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Abstract

Aphids are serious pests of agricultural and ornamental plants and important model systems for hemipteran–plant interactions. The long evolutionary history of aphids with their host plants has resulted in a variety of systems that provide insight into the different adaptation strategies of aphids to plants and vice versa. In the past, various plant–aphid interactions have been documented, but lack of functional tools has limited molecular studies on the mechanisms of plant–aphid interactions. Recent technological advances have begun to reveal plant–aphid interactions at the molecular level and to increase our knowledge of the mechanisms of aphid adaptation or specialization to different host plants. In this article, we compile and analyze available information on plant–aphid interactions, discuss the limitations of current knowledge, and argue for new research directions. We advocate for more work that takes advantage of natural systems and recently established molecular techniques to obtain a comprehensive view of plant–aphid interaction mechanisms.

1. INTRODUCTION

Plant–insect interactions first evolved approximately 400 million years ago (112), driving selection on plants to reinforce and reinvent their defenses and on insects to develop new mechanisms to overcome them or to exploit new plant species (6, 26, 63). However, the molecular mechanisms that underlie the adaptation and specialization of an insect to a specific plant and those that allow a generalist insect to feed on a wide range of plant species remain relatively poorly understood. To understand plant–insect interactions at the molecular level, in particular, those involving sap feeders, we usually refer to the concepts developed in research on plant–microbial pathogen interactions because more studies have been done in this field (43, 53). However, there is no established model to explain the host specificity of pathogens and resistance of plants to nonadapted pathogens (nonhost resistance). Based on the zig-zag model (50), plants recognize pathogen-associated molecular patterns (PAMPs) that induce pattern-triggered immunity (PTI). However, host-specialized pathogens can secrete effector proteins to overcome PTI without triggering effector-triggered immunity (ETI). Nonhost resistance may consist of PTI and ETI but also a combination of many other plant-specific constitutive defenses; thus, knowledge of nonhost resistance developed in one plant system may not be applicable to others. Unlike pathogens, insects have evolved a large repertoire of behaviors to locate and exploit their host plants, as well as a wide range of feeding strategies. Therefore, relying on the models established for plant–microbe interactions can limit understanding of plant–insect interactions. Recently, next-generation sequencing has expanded research beyond model organisms and provided an unprecedented wealth of genomic and transcriptomic information. Thus, we now have the tools to study various naturally occurring systems and examine the different mechanisms that determine the compatibility of plant–insect interactions. In this review, we focus on aphids because they belong to an important group of insect herbivores on which a significant amount of knowledge has accumulated recently.

Aphids are phloem-feeding hemipterans that belong to the superfamily Aphidoidea, among which many species cause huge economic losses either directly through sap ingestion or indirectly by transmitting plant viruses. Most aphid species are specialized to a few host plants belonging to a single family or closely related taxonomic families, and only fewer than 1% of species can feed on plants belonging to several taxonomic families (69, 95). Within aphid species, it is common to find some host plant–based genetic differentiation between populations, resulting in the existence of multiple biotypes specialized to feed on a limited number of host plants. In addition, host alternation, which is present in approximately 10% of aphid species (82), is a striking example of the ability of aphids to accommodate unrelated plants with distinct chemistry. These diverse aphid–plant interactions provide valuable systems for understanding the molecular mechanisms of host adaptation. Currently, most of the knowledge on molecular plant–aphid interactions has been found using model systems, such as the green peach aphid, *Myzus persicae*, and the thale cress, *Arabidopsis thaliana*, although this interaction is rare in nature. In addition, previous studies have mostly focused on plant resistance against aphids (44, 87, 146) but rarely investigated the mechanisms underlying aphid adaptation strategies in different plant–aphid systems. In this review, we summarize the main challenges of aphid colonization and how host-adapted aphids overcome them. We then give an overview of the potential mechanisms that contribute to promoting aphid variation in plant use and finally propose avenues for future research on plant–aphid interactions.

2. CHALLENGES FOR APHIDS TO FEED ON NEW PLANTS

Aphids face several challenges to exploiting their host plants. First, they use specific cues to recognize hosts among nonhosts. Physical and chemical barriers in plants thus prevent aphids from establishing a feeding site. Various plant defense responses and toxic metabolites also provide resistance to aphids. These challenges are detailed in this section.

Zig-zag model: a model to explain the plant immune system by induction and suppression of plant immunity by biotrophic pathogens

Pathogen-associated molecular patterns (PAMPs): conserved (slowly evolving) molecular patterns associated with pathogens and detected by plants; examples include bacterial lipopolysaccharides, flagellin, fungal chitin, and elongation factor Tu

Pattern-triggered immunity (PTI): a set of plant responses, such as ROS production, triggered by the recognition of PAMPs by membrane-localized pattern recognition receptors

Effector-triggered immunity (ETI): a set of plant responses triggered by the recognition of pathogen effectors

Biotype: a group of individuals sharing a similar genotype, such as a particular plant-specialized population of an insect species

Host alternation: obligate migration between host plants of distinct botanical families, such as between woody and herbaceous hosts

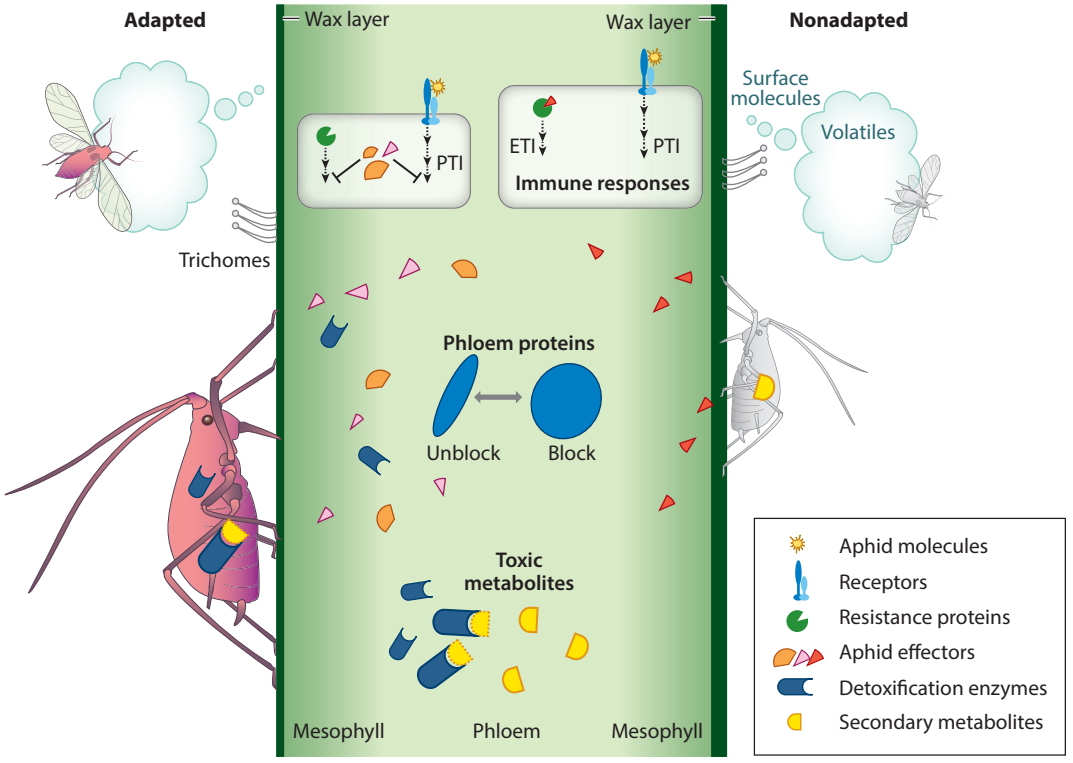

Figure 1

Challenges for aphids in feeding on new plants. Volatiles released from plants are crucial cues for aphids to recognize their hosts. After landing on a plant, wax and trichomes on the leaf surface could act as barriers to aphid infestation. When aphids probe plants, plant immune receptors may recognize aphid molecules to trigger pattern-triggered immunity (PTI), but the defense response can be suppressed by aphid salivary effectors. Some plants may also produce resistance proteins that recognize some aphid effectors and trigger effector-triggered immunity (ETI). Phloem proteins in certain plant species can block phloem flow to inhibit aphid ingestion, but adapted aphids can effectively avoid this. Plants produce toxic secondary metabolites that reduce aphid fitness. However, adapted aphids can deal with toxic compounds through a range of detoxifying systems.

2.1. Long-Distance Identification of Host Plants by Aphids

In addition to visual signals, volatiles emitted by plants are important cues for aphids to find host plants in environments that are usually complex in terms of diversity and spatial arrangement (**Figure 1**). Laboratory and field studies indicate that aphids can recognize host and nonhost volatiles (99), which would influence their flight behavior (89). Volatiles that are attractive or repellent to aphids were also identified in various plants. For example, the mixture of 15 active compounds identified from broad bean were attractive to the black bean aphid, *Aphis fabae* (137).

Multiple chemosensory proteins (CSPs) and odorant-binding proteins (OBPs), olfactory receptors (ORs), and gustatory receptors (GRs) are likely involved in distinguishing volatiles from host and nonhost plants. The corresponding genes for these proteins and receptors have been recently identified in some aphid species (54, 136). Transcriptomic analysis showed that many OBPs are highly expressed in heads or antennae, which indicates that they play roles in detecting environmental molecules (54, 136, 141). The aphid alarm pheromone, (E)-β-farnesene, is produced not only by aphids but also by several plant species and is hypothesized to repel aphids (99). Wang

Chemosensory proteins (CSPs) and odorant-binding proteins (OBPs): two families of small water-soluble proteins that are thought to bind to odorant molecules, then activate the receptors

et al. (134) reported recently that three OBPs, MperOBP3/7/9, coordinately mediate *M. persicae* response to (E)-β-farnesene, suggesting a mechanism by which aphids might recognize various plant volatiles using a limited number of OBPs.

2.2. Establishment of a Feeding Site

After landing on a plant surface, aphids penetrate plants with their stylets to establish a feeding site, a step that is influenced by several plant barriers and cues (**Figure 1**). Trichomes can act as barriers and enhance plant resistance to aphids on potato, cotton, and tomato. Such resistance may be mediated by glandular trichomes, which synthesize and secrete various metabolites (107). Epicuticular waxes also provide a barrier against nonadapted aphids. Stripping epicuticular waxes from a nonhost plant oat promotes an earlier stylet penetration of *A. fabae* than on unstripped plants (103). Stylet penetration by *A. fabae* was delayed when a major lipid component of oat epicuticular lipids, 1-hexacosanol, was applied, indicating that epicuticular lipids are involved in the sensing of nonhost plants (103).

Once aphid stylets penetrate plant tissues to find the phloem, cues such as sugar concentration and pH are important for their navigation to vascular tissues (42). Adapted aphids can easily penetrate mesophyll to reach phloem without much probing, but nonadapted aphids may repeatedly probe or even avoid probing when they are on nonhost plants. The bird cherry-oat aphid, *Rhopalosiphum padi*, displays more frequent probing behavior on the nonhost plant *Arabidopsis* than on the host plant barley, and stylet penetration is limited to mesophyll (28). The clover- and alfalfa-adapted biotypes of the pea aphid, *Acyrthosiphon pisum*, have shorter penetration time on their nonhost plants (10), and plant factors in mesophyll and sieve elements may play critical roles in the determination of host specificity (113). These results suggest that lack of phagostimulants and/or the presence of some barriers prevent nonadapted aphids from reaching the phloem (see the sidebar titled Aphid Feeding Behavior).

Nutrient content may also affect host plant selection by aphids. A study using an electrical penetration graph (EPG) showed that nitrogen and sugar concentrations are important cues used by aphids to assess plant quality (42). For example, *M. persicae* prefers to settle and shows longer phloem ingestion time on young cabbage leaves, which contain higher amino acid to sugar ratios than older leaves (11). However, several studies suggest that plant nutrients play less important roles in host selection and acceptance by aphids than the other cues presented above (104).

2.3. Overcoming Further Plant Defenses

Plants have developed different lines of defense that can involve the immune system and induced or constitutive metabolites that are toxic for aphids. These lines of plant defense are presented in this section.

APHID FEEDING BEHAVIOR

Aphid feeding behavior can be studied using an electrical penetration graph (EPG), which is a system to create an electrical circuit using a live aphid and a plant and record the waveforms of the electric signal. When the aphid inserts its stylets into a plant, the circuit is formed, and an electric signal is observed. Aphids produce specific waveforms when the stylets navigate through plant tissues, salivate, and establish feeding at phloem sieve cells. When the waveforms are recorded for several hours, the proportion of time spent on each feeding step can be examined and compared between different aphids or conditions.

2.3.1. Innate immunity against aphids. Pathogen recognition has been well studied in plants; PAMPs such as conserved peptide sequences of flagellin (36), elongation factor Tu (145), or chitin (80) are recognized by plants and induce PTI. Microbial recognition usually requires a coreceptor such as BRASSINOSTEROID INSENSITIVE1-ASSOCIATED KINASE1 (BAK1) and signal transmission by mitogen-activated protein kinase (MAPK)-signaling cascades and cytosolic calcium elevation. This signaling induces the production of reactive oxygen species (ROS), callose deposition, defense hormone accumulation, and immune marker gene expression (88). Several aphid-related molecules have been shown to induce plant PTI-like responses, and some PTI components work against both pathogens and aphids (**Figure 1**). For example, BAK1 induces rapid elevation of cytosolic calcium in epidermal and mesophyll cells surrounding the *M. persicae* penetration site by mediating the activation of both plasma membrane and vacuolar ion channels (132). In addition, the legume specialist *A. pisum* survives longer on the *bak1–5* mutant than on wild-type *Arabidopsis*, which indicates that BAK1 also confers nonhost resistance (105). Several aphid salivary proteins were identified as inducing the PTI-like responses, including the *Macrosiphum euphorbiae* effector, Me47, which induces the expression of PAMP-responsive genes in tomato (56).

Reactive oxygen species (ROS): highly reactive molecules containing oxygen; they are toxic to organisms and are involved in signal transduction

Chitin is a primary component of fungal cell walls but also of aphid exoskeleton. Although stylets are usually covered by gel saliva during penetration (129), chitin may come into contact with plant cells during aphid feeding. However, aphid extract that contains chitin induces ROS production in the *Arabidopsis fls2/efr1/cerk1* triple mutant, which cannot recognize PAMPs including fungal chitin (105). This result suggests that *Arabidopsis* may use unknown receptors to recognize aphid chitin or some other aphid-derived elicitors. In addition, many plant cell wall–degrading enzymes, including cellulases and pectinase, are found in gel saliva, and compounds from digested plant cell walls, such as oligogalacturonides, may trigger local defense (129, 139).

2.3.2. Hormone-mediated defense reactions. Induction of PTI usually involves the accumulation of phytohormones such as salicylic acid (SA) and jasmonic acid (JA) and activation of downstream signaling pathways. SA or JA accumulation could induce defense gene expression, secondary metabolite production, cell death, or even systemic acquired resistance, which confer resistance against various pathogens and herbivores. Induction of SA by aphid infestation was reported in various plant species (13, 68, 81). For example, the cotton aphid, *Aphis gossypii*, induces the expression of SA biosynthesis and signaling genes in zucchini, and the application of methyl-SA reduces the number of *A. gossypii* individuals on the plants (18). JA usually acts antagonistically to SA, and responds to wounding or necrotrophic pathogen infection. Although aphid stylet insertion does not cause significant wounding, aphid infestation can activate JA signaling pathways in certain plant species (72, 111). Application of methyl-JA on the plant surface also confers aphid resistance in some plant species: Methyl-JA treatment reduces fecundity of the blue alfalfa aphid, *Acyrthosiphon kondoi*, on *Medicago truncatula* cultivar A17 but not on Jester (34), and *M. persicae* exhibits reduced reproductive rate on methyl-JA-treated *Arabidopsis* (24). The timing and strength of phytohormone response to aphid infestation may vary among plant–aphid interaction systems. Weaker SA and JA induction was observed in various legumes infested by adapted *A. pisum* biotypes compared with nonadapted biotypes (111). However, another study showed clear induction of SA and JA in pea plants infested by pea-adapted aphids (72). These contrasting results may be due to the different cultivars used or variation in other experimental conditions such as aphid abundance. The diversity in plant SA and JA responses emphasizes the complexity of defense hormone signaling in aphid resistance.

In addition to SA and JA, involvement of other phytohormones such as ethylene, abscisic acid, and gibberellic acid in plant responses to aphid infestation is indicated. We invite interested readers to find more information in excellent reviews (e.g., 27, 83).

Resistance (R) genes: involved in recognition of effectors and conferring resistance to the parasite; often encode nucleotide-binding site and leucine-rich repeat (NBS-LRR) proteins

Effectors: molecules (often proteins) released by parasites into host plants to alter the biological processes of the host to promote infection

Genome-wide association study (GWAS): study to detect associations between genetic variants and phenotypic traits such as insect resistance in plants

Phytoalexin: molecules produced by plants that have toxic effects on the parasite

2.3.3. Resistance genes and their encoded proteins. In addition to the aforementioned immune responses, resistance (R) genes protect the plant against specific pest species or biotypes (**Figure 1**). R proteins may activate JA and SA signaling or ROS production to inhibit aphid feeding. Tomato *Mi-1* was the first R gene against aphids to be cloned. It encodes a nucleotide-binding site and leucine-rich repeat (NBS-LRR) protein (79, 110), which is involved in the recognition of pathogen effectors. *Mi-1* is constitutively expressed in both roots and leaves (20) and confers resistance to *M. euphorbiae*, the nematode *Meloidogyne incognita*, and the whitefly *Bemisia tabaci* via MAPK and SA signaling pathways (68). *Vat* is another cloned R gene from melon and also a member of the NBS-LRR family. It confers resistance to both *A. gossypii* infestation and *A. gossypii*–mediated virus transmission (22). Other NBS-LRR genes associated with aphid resistance have been reported, highlighting their importance in plant defense against these insects. This is the case for the *Rag6* and *Rag3c* loci in soybean, which contain three and one NBS-LRR genes, respectively, and other genes conferring resistance to *Aphis glycines* (143). A lettuce locus, *Ra*, which is linked to an NBS-LRR cluster, confers resistance to the aphid, *Pemphigus bursarius*, and silencing the NBS-LRR genes in the locus reduces the resistance against the aphid, indicating involvement of the NBS-LRR genes in *P. bursarius* resistance (140). Unlike these R genes, which exist in specific cultivars and work against host-adapted aphids, the *RAP1* locus in *M. truncatula* confers resistance against the *A. pisum* pea-adapted biotype but not against the *Medicago*-adapted biotype, indicating that it plays a role in nonhost resistance (119).

Although several R loci and genes were identified in different plant species, it is still not clear how they recognize aphid attacks. The aphid components that activate R proteins also remain to be identified.

2.3.4. Phloem-localized proteins. Several phloem proteins function to control sap flow, which may influence aphid feeding (**Figure 1**). Forisomes are Fabaceae-specific proteins that form a spindle-shaped complex located in sieve tubes (97). Rapid calcium elevation in response to environmental stimuli can trigger dispersion of forisomes, which block sap flow (98). The generalist aphids *M. persicae* and *M. euphorbiae* trigger the phloem occlusion by forisomes when feeding on broad bean, resulting in the withdrawal of their stylets or additional salivation, but this is not observed in *A. pisum*, which is adapted to broad bean (78).

SIEVE ELEMENT-LINING CHAPERONE1 (SLI1), a small heat shock–like protein, was identified by a genome-wide association study (GWAS) of aphid behavior on *Arabidopsis* ecotypes (60). SLI1 does not seem to occlude sieve tubes, but *M. persicae* and the cabbage aphid, *Brevicoryne brassicae*, produce more offspring on *sli1* mutants than on wild-type *Arabidopsis* (61). SLI1 localizes at sieve element margins and is thought to limit phloem ingestion by aphids by anchoring organelles and phloem proteins (61).

2.4. Toxic Secondary Metabolites

Many plant secondary metabolites are important defense molecules against pathogens and herbivores. These metabolites can be transported via the phloem and ingested by aphids (**Figure 1**). Camalexin is a phytoalexin known to contribute to plant defense against microbial pathogens and also aphids (2). Infestation of *Arabidopsis* by *B. brassicae* induces the expression of camalexin biosynthesis enzymes like PAD3, and aphid fecundity is enhanced in the *pad3-1* mutant (64). Feeding behavior monitored by EPG shows that *M. persicae* more easily establishes phloem feeding in the mutant of *pae9*, which contains lower basal levels of camalexin (59), and of *pad4*, which does not synthesize camalexin (96). *Myzus persicae* fecundity is reduced when it is fed on an artificial diet containing camalexin, confirming camalexin's toxicity (55). Glucosinolates compose another

important class of defense metabolites in Brassicaceae, and their toxicity is enhanced when they are hydrolyzed into isothiocyanates by myrosinase upon attacks by pathogens or insects. The concentration of an indole glucosinolate, 4MI3M (4-methoxy-indol-3-ylmethyl-glucosinolate), increases in *M. persicae* fed on *Arabidopsis* and cabbage, and aphid fecundity is reduced on an artificial diet containing indole glucosinolate and myrosinase (57, 58). These results suggest that both indole glucosinolates and their hydrolysis products such as isothiocyanates play major roles in resistance to *M. persicae*. Plant alkaloids such as nicotine also demonstrate toxicity to aphids. For example, the fecundity of a non-tobacco-adapted *M. persicae* lineage, but not that of the tobacco-adapted one, was totally inhibited when it was fed on an artificial diet containing 100 μM nicotine (106). Cardenolides, which are produced in many Apocynaceae species, such as milkweeds, inhibit Na^+/K^+ ATPase and confer toxicity to aphids (1). Cardenolide concentration of *Asclepias curassavica* is influenced by the oleander aphid, *Aphis nerii*, in a density-dependent manner (73), and the fitness of *A. nerii* is negatively correlated with cardenolide concentration in various milkweed plants (7). Although the aforementioned defense metabolites confer resistance to aphids, it is not known if and how reactions such as PTI and ETI regulate the production of these metabolites. In addition, it remains to be determined whether the concentration of defense metabolites is high enough in the phloem to ensure resistance to aphids.

3. MECHANISMS OF APHIDS TO OVERCOME PLANT DEFENSES

Although plants use a variety of strategies to protect themselves from aphids, adapted aphids are able to overcome them. Counterstrategies used by aphids involve suppressing plant defense and detoxifying or sequestering toxic metabolites. In this section, we present the current knowledge on these strategies.

3.1. Evidence for Suppression of Plant Defenses

Aphids have evolved various strategies to manipulate host plant immunity or to avoid recognition. Whereas the infestation by an avirulent clone of *M. persicae* induces expression of ROS-production genes in pepper, virulent clones induce ROS-scavenging genes and repress ROS-production genes in pepper (121). Co-infestation of a virulent and an avirulent biotype of the lettuce aphid, *Nasonovia ribisnigri*, increases the phloem-feeding duration of the avirulent biotype on the resistant cultivar of *Lactuca sativa* (124). Manipulating SA and JA accumulation and signaling pathway activation is one way for aphids to overcome host plant immunity. The JA, but not the SA, signaling pathway is attenuated in tomato after two days postinfestation with *M. persicae* (123). Broad beans preinfested by *A. pisum* produce much less JA after the second infestation, which accelerates aphid development (122). These alterations of hormone signaling may be mediated by aphid effectors, as discussed below.

3.2. Salivary Proteins Interfere with Various Plant Defense Mechanisms

Aphids secrete effector proteins and noncoding RNA into plants during infestation, and there is growing evidence, especially for effectors, that they can manipulate host plant immunity in various ways (**Figure 1**). For example, Mp55, a salivary protein identified in *M. persicae*, reduces ROS production and callose deposition when expressed in *Arabidopsis* and enhances *M. persicae* reproduction (25). MpMIF1, another salivary protein of *M. persicae*, can suppress both PR gene expression and immune responses in *Nicotiana benthamiana*. Silencing MpMIF1 in *M. persicae* decreased aphid fecundity, but normal fecundity was recovered when the silenced aphids were grown on transgenic plants expressing *MpMIF1* (86). Avoiding triggering plant immunity by reducing avirulent

effector secretion is another strategy used by aphids. An *M. persicae*–secreted cysteine protease, Cathepsin B3, is recognized by a tobacco cytoplasmic kinase EDR1-like protein and induces ROS production in phloem, which restricts aphid survival on tobacco. However, the tobacco-adapted lineage of *M. persicae* secretes less Cathepsin B3 than does the nonadapted lineage, which prevents ROS production and facilitates aphid feeding on tobacco (38).

How salivary effectors suppress host immunity is not clear in most cases. C002, which is important for establishing phloem feeding, was the first aphid effector protein to be identified (84). Silencing *C002* expression reduces survival of *A. pisum* (85) and *Schizaphis graminum* (144) and fecundity of *M. persicae* (100). Using *C002* transgenic plants further reveals that the C002 from *A. pisum* (ApC002) does not function like that of *M. persicae* (MpC002) because ApC002 lacks a repeat sequence that is present in MpC002. These species-specific effects were also found in other salivary effectors. Expression of the effectors *Mp1* and *Mp2* promotes *M. persicae* colonization on *Arabidopsis*, but expression of their orthologs from *A. pisum* (*ApPIntO1* and *ApPIntO2*) does not (101). In addition, *Mp1*, but not its orthologs, specifically interacts with the host Vacuolar Protein Sorting Associated Protein 52 (VPS52) of potato (*Solanum tuberosum*) and *Arabidopsis* (109). Because phloem-specific expression of *StVPS52* negatively impacts *M. persicae* virulence on *N. benthamiana*, targeting StVPS52 may be a way to promote aphid fitness on host plants. Unlike these host plant–specific effectors, the *M. euphorbiae* salivary effector Me10 enhances the fecundity of *M. euphorbiae* and *M. persicae* on tomato and *N. benthamiana*, respectively (3). Me10 and Ag10k, the homolog of Me10 in *A. gossypii*, interact with tomato 14-3-3 isoform 7 (TFT7), and the silencing of TFT7 in tomato improves longevity and fecundity of the nonhost aphid *A. gossypii* (15), which suggests that TFT7 is involved in basal resistance to aphids. In addition to effector proteins, a long noncoding RNA, *Ya1*, in *M. persicae* was reported as a virulence factor that promotes aphid fecundity in *Arabidopsis* (16). However, the modes of action of most of the effector proteins and the long noncoding RNA are unknown.

3.3. Degradation and Sequestration of Toxic Plant Metabolites

Aphids use different detoxification enzymes to overcome toxic plant metabolites (**Figure 1**). One main type of these enzymes, which includes cytochrome P450 (CYP450), catalyzes metabolites. The other type, which includes glutathione S-transferases (GSTs) and Uridine diphosphate (UDP)-glycosyltransferases, conjugates metabolites with polar molecules to detoxify them (41). The detoxified toxic metabolites could be excreted or sequestered in aphids.

Tobacco-adapted *M. persicae* plants have a higher nicotine tolerance than nonadapted ones and even show higher fecundity on a diet with 100 μM nicotine than on a diet without nicotine (106), which indicates their ability to detoxify nicotine. Relative to a nonadapted clone, 10 UDP-glycosyltransferase genes were reported to be highly expressed in tobacco-adapted *M. persicae*, and silencing four of them significantly increased the nicotine sensitivity of tobacco-adapted *M. persicae*, suggesting the involvement of these genes in nicotine tolerance and adaptation to tobacco (93). Moreover, two CYP450s, CYP6CY3 and CYP6CY4, were identified to confer nicotine resistance in tobacco-adapted *M. persicae*. Heterologous expression of the two genes confirmed their abilities to catalyze nicotine into nontoxic compounds, which protects both the aphid and its obligate endosymbiont, *Buchnera aphidicola* (5, 116). A similar strategy is observed in *A. nerii*, where several CYP450 and UDP-glycosyltransferase genes are induced to a greater extent upon feeding on more toxic milkweed species than on less toxic species (7).

When *M. persicae* feeds on *Arabidopsis* that overproduces indole glucosinolate, several aphid CYP450 genes are overexpressed, which grants the aphid a better tolerance to this compound (47). GST activities were also detected in *Sitobion avenae* and *M. persicae* fed on diets with

glucosinolates and their hydrolyzed compounds (33). A salivary effector, Me47, was identified in *M. euphorbiae* as a GST that metabolizes isothiocyanates and enhances fecundity on tomato, suggesting that aphids actively detoxify plant metabolites by injecting GSTs (56).

In addition to detoxifying toxic metabolites, some specialist aphid species can sequester metabolites and use them as weapons against predators. For example, the cabbage aphid *B. brassicae* can selectively sequester glucosinolates from host plants, thus avoiding generating toxic hydrolyzed products. *Brevicoryne brassicae* produces its own myrosinases that can hydrolyze aliphatic glucosinolates (48, 49, 102), and the hydrolysis products are toxic for predators: The developmental time of the predators is affected by feeding on *B. brassicae* grown on different host plants with different glucosinolate profiles (62). The oleander aphid, *A. nerii*, can also sequester toxic cardenolide from milkweeds (147). Parasitoid larval mortality is increased on *A. nerii* from milkweeds with a high concentration of cardenolides (21).

Epigenetic regulation: controls gene expression heritably without changing gene sequence

Quantitative trait locus (QTL): a genetic region that correlates with a quantitative phenotypic trait, such as a type of insect resistance

4. MECHANISMS OF APHID ADAPTATION TO A NEW HOST PLANT

Studies of plant–aphid interactions have identified various mechanisms and genes involved in aphid adaptation to specific plant species. Variation in amino acid sequences or expression patterns of these key genes provides opportunities for aphids to adapt to a new host plant. These differences can be genetically determined or involve epigenetic regulation, but they can also entail aphid symbionts. In this section, we discuss how aphids expand their host range via these different sources of variation.

4.1. Genetic Variation Promotes Aphid Adaptation to New Host Plants

As sequencing technologies improve, aphid genomic resources including reference genomes are rapidly accumulating (75), allowing the investigation of different plant adaptation strategies resulting from selection on aphid genetic variation. These genetic variations can be caused by mutations in small regions of sequence; by chromosome structure rearrangement; or by horizontal transfer, which results in sequence polymorphism, gene duplication, or new gene acquisition (142). Some of these variants may have become fixed in the aphid species, biotypes, or lineages showing distinct host specificity as a result of specialization and subsequent differentiation.

For example, quantitative trait locus (QTL) mapping on biotypes of *A. pisum* revealed several QTLs controlling specificity to clover or alfalfa (40), and further genome scan analysis identified more precisely the genomic regions associated with host specialization in different biotypes (45, 90, 91). Genome-wide characterization of the polymorphisms among three *A. pisum* biotypes further revealed that candidate salivary genes, which are expressed in salivary glands and encode secreted proteins, were enriched in the loci associated with plant specialization (90), suggesting the importance of these genes in the evolution of host adaptation. In support of this, *A. pisum* candidate salivary genes encode many aphid-specific genes, and their evolutionary rates are faster than those of other salivary gland–expressed genes (8). Similarly, sequence comparison between *Myzus cerasi*, *M. persicae*, and *R. padi* showed faster evolution in putative aphid effectors (secreted salivary genes) than in noneffectors (126). These results suggest that species- or biotype-specific salivary proteins have evolved and specialized to be effective effectors in the specific host plants by acquiring functional mutations that suppress plant immunity while avoiding plant recognition.

Gene duplication is an important source of evolutionary innovation that may affect gene expression level. OR and GR gene families, as well as salivary gene families, have expanded in the genome of *A. pisum*, and some copies show signs of positive selection, suggesting their neofunctionalization and possible involvement in plant adaptation (8, 117). In addition, the gene copy

numbers of OR and GR genes also differ among *A. pisum* biotypes (23), and a focused approach revealed several OR and GR genes that are highly differentiated among these biotypes and that may be involved in aphid host specialization (118). This ample genetic variation in chemosensory genes may fuel variation in aphids' ability to discriminate plant volatiles and enhance host plant selection.

As mentioned above, many CYP450 enzymes play key roles in the detoxification of plant secondary metabolites. In *A. pisum*, copy numbers of P450 genes are variable across biotypes with distinct host plant specificity (23), which may facilitate adaptation to new hosts. The genetic changes involved in the different evolutionary paths between tobacco-adapted and nonadapted lineages of *M. persicae* were recently revealed (116). Chromosomal rearrangement in the tobacco-adapted lineage not only increased the copy number of the genes at these loci, but also generated a chimeric gene. Further mutation, deletion, or insertion within the amplified region could eliminate the duplicated genes with no fitness benefit while maintaining high expression levels of the adaptive genes such as P450s. In addition, transposable elements also led to the amplification of P450s at different positions of the genome. These genetic changes cause higher expression levels of specific P450s compared to non-tobacco-adapted *M. persicae* and confer a protection mechanism to the aphid and its obligatory symbiont against nicotine (116).

Gene copy number: number of copies of a particular gene in the genome of an individual; copy number variation is caused by changes in DNA structure involving various processes such as duplication, deletion or insertion

Methylation: a heritable epigenetic mark that refers to the addition of a methyl group to the cytosine of DNA

Small RNAs (sRNAs): the general term that indicates short (approximately 200 nucleotide) noncoding RNAs that are often processed into 20–30 nucleotides and regulate gene expression

MicroRNA (miRNA): a class of single-stranded noncoding sRNAs that often negatively regulate gene expression

Chromatin: a complex of DNA and proteins such as histones

Histones: proteins involved in DNA condensation and packaging in the nucleus

4.2. Epigenetic Regulation Enhances Plastic Response of Aphids

Transcriptional changes associated with a shift between different plant species have been revealed in different aphid systems (19, 54, 74, 127) and likely involve epigenetic regulation. Epigenetic mechanisms are reported in many insect species as regulating gene expression and protein translation (35). DNA methylation and histone modification play an important role in regulating local gene expression. Small RNAs (sRNAs) such as microRNA (miRNA) are major players in post-transcriptional regulation (35). Alternative splicing enhances protein diversity from a single precursor messenger RNA (mRNA) or regulates mRNA abundance (76). These regulations are well studied in plants and vertebrates but considerably less well studied in insects, especially in the context of host plant adaptation.

Methylation of DNA CpG islands is known to regulate gene expression through transcriptional silencing in a tissue-specific manner (51). In *A. pisum*, genes that encode DNA methyltransferases and the associated proteins were annotated, and the general methylation patterns were also characterized (133). Compared to plants and vertebrates, lower levels of methylated CpGs were observed in the *A. pisum* genome, and the methylation sites were more enriched in gene bodies than in regulatory elements, which seems to be common in invertebrates (71, 133). DNA methylation in regulatory elements usually suppresses transcription; however, DNA methylation in gene bodies can be associated with enhanced gene expression in aphids (51). Esterase E4 genes confer resistance to both organophosphate and carbamate insecticides in *M. persicae* (4). In some insecticide-resistant *M. persicae* clones, E4 genes are amplified, highly methylated, and highly expressed. Interestingly, in the absence of insecticide pressure, the resistance mechanism can be lost in one generation and is associated with a demethylation of E4 genes, resulting in their reduced expression (32). This example clearly shows the importance of (de)methylation of key genes in fast adaptation to sudden environmental changes.

Histone proteins play a major role in the regulation of the chromatin structure. They can be post-translationally altered by various modifications such as (de)methylation and (de)acetylation or replaced by alternative histones, which results in the alteration of local chromatin accessibility and gene expression. The genome of *A. pisum* contains a comprehensive catalog of histone-modifying enzymes, and the members of this catalog are clearly more diverse than enzymes in

other known arthropod species (108). Some histone variants were also identified in *A. pisum* that may provide different binding abilities with chromatin and affect its accessibility (108).

The miRNAs produced by the miRNA machinery usually target specific genes' mRNAs to suppress their translation, which may affect the expression of key genes of host adaptation in aphids. Unlike vertebrates, the *A. pisum* genome encodes multiple copies of the miRNA machinery, and these copies were shown to evolve rapidly in aphids (46). Expression profiles of these copies revealed that they were differentially expressed at different morphological stages, which indicates that they play roles in regulating developmental gene expression. Many miRNAs have been predicted to exist in the aphid genomes (46, 66), but most of them have no characterized function in host adaptation.

Alternative splicing enables different translation of protein variants from a single precursor mRNA or regulation of mRNA abundance through nonsense-mediated mRNA decay (76). In *A. pisum*, 34% of expressed genes exhibited alternative splicing in different morphs (37). Involvement of alternative splicing in aphid adaptation to host plant is not known.

4.3. Aphid Symbionts May Affect Plant–Aphid Interactions

Many mechanisms underlying adaptation to host plants are encoded by the aphid genome; others may involve aphids' symbiotic bacteria and viruses. The primary endosymbiont *Buchnera* is essential for aphids by providing nutrients such as essential amino acids and vitamins lacking in their diet. Curiously, upon feeding, aphids inject GroEL, a protein produced in high quantity by *Buchnera*, which is recognized by the plant and elicits PTI responses (14). However, aphid feeding is not altered, suggesting that aphids might inject other effectors into the plant to overcome or suppress the GroEL-induced response (120). A recent study also showed that the expression profiles of *Buchnera* sRNA differ between *A. pisum* feeding on broad bean or those feeding on alfalfa (125). The authors of this study hypothesized that the plant-specific expression patterns of *Buchnera* sRNA may be caused by the variation in plant metabolites (which include amino acids and plant defense compounds) or by stress responses of *Buchnera*. Although they are difficult to perform, functional studies are needed to verify the roles of the sRNA in plant–aphid interaction. GWASs on *A. pisum* genotypes revealed associations between variation on the *Buchnera* genome and the pea aphid performance on a histidine-free diet. Interestingly, association peaks involved two *Buchnera* genes encoding the histidine biosynthesis pathway (17). Thus, genetic variation in *Buchnera* lineages could translate into different nutrient acquisition efficiency in the host aphids, which may affect the aphids' abilities to feed on different host plants.

In addition to *Buchnera*, aphids harbor a range of facultative bacterial symbionts, which may also influence interactions with plants (92). It was found that *Regiella insecticola*, a facultative symbiont of *A. pisum*, promotes pea aphid fecundity on white clover (*Trifolium repens*) specifically (128); however, this result was not reproduced in other pea aphid–*R. insecticola* or –facultative symbiont interactions (30, 77). A clone of the wheat aphid (*Sitobion miscanthi*) infected by the *Hamiltonella defensa* facultative symbiont developed faster and had higher fecundity on wheat than did an uninfected one; these results were correlated with lower SA and JA accumulation and repression of the downstream genes in the infected clone (67). In addition, *Serratia symbiotica*–infected pea aphids repressed ROS production and the SA and JA pathways and fed for longer on *M. truncatula* compared to uninfected aphids. A salivary gene, *ApHRC*, was highly upregulated in the *Serratia*-infected aphid, and silencing this gene increased ROS production upon feeding (135). However, how *Serratia* infection induces specific salivary genes is not known. Besides bacterial symbionts, the *Acyrthosiphon pisum* virus (APV) was shown to increase pea aphid survival rate on unsuitable plants; this increase in survival coincided with reduced JA production (70). Taken together, this evidence

indicates that the involvement of microbial symbionts in determining aphid plant specificity seems to be elusive and cannot be generalized to all aphid–symbiont interactions.

5. FUTURE DIRECTIONS OF RESEARCH ON MOLECULAR PLANT–APHID INTERACTIONS

Current knowledge on plant–aphid interactions at the molecular level has been generated primarily by studies of the *Arabidopsis–M. persicae* and tomato–*M. euphorbiae* interactions, taking advantage of various resources developed in the model plants *Arabidopsis* and tomato and the recently published genome of *M. persicae* and other accumulating genomic resources. Studies on other systems are complicated due to the lack of experimental tools and genetic resources for both the plants and the aphids. Nevertheless, these pioneering studies have provided a first glimpse of the complexity of the mechanisms underlying plant–aphid interactions. To advance this important area of research, we propose that future studies of plant–aphid interactions focus more on systems that are closer to natural situations and consider the different time scales at which the molecular mechanisms operate. This section discusses some examples of such research programs presented from the long to the short time scale of molecular changes involved.

Unrelated aphid species may infest the same host plant by adapting the plant species independently (**Figure 2*a***). For example, both *Aphis spiraecola* and *Toxoptera citricida* are able to feed on sweet orange (*Citrus sinensis*), while both *Megoura viciae* and *A. pisum* are able to feed on vetch (*Vicia sativa*). The genome of these aphids sharing the same hosts may encode common or specific pathways allowing them to exploit the hosts. Previous studies on plant–pathogen interactions have revealed that functionally convergent effectors are used by different pathogens to suppress ROS production by targeting conserved host proteins in ROS signaling or metabolism (52). An investigation of interactions between *Arabidopsis* proteins and effectors from three kingdoms of

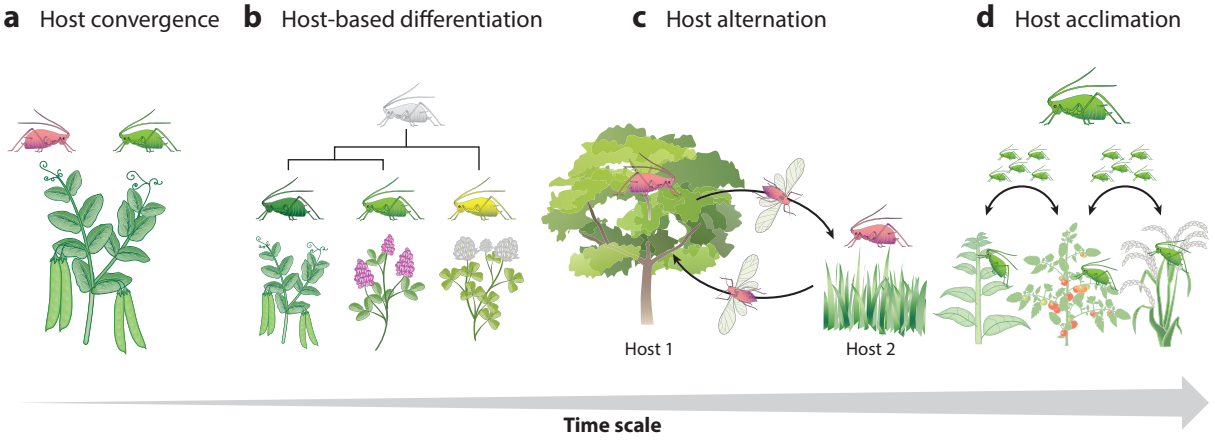

Figure 2

Different time scales and processes of colonization of new host plants by aphids. The molecular mechanisms underlying the colonization of new plants by aphids can be characterized according to the time scale at which they operate. (*a*) Different aphid species that diverged a long time ago may have adapted to the same host plant independently. (*b*) Some aphid species have developed biotypes that are genetically related but adapted to specific plants. (*c*) Approximately 10% of aphid species migrate between unrelated host plants (generally woody and herbaceous plants) to complete their annual life cycle. This host alternation requires rapid adjustments of migrant morphs to the unrelated host. (*d*) Unlike most specialist aphids, generalist species can colonize a very wide range of hosts from different plant families and shift from one plant to another during their lifetime.

pathogens also demonstrated common targets of host proteins, indicating convergent evolution among these pathogens (138). Therefore, comparative genomics and transcriptomics of aphid species sharing the same host could help us to identify those shared or specific adaptation genes and their common plant targets.

Host-specialized biotypes are reported in several aphid species, such as *A. gossypii* (12, 130), *A. pisum* (31, 94, 131), and *M. persicae* (115). Such biotype complexes offer opportunities to elucidate the molecular basis of plant specialization and the evolutionary processes leading to biotype divergence. In this context, *A. pisum*, which comprises at least 15 biotypes, provides a valuable system to decipher the molecular determinants of plant specificity and, more particularly, to interrogate whether biotype formation relies on common or specific mechanisms (114). These biotypes share similar genome sequences but are very specialized to feed on a limited number of host legume species (**Figure 2*b***). Comparative analyses of different biotypes have revealed biotype-specific genomic and expression patterns. Many of these sequence and expression differences are found in chemosensory and salivary genes, suggesting their involvement in plant specialization (9, 23, 29, 90, 117, 118). Given the development of functional validation tools (39, 65), the *A. pisum* complex is an emerging system that has considerable potential to advance understanding of the mechanisms of adaptation to specific host plants in their functional and evolutionary dimensions.

Another interesting system offering the possibility of understanding molecular mechanisms determining plant specificity is provided by host-alternating aphids, which have an obligate shift between unrelated host plants (82) (**Figure 2*c***). For example, *M. cerasi* uses *Prunus* trees as primary hosts in winter and many herbaceous plants as secondary hosts in summer. Host alternation is accomplished by specialized morphs produced by the same clone under unknown cues; therefore, it does not involve any genetic changes. Host alternation certainly induces the tuning of chemosensory receptors to locate the host and the production of specific proteins to overcome plant defenses and acquire nutrients. We are only at a very early stage of understanding the molecular basis of host alternation in aphids. To the best of our knowledge, only two studies, one on *M. cerasi* (127) and the other on *Hyalopterus persikonus* (19), have examined gene expression differences between aphid morphs on woody and herbaceous hosts using RNA sequencing. Both studies found an enrichment of salivary and detoxifying function categories in the differentially expressed gene set (19, 127), suggesting that these two functions, at least, might be involved in plant specialization.

Unlike the aforementioned plant-specialized species, biotypes, or morphs, some generalist aphid clones can colonize a very wide range of divergent host plants and make immediate shifts from one plant to another (**Figure 2*d***). Since aphids reproduce mainly via parthenogenesis, the mechanisms underlying plasticity in host range in such generalist aphids rely on expression (epigenetic) changes and not on genetic changes. Therefore, generalist aphids may provide another perspective on the molecular basis of plant adaptation. A study on a generalist *M. persicae* clone that shifted between different unrelated plant species identified several coregulated clusters of genes involved in the adjustment to new hosts, among them cathepsin B and cuticular genes (74). Further work is needed to determine how this transcriptional plasticity is controlled and the modes of action of the genes specifically associated with host plant shifts. In addition, aphids also rely on plant cues to select their hosts, and the chemosensory mechanisms involved in the selection of multiple hosts have to be examined using appropriate experimental designs.

Another ideal system for investigating the molecular basis of plasticity in plant choice in aphids is again provided by host-alternating species, which typically show highly specialized morphs on the winter hosts and much more flexible morphs able to feed on a wide range of summer hosts. For example, *A. fabae* and *Macrosiphum rosae* exclusively use spindle trees (*Euonymus europaeus*) and *Rosa* species as winter hosts, respectively, but feed on many summer hosts belonging to different families. Comparing gene expression patterns of the aphids feeding on the primary host and those

feeding on the multiple secondary hosts may reveal how specialism and generalism are regulated at a clonal level.

SUMMARY POINTS

1. Most aphid species are specialized to one or a few host plants, but the molecular mechanisms underlying host adaptation are poorly known.
2. Throughout their interactions with plants, aphids have evolved a series of adaptive mechanisms to overcome the different challenges posed by their host plants.
3. Recent progress on aphid–plant systems studied in the laboratory has increased our understanding of mechanisms of suppression of plant defense via salivary proteins and of sequestration and detoxification of secondary plant metabolites.
4. Sequence variation, epigenetic regulatory mechanisms, and interactions with microbial symbionts can fuel innovations that allow aphids to acquire a new host plant.
5. While there are increasing numbers of examples of the role of genetic changes in aphid adaptation to a new plant, little is known about the importance of epigenetic regulation in host plant shifts and the actual influence of symbionts on aphid plant specificity.
6. Future studies of plant–aphid interactions should focus more on systems that are closer to natural situations and consider the different time scales at which the molecular mechanisms operate.

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LITERATURE CITED

1. Agrawal AA, Petschenka G, Bingham RA, Weber MG, Rasmann S. 2012. Toxic cardenolides: chemical ecology and coevolution of specialized plant–herbivore interactions. *New Phytol.* 194:28–45
2. Ahuja I, Kissen R, Bones AM. 2012. Phytoalexins in defense against pathogens. *Trends Plant Sci.* 17:73–90
3. Atamian HS, Chaudhary R, Cin VD, Bao E, Girke T, Kaloshian I. 2013. In planta expression or delivery of potato aphid *Macrosiphum euphorbiae* effectors *Me10* and *Me23* enhances aphid fecundity. *Mol. Plant. Microbe Interact.* 26:67–74
4. Bass C, Puinean AM, Zimmer CT, Denholm I, Field LM, et al. 2014. The evolution of insecticide resistance in the peach potato aphid, *Myzus persicae*. *Insect Biochem. Mol. Biol.* 51:41–51
5. Bass C, Zimmer CT, Riveron JM, Wilding CS, Wondji CS, et al. 2013. Gene amplification and microsatellite polymorphism underlie a recent insect host shift. *PNAS* 110:19460–65
6. Becerra JX. 2007. The impact of herbivore-plant coevolution on plant community structure. *PNAS* 104:7483–88
7. Birnbaum SSL, Rinker DC, Gerardo NM, Abbot P. 2017. Transcriptional profile and differential fitness in a specialist milkweed insect across host plants varying in toxicity. *Mol. Ecol.* 26:6742–61

8. Boulain H, Legeai F, Guy E, Morlière S, Douglas NE, et al. 2018. Fast evolution and lineage-specific gene family expansions of aphid salivary effectors driven by interactions with host-plants. *Genome Biol. Evol.* 10:1554–72
9. Boulain H, Legeai F, Jaquiéry J, Guy E, Morlière S, et al. 2019. Differential expression of candidate salivary effector genes in pea aphid biotypes with distinct host plant specificity. *Front. Plant Sci.* 10:1301
10. Caillaud MC, Via S. 2000. Specialized feeding behavior influences both ecological specialization and assortative mating in sympatric host races of pea aphids. *Am. Nat.* 156:606–21
11. Cao H-H, Zhang Z-F, Wang X-F, Liu T-X. 2018. Nutrition versus defense: why *Myzus persicae* (green peach aphid) prefers and performs better on young leaves of cabbage. *PLOS ONE* 13:e0196219
12. Carletto J, Lombaert E, Chavigny P, Brévault T, Lapchin L, Vanlerberghe-Masutti F. 2009. Ecological specialization of the aphid *Aphis gossypii* Glover on cultivated host plants. *Mol. Ecol.* 18:2198–212
13. Chaman ME, Copaja SV, Argandoña VH. 2003. Relationships between salicylic acid content, phenylalanine ammonia-lyase (PAL) activity, and resistance of barley to aphid infestation. *J. Agric. Food Chem.* 51:2227–31
14. Chaudhary R, Atamian HS, Shen Z, Briggs SP, Kaloshian I. 2014. GroEL from the endosymbiont *Buchnera aphidicola* betrays the aphid by triggering plant defense. *PNAS* 111:8919–24
15. Chaudhary R, Peng H-C, He J, MacWilliams J, Teixeira M, et al. 2019. Aphid effector Me10 interacts with tomato TFT7, a 14-3-3 isoform involved in aphid resistance. *New Phytol.* 221:1518–28
16. Chen Y, Singh A, Kaithakottil GG, Mathers TC, Gravino M, et al. 2020. An aphid RNA transcript migrates systemically within plants and is a virulence factor. *PNAS* 117:12763–71
17. Chung SH, Parker BJ, Blow F, Brisson JA, Douglas AE. 2020. Host and symbiont genetic determinants of nutritional phenotype in a natural population of the pea aphid. *Mol. Ecol.* 29:848–58
18. Coppola M, Manco E, Vitiello A, Di Lelio I, Giorgini M, et al. 2018. Plant response to feeding aphids promotes aphid dispersal. *Entomol. Exp. Appl.* 166:386–94
19. Cui N, Yang P-C, Guo K, Kang L, Cui F. 2017. Large-scale gene expression reveals different adaptations of *Hyalopterus persikonus* to winter and summer host plants. *Insect Sci.* 24:431–42
20. de Ilarduya OM, Kaloshian I. 2001. *Mi-1.2* transcripts accumulate ubiquitously in resistant *Lycopersicon esculentum*. *J. Nematol.* 33:116–20
21. Desneux N, Barta RJ, Hoelmer KA, Hopper KR, Heimpel GE. 2009. Multifaceted determinants of host specificity in an aphid parasitoid. *Oecologia* 160:387–98
22. Dogimont C, Chovelon V, Pauquet J, Boualem A, Bendahmane A. 2014. The *Vat* locus encodes for a CC-NBS-LRR protein that confers resistance to *Aphis gossypii* infestation and *A. gossypii*-mediated virus resistance. *Plant J.* 80:993–1004
23. Duvaux L, Geissmann Q, Gharbi K, Zhou JJ, Ferrari J, et al. 2015. Dynamics of copy number variation in host races of the pea aphid. *Mol. Biol. Evol.* 32:63–80
24. Ellis C, Karafyllidis I, Turner JG. 2002. Constitutive activation of jasmonate signaling in an *Arabidopsis* mutant correlates with enhanced resistance to *Erysiphe cichoracearum*, *Pseudomonas syringae*, and *Myzus persicae*. *Mol. Plant Microbe Interact.* 15:1025–30
25. Elzinga DA, De Vos M, Jander G. 2014. Suppression of plant defenses by a *Myzus persicae* (green peach aphid) salivary effector protein. *Mol. Plant Microbe Interact.* 27:747–56
26. Endara MJ, Coley PD, Ghabash G, Nicholls JA, Dexter KG, et al. 2017. Coevolutionary arms race versus host defense chase in a tropical herbivore-plant system. *PNAS* 114:E7499–505
27. Erb M, Meldau S, Howe GA. 2012. Role of phytohormones in insect-specific plant reactions. *Trends Plant Sci.* 17:250–59
28. Escudero-Martinez C, Leybourne DJ, Bos JIB. 2020. Plant resistance in different cell layers affects aphid probing and feeding behaviour during non-host and poor-host interactions. *Bull. Entomol. Res.* 111:31–38
29. Eyres I, Jaquiéry J, Sugio A, Duvaux L, Gharbi K, et al. 2016. Differential gene expression according to race and host plant in the pea aphid. *Mol. Ecol.* 25:4197–215
30. Ferrari J, Scarborough CL, Godfray HCJ. 2007. Genetic variation in the effect of a facultative symbiont on host-plant use by pea aphids. *Oecologia* 153:323–29
31. Ferrari J, West JA, Via S, Godfray HCJ. 2012. Population genetic structure and secondary symbionts in host-associated populations of the pea aphid complex. *Evolution* 66:375–90

32. Field LM, Blackman RL, Tyler-Smith C, Devonshire AL. 1999. Relationship between amount of esterase and gene copy number in insecticide-resistant *Myzus persicae* (Sulzer). *Biochem. J.* 339(Part 3):737–42
33. Francis F, Vanhaelen N, Haubruge E. 2005. Glutathione S-transferases in the adaptation to plant secondary metabolites in the *Myzus persicae* aphid. *Arch. Insect Biochem. Physiol.* 58:166–74
34. Gao LL, Anderson JP, Klingler JP, Nair RM, Edwards OR, Singh KB. 2007. Involvement of the octadecanoid pathway in bluegreen aphid resistance in *Medicago truncatula*. *Mol. Plant Microbe Interact.* 20:82–93
35. Glastad KM, Hunt BG, Goodisman MAD. 2019. Epigenetics in insects: genome regulation and the generation of phenotypic diversity. *Annu. Rev. Entomol.* 64:185–203
36. Gomez-Gomez L, Boller T. 2000. FLS2: an LRR receptor-like kinase involved in the perception of the bacterial elicitor flagellin in *Arabidopsis*. *Mol. Cell* 5:1003–11
37. Grantham ME, Brisson JA. 2018. Extensive differential splicing underlies phenotypically plastic aphid morphs. *Mol. Biol. Evol.* 35:1934–46
38. Guo H, Zhang Y, Tong J, Ge P, Wang Q, et al. 2020. An aphid-secreted salivary protease activates plant defense in phloem. *Curr. Biol.* 30:4826–36
39. Guy E, Boulain H, Aigu Y, Le Pennec C, Chawki K, et al. 2016. Optimization of agroinfiltration in *Pisum sativum* provides a new tool for studying the salivary protein functions in the pea aphid complex. *Front. Plant Sci.* 7:1171
40. Hawthorne DJ, Via S. 2001. Genetic linkage of ecological specialization and reproductive isolation in pea aphids. *Nature* 412:904–7
41. Heidel-Fischer HM, Vogel H. 2015. Molecular mechanisms of insect adaptation to plant secondary compounds. *Curr. Opin. Insect Sci.* 8:8–14
42. Hewer A, Will T, van Bel AJ. 2010. Plant cues for aphid navigation in vascular tissues. *J. Exp. Biol.* 213:4030–42
43. Hogenhout SA, Bos JIB. 2011. Effector proteins that modulate plant–insect interactions. *Curr. Opin. Plant Biol.* 14:422–28
44. Jaouannet M, Rodriguez PA, Thorpe P, Lenoir CJ, MacLeod R, et al. 2014. Plant immunity in plant-aphid interactions. *Front. Plant Sci.* 5:663
45. Jaquiéry J, Stoeckel S, Nouhaud P, Mieuzet L, Mahéo F, et al. 2012. Genome scans reveal candidate regions involved in the adaptation to host plant in the pea aphid complex. *Mol. Ecol.* 21:5251–64
46. Jaubert-Possamai S, Rispe C, Tanguy S, Gordon K, Walsh T, et al. 2010. Expansion of the miRNA pathway in the hemipteran insect *Acyrthosiphon pisum*. *Mol. Biol. Evol.* 27:979–87
47. Ji R, Lei J, Chen IW, Sang W, Yang S, et al. 2021. Cytochrome P450s CYP380C6 and CYP380C9 in green peach aphid facilitate its adaptation to indole glucosinolate-mediated plant defense. *Pest Manag. Sci.* 77:148–58
48. Jones AME, Bridges M, Bones AM, Cole R, Rossiter JT. 2001. Purification and characterisation of a non-plant myrosinase from the cabbage aphid *Brevicoryne brassicae* (L.). *Insect Biochem. Mol. Biol.* 31:1–5
49. Jones AME, Winge P, Bones AM, Cole R, Rossiter JT. 2002. Characterization and evolution of a myrosinase from the cabbage aphid *Brevicoryne brassicae*. *Insect Biochem. Mol. Biol.* 32:275–84
50. Jones JDG, Dangl JL. 2006. The plant immune system. *Nature* 444:323–29
51. Jones PA. 2012. Functions of DNA methylation: islands, start sites, gene bodies and beyond. *Nat. Rev. Genet.* 13:484–92
52. Jwa N-S, Hwang B. 2017. Convergent evolution of pathogen effectors toward reactive oxygen species signaling networks in plants. *Front. Plant Sci.* 8:1687
53. Kaloshian I, Walling LL. 2005. Hemipterans as plant pathogens. *Annu. Rev. Phytopathol.* 43:491–521
54. Kang ZW, Liu FH, Pang RP, Yu WB, Tan XL, et al. 2018. The identification and expression analysis of candidate chemosensory genes in the bird cherry-oat aphid *Rhopalosiphum padi* (L.). *Bull. Entomol. Res.* 108:645–57
55. Kettles GJ, Drurey C, Schoonbeek H-J, Maule AJ, Hogenhout SA. 2013. Resistance of *Arabidopsis thaliana* to the green peach aphid, *Myzus persicae*, involves camalexin and is regulated by microRNAs. *New Phytol.* 198:1178–90
56. Kettles GJ, Kaloshian I. 2016. The potato aphid salivary effector Me47 is a glutathione-S-transferase involved in modifying plant responses to aphid infestation. *Front. Plant Sci.* 7:1142

57. Kim JH, Jander G. 2007. *Myzus persicae* (green peach aphid) feeding on *Arabidopsis* induces the formation of a deterrent indole glucosinolate. *Plant J.* 49:1008–19
58. Kim JH, Lee BW, Schroeder FC, Jander G. 2008. Identification of indole glucosinolate breakdown products with antifeedant effects on *Myzus persicae* (green peach aphid). *Plant J.* 54:1015–26
59. Kloth KJ, Abreu IN, Delhomme N, Petřík I, Villard C, et al. 2019. PECTIN ACETYLESTERASE9 affects the transcriptome and metabolome and delays aphid feeding. *Plant Physiol.* 181:1704–20
60. Kloth KJ, Busscher-Lange J, Wiegers GL, Kruijer W, Buijs G, et al. 2017. SIEVE ELEMENT-LINING CHAPERONE1 restricts aphid feeding on Arabidopsis during heat stress. *Plant Cell* 29:2450–64
61. Kloth KJ, Shah P, Broekgaarden C, Ström C, Albrectsen BR, Dicke M. 2021. SLI1 confers broad-spectrum resistance to phloem-feeding insects. *Plant Cell Environ.* 44:2765–76
62. Kos M, Kabouw P, Noordam R, Hendriks K, Vet LEM, et al. 2011. Prey-mediated effects of glucosinolates on aphid predators. *Ecol. Entomol.* 36:377–88
63. Kursar TA, Dexter KG, Lokvam J, Pennington RT, Richardson JE, et al. 2009. The evolution of antiherbivore defenses and their contribution to species coexistence in the tropical tree genus *Inga*. *PNAS* 106:18073–78
64. Kuśnierczyk A, Winge P, Jørstad TS, Troczyńska J, Rossiter JT, Bones AM. 2008. Towards global understanding of plant defence against aphids: timing and dynamics of early *Arabidopsis* defence responses to cabbage aphid (*Brevicoryne brassicae*) attack. *Plant Cell Environ.* 31:1097–115
65. Le Trionnaire G, Tanguy S, Hudaverdian S, Gleonnec F, Richard G, et al. 2019. An integrated protocol for targeted mutagenesis with CRISPR-Cas9 system in the pea aphid. *Insect Biochem. Mol. Biol.* 110:34–44
66. Legeai F, Rizk G, Walsh T, Edwards O, Gordon K, et al. 2010. Bioinformatic prediction, deep sequencing of microRNAs and expression analysis during phenotypic plasticity in the pea aphid, *Acyrthosiphon pisum*. *BMC Genom.* 11:281
67. Li Q, Fan J, Sun J, Zhang Y, Hou M, Chen J. 2019. Anti-plant defense response strategies mediated by the secondary symbiont *Hamiltonella defensa* in the wheat aphid *Sitobion miscanthi*. *Front. Microbiol.* 10:2419
68. Li Q, Xie Q-G, Smith-Becker J, Navarre DA, Kaloshian I. 2006. *Mi-1*-mediated aphid resistance involves salicylic acid and mitogen-activated protein kinase signaling cascades. *Mol. Plant Microbe Interact.* 19:655–64
69. Loxdale HD, Balog A, Harvey JA. 2019. Generalism in nature. . . The great misnomer: aphids and wasp parasitoids as examples. *Insects* 10:314
70. Lu H, Zhu J, Yu J, Chen X, Kang L, Cui F. 2020. A symbiotic virus facilitates aphid adaptation to host plants by suppressing jasmonic acid responses. *Mol. Plant Microbe Interact.* 33:55–65
71. Lyko F, Maleszka R. 2011. Insects as innovative models for functional studies of DNA methylation. *Trends Genet.* 27:127–31
72. Mai VC, Drzewiecka K, Jeleń H, Narożna D, Rucińska-Sobkowiak R, et al. 2014. Differential induction of *Pisum sativum* defense signaling molecules in response to pea aphid infestation. *Plant Sci.* 221–22:1–12
73. Martel JW, Malcolm SB. 2004. Density-dependent reduction and induction of milkweed cardenolides by a sucking insect herbivore. *J. Chem. Ecol.* 30:545–61
74. Mathers TC, Chen Y, Kaithakottil G, Legeai F, Mugford ST, et al. 2017. Rapid transcriptional plasticity of duplicated gene clusters enables a clonally reproducing aphid to colonise diverse plant species. *Genome Biol.* 18:27
75. Mathers TC, Mugford ST, Wouters RHM, Heavens D, Botha A-M, et al. 2022. *Aphidinae comparative genomics resource (version v1)*. Data set: Zenodo, CERN, Meyrin, Switz, updated Feb. 4. **https://doi.org/10.5281/zenodo.5908005**
76. McGlincy NJ, Smith CWJ. 2008. Alternative splicing resulting in nonsense-mediated mRNA decay: What is the meaning of nonsense? *Trends Biochem. Sci.* 33:385–93
77. McLean AHC, van Asch M, Ferrari J, Godfray HCJ. 2011. Effects of bacterial secondary symbionts on host plant use in pea aphids. *Proc. Biol. Sci.* 278:760–66
78. Medina-Ortega KJ, Walker GP. 2015. Faba bean forisomes can function in defence against generalist aphids. *Plant Cell Environ.* 38:1167–77

79. Milligan SB, Bodeau J, Yaghoobi J, Kaloshian I, Zabel P, Williamson VM. 1998. The root knot nematode resistance gene *Mi* from tomato is a member of the leucine zipper, nucleotide binding, leucine-rich repeat family of plant genes. *Plant Cell* 10:1307–19
80. Miya A, Albert P, Shinya T, Desaki Y, Ichimura K, et al. 2007. CERK1, a LysM receptor kinase, is essential for chitin elicitor signaling in *Arabidopsis*. *PNAS* 104:19613–18
81. Mohase L, van der Westhuizen AJ. 2002. Salicylic acid is involved in resistance responses in the Russian wheat aphid-wheat interaction. *J. Plant Physiol.* 159:585–90
82. Moran NA. 1992. The evolution of aphid life cycles. *Annu. Rev. Entomol.* 37:321–48
83. Morkunas I, Mai VC, Gabryś B. 2011. Phytohormonal signaling in plant responses to aphid feeding. *Acta Physiol. Plant.* 33:2057–73
84. Mutti NS, Louis J, Pappan LK, Pappan K, Begum K, et al. 2008. A protein from the salivary glands of the pea aphid, *Acyrthosiphon pisum*, is essential in feeding on a host plant. *PNAS* 105:9965–69
85. Mutti NS, Park Y, Reese JC, Reeck GR. 2006. RNAi knockdown of a salivary transcript leading to lethality in the pea aphid, *Acyrthosiphon pisum*. *J. Insect Sci.* 6:38
86. Naessens E, Dubreuil G, Giordanengo P, Baron OL, Minet-Kebdani N, et al. 2015. A secreted MIF cytokine enables aphid feeding and represses plant immune responses. *Curr. Biol.* 25:1898–903
87. Nalam V, Louis J, Shah J. 2019. Plant defense against aphids, the pest extraordinaire. *Plant Sci.* 279:96–107
88. Ngou BPM, Jones JDG, Ding P. 2021. Plant immune networks. *Trends Plant Sci.* 27:255–73
89. Nottingham SF, Hardie J. 1993. Flight behaviour of the black bean aphid, *Aphis fabae*, and the cabbage aphid, *Brevicoryne brassicae*, in host and non-host plant odour. *Physiol. Entomol.* 18:389–94
90. Nouhaud P, Gautier M, Gouin A, Jaquiéry J, Peccoud J, et al. 2018. Identifying genomic hotspots of differentiation and candidate genes involved in the adaptive divergence of pea aphid host races. *Mol. Ecol.* 27:3287–300
91. Nouhaud P, Peccoud J, Mahéo F, Mieuzet L, Jaquiéry J, Simon JC. 2014. Genomic regions repeatedly involved in divergence among plant-specialized pea aphid biotypes. *J. Evol. Biol.* 27:2013–20
92. Oliver KM, Degnan PH, Burke GR, Moran NA. 2009. Facultative symbionts in aphids and the horizontal transfer of ecologically important traits. *Annu. Rev. Entomol.* 55:247–66
93. Pan Y, Xu P, Zeng X, Liu X, Shang Q. 2019. Characterization of UDP-glucuronosyltransferases and the potential contribution to nicotine tolerance in *Myzus persicae*. *Int. J. Mol. Sci.* 20:3637
94. Peccoud J, Ollivier A, Plantegenest M, Simon J-C. 2009. A continuum of genetic divergence from sympatric host races to species in the pea aphid complex. *PNAS* 106:7495–500
95. Peccoud J, Simon J-C, von Dohlen C, Coeur d'acier A, Plantegenest M, et al. 2010. Evolutionary history of aphid-plant associations and their role in aphid diversification. *C. R. Biol.* 333:474–87
96. Pegadaraju V, Louis J, Singh V, Reese JC, Bautor J, et al. 2007. Phloem-based resistance to green peach aphid is controlled by Arabidopsis *PHYTOALEXIN DEFICIENT4* without its signaling partner *ENHANCED DISEASE SUSCEPTIBILITY1*. *Plant J.* 52:332–41
97. Pélissier HC, Peters WS, Collier R, van Bel AJE, Knoblauch M. 2008. GFP tagging of sieve element occlusion (SEO) proteins results in green fluorescent forisomes. *Plant Cell Physiol.* 49:1699–710
98. Peters WS, van Bel AJE, Knoblauch M. 2006. The geometry of the forisome–sieve element–sieve plate complex in the phloem of *Vicia faba* L. leaflets. *J. Exp. Bot.* 57:3091–98
99. Pickett JA, Wadhams LJ, Woodcock CM, Hardie J. 1992. The chemical ecology of aphids. *Annu. Rev. Entomol.* 37:67–90
100. Pitino M, Coleman AD, Maffei ME, Ridout CJ, Hogenhout SA. 2011. Silencing of aphid genes by dsRNA feeding from plants. *PLOS ONE* 6:e25709
101. Pitino M, Hogenhout SA. 2012. Aphid protein effectors promote aphid colonization in a plant species-specific manner. *Mol. Plant Microbe Interact.* 26:130–39
102. Pontoppidan B, Ekbom B, Eriksson S, Meijer J. 2001. Purification and characterization of myrosinase from the cabbage aphid (*Brevicoryne brassicae*), a brassica herbivore. *Eur. J. Biochem.* 268:1041–48
103. Powell G, Maniar SP, Pickett JA, Hardie J. 1999. Aphid responses to non-host epicuticular lipids. *Entomol. Exp. Appl.* 91:115–23
104. Powell G, Tosh CR, Hardie J. 2005. Host plant selection by aphids: behavioral, evolutionary, and applied perspectives. *Annu. Rev. Entomol.* 51:309–30

105. Prince DC, Drurey C, Zipfel C, Hogenhout SA. 2014. The leucine-rich repeat receptor-like kinase BRASSINOSTEROID INSENSITIVE1-ASSOCIATED KINASE1 and the cytochrome P450 PHYTOALEXIN DEFICIENT3 contribute to innate immunity to aphids in Arabidopsis. *Plant Physiol.* 164:2207–19
106. Ramsey JS, Elzinga DA, Sarkar P, Xin YR, Ghanim M, Jander G. 2014. Adaptation to nicotine feeding in *Myzus persicae*. *J. Chem. Ecol.* 40:869–77
107. Riddick EW, Simmons AM. 2014. Do plant trichomes cause more harm than good to predatory insects? *Pest Manag. Sci.* 70:1655–65
108. Rider SD Jr., Srinivasan DG, Hilgarth RS. 2010. Chromatin-remodelling proteins of the pea aphid, *Acyrthosiphon pisum* (Harris). *Insect Mol. Biol.* 19:201–14
109. Rodriguez PA, Escudero-Martinez C, Bos JIB. 2017. An aphid effector targets trafficking protein VPS52 in a host-specific manner to promote virulence. *Plant Physiol.* 173:1892–903
110. Rossi M, Goggin FL, Milligan SB, Kaloshian I, Ullman DE, Williamson VM. 1998. The nematode resistance gene *Mi* of tomato confers resistance against the potato aphid. *PNAS* 95:9750–54
111. Sanchez-Arcos C, Reichelt M, Gershenzon J, Kunert G. 2016. Modulation of legume defense signaling pathways by native and non-native pea aphid clones. *Front. Plant Sci.* 7:1872
112. Schatz B, Sauvion N, Kjellberg F, Nel A. 2017. Plant–insect interactions: a palaeontological and an evolutionary perspective. In *Advances in Botanical Research*, Vol. 81, ed. N Sauvion, D Thiéry, P-A Calatayud, pp. 1–24. Amsterdam: Elsevier
113. Schwarzkopf A, Rosenberger D, Niebergall M, Gershenzon J, Kunert G. 2013. To feed or not to feed: plant factors located in the epidermis, mesophyll, and sieve elements influence pea aphid's ability to feed on legume species. *PLOS ONE* 8:e75298
114. Simon J-C, d'Alençon E, Guy E, Jacquin-Joly E, Jaquiéry J, et al. 2015. Genomics of adaptation to host-plants in herbivorous insects. *Brief. Funct. Genom.* 14:413–23
115. Singh KS, Cordeiro EMG, Troczka BJ, Pym A, Mackisack J, et al. 2021. Global patterns in genomic diversity underpinning the evolution of insecticide resistance in the aphid crop pest *Myzus persicae*. *Commun. Biol.* 4:847
116. Singh KS, Troczka BJ, Duarte A, Balabanidou V, Trissi N, et al. 2020. The genetic architecture of a host shift: an adaptive walk protected an aphid and its endosymbiont from plant chemical defenses. *Sci. Adv.* 6:eaba1070
117. Smadja C, Shi P, Butlin RK, Robertson HM. 2009. Large gene family expansions and adaptive evolution for odorant and gustatory receptors in the pea aphid, *Acyrthosiphon pisum*. *Mol. Biol. Evol.* 26:2073–86
118. Smadja CM, Canbäck B, Vitalis R, Gautier M, Ferrari J, et al. 2012. Large-scale candidate gene scan reveals the role of chemoreceptor genes in host plant specialization and speciation in the pea aphid. *Evolution* 66:2723–38
119. Stewart SA, Hodge S, Ismail N, Mansfield JW, Feys BJ, et al. 2009. The *RAP1* gene confers effective, race-specific resistance to the pea aphid in *Medicago truncatula* independent of the hypersensitive reaction. *Mol. Plant Microbe Interact.* 22:1645–55
120. Sugio A, Dubreuil G, Giron D, Simon J-C. 2015. Plant–insect interactions under bacterial influence: ecological implications and underlying mechanisms. *J. Exp. Bot.* 66:467–78
121. Sun M, Voorrips RE, van Kaauwen M, Visser RGF, Vosman B. 2020. The ability to manipulate ROS metabolism in pepper may affect aphid virulence. *Hortic. Res.* 7:6
122. Takemoto H, Uefune M, Ozawa R, Arimura G-I, Takabayashi J. 2013. Previous infestation of pea aphids *Acyrthosiphon pisum* on broad bean plants resulted in the increased performance of conspecific nymphs on the plants. *J. Plant Interact.* 8:370–74
123. Tan XL, Chen JL, Benelli G, Desneux N, Yang XQ, et al. 2017. Pre-infestation of tomato plants by aphids modulates transmission-acquisition relationship among whiteflies, Tomato Yellow Leaf Curl Virus (TYLCV) and plants. *Front. Plant Sci.* 8:1597
124. ten Broeke CJM, Dicke M, van Loon JJA. 2017. The effect of co-infestation by conspecific and heterospecific aphids on the feeding behaviour of *Nasonovia ribisnigri* on resistant and susceptible lettuce cultivars. *Arthropod-Plant Interact.* 11:785–96
125. Thairu MW, Hansen AK. 2019. Changes in aphid host plant diet influence the small-RNA expression profiles of its obligate nutritional symbiont, *Buchnera*. *mBio* 10:e01733-19

126. Thorpe P, Cock PJA, Bos JIB. 2016. Comparative transcriptomics and proteomics of three different aphid species identifies core and diverse effector sets. *BMC Genom.* 17:172
127. Thorpe P, Escudero-Martinez CM, Eves-van den Akker S, Bos JIB. 2020. Transcriptional changes in the aphid species *Myzus cerasi* under different host and environmental conditions. *Insect Mol. Biol.* 29:271–82
128. Tsuchida T, Koga R, Fukatsu T. 2004. Host plant specialization governed by facultative symbiont. *Science* 303:1989
129. van Bel AJE, Will T. 2016. Functional evaluation of proteins in watery and gel saliva of aphids. *Front. Plant Sci.* 7:1840
130. Vanlerberghe-Masutti F, Chavigny P. 1998. Host-based genetic differentiation in the aphid *Aphis gossypii* Glover, evidenced from RAPD fingerprints. *Mol. Ecol.* 7:905–14
131. Via S. 1991. The genetic structure of host plant adaptation in a spatial patchwork: demographic variability among reciprocally transplanted pea aphid clones. *Evolution* 45:827–52
132. Vincent TR, Avramova M, Canham J, Higgins P, Bilkey N, et al. 2017. Interplay of plasma membrane and vacuolar ion channels, together with BAK1, elicits rapid cytosolic calcium elevations in Arabidopsis during aphid feeding. *Plant Cell* 29:1460–79
133. Walsh TK, Brisson JA, Robertson HM, Gordon K, Jaubert-Possamai S, et al. 2010. A functional DNA methylation system in the pea aphid, *Acyrthosiphon pisum*. *Insect Mol. Biol.* 19:215–28
134. Wang Q, Liu J-T, Zhang Y-J, Chen J-L, Li X-C, et al. 2021. Coordinative mediation of the response to alarm pheromones by three odorant binding proteins in the green peach aphid *Myzus persicae*. *Insect Biochem. Mol. Biol.* 130:103528
135. Wang Q, Yuan E, Ling X, Zhu-Salzman K, Guo H, et al. 2020. An aphid facultative symbiont suppresses plant defence by manipulating aphid gene expression in salivary glands. *Plant Cell Environ.* 43:2311–22
136. Wang Q, Zhou JJ, Liu JT, Huang GZ, Xu WY, et al. 2019. Integrative transcriptomic and genomic analysis of odorant binding proteins and chemosensory proteins in aphids. *Insect Mol. Biol.* 28:1–22
137. Webster B, Bruce T, Dufour S, Birkemeyer C, Birkett M, et al. 2008. Identification of volatile compounds used in host location by the black bean aphid, *Aphis fabae*. *J. Chem. Ecol.* 34:1153–61
138. Weßling R, Epple P, Altmann S, He Y, Yang L, et al. 2014. Convergent targeting of a common host protein-network by pathogen effectors from three kingdoms of life. *Cell Host Microbe* 16:364–75
139. Will T, van Bel AJE. 2008. Induction as well as suppression: how aphid saliva may exert opposite effects on plant defense. *Plant Signal. Behav.* 3:427–30
140. Wroblewski T, Piskurewicz U, Tomczak A, Ochoa O, Michelmore RW. 2007. Silencing of the major family of NBS–LRR-encoding genes in lettuce results in the loss of multiple resistance specificities. *Plant J.* 51:803–18
141. Xue W, Fan J, Zhang Y, Xu Q, Han Z, et al. 2016. Identification and expression analysis of candidate odorant-binding protein and chemosensory protein genes by antennal transcriptome of *Sitobion avenae*. *PLOS ONE* 11:e0161839
142. Zhang L, Reifová R, Halenková Z, Gompert Z. 2021. How important are structural variants for speciation? *Genes* 12:1084
143. Zhang S, Zhang Z, Wen Z, Gu C, An Y-QC, et al. 2017. Fine mapping of the soybean aphid-resistance genes *Rag6* and *Rag3c* from *Glycine soja* 85–32. *Theor. Appl. Genet.* 130:2601–15
144. Zhang Y, Fan J, Sun J-R, Chen J-L. 2015. Cloning and RNA interference analysis of the salivary protein C002 gene in *Schizaphis graminum*. *J. Integr. Agric.* 14:698–705
145. Zipfel C, Kunze G, Chinchilla D, Caniard A, Jones JD, et al. 2006. Perception of the bacterial PAMP EF-Tu by the receptor EFR restricts *Agrobacterium*-mediated transformation. *Cell* 125:749–60
146. Züst T, Agrawal AA. 2016. Mechanisms and evolution of plant resistance to aphids. *Nat. Plants* 2:15206
147. Züst T, Agrawal AA. 2016. Population growth and sequestration of plant toxins along a gradient of specialization in four aphid species on the common milkweed *Asclepias syriaca*. *Funct. Ecol.* 30:547–56

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