all likely derived from Mucoromycotina.[16,110] Functional studies, including those in *Myzus persicae* (green peach aphid, GPA), confirmed *Tor* as essential for red carotenoid production and *CarRP* for cyclic carotenoid synthesis, together underpinning aphid body coloration.[16,110,111] However, targeted silencing of *Tor*, *CarRP* induced no significant changes in body coloration or mortality, though *Tor* and *CarRP* suppression decreased both gene expression and progeny production.[62] Similar fungal-origin HTGs linked to carotenoids were also reported in gall midges (*Asteromyia carbonifera* and *Mayetiola* destructor), where they are thought to facilitate herbivory.[112] Beyond pigmentation, many other fungi-derived HGTs have been reported linked to defense and metabolism: in *Bemisia tabaci*, *BtFTSP1* encodes a salivary protein suppressing NtFD1-mediated plant defenses and critical for feeding success,[113] while in Lepidoptera, the widespread fungal-origin gene *DODA* (4,5-DOPA dioxygenase) was found with high expression levels in *Bombyx mori* midgut and head that largely induced by bacterial pathogens, revealing it functions of dopa metabolism and antimicrobial activity.[114] Additional examples include *ChtPE* in *Diaphorina citri*, a chitinase with plant/fungi-like CBD domains proposed to originate via HGT,[115] and fungal-transferred dioxygenases in *Bombyx mori*, *Danaus plexippus*, and *Heliconius melpomene*,[5,85] though their precise functional relevance remains unclear. Collectively, these findings highlight fungi as recurrent donors of ecologically significant genes shaping insect pigmentation, defense, and metabolic versatility.

Insect HTGs from viridiplantae

Compared with the numerous bacterial- and fungal-derived HTGs, viridiplantae-origin HGTs in insects are relatively rare and mainly reported in Hemiptera and Diptera. A well-known example is the ribosome-inactivating protein (*RIP*) gene family. A well-characterized example is the ribosome-inactivating protein (*RIP*) gene family. Initially identified in viridiplantae and bacteria, *RIP* genes were first reported in metazoans in two mosquito species (*Aedes aegypti* and *Culex quinquefasciatus*, belonging to Culicidae)[116] and later confirmed in *Aedes aegypti* and *Aedes albopictus* as cyanobacteria-derived HGTs.[117] More recently, additional *RIP* HGTs were identified in *Contarinia nasturtii* and *Bradysia odoriphaga*, with stage-specific expression in early development and higher activity in thorax and abdomen tissues.[118] Recurrent HGT events have facilitated the acquisition of *RIP* genes across diverse insect lineages, resulting in both active transcripts and null alleles in mosquitoes, alongside functional, intron-containing copies in *Bemisia tabaci*.[88,119] These genes exhibit prominent expression in the thorax and abdomen, particularly during early ontogeny.[118,119] Serving as immune effectors, their expression is significantly upregulated following pathogen infection to exert RNA N-glycosidase activity, confirmed in *Aedes aegypti* via the depurination of parasite ribosomal RNA, mirroring the defensive utility of *RIP* genes observed in *Spiroplasma*.[108,117–119] The recurrent acquisition of *RIP* genes highlights a potent selective advantage in ecological niches with high parasite or microbial pressures, where they serve as "off-the-shelf" molecular weaponry. While providing systemic defense in mosquitoes and whiteflies, their stage- and tissue-specific expression suggests functional diversification toward protecting specialized developmental niches or regulatory co-option.[88,108,117–119] The sporadic maintenance of *RIP* genes across insect lineages likely reflects an evolutionary trade-off between the high metabolic costs of harboring such potent toxins and the indispensable defensive benefits required by certain niche-specialized species.

Beyond *RIP*, several other viridiplantae-derived HGTs have been reported, particularly in *Bemisia tabaci*. For example, Xia et al.[19] found a plant-origin HTGs *BtPMaT1* enables detoxification of plant phenolic glucosides, thereby enhancing *Bemisia tabaci* herbivore resistance to host defenses. Gilbert and Maumus[60] identified 49 plant-origin HTGs in *Bemisia tabaci* from at least 24 independent events, most associated with plant-pathogen interactions. Within this set, *BtFAD2* genes were shown to facilitate PUFA biosynthesis, with *BtFAD2-9* playing a key role in PGE_2 biosynthesis levels and *Bemisia tabaci* fecundity, as demonstrated by RNAi knockdowns.[20] Similarly, Plant-derived thaumatin-like proteins (TLPs) have evolved divergent defensive functions in whiteflies: in *Bemisia tabaci*, TLP acts as a salivary effector that suppresses plant jasmonate-mediated defenses by interacting with OPR3, whereas in *Trialeurodes vaporariorum*, the corresponding TLP variant provides critical immune protection against entomopathogenic fungi.[74] Expanding these findings, Colinet et al.[22] catalogued 255 HTGs in *Bemisia tabaci* across 136 events, of which 200 overlapped with those previously reported by Chen,[21] Li[5] and Gilbert,[60] while 41 were newly identified and 14 were absent. Their analysis further revealed that piercing-sucking insects like *Bemisia tabaci* have acquired carbohydrate-active enzymes from multiple plant donor species, while notably reported for the first time plant-derived glycoside hydrolase families GH17 and GH152 in insects.[22,120]

Insect HTGs from virus

The earliest reported viral-origin HTGs in insects is the *Bombyx mori* chitinase gene *BmChi-h*, which encodes a highly conserved enzyme involved in chitin degradation during molting.[97,98] However, this gene also exhibits high sequence identity with bacterial homologs, complicating definitive donor attribution.[44,82,98] Since then, more definitive virus-origin HGTs have been observed, particularly in Lepidoptera. Examples include *gasmin* and *Se-BLL* genes in *Spodoptera* species, which modulate cellular immune responses against bacterial and viral infections.[121–124] Interestingly, *gasmin* in *Spodoptera littoralis* appears to have originated indirectly via parasitic wasps carrying symbiotic viruses.[124] Another virus-derived HTGs, the parasitoid killing factors (PKFs) family genes, has been identified in *Helicoverpa*, *Heliothis*, and *Spodoptera*, with experimental evidence in *Spodoptera exigua* showing toxic effects against parasitoids through apoptosis and DNA fragmentation.[18]

Virus-origin HTGs have also been characterized in Hemiptera and Diptera. In aphids, transcriptome analyses unexpectedly revealed two viral-derived genes (*Apns-1* and *Apns-2*) linked to wing plasticity, with RNAi experiments confirming their regulatory roles in aphid wing plastic traits.[17] In the brown planthopper (*Nilaparvata lugens*), nudivirus-derived sequences contributed ten functional ORFs expressed mainly in the digestive tract.[125] Similarly, bacteriophage-derived *cdtB* genes, transferred from the endosymbiont *Candidatus Hamiltonella defensa* to *Acyrthosiphon pisum*, were identified providing defense against parasitoid wasps.[126] Homologs of *cdtB* and the related *aip56* were later identified in multiple *Drosophila* species, where they occur either singly or as *cdtB::aip56* fusion variants (*fusionA* and *fusionB*).[127] Functional analyses indicate that the single-copy *cdtB* is expressed in embryos, while the *fusionB* variant acts as a nuclease and provides innate immune defense against parasitoid wasp embryos.[127,128] However, targeted silencing of *cdtB* induced no significant changes in mortality of aphid.[62] In contrast, the *fusionB* is like a double edged sword, delaying the *Drosophila* larvae development and finally causing their death when expressed ubiquitously, which necessitates host mitigation mechanisms.[128]

Other types of insect HTGs

Beyond the well-characterized HTGs originating from bacteria, fungi, plants, and viruses, numerous additional HGT events have been identified across insect lineages, though many remain functionally uncharacterized. For instance, Li et al.[5] documented 1,410 HTGs across 218 insect species, tracing their origins to approximately 670 putative donor lineages but most with only annotated functional information. Subsequent research by Wang et al.[90] expanded this catalog by reporting 143 additional HTGs across seven *Papilio* species. In Lepidoptera, a family of *Spiroplasma*-derived propeller-shaped proteins has undergone extensive duplication, though their biological roles remain to be elucidated.[129] In Hemiptera, complementary genomic surveys revealed extensive HGT repertoires in other aphids, including 212–338 events across six aphid species[130] and 14 HTGs in *Sitobion avenae* inferred to be involved in carotenoid biosynthesis and LD carboxypeptidases,[131] but functional validation of these genes remains pending.

HTGs from more phylogenetically divergent donors have also been identified. A novel dual-specificity kinase gene, the mycetozoa protein kinase-like (*MPKL*) gene was found horizontally transferred from Mycetozoa to *Locusta migratoria*,[132] where RNAi experiments confirmed its function in regulating photoperiodic diapause via altered phosphorylation levels in ovaries and reactive oxygen species (ROS) dynamics.[132] Additionally, the origin of the conserved reproduction gene *oskar* has been linked to an HGT-mediated domain fusion: a bacterial OSK domain integrated near the ancient insect LOTUS locus, forming the long *oskar* domain that subsequently underwent de novo coding evolution.[133] This case exemplifies how unconventional gene origins give rise to gene in insects.[133]

REPRESENTATIVE FUNCTIONS OF INSECT HTGS

Although numerous insect HTGs remain functionally uncharacterized, thousands have been experimentally validated with clearly defined biological roles, as exemplified in section 3. Enrichment analyses reveal that HTGs exhibit lineage-specific functional biases, with different insect orders showing distinct enriched biological pathways (Figure S1). Among the diverse functional categories identified, the most prominent are plant cell wall-degrading enzymes (PCWDEs; 765 out of 3336 HTGs) and symbiosis-related genes (222 out of 3,336 HTGs). Nevertheless, a substantial proportion of HTGs lack clear functional annotation, remain poorly characterized, or originate from less common donor sources such as other metazoans (Figure S2). In the following sections, we provide a detailed overview of these two major functional categories, highlighting representative studies and key mechanistic insights.

Insect HTGs for symbiosis

Since the first discovery of *Wolbachia* DNA fragments in the X chromosome of *Callosobruchus chinensis* in 2002[134] and their subsequent experimental confirmation,[135] *Wolbachia*-to-host HGT events have been widely reported across insect taxa. Endosymbionts such as *Wolbachia*, *Portiera*, *Hamiltonella*, and *Rickettsia*, owing to their cytoplasmic inheritance and intimate interactions with hosts, represent major sources of horizontally acquired symbiosis-related genes.[6,7] These kinds of "symbiotic" HGTs can be generally categorized as: (i) endosymbiont gene transfers (EGTs) that directly from resident symbionts,[136] (ii) gene transfers from other symbiont lineages, and (iii) genes of non-symbiont origin but contribute to host–symbiont metabolic integration.

To be specific, EGT has been detected in nearly all insect harboring symbionts, spanning Diptera (e.g., *Drosophila* species and mosquitoes),[45–47,49,135,137–139] Coleoptera (e.g., *Callosobruchus chinensis* and *Monochamus alternatus*),[140] Hymenoptera (e.g., *Nasonia vitripennis*, *Melittobia digitata* and *Formica exsecta*),[135,141] Orthoptera (e.g., *Chorthippus parallelus*)[142] and the Hemipteran species such as psyllids (*Pachypsylla venusta*),[65] whiteflies (*Bemisia tabaci*),[92] the bed bug (*Cimex lectularius*),[143] milkweed bug (*Oncopeltus fasciatus*) and stink bug (*Halyomorpha halys*).[144,145] Early studies primarily employed PCR-based screening to detect endosymbiotic sequence insertions, such as *Wolbachia*-origin *ftsZ* in *M. alternatus*,[140,146] three other EGT genes (*16S rRNA*, *fbpA* & *wsp*) identified in the tsetse fly,[45–47] dozens of *Wolbachia*-derived genes in *Callosobruchus chinensis*,[147] and two *Wolbachia*-to-mosquito HTGs (*AAEL004181* and *AAEL004188*).[137,138] With advancing sequencing, parametric and phylogenetic approaches became widely used, exemplified by BLSOM-based detection of 1,289 bacterial contigs in tsetse flies, including 36 of *Wolbachia* origin,[49] and the numerous endosymbiont-origin HTGs and homologs identified in aphids.[2,148,149]

Functional studies suggest that EGTs often compensate for symbiont genome reduction. In aphids, horizontally acquired genes such as *ldcA*, *rlpA*, *amiD*, and *bLys* are highly expressed in bacteriocytes but absent from the primary symbiont *Buchnera*, while RNAi knockdown of *ldcA* and *amiD* impaired *Buchnera* abundance and aphid fitness, linking these HTGs to peptidoglycan metabolism and symbiosis maintenance.[2,81,148–150] Similar compensation is seen in psyllids, where duplicated EGT-derived genes show bacteriome-preferential expression, and *ribC* in *Diaphorina citri* complements a pathway loss in its endosymbiont *Profftella*.[65] Besides compensate for symbionts metabolic pathways, the EGT genes were also found can compensate for host insects. For example, in *Bemisia tabaci*, multiple EGT genes sourced from the endosymbiont *Portiera* were identified linked to novel amino acid biosynthesis,[92] while analogous EGT sequences from endosymbionts *Wolbachia* and *Arsenophonus* also occurred in *Cimex lectularius*.[143] In Hymenoptera, a prominent *Wolbachia*-to-insect HGT case of the embryonic dorsoventral (DV) Chalcidoidea Lineage-specific ANKyrin domain-encoding gene (CLANK) family were identified in *Nasonia vitripennis* and *Melittobia digitata*, with knockdown experiments showing their essential roles in dorsoventral embryonic patterning, where loss often proved lethal.[151] Similar genetic insertions of *Wolbachia* DNA fragments have been found in the woodwasp *Sirex noctilio*, where 12 *Wolbachia*-like open reading frames (ORFs) were inferred to mediate cytoplasmic incompatibility.[152]

The second category of symbiosis-related HGT involves transfers from symbionts not stably associated with the host, which often inferred through phylogenetic analyses and were frequently found in species compatible with symbiont bacterial infection. Specifically, in *Bemisia tabaci*, Luan et al.[153] identified 10 HTGs with phylogenetic bacterial-origin (likely from other sap-feeding insect symbioses) and highlighted the genomic decay of its symbiotic bacteria *Portiera* and *Hamiltonella* drove the host to acquire metabolic genes for compensating symbiotic functional losses. This catalog was later expanded to 142 HTGs with moderate-to-high expression and predicted enzymatic roles in *Bemisia tabaci*.[21] Among them, the vitamin B7 synthesis genes, *bioA*, *bioD* and *bioB*, were traced originated from *Wolbachia* strains rather than directly from *Bemisia tabaci* own endosymbiont *Hamiltonella*.[154] These genes exhibit bacteriome-specific expression, and their knockdown reduces biotin levels, host survival, and fecundity.[154] Orthologous *bioD* and *bioB* were subsequently validated in *Icerya aegyptiaca*, with similar functions in symbiotic relationships.[155] Likewise, lysine synthesis genes (*dapB*, *dapF*, *lysA*), derived from multiple bacterial lineages (Rickettsiales, Enterobacteriales and Planctomycetes), were found can encoding proteins helping the endosymbiont *Portiera* and *Rickettsia* for synthesizing lysine, while silencing *lysA* reduced fecundity and symbiont titers either with or without another lysine producer endosymbiont *Hamiltonella*.[156] In mealybugs, 22 HTGs of *Planococcus citri*, likely originated from *Wolbachia* or other proteobacteria, were discovered contributing to lysine, vitamin and peptidoglycan biosynthesis that lost in *Planococcus citri* endosymbiont *Tremblaya* and *Moranella*.[71] Ten of those HTGs were further proved collaborate with retained genes of *Planococcus citri* endosymbiont *Moranella* for Peptidoglycan (PGN) production in symbiosis, among which *MurF*-translated peptide was discovered transported into *Moranella* cytoplasm.[157] Similar HGT complement cases have also been documented in *Trabutina mannipara* (9 genes) and mealybug *Maconellicoccus hirsutus* (part of 47 genes), with ancestral donors likely being *Rickettsia* or *Wolbachia*.[158] Hymenoptera examples include a *Wolbachia*-derived HTGs under positive selection in *Bombus terrestris*, hypothesized to mediate cytoplasmic incompatibility.[159]

Beyond direct acquisition from endosymbionts, some HTGs originate from unrelated lineages but nonetheless compensate or contribute to symbiotic function. For example, *Diaphorina citri* harbors a polyketide synthase (PKS) gene originated from non-symbiont bacteria, which complements the drastically reduced genomes of its endosymbionts *Profftella* and *Carsonella*.[160] In psyllids, 15 bacterial-origin HTGs in *Bactericera cockerelli* (including multiple duplicates) were identified, most of which involved in *B. cockerelli* amino acid metabolism and with up-regulated bacteriome-preferential expression, suggesting their essential symbiotic mediating roles in symbiosis.[63–65] In *Bemisia tabaci*, Ren et al.[161] reported a bacterial-origin fusion gene (*panBC*) that compensates for the loss of the pantothenate biosynthesis pathway in *Portiera*, enhancing host survival and symbiont fitness, while subsequent work showed that additional HTGs in *Bemisia tabaci* are regulated by miRNAs and can collaborate play roles in *panBC*-mediating *Bemisia tabaci*-*Portiera* symbiosis.[162] Similarly, two leafhopper species, *Macrosteles quadrillineatus* and *Homalodisca vitripennis*, harbored at least 30 and 14 bacterial-origin HTGs respectively, which were illustrated highly expressed in bacteriocytes and localized to chromosomal regions consistent with symbiosis-related functions.[163–165]

HTGs belong to Glycoside hydrolases families

The glycoside hydrolases (GH) family comprise a diverse group of enzymes that hydrolyze glycosidic bonds, classified into numerous families

based on distinct biochemical rules continually updated in the Carbohydrate-Active Enzymes database (CAZy).[166] Insects have acquired at least 19 GH families via HGT from fungi, bacteria, plants, or viruses, including CE8 (pectin methylesterase), GH5 (including mannanase, cellulase, xyloglucanase or xylanase), GH7 & GH9 (including endoglucanase and cellobiohydrolase), GH10 & GH11 (most are xylanase), GH16 (most are β-glycanase), GH17 (glucan endohydrolase), GH18 (chitinase), GH25 (lysozyme), GH26 (mannosidase), GH28 (polygalacturonases (PGs) or pectinase), GH31 (most are α-glucosidase), GH32 (including inulinase, exohydrolase, fructosyltransferase and levanase), GH43 (most are arabinofuranosidase and xylosidase), GH44 (cellulase including endoglucanase and xyloglucanase), GH45 (endoglucanase), GH48 (exocellulase), GH78 (rhamnosidases), GH152 (β-1,3-glucanase) and PL4 (rhamnogalacturonan lyases).[22,23,120,167–169] Most of these GH families (8/12) have been found occur in Lepidoptera and Coleoptera (phytophaga), where they facilitate insect dietary adaptation and enable insects to exploit novel ecological niches by digesting previously inaccessible plant materials.

The insect plant cell wall-degrading enzymes (PCWDEs) genes, as a major subset of functional HGT-derived GHs, are found essential to insect herbivory.[23,168,170,171] The horizontally transferred PCWDEs encompass CE8, PL4, GH5, GH7, GH10, GH11, GH16, GH26, GH28, GH31, GH32, GH45, GH48, and GH53 families, distinct from the vertically inherited GH1 and GH9.[23,168,172,173] Most HGT-derived PCWDEs have undergone gene family expansions driven by symbiont acquisitions, resulting in functional redundancy despite dynamic evolutionary trajectories involving gene gain, loss, and replacement.[23,168,172–174] Among them, HGT-derived PCWDEs belonging to GH28 family genes are the best-studied, initially identified in the weevil *Sitophilus oryzae* as fungal transfers.[175] This HGT-derived gene family genes, mainly consists of the polygalacturonases (PGs) genes, are of great benefits in the shape of insect herbivory and functional repertoire expansion. For example, knockdown of four fungal-derived PG genes reduced enzymatic activity and fitness, which could be rescued by supplementation with PG enzyme.[174] Hemipteran mirid bugs were also reported harboring numerous fungal-origin PGs, with expression linked to feeding mode.[93,176] Additional bacterial-derived GH28 PCWDE genes were also identified in beetles (*Callosobruchus maculatus*), stick and leaf insects (Phasmatodea) and the cockroach (*Blattella germanica*), where functional assays also confirmed their catalytic activity against plant tissues.[23,177–180]

Among the acquired PCWDEs, GH5 family exhibits exceptional paralog diversity with multiple subfamilies (GH5-2, 8, 10, 12), multiple independent origins from both bacterial and fungal donors.[168,169,173,181] Early reported horizontally-acquired GH5 gene can be traced back to 2012, where the gene *HhMAN1* in *Hypothenemus hampei* (subfamily GH5_8), was suggested derived from bacteria with inferred function of hydrolyze galactomannan.[23,182] Subsequent studies identified other HGT subfamilies, including bacterial-derived GH5_2 and GH5_10, and fungal-derived GH5_12, in Cerambycidae (longhorned beetles), Chrysomelidae species (e.g., *Gastrophysa viridula*, *Callosobruchus maculatus* and *Diabrotica virgifera virgifera*) and Thysanoptera species (*Frankliniella occidentalis*).[22,23,120,183–185] This recurrent recruitment and expansion of GH5 subfamilies enable insects to degrade a broad spectrum of polysaccharides ranging from cellulose to mannan. In contrast, the GH32 family, despite its uniform bacterial origin, represents a conserved metabolic adaptation to plant-based diets. Since the early identification of the bacterial-origin beta-fructofuranosidase genes (*BmSUC1*/*BmSUC2*) in *Bombyx mori*,[186] these genes were subsequently confirmed comprising three main clusters exhibiting divergent expression patterns and enzymatic properties, and are critical for larval sucrase activity and fructan digestion.[187,188] Other GH32 HTGs were later identified in Coleopteran species (*Dendroctonus ponderosae*, *Agrilus planipennis*, and *Sphenophorus levis*), Dipteran species (*Mayetiola destructor*) and Thysanoptera species (*F. occidentalis*).[22,83,120,189–191] Despite their diverse hosts, all GH32 HTGs share a uniform bacterial origin and exhibit highly conserved digestive functions (e.g., inulinase and invertase activity) and midgut-specific expression patterns.[22,83,120,189–191]

Other GH family PCWDEs show similar ecological importance. The bacterial or fungal origin GH45 PCWDE genes, have been functionally validated in cerambycids (e.g., *Apriona japonica* and *Anoplophora glabripennis*) as endo-β-1,4-glucanases degrading amorphous cellulose, xyloglucan, and glucomannan.[169,181,192,193] The bacterial-origin GH48 family PCWDEs were identified in polyphagan beetles with cellulose degradation capability, and found critical for larvae growth and survival in *Plagiodera versicolora*.[23,93,181] The HGT GH26 family PCWDE was first documented in Pentatomidae as a bacterial-origin transfer event, encompassing two genes in *Oncopeltus fasciatus* and nine in *Halyomorpha halys*, with inferred roles in plant cell metabolism,[144] while Walt et al.[167] further detected expanded existence of an HGT-derived GH26 event in Pentatomoidea and Lygaeoidea species, with biased expression in digestive tissues. GH31 PCWDE genes of bacterial origin were identified occur in Lepidoptera (e.g., *Bombyx mori* and *Plutella xylostella*) and Coleoptera (e.g., *Diabrotica virgifera virgifera* and *Dendroctonus ponderosae*), with functions also in digestion and development (like pupal process).[23,56,194] Other identified GH families that PCWDEs belonging to include GH7, GH10, GH11, GH16, CE8, GH43, GH44, GH78 and GH53, each documented in specific phytophagous lineages transferred from bacteria or fungi, and also with similar but essential digestive roles.[84,168,172,185,195–199]

Beyond digestion, the HGT-derived GHs were also found contribute to immunity. GH25 lysozymes of probable *Wolbachia* origin are found in aphid (*Acyrthosiphon pisum*), bugs (*Halyomorpha halys* and *Riptortus pedestris*) and gall midge (Cecidomyiidae), with the demonstrated function of antibacterial defense.[9,183,200] GH19 chitinases HTGs, independently acquired from unicellular microsporidia in parasitoid wasps and mosquitoes, are found highly expressed in wasps' venom gland while facilitate both antifungal defense and the degradation of host chitin structures, and thereby improving insect access to host nutritional contents.[201] Another chitinase family GH18, have been recorded with an HTG *HcuChiA*, serving as a broad-spectrum antifungal barrier in the digestive tract and playing a vital role in gut immunity and host adaptation.[94] This HGT-derived immune enhancement helps larvae better thrive on suboptimal host plants, significantly facilitating rapid host range expansion.[94]

COMMON DOMESTICATION AND FUNCTIONAL PATTERNS OF INSECT HGT

HGT represents a pivotal yet underappreciated mechanism driving insect evolutionary innovation, enabling the acquisition of pre-adapted genetic modules that bypass gradual mutation-selection processes. In a macroevolutionary context, HGT is significantly less frequent in eukaryotes than in prokaryotes, mainly due to their different selectively ecological strategies.[202] Prokaryotes primarily acquire nutrients through extracellular heterotrophy, making their fitness strongly dependent on metabolic enzymes and transporters that can be readily gained as fully functional units via HGT.[202] In contrast, eukaryotes mainly access resources through complex behavior like phagocytosis and thus adapt predominantly through complex changes in regulatory or developmental networks, point mutation and gene duplications that are not readily available by HGT.[202] Once integrated, foreign sequences undergo a process of genomic "domestication", during which introns are gained and expression patterns adjusted, ultimately determining whether these genes persist as functional assets or are eroded by selection.[5,73,113,144,167] Most HGTs in eukaryotes are transient and subject to rapid loss, and their long-term retention is governed by "selective sieve" that only sequences providing substantial fitness advantages survive stringent cellular and regulatory purging mechanisms.[202] The evolutionary trajectories of the integrated HTGs, in general, are shaped by two cardinal forces: functional necessity and ecological opportunity. In 2018, Husnik and McCutcheon have summarized these two aspects and proposed two new items: "maintenance" and "innovation", which illustrated that HTGs seem to either maintain ancestral functional states, or provide novel functions for host or symbiosis adaptation.[203] These dual pathways reflect a genomic "divide-and-conquer" strategy: while maintenance ensures metabolic continuity, innovation propels ecological diversification. Representative cases of "maintenance" include *ribC* in psyllids and mealybugs restoring riboflavin biosynthesis,[65,160] the EGT genes such as *ldcA*, *rlpA*, and *amiD* maintaining symbiosis,[2,62,110,148,149] and the HGT toxin genes (*Lar* & *Warm*) help wasps inhibit or evade host *Drosophila* immunity for survival maintenance.[109] Conversely, the widely-found PCWDE gene families acquired in Hemiptera, Coleoptera and Lepidoptera that help shape the insect herbivory, and the *Sl gasmin* gene derived from virus to *Spodoptera* species

that help protect against bacterial and viral infections[124,168,177,192,193] exemplify "innovation". Such dual domestication strategies collectively shape insect adaptability while providing insects multitudinous exploration of survival or fecundity under selection and evolution.

As introduced in section 3, the insect HTGs exhibit diverse specific functional roles. Accordingly, these "maintenance-innovation" strategies can be further categorized into four distinct patterns (Figure 5):

(1) Ecological versatility: this pattern reflects how HGT expands or unlock novel nutritional pathways or dietary of insects. Typical examples include the nitrogenous metabolism HTGs *BtUCA* and *BtAtzF* that help control nitrogen recycling capacity, and the nutrition-synthesized gene *BtFAD2-9* that help increase fecundity,[20,75] and diverse HTGs belonging to GH/PCWDE families that enable phytophagous insects to digest cellulose and pectin and thus exploit novel plant resources.[168,169,173,181,192,198,204]

(2) Weaponized innovation: this pattern reflects how HGT provides offensive or defensive modules borrowed across lineages. It is like a cross-organism "gene piracy" where insects integrate necessary functional modules from organisms outside their direct antagonistic relationships, enabling insects to bypass the probable evolutionary constraints in direct "arms races", to create novel offensive/defensive capacity against enemies or prey. Examples include the parasitoid wasp HTGs (*Lar, Warm*) suppressing or evading host immunity,[109] microsporidia-derived GH19 chitinase genes manipulating host defenses,[201] and *RIP*, *cdtB*, and *DODA* genes conferring resistance against nematodes, parasitoids, and pathogens.[88,114,117,118,126]

(3) Adversary subversion: this pattern reflects insects' ability to co-opt molecular tools originally deployed by other organisms in antagonistic contexts. Unlike "weaponized innovation", it establishes an asymmetric "warfare", where victims counterattack by stealing the aggressors' own weapons, thereby fundamentally reshaping defender-aggressor dynamics while expanding the ecological adaptability under rapid coevolution. Representative examples include the bacterial-origin lysozyme genes in Pentatomoidea and Aphids that help defend bacterial infection,[183,200] the hijacked *cwh* genes from bacteria for combating bacterial threats,[89] the virus-origin *Sl gasmin* gene that allows Spodoptera species resisting bacterial and viral infections,[121–124] and the plant-origin gene *BtPMaT1* possessed *Bemisia tabaci* with detoxification ability to neutralize the plant defensive phenolic glucosides.[19]

(4) Symbiotic synergy: this pattern reflects how HGT sustains insect-symbiont partnerships. It transforms insects and their symbionts into a unified metabolic entity, with host genomes evolving as dynamic "patchworks" that compensate for symbiont genome reduction or losses in host biosynthetic pathways, ultimately driving insect-symbiont interactions to a win-win situation across ecological niches. Key examples include the peptidoglycan synthesis genes (*amiD, rlpA, ldcA*) in aphids compensating the endosymbiont biopathways,[2,62,110,148,149] the biotin synthesis genes (*bioA, bioD, bioB*) in whiteflies that complement the nutritional provisioning of the endosymbiont *Portiera*,[154] and the *ribC* gene retained in psyllids to restore riboflavin biosynthesis despite symbiont deficiencies.[65]

The proposed functional framework serves as a heuristic summary of currently documented cases rather than a rigid, exhaustive taxonomy of all possible evolutionary outcomes. These adaptive patterns often exist on a functional continuum with potential overlaps, representing a conceptual roadmap that will likely expand as future genomic discoveries reveal novel HGT-mediated innovations.

Beyond these discrete functional patterns, the collective domestication of HTGs frequently acts as a macroevolutionary engine that propels insects toward new adaptive horizons. The evolutionary history of plant cell wall degradation in beetles highlights the importance of diverse plant cell wall degrading enzymes in facilitating herbivorous lifestyles.[23,168,174,204] Different lineages exhibit a dynamic combination of gene retention, loss, horizontal replacement, and symbiont mediated supplementation, reflecting strong ecological associations with host plant chemistry and feeding strategies.[23,168,174,204] These patterns illustrate how the integration of HTGs has shaped the diversification of digestive capabilities in beetles and contributed to their adaptation to plant-based diets.[23,168,174,204] Moreover, recent studies reveal that HTGs are deeply integrated into host biological systems through multi-dimensional regulatory and interaction networks. These foreign genes are not only precisely tuned by endogenous host elements, such as miRNAs[162] and transcription factors (e.g., *HcuZBTB1* interacting with *HcuChiA*[94]) that activate their expression, but they also engage in direct protein-protein interactions with both host and environmental targets (e.g., *BtFTSP1* degrading plant defense proteins[113]). Such complex interplay demonstrates that HTGs have transitioned from isolated genomic insertions to core functional components that actively shape the host's physiological and ecological landscape. Beyond protein-level interaction, a frontier in HGT domestication is the detailed integration process of these sequences into the host's gene regulatory networks (GRNs). The stabilization of HTGs likely occurs via two regulatory pathways: inserted near host-specific domains or regulatory elements to 'hitchhike' on established circuits (e.g., the bacteria-derived *OSK* sequence),[133] or through a possible *de novo* construction process of novel promoters and enhancers. Despite its significance, the precise mechanistic transition from a genomic 'invader' to a regulated host component remains a major 'black box.' Current research often identifies surrounding genomic regions or broad functional networks,[93,94,102,104,188] yet how these alien sequences are 'legally' hardwired into the host's regulatory architecture required further exploration.

DISCUSSION AND CONCLUSION

In this review, we synthesize recent advances in the identification of insect horizontal gene transfer (HGT) events, their donor–recipient relationships, and associated biological functions. The expanding body of insect HGT research is reshaping our understanding of adaptive evolution, revealing that horizontally transferred genes (HTGs) contribute to key innovations across Hemiptera, Coleoptera, Diptera, Hymenoptera, and Lepidoptera. Despite this progress, major challenges persist in methodological rigor, taxonomic completeness, and functional validation.

Despite the growing availability of insect HGT detection pipelines, methodologies remain fragmented and often rely on customized workflows with inconsistent thresholds, which compromises cross-study reproducibility. To begin with, methodological subjectivity—especially in database selection and parameter settings—also hampers reproducibility, contributing both to inflated estimates, as in the disputed tardigrade HGT cases later attributed to contamination, and to underestimates caused by database biases.[205-207] Technical constraints in sequencing depth, alignment quality, and contamination control continue to limit the accuracy of donor inference and divergence timing. Moreover, tracing evolutionary trajectories is hindered by limited phylogenetic breadth, making it difficult to distinguish ancient inheritance from independent convergence, as seen in the DUF1963-containing genes of distantly related Coccinellidae and Hemiptera.[95] Under the phylogenetic identification, the inferred HGT donors typically represent the closest extant lineages rather than the actual ancestral organisms involved in transfer events occurring millions of years ago. Such patterns also suggest overlooked 'gain-loss-regain' dynamics that current models often fail to capture. Researchers should therefore adopt taxonomic conservatism by prioritizing broader classifications over specific species to account for extinct or uncharacterized donors without further proofs. Thirdly, unlike standardized prokaryotic pipelines, insect-focused research urgently requires unified criteria and AI-enhanced workflows to resolve these complex evolutionary histories across diverse lineages. Moreover, while the current HTG landscape is heavily weighted toward Lepidoptera, Hemiptera, and Coleoptera, it remains to be determined whether this reflects intrinsic biological patterns or a concentration of research effort. A balanced approach is essential for reconstructing the true nature of ancient horizontal transfer events, requiring researchers to look beyond the insect host and integrate the evolutionary dynamics of donor and recipient lineages across plant and microbial domains. Considering factors such as genome reduction in symbiotic bacteria and the adaptive pressures of plant defense mechanisms provides a more holistic framework for understanding how these cross-lineage genetic exchanges are facilitated and fixed over evolution. Future progress will require unified criteria, expanded phylogenetic breadth, AI-enhanced and more balanced workflows, and systematic surveys of more underrepresented taxa or species to strengthen the resolution and comparability of HGT events across diverse lineages for more accurate and balanced perspectives.

Functionally, most insect HTGs characterized to date are involved in

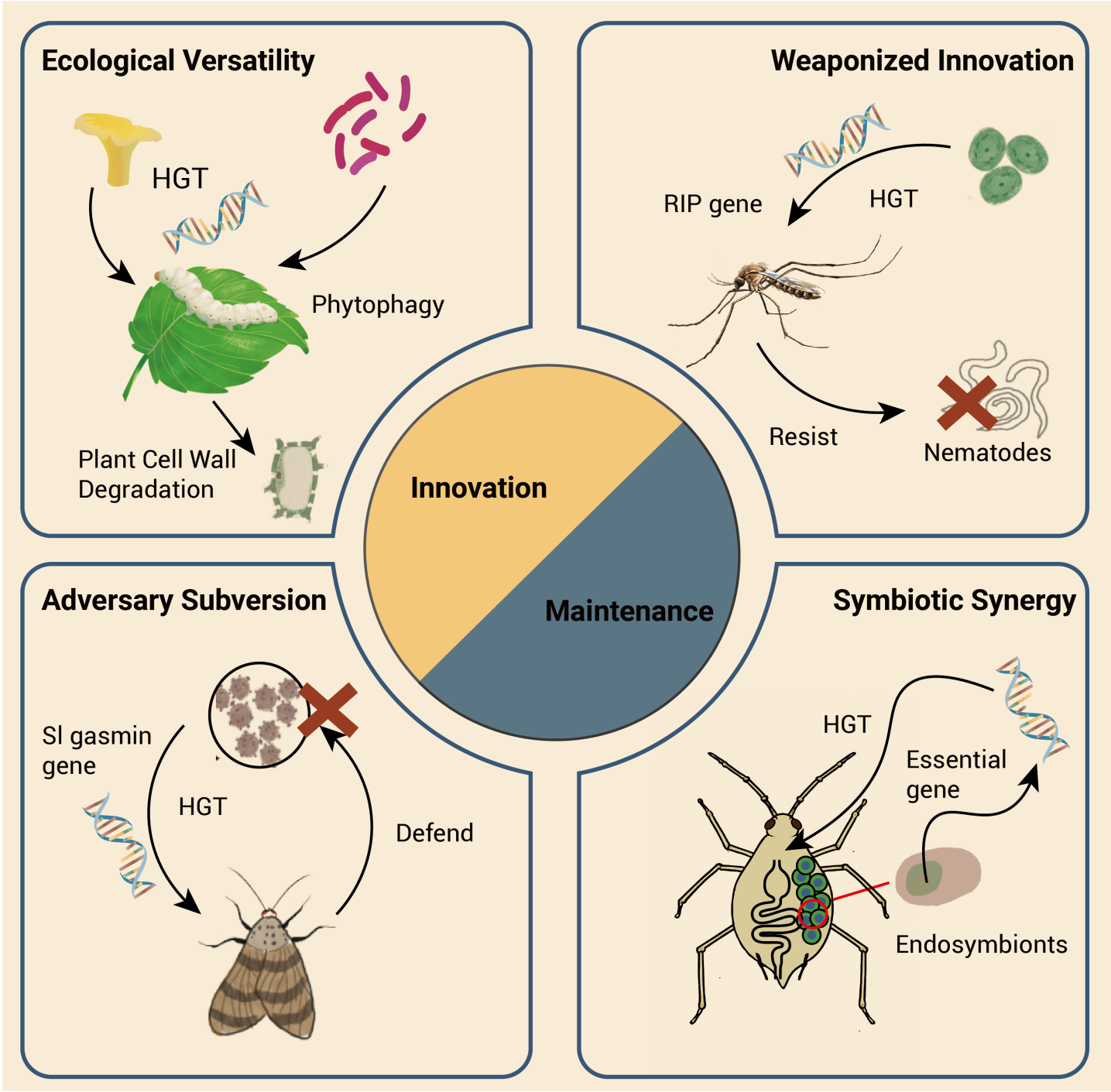

Figure 5. Roles and functional patterns of insect HGT Insect HGT can be summarized by either "maintenance" or "innovation" strategies, which can be further categorized into four patterns: ecological versatility, weaponized innovation, adversary subversion and symbiotic synergy.

herbivory, parasitism, symbiosis, or detoxification, yet major gaps remain in understanding HGT across evolutionary timescales—particularly regarding regulatory integration, transfer frequency, and parallels to endosymbiotic gene transfer.[208] Current findings suggest insect HTGs follow two domestication trajectories: "maintenance", stabilizing ancient symbiotic functions, and "innovation", driving ecological diversification. Notably, some HTG functions already provide applied value, for example, the plant-derived HTG *BtPMaT1*[19] enables novel pest-control strategies targeting detoxification pathways in whiteflies. However, interactions among distinct HTG systems still remain confused. Take aphid as an example, previous studies have found red pea aphid can have more winged offspring, suggesting a possible association between these two HGT-derived traits, wing plasticity (viral-derived *Apns* genes) and body coloration (fungal-derived *Tor* genes).[209-211] However, another recent research findings illustrated the plasticity variation impacted more by other genetic variation, rather than the body color traits.[212] Besides, numerous putative HTGs from earlier studies still lack peptide evidence or functional assays due to incomplete proteomic annotation. Future integration of advanced transcriptomic, proteomic, and gene-editing technologies with standardized performance metrics will be essential for systematically resolving functional landscapes and evolutionary integration mechanisms of horizontally acquired genes.

Overall, insect HGT research is entering a rapid expansion phase. Future efforts should extend functional studies to underrepresented insect orders, dissect ecological consequences of HTG-mediated adaptation, and clarify

interactions between HTGs and host genomes. Collectively, these directions will advance our understanding of genomic plasticity and inform biotechnological applications in sustainable agriculture and precision pest management.

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FUNDING AND ACKNOWLEDGMENTS

We sincerely thank Prof. Shuo Yan and Prof. Fan Song for their valuable suggestions and guidance in the conception and writing of this manuscript. We also thank Mr. Vincent Senyang Xue and Mrs. Xinyi Guo for their kind help in bioinformatics. Their insightful advice greatly improved the clarity and quality of this work. The work was supported by the grants from National Key Research and Development Program of China (Nos. 2024YFC2607800 and 2024YFC2607804), National Natural Science Foundation of China (Nos. 31730086 and 31922012), the Postdoctoral Fellowship Program of CPSF (No. GZC20241945) and the 2115 Talent Development Program of China Agricultural University. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

AUTHOR CONTRIBUTIONS

W.C. and H.L.: Conceptualization and supervision.D.Z. and Z.W.: Writing original draft. D.Z., J.X., Y.D. and H.L.: Writing, review, and editing. All authors contributed to the manuscript and approved the final version.

DECLARATION OF INTERESTS

The authors declare no competing interests.

ETHICAL STATEMENT AND PATIENT CONSENT

Not applicable.

DATA AND CODE AVAILABILITY

Not applicable.

SUPPLEMENTAL INFORMATION

It can be found online at https://doi.org/10.59717/j.xinn-life.2026.100223