



From basal defenses to chromatin landscapes: how *Arabidopsis* genetic diversity modulates potyvirus evolutionary dynamics

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Abstract

Host genetic variability strongly shapes virus evolution by defining the selective pressures that drive pathogens to either diversify across resistance alleles or specialize on the most susceptible genotypes. These dynamics can also shift virulence, though the direction of change is not always predictable. Experimental evolution with potyviruses in different *Arabidopsis thaliana* genotypes offers clear evidence. Across genotypes classified as permissive, wild-type-like, or restrictive, adaptation proceeded faster in restrictive hosts than in permissive ones. Cross-infection assays showed that restrictive genotypes favored generalist viruses able to overcome multiple barriers, whereas permissive genotypes selected specialists optimized for high fitness in a single host. Together, these results highlight how host heterogeneity—whether from natural variation, targeted mutations, or epigenetic regulation—determines the tempo and mode of virus evolution, with implications for predicting pathogen emergence and designing durable resistance strategies.

Keywords Emerging viruses · Experimental evolution · *Potyvirus* · Trade-offs · Virus evolution

Introduction

Genetic diversity within host populations is a key determinant of ecosystem stability and pathogen dynamics. High within-species diversity enhances resilience to disturbance and speeds recovery, whereas low diversity can increase vulnerability to infectious agents (Loreau et al. 2001; Reusch et al. 2005). Parasites, including plant RNA viruses, exert pervasive selective pressures that shape both host and pathogen evolution (Poulin 2007). Beyond immediate epidemiological effects, host genetic variability, particularly at loci governing resistance and susceptibility, strongly influences pathogen evolutionary trajectories (Keesing et al. 2006; Altermatt and Ebert 2008).

Across taxa, genetically homogeneous populations often exhibit higher infection prevalence and more severe disease than heterogeneous ones (Mundt 2002; Dennehy et al. 2007; Ganz and Ebert 2010). In plants, variation in susceptibility

frequently arises from polymorphisms in basal and inducible defenses, including translation-initiation factors and hormone-regulated signaling pathways (Soosaar et al. 2005; Carr et al. 2010; Mandadi and Scholthof 2013). These host mechanisms interact with viral strategies for resource exploitation, fueling a dynamic coevolutionary arms race. From an evolutionary perspective, basal defenses are expected to impose early, steep fitness gradients, whereas inducible defenses generate later, shallower selective pressures.

Eco-evolutionary theory offers a useful framework. In genetically uniform populations, parasites are expected to evolve strategies that maximize transmission while limiting virulence, as excessive damage reduces host availability (Haraguchi and Sasaki 2000; Regoes et al. 2000; Gandon 2004). In heterogeneous populations, selection favors broader infectivity, potentially at the cost of increased virulence or reduced specialization (Regoes et al. 2000; Moreno-Gómez et al. 2013). Gene-for-gene (GFG) and matching-alleles (MA) models formalize these interactions: GFG predicts nested infection networks dominated by generalist pathogens, whereas MA anticipates modular structures driven by negative frequency-dependent selection (Flor 1956; Frank 1993; Thrall et al. 2012). Network analyses of virus-host systems support these expectations, revealing nestedness along generalist-specialist gradients

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and modularity under strong genotype-specific constraints (Flores et al. 2011; Weitz et al. 2013).¹

Experimental evolution with potyviruses such as tobacco etch virus (TEV; species *Potyvirus nicotianainsculpensis*) and turnip mosaic virus (TuMV; species *Potyvirus rapae*) in diverse *Arabidopsis thaliana* genotypes differing in their degree of susceptibility to infection confirms that host heterogeneity modulates viral adaptation. Hereafter, I refer to plant genotypes that support high viral replication as “permissive”. In contrast, “restrictive” genotypes are those in which viral replication is low relative to the wild-type plants. Viruses evolving in permissive plant genotypes often exhibit increased accumulation and virulence, sometimes expanding their host range, whereas adaptation in restrictive plant genotypes can lead to specialization (Agudelo-Romero et al. 2008; Lalić et al. 2010; Hillung et al. 2014; González et al. 2020; Navarro et al. 2022; Ambrós et al. 2024; Elena et al. 2025). Intermediate levels of host resistance can maximize the likelihood of evolutionary emergence, aligning with recent theory (Chabas et al. 2018).

Herewith, I synthesize recent work testing how host heterogeneity in *Arabidopsis* susceptibility to potyvirus infection shapes the patterns and dynamics of potyvirus evolution, the molecular targets of selection, and the consequences of viral adaptation for host responses. This review advances a unified framework for how distinct layers of host diversity, (i) natural genetic variation among *Arabidopsis* genotypes, (ii) differences in basal defenses and susceptibility factors and (iii) resistance-related and epigenetic constraints, shape the tempo and mode of potyvirus evolution. Across these layers, I show that restrictive contexts consistently favor generalist viruses with broader host range (often at increased virulence), whereas permissive contexts favor specialists optimized for high replication in a single background; intermediate resistance levels can maximize the probability of emergence. I further highlight VPg as a recurring molecular nexus linking these ecological patterns to mechanisms. Table 1 summarizes the studies discussed and their main evolutionary conclusions.

¹ In an infection network, nestedness describes a hierarchical pattern in which the set of hosts that a specialist virus can infect is a subset of the hosts that more generalist viruses can infect. Highly susceptible hosts tend to be infected by all viral genotypes. Highly resistant hosts are infected only by the most generalist viral lineages. This creates a matrix structure where interactions of specialists are nested within those of generalists, producing a predictable, ordered pattern of infectivity. Modularity refers to the presence of distinct clusters in the infection network, where subsets of viruses interact primarily with specific subsets of hosts. Each module represents a group of hosts and viral genotypes that interact strongly among themselves but weakly with other groups. Modular networks thus indicate strong specificity and reduced cross-infection between clusters (Flores et al. 2011; Weitz et al. 2013).

Genetic variation for susceptibility to infection among ecotypes

Phenotypic patterns of adaptation

Experimental evolution with TEV (Agudelo-Romero et al. 2008; Hillung et al. 2014, 2015) and TuMV (González et al. 2020; Elena et al. 2025) in different *A. thaliana* ecotypes (Table 1) shows that genome-wide host diversity strongly influences viral adaptation. In genetically homogeneous plant populations, viruses rapidly adapt to the local ecotype, achieving high fitness and infectivity there but often at a cost in alternative hosts ecotypes. By contrast, heterogeneous or gradually changing host populations impose fluctuating selection that slows adaptation yet favors generalist strategies, broader host range, and, ultimately, increased virulence (Osnas and Dobson 2012; Berngruber et al. 2015; White et al. 2020).

The pace of phenotypic evolution depends on host population structure. Traits related to virulence, such as symptom progression and infectiousness, evolve faster in homogeneous demes than in heterogeneous populations, reflecting stronger and more consistent selection in uniform environments (González et al. 2020). Variable environments slow adaptation but promote broader host range and higher end-point virulence (González et al. 2020; Elena et al. 2025), consistent with theory that constant regimes accelerate adaptation whereas temporal or spatial variability favors slower, more versatile trajectories (Bell 2010; Chaturvedi and Chatterjee 2024).

Infection network structure

Cross-infection experiments show that interactions between viral lineages and host ecotypes often yield infection matrices with significant nestedness (Hillung et al. 2014; González et al. 2020), consistent with a GFG model (Flores et al. 2011; Weitz et al. 2013). Highly susceptible ecotypes are infected by all viral lineages, whereas resistant ecotypes restrict infection only to generalist viral lineages. Modularity is generally weak, indicating that hierarchical differences in host resistance and viral adaptability dominate. This pattern implies that permissive hosts tend to select specialist viruses, whereas restrictive hosts favor generalist viruses capable of overcoming multiple resistance barriers.

Molecular signatures of adaptation

Genomic analyses consistently identify convergent evolution in key viral proteins, particularly VPg, which interacts with host translation initiation factors. Recurrent nonsynonymous changes in VPg (e.g., positions 2038–2042) indicate strong positive selection for improved viral

Table 1 Summary of evolution experiments and observed phenotypic changes and evolutionary consequences

Study	<i>Arabidopsis</i> genotypes	Pathways affected	Phenotypes observed	Effects on Potyvirus evolution
Hillung et al. (2014)	ecotypes	Genome-wide differences. Focus on differences in <i>RTM</i> loci ¹	Increased infectivity, virulence, and viral load	Restrictive hosts select generalists, permissive ones for specialists. VPg as key target of adaptation
González et al. (2020)	ecotypes	Genome-wide differences	Increased infectivity, virulence and viral load	Restrictive hosts select generalists, permissive ones specialists
Elena et al. (2025)	ecotypes	Genome-wide differences	Increased infectivity, virulence, and viral load	Ecological succession between susceptible and restrictive hosts affect rates of adaptation
Navarro et al. (2022)	mutants	Basal and inducible immunity	Increased infectivity, virulence and viral load	Restrictive hosts select generalists. Faster evolution in restrictive host
Ambrós et al. (2024)	mutants	DNA methylation and histone modification	Increased infectivity, virulence, and viral load	Faster evolution in restrictive hosts. VPg as key target of adaptation

¹Restricted TEV movement. The RTM genes form a dominant resistance system in *Arabidopsis* that blocks TEV (and other potyviruses) long-distance movement. They do not trigger classical immune responses but act as a physical or functional block. There are three core RTM loci: *RTM1*: encodes a HSP20-like family protein localized in the phloem. It is believed to contribute to a structural barrier or regulatory complex that prevents viral entry into phloem (Whitham et al. 1999). *RTM2*: encodes a small LRR receptor-like protein with a secretory signal peptide and noncanonical LRR arrangement. Localizes in endomembrane system and phloem. Confers recognition-like restriction, probably acting as part of a protein complex blocking viral long-distance movement (Chisholm et al. 2000). *RTM3*: encodes a meprin and TRAF homology (MATH) domain-containing protein. Likely a scaffolding or regulatory component of the RTM antiviral complex (Cosson et al. 2010)

genome transcription and more efficient host exploitation. Synonymous changes also converge, likely reflecting selection for translational efficiency and codon usage (Agudelo-Romero et al. 2008; Hillung et al. 2015). Gradual host transitions maintain higher mutational richness and polymorphism, whereas abrupt shifts favor fixation of fewer, large-effect mutations (Elena et al. 2025). These patterns align with adaptive-walk theory under moving fitness optima: abrupt environmental change selects larger-effect mutations, while gradual change promotes diversity and smaller-effect adaptations (Hadany 2003).

Host transcriptomic landscape shows differential responses to ancestral and evolved viral lineages

Transcriptomic analyses further support the role of host genetic diversity in shaping susceptibility to TEV infection. Hillung et al. (2012) demonstrated that *Arabidopsis* ecotypes exhibit distinct transcriptional responses to infection with an evolved TEV lineage, with ecotypes clustering into two groups based on gene expression profiles. Ecotypes with lower susceptibility upregulated genes involved in abiotic stress and tissue development, while more susceptible ecotypes activated defense-related pathways. Building on this, Hillung et al. (2016) showed that viral lineages evolved in the same ecotype induced convergent transcriptomic responses, yet the functional categories affected varied across ecotypes. Notably, generalist viruses elicited uniform transcriptomic changes across hosts, whereas specialist viruses triggered

ecotype-specific responses, particularly in defense-related genes. These findings underscore the complex interplay between host genotype and viral adaptation, highlighting how standing genetic variation in susceptibility not only influences infection outcomes but also constrains the evolutionary trajectories of plant viruses.

Integration with theoretical predictions

The observed dynamics align with evolutionary epidemiology theory. In genetically uniform hosts, parasites tend to maximize transmission with lower virulence, whereas heterogeneous hosts select for broader host range and often higher virulence (Regoes et al. 2000; Gandon 2004; Keesing et al. 2006; Altermatt and Ebert 2008). Our empirical work mirrors these expectations: homogeneous environments accelerate adaptation but promote specialization and lower virulence; heterogeneous environments slow adaptation but favor generalism and higher virulence. The emergence of nested infection networks matches GFG expectations, and the general absence of strong modularity suggests a limited role for MA dynamics in these plant-virus systems.

Effect of point mutations in basal resistances in potyvirus evolutionary patterns

Navarro et al. (2022) examined how defects in plant immunity shape TuMV evolution (Table 1) by evolving the virus in *Arabidopsis* mutants with disruptions in basal and

inducible defense pathways. TuMV evolved faster in restrictive hosts and slower in permissive ones. Restrictive genotypes selected generalists; permissive genotypes selected specialists.

Both ecotype-based and pathway-specific studies converge on the same principle, host heterogeneity shapes virus evolution, but this work adds nuance by showing that the type of defense mechanism matters. Viruses evolved faster in hosts with defects in basal resistance, such as mutations in susceptibility genes like *eIF(iso)4G*, than in hosts with impaired inducible defenses (e.g., salicylic or jasmonic acid signaling pathways). Basal defenses impose stronger and more immediate constraints on viral replication, creating steeper fitness gradients and accelerating adaptation, whereas inducible defenses, activated later, exert weaker selection and slow evolutionary change. Despite this difference in tempo, the qualitative pattern remains: restrictive hosts select generalists; permissive hosts favor specialists. VPg again emerges as a recurrent adaptive hotspot.

Adaptation by altering VPg-host protein–protein interaction network (PPIN)

Beyond amino acid change per se, VPg's role as a major target of viral adaptation includes rewiring its interaction network with host proteins. Using high-throughput yeast two-hybrid screens, Carrasco et al. (2024) showed that evolutionarily fixed mutations such as D113G and R118H modify VPg's binding affinities to key host factors. Both mutations weaken the canonical interaction with *eIF(iso)4E*, essential for potyvirus replication, and reshape contacts with proteins involved in stress signaling and epigenetic regulation. For example, D113G reduces affinity for ROS1-associated homeodomain protein 1 (RHD1), linked to DNA demethylation and infection tolerance (Liu et al. 2021), whereas R118H strengthens interactions with OBERON1 (OBE1), a PHD-finger nuclear protein that remodels chromatin via interactions with WRKY transcription factors and histones (Du et al. 2023), and with class XI myosins that influence intracellular trafficking and transport of viral components (Amari et al. 2011).

These findings indicate that VPg adaptation is not limited to overcoming resistance alleles but involves broader reconfiguration of the host-virus PPIN, with consequences for viral fitness, virulence, and host tolerance. This mechanistic view complements evidence that VPg is a recurrent hotspot of positive selection and underscores the value of network-level interpretations of molecular signatures of adaptation.

Epigenetically-regulated resistances

Building on observations that TuMV infection affects epigenetic marks (Corrêa et al. 2020, 2024; Navarro et al. 2022), Ambrós et al. (2024) tested how mutations in epigenetic regulatory pathways influence TuMV evolution. They evolved TuMV lineages in genotypes with defects in DNA methylation (e.g., *ddm1*, *polv*) and histone demethylation (*jmj14*). Over 12 serial passages, the virus adapted to each host genotype, becoming more virulent and accumulating to higher titers. Defects in DNA methylation and histone modification pathways imposed strong selection, driving notable increases in infectivity, virulence, and viral load, with magnitudes depending on the disrupted pathway. Notably, histone demethylation mutant *jmj14* imposed the strongest constraints and the fastest phenotypic evolution for replication, whereas highly permissive RNA-directed DNA methylation (RdDM) mutant *dcl2 dcl3 dcl4* produced the slowest rates, consistent with the general principle that adaptation accelerates under restrictive conditions.

Olmo-Uceda et al. (2024) complemented these results with transcriptomic signatures of TuMV adaptation in epigenetic plant mutants. Evolved viruses broadly reprogrammed defense networks, with enrichment of genes near transposable elements and altered expression of regulators such as TGAGG motif-binding protein (TGA1), a salicylic acid-responsive activator of systemic acquired resistance, and RHD1. Integration of transcriptomic data with a virus-host PPIN highlighted key host genes and viral proteins, including a potentially important interaction between the potyviral viroporin 6K1 and phenylalanine ammonia-lyase 1 (PAL1), a phenylpropanoid enzyme associated with increased resistance to viral infection (Kavil et al. 2021). This points to a mechanistic link between viral evolution and host metabolic reprogramming.

Together, these studies show how epigenetic regulation intersects with viral infection and adaptation in plants. Epigenetic pathways not only modulate susceptibility but also shape the tempo and mode of virus evolution, reinforcing VPg's central role in adaptation and revealing that evolutionary responses extend to network-level and chromatin-associated processes. The host's epigenetic makeup influences which viral variants thrive, while viral fitness determines the extent of host transcriptomic and epigenomic reprogramming, underscoring a dynamic interplay between viral adaptation and host regulatory landscapes.

Discussion

Experimental evolution studies with potyviruses in arabidopsis demonstrate that host genetic architecture—whether natural ecotypic variation, targeted mutations in defense pathways, or disruptions of epigenetic regulation—profoundly shapes viral evolution. A consistent pattern emerges: restrictive hosts impose strong selection that accelerates adaptation and favors generalists; permissive hosts slow adaptation and select specialists. This dynamic agrees with GFG predictions of nested infection networks in which resistant hosts primarily admit generalists and susceptible hosts select specialists. Nevertheless, inferences drawn from infection-network architecture warrant caution: estimates of nestedness and modularity are sensitive to sampling intensity, species abundances, and the choice of null models, and binary presence-absence matrices can overstate nestedness relative to quantitative data. More broadly, single-time snapshot networks abstract inherently dynamic eco-evolutionary processes; where possible, abundance-informed (fixed–fixed) null models and longitudinal, weighted networks should be used to qualify these patterns (Ulrich et al. 2009; Staniczenko et al. 2013).

The tempo of adaptation varies with the defense mechanism. Mutations that alter basal resistance, such as those in susceptibility genes (*e.g.*, *eIF(iso)4G*), typically impose stronger constraints than do defects in inducible defenses, yielding steeper fitness gradients and faster evolution. Epigenetic pathways add another layer: defects in DNA methylation and histone modification can markedly shift the pace and mode of TuMV evolution, with histone demethylation mutants producing the strongest constraints and most rapid increases in viral replication; highly permissive RdDM mutants yield the slowest adaptation (Ambrós et al. 2024). Thus, both the degree and the nature of host resistance determine evolutionary outcomes.

At the molecular level, VPg consistently emerges as the principal target of selection. Beyond its canonical interaction with *eIF(iso)4G*, our work shows that VPg adaptation rewires host interactions, including with factors linked to chromatin remodeling and stress signaling (Carrasco et al. 2024). This network perspective suggests that viral adaptation extends beyond overcoming single resistance alleles to a broader reconfiguration of host-virus interaction landscapes, with potential consequences for viral fitness, virulence, and host tolerance. Collectively, VPg concentrates selection because it is the principal viral interface with host translation factors (*eIF4E/eIF(iso)4E/eIF4G*) (Nicaise et al. 2007), sits in a highly intrinsically disordered (Charon et al. 2016), mutationally robust region, and presents many contact points for adaptively rewiring host interactions. In contrast, proteins with tighter catalytic or architectural constraints (*e.g.*,

HC-Pro, NIa-Pro, NIb, or CP) appear more evolutionarily canalized (Torres-Barceló et al. 2010), so breaking or bypassing recessive *eIF4E*-mediated resistances recurrently funnels adaptation through VPg. These features explain the repeated mapping of resistance-breaking and host-range changes to VPg across crops and experimental systems.

A clearer connection can be drawn between these molecular findings and the phenotypic patterns described earlier. The recurrent targeting of VPg, as well as its role in rewiring interactions with host translation factors, stress-response proteins, and chromatin regulators, provides a mechanistic basis for why restrictive hosts tend to select generalist viruses, whereas permissive hosts favor specialists. By reshaping the VPg-centered PPIN, adaptive mutations enable viruses to navigate different constellations of host defenses, either broadening compatibility across diverse restrictive genotypes or fine-tuning replication within permissive ones. Thus, the network level consequences of VPg evolution offer a molecular bridge linking host-driven selection pressures to emergent differences in viral infectivity, host range, and virulence observed across experimental evolution studies.

Transcriptomic analyses further illuminate this interplay. TuMV adaptation in epigenetic mutants triggers extensive reprogramming of defense networks, with enrichment near transposable elements and modulation of regulators such as TGA1. Integrating these data with interactomes identifies critical nodes, such as the 6K1—PAL1 interaction, linking viral adaptation to host metabolic pathways (Olmo-Uceda et al. 2024; Kavil et al. 2021). Similar transcriptomic shifts were observed by Hillung et al. (2014), who reported that TEV adaptation in resistant ecotypes alters expression of stress-related and immune signaling genes, reinforcing the view that viral evolution reshapes host regulatory landscapes. Epigenetic instability appears to amplify transcriptional plasticity, shaping both viral and host evolutionary responses.

Parallelism with potyvirus evolution in the wild and implications for disease management

Interestingly, the results of our experimental evolution studies, especially the repeated identification of VPg as a major target of adaptation to diverse host genotypes, parallel patterns observed in natural potyvirus populations. VPg has long been recognized as a key determinant of host compatibility in crops carrying resistance genes. For example, one of the most widely deployed resistance genes against potato virus Y (PVY; species *Potyvirus solani*) in commercial pepper cultivars is *pvr²*, a locus with numerous allelic variants (Nicaise et al. 2007; Charron et al. 2008). *pvr²* encodes the *eIF4E* translation initiation factor, which must interact correctly with VPg to support PVY replication in pepper.

Consistent with this, all resistance-breaking PVY isolates identified to date contain mutations in the VPg cistron (Duprat et al. 2002; Moury et al. 2004; Ayme et al. 2007). These field observations reinforce the central role of VPg in mediating virus-host compatibility across both experimental and natural evolutionary contexts.

These findings also carry important implications for agriculture and plant disease management. Strategies that increase or preserve host genetic diversity may slow the overall pace of viral adaptation, but they also risk selecting for more virulent, generalist strains capable of overcoming multiple resistance backgrounds. Conversely, genetically uniform cropping systems can accelerate viral adaptation yet tend to favor specialist viruses with narrow host ranges and often lower virulence. Understanding these trade-offs is essential for designing sustainable resistance-deployment strategies and for anticipating how plant pathogens may evolve under different management regimes.

Beyond host genetic composition, several ecological processes in the field can modulate these evolutionary outcomes. First, recombination and genome modularity can rapidly generate resistance-breaking or host-range variants in potyviruses, well documented for PVY, where recombinant genotypes are common and epidemiologically consequential (*e.g.*, PVY^{NTN} and other mosaics) (Gibbs et al. 2020; Rodríguez-Rodríguez et al. 2020; Mao et al. 2019). Second, mixed infections (coinfection/superinfection) are frequent in crops and can produce synergism or antagonism via complementation or interference, altering virulence, transmission, and the selective advantage of generalist vs specialist strategies (Martínez et al. 2013; Moreno and López-Moya 2019; Singhal et al. 2021). Third, vector-mediated transmission introduces strong, recurrent bottlenecks and trait-based filters (*e.g.*, aphid behavior and non-persistent transmission), shaping adaptation, epidemic spread, and the payoffs to virulence in potyviruses (Gadhave et al. 2020). Finally, spatial structure and landscape heterogeneity (*e.g.*, field mosaics, host turnover and metapopulations) can either impede or accelerate the spread of more virulent or generalist types depending on mixing and transmission mode, thereby shifting the evolutionarily favored strategy at scale (Berngruber et al. 2015; González et al. 2019; McLeish et al. 2024). These factors argue for integrating genetic deployments with vector control, surveillance of recombinants/coinfections (via high-throughput sequencing), and landscape-level planting schemes to steer viral evolution toward less damaging equilibria.

Concluding remarks

Host genetic and epigenetic diversity jointly determine the pace and direction of virus evolution, shaping phenotypic traits, genomic architecture, and epidemiological outcomes. Homogeneous host populations tend to accelerate adaptation but promote specialization, whereas heterogeneous or epigenetically unstable populations slow adaptation while selecting for generalists with broader host ranges and potentially higher virulence. Future work should integrate multi-omics—combining genomic, transcriptomic, and interactomic data—to resolve mechanisms of virus adaptation in complex host environments. Particular attention should be given to epigenetic regulation and to the ecological and evolutionary consequences of resistance gene deployment in agriculture. Bridging experimental evolution with predictive modeling will improve forecasts of viral evolutionary trajectories and inform strategies for durable crop resistance.

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Declarations

Conflict of interest The author declares no competing financial interests or personal relationships that could have influenced the work reported in this paper.

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