

# RNAi-Based Antiviral Innate Immunity in Plants

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**Abstract:** Multiple antiviral immunities were developed to defend against viral infection in hosts. RNA interference (RNAi)-based antiviral innate immunity is evolutionarily conserved in eukaryotes and plays a vital role against all types of viruses. During the arms race between the host and virus, many viruses evolve viral suppressors of RNA silencing (VSRs) to inhibit antiviral innate immunity. Here, we reviewed the mechanism at different stages in RNAi-based antiviral innate immunity in plants and the counteractions of various VSRs, mainly upon infection of RNA viruses in model plant *Arabidopsis*. Some critical challenges in the field were also proposed, and we think that further elucidating conserved antiviral innate immunity may convey a broad spectrum of antiviral strategies to prevent viral diseases in the future.

**Keywords:** virus; antiviral innate immunity; RNAi; small RNA; VSR

## 1. Introduction

The phenomenon of RNA silencing was first observed in plants in 1990 when the introduction of chalcone synthase transgene into petunia led to the suppression of endogenous homologous genes [1,2]. In 1998, Andrew Fire and Craig Mello found that double-stranded RNAs (dsRNA) caused potent and specific interference in *Caenorhabditis elegans* [3] and termed the phenomenon RNA interference (RNAi), which won the Nobel Prize in Physiology and Medicine in 2006 and opened up a revolution in the field of biology [3,4]. Numerous studies showed that RNAi was evolutionarily conserved in eukaryotes, and it regulated all aspects of biological events [5,6]. RNAi signaling was established with the identification of some key components in the pathway. It was found that noncoding small RNA is triggered by either self-complementary or double-stranded RNA (dsRNA) and functions as the true signal and specificity determinant of gene silencing. Primary duplex small RNA is, respectively, produced by processing hair-pin RNA or dsRNA to microRNA or siRNA using a specific Dicer [7]. Additionally, secondary small RNA usually needs to be produced through amplification by RNA-dependent RNA polymerase (RdRP) for efficient gene silencing. Duplex small RNA can then be methylated by HEN1 to increase stability and is loaded into effector Argonaute (AGO) proteins [8]. The passage strand of duplex small RNA is degraded by AGOs, and the guided strand will remain to form an RNA-induced silencing complex (RISC) [9]. RISC then targets complementary RNA by base-pairing to mediate degradation or translation inhibition in post-transcription gene silencing (PTGS) or induce transcription gene silencing (TGS).

There are two major classes of endogenous small RNA in plants: microRNAs (miRNAs) and siRNAs [10]. miRNAs and siRNA are, respectively, produced from the processing of hair-pin RNA or dsRNA by a specific Dicer. miRNA, usually 21 nt in length, is produced by Dicer-like 1 (DCL1) in *Arabidopsis*. Endogenous miRNAs usually mediate PTGS and play an essential role in all aspects of plant developmental processes. Furthermore, 21, 22, and 24 nt siRNAs are, respectively, produced by DCL4, DCL2, or DCL3 in *Arabidopsis* and also regulate various biological processes. While 21 and 22 nt endogenous siRNAs usually



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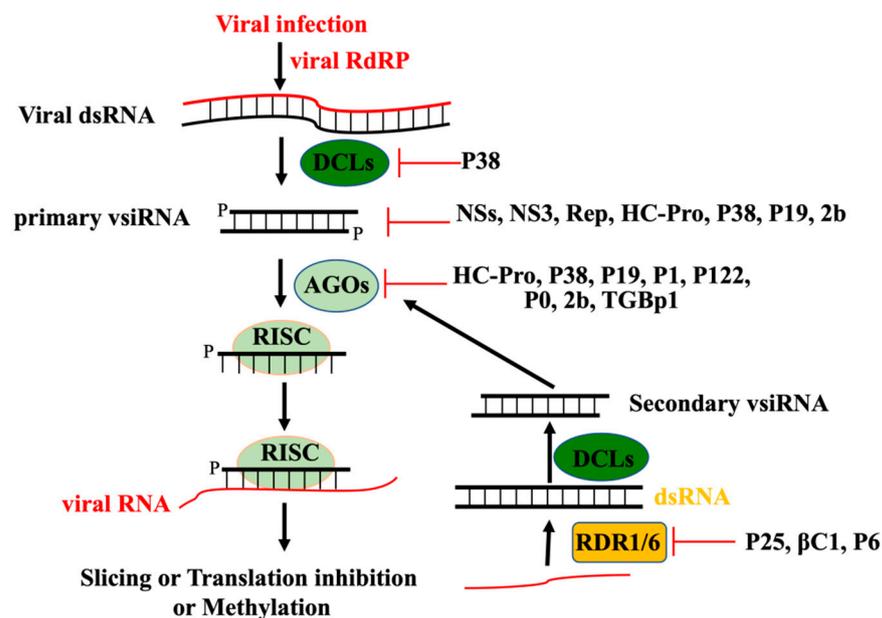
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mediate PTGS, such as 21 nt tasiRNA involved in leaf morphogenesis, 24 nt endogenous siRNAs mainly mediate TGS through DNA methylation.

Upon pathogen infection, different sizes of pathogen RNA-derived siRNAs are also produced to induce RNAi-based antimicrobial immunity to confer host resistance [10,11]. RNAi-based antiviral defense was first discovered in plants [12,13]. It was then found to play a vital role in antiviral immunity in invertebrates [14] and mammals [15,16]. Based on the findings in transgene silencing and endogenous gene silencing, the function of DCLs, AGOs, and RDRs (RNA dependent RNA Polymerases) in antiviral immunity were characterized. Now it is recognized that RNAi-based antiviral innate immunity will be induced to prevent aggression of all kinds of RNA or DNA viruses in almost all eukaryotes (Figure 1). On the other hand, many viruses, especially pathogenic viruses, evolve to encode VSRs to attack different steps of the RNAi-based antiviral pathway (Figure 1). The prevalence of VSR contributes to viral epidemics; it also blinds our appreciation to RNAi-based antiviral innate immunity. In addition, VSR also hindered us using classical genetic screen to identify new regulators in the antiviral pathway for decades until recently an efficient genetic method was developed to bypass the barrier [17,18].



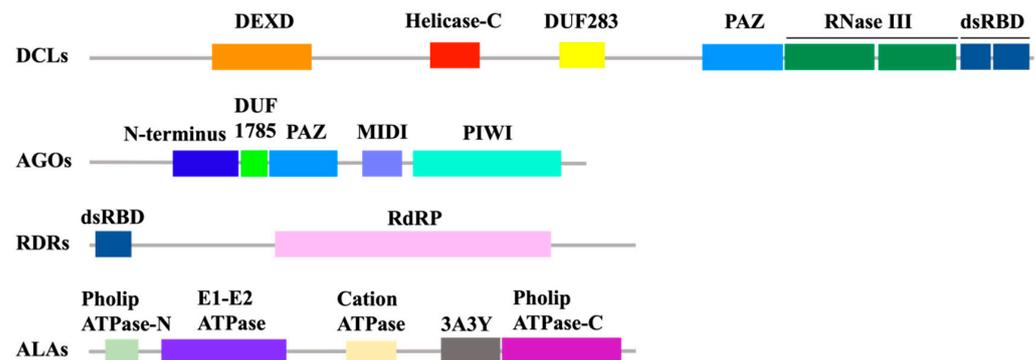
**Figure 1.** RNAi-based antiviral pathway in model plant *Arabidopsis*. After viral infection, the double-stranded viral RNA replicate intermediate will be perceived and processed into 21, 22, or 24 nt duplex primary viral siRNAs, respectively, by DCL4, DCL2, or DCL3. These 21 and 22nt primary viral siRNAs will then be uploaded into AGO1 or AGO2 to form RISC to mediate the slicing or translation inhibition of RNA viruses through PTGS. In contrast, 24nt vsiRNA will be uploaded to AGO4, AGO6, or AGO9 to form RISC to induce DNA methylation or histone modification through TGS to silence DNA viruses. Secondary viral siRNAs produced through amplification by RDR1/RDR6 or RDR2 are, respectively, required to enforce RNAi-based antiviral defense against RNA viruses or DNA viruses. Various VSRs of plant viruses target different steps to inhibit antiviral immunity.

Here, we will review the perception of viral RNA and the initiation of RNAi-based antiviral defense, production, and amplification of viral siRNA (vsiRNA) and the functions of antiviral RNAi effector Argonautes, with an emphasis on the recent progress in the field, challenging the existing questions on model plant *Arabidopsis*. Some VSRs of plant viruses and their functions were also summarized for a better understanding of the arms race between plant hosts and viruses. We apologize that some research progresses in the field may not be included.

## 2. Perception of Viral RNA and Initiation of RNAi-Based Antiviral Defense

Viruses are almost the smallest organisms on Earth, with a classical structure in which genetic material, RNA or DNA, is packaged in coat protein. Viruses need to be paralyzed in the host and propagated using the materials and energy of the host. Unlike other microbial pathogens, pattern-recognition receptors (PRRs) are not found to perceive viruses on the cell membrane of the host. After virus enters the host cell, double-strand viral RNAs will be produced during viral replication through viral replicases, host Dicer proteins will perceive and dice the double-strand viral RNAs to produce 21–24 nt lengths of vsiRNA. Thus, Dicer protein may be regarded as a viral PRR used to initiate the RNAi-based antiviral pathway.

Dicer belongs to the RNaseIII-like family and has highly conserved endonuclease in eukaryotes [19]. In Arabidopsis, there are four Dicer-like proteins (DCL): DCL1, DCL2, DCL3, and DCL4. They all contain five domains which are DEXD-helicase, helicase-C, domain of unknown function 283 (DUF283), Piwi/Argonaute/Zwille (PAZ) domain, two tandem RNase III domains, and one or two dsRNA-binding domains (dsRBDs) from the N-terminus to C-terminus [20] (Figure 2). DCL3 does not have a helicase-C domain. In general, the helicase domain utilizes ATP hydrolysis to facilitate the unwinding of dsRNA [19,21]. The DUF283 domain was recently described to facilitate RNA–RNA base pairing and RNA-binding [22,23]. The PAZ and RNase III domains are vital for dsRNA cleavage, the PAZ domain recognizes the terminus of the dsRNA and RNase III domains and cuts one of the strands of dsRNA, and the distance between the PAZ domain and RNase III domains is determined by the length of the products [22,24]. The dsRBD domain facilitates dsRNA binding and also serves as a nonclassical nuclear localization signal [23].



**Figure 2.** Protein structure diagram of DCLs, AGOs, RDRs, and ALAs. Function domains of each protein are shown with different colored boxes.

DCL1 is mainly involved in the biogenesis pathway of 21 nt micro-RNAs (miRNA), which play essential roles in all aspects of plant development and plant responses to environmental stimuli [25]. DCL1, DsRNA binding protein 1 (DRB1) (also known as HYPONASTIC LEAVES 1, HYL1), and SERRATE (SE) form nuclear dicing bodies to recognize the hair-pin structure of pri-miRNA, and sequentially cut pri-miRNA to precursor miRNA (pre-miRNA) and pre-miRNA to mature miRNA [21,26]. Recently it was reported that phase separation of SE drives dicing body assembly and promotes miRNA processing by DCL1 in Arabidopsis [27]; SE-Associated Protein 1 also promotes miRNA biogenesis by modulating pri-miRNA splicing, processing, and stability [28]. Therefore, loss-of-function DCL1 mutants, embryonic lethal, and even hypomorphic mutant DCL1 also showed pleiotropic developmental defects due to disrupted miRNA biogenesis [29]. DCL1 may indirectly function in RNAi-based antiviral innate immunity through controlling the biogenesis of some miRNAs. It was reported that miR168 negatively regulates AGO1 accumulation in plants [30], and miR482 or miR6019/miR6020, respectively, decrease antiviral resistance of R-genesin tomato or tobacco [31,32]. DCL1 could also promote the other DCLs mediated biogenesis of vsiRNA [33,34].

DCL2 is responsible for processing exogenous double-stranded RNA (dsRNA) molecules or natural antisense siRNAs into 22-nt siRNAs in Arabidopsis [35,36]. However, DCL2 only subrogates to initiate RNAi-based antiviral innate immunity in Arabidopsis when the function of DCL4 is abrogated [37,38]. Interestingly, recent studies showed that massive endogenous 22 nt siRNAs can be accumulated when the cytoplasmic RNA decay pathway and function of DCL4 is defective; these siRNAs can trigger gene-specific and global translational repression and lead to pleiotropic growth disorders [39]. However, multiple orthologs of DCL2 exist in other plants and can evolve to possess functions. For example, a study demonstrated that DCL2b, one DCL2 homolog out of four in tomatoes, played a vital role against *tomato mosaic virus* (ToMV) infection by producing 22 nt vsiRNA in tomatoes [40].

DCL3 generates 24nt siRNAs to regulate RNA-dependent DNA methylation (RdDM) in transcriptional gene silencing (TGS) in Arabidopsis [41]. Recently, DCL3-pre-siRNA structure revealed that DCL3 used a positively charged pocket and an aromatic cap to, respectively, recognize the 5'-phosphorylated adenosine of the guide strand and the 3' overhang of the complementary strand. The paired RNase III domains of DCL3 cut both strands of the RNA, determining the precise length of the product small RNA [42]. Endogenous 24 nt siRNAs are mainly produced from heterochromatin or the repeated-sequence rich region by DCL3 to maintain transposon silencing or genome stability; 24 nt siRNAs also repress transcription of the transgene or other exogenous DNA, such as DNA viruses [43–45]. It was reported that after the infection of the DNA virus, 24 nt vsiRNAs were produced to modulate DNA methylation and histone modification of viral DNA and to prevent viral infection [46,47].

DCL4 cleaves long endogenous dsRNA to produce 21 nt siRNAs, such as trans-acting siRNAs (ta-siRNAs), which are crucial for plant development [48–51]. Arabidopsis *dcl4* mutant showed a phenotype of elongated, downward curled rosette leaves [51,52] and augmented anthocyanin accumulation [53,54]. In RNAi-based antiviral innate immunity, DCL4 perceives and cuts long viral dsRNA to produce 21 nt vsiRNA to prevent viral infection, especially after the infection of RNA virus in Arabidopsis and other plants [49].

Although each DCL is responsible for the production of distinct small RNA, they may function redundantly or hierarchically in RNAi-based antiviral innate immunity. For example, DCL4 was regarded as an endogenous suppressor to repress DCL2-mediated production of 22 nt siRNAs [39,55]; however, DCL2 functions redundantly in RNAi-based antiviral innate immunity, especially when the function of DCL4 is compromised [56]. Thus, in the absence of both DCL2 and DCL4, virus titers would be dramatically increased [18,57,58]. Furthermore, 21 nt siRNA produced by DCL4 could also facilitate the RdDM pathway to defend against the infection of DNA viruses [41]. DCL2 and DCL3 need to function together in the defense against *potato spindle tuber viroid* [59]. In addition, DCL1 has the potential to produce 21 nt vsiRNA in the absence of DCL2, DCL3, and DCL4 [55,57].

DsRNA-binding (DRB) proteins are also required for the proper perception and dicing of viral RNAs by DCLs [60]. The Arabidopsis genome encodes five DRB proteins: DRB1/HYL1, DRB2, DRB3, DRB4, and DRB5 [61]. They contain one to three conserved dsRNA-binding motifs (dsRBMs), which consist of about 70 amino acids, forming  $\alpha$ - $\beta$ - $\beta$ - $\beta$ - $\alpha$  folds and two  $\alpha$ -helices to interact with dsRNA [62,63]. DRBs interact with specific DCLs to execute their special function in small RNA biogenesis and antiviral defense [60]. For example, the interaction between DRB1 (HYL1) and DCL1 is required for miRNA biogenesis and is involved in selecting the guide strand loaded into RISC [64–66]. DRB4 interacts with DCL4 to form another kind of dicing body for the efficient processing of siRNAs. It was reported that the DRB4 mutation resulted in defective antiviral defense to the infection of *turnip yellow mosaic virus* (TYMV) [67]. The *drb3* mutant was hyper-susceptible to *cabbage leaf curl virus* (CaLCuV) and *beet curly top virus* (BCTV) infection, and the viral genome methylation was substantially reduced in *drb3* [47]. DRB2 was recently characterized as a wide-spectrum antiviral effector; overexpression of DRB2 decreased the accumulation of

several different RNA viruses, including *tobacco rattle virus* (TRV), *tomato bushy stunt virus* (TBSV), *potato virus X* (PVX), and *grapevine fanleaf virus* (GFLV) [68].

### 3. Production and Amplification of vsiRNA

After the perception and dicing of viral dsRNA through DCL, primary vsiRNA will be produced. However, adequate secondary vsiRNA must be produced through amplification for efficient antiviral defense. Host RNA-dependent RNA Polymerase (RdRP) proteins are core factors for secondary vsiRNA amplification in plants and *Caenorhabditis elegans*. They exponentially generate viral dsRNA, which serves as DCLs substrates for vsiRNA biogenesis, probably using truncated viral RNAs as templates [18,69,70].

There are six RdRP proteins in Arabidopsis (RDR1 to RDR6). RDR1, RDR2, and RDR6 all share the C-terminal canonical catalytic DLDGD motif of eukaryotic RDRs and have orthologs in many plant species, while RDR3, RDR4, and RDR5 share an atypical DFDGD amino acid motif in the catalytic domain [71]. RDR1, RDR2, and RDR6 are well demonstrated to control RNAi-based antiviral innate immunity in Arabidopsis, although the function of the tandem-repeated RDR3, RDR4, and RDR5 in the Arabidopsis genome are not identified.

RDR1 can be induced by the infection of the virus [72], viroid [73], or salicylic acid treatment [74]. It was found to amplify 21 nt or 22 nt vsiRNA in RNAi-based antiviral innate immunity, especially upon the infection of RNA viruses. RDR1 does not regulate either endogenous siRNA biogenesis or plant development. However, it was found that RDR1 mediated the production of virus-activated endogenous siRNA (vasiRNA), a novel class of host siRNAs that may contribute to antiviral defense in plants [72].

RDR6 is constitutively-expressed in various tissues in Arabidopsis. RDR6 not only promotes RNAi-based antiviral innate immunity by mediating vsiRNA biogenesis, especially after the infection of RNA viruses, it also controls plant development by mediating the biogenesis of endogenous siRNA, such as tasiRNAs [75,76]. RDR6 usually forms siRNA bodies with a suppressor of gene silencing 3 (SGS3) to cooperatively function in the processes [77–80]. Thus, the *rdr6* mutant and *sgs3* mutant display the same defects in antiviral defense and development [78,81–83]. Interestingly, RDR6 and miR472 may also negatively regulate PAMP-triggered immunity (PTI) and effector-triggered immunity (ETI) through the post-transcriptional control of disease resistance genes [84] and contribute to double-strand break formation in meiosis in other plants [75]. Besides, rice (*Oryza sativa*) RDR6 plays an antiviral role in the defense against *rice stripe virus* (RSV) [85].

RDR2 mainly associates with Pol IV to form a complex for transcribing short dsRNA precursors, which are cleaved by DCL3 to produce 24 nt siRNAs for directing DNA methylation [86–89], although RDR2 might also be able to generate 23 to 27 nt small RNAs from MIR genes to mediate DNA methylation [90]. It was reported that RDR2, Pol IV, and DCL3, core components in the RdDM pathway, mediated 24 nt vsiRNA production and played major roles against the infection of DNA viruses, such as geminiviruses [44,45]. Interestingly, 21 nt vsiRNA amplified through RDR1 and RDR6 could also facilitate the RdDM pathway and contribute to plant defense against DNA viruses [91,92].

Several novel factors involved in the amplification of secondary vsiRNA were also recently discovered. Antiviral RNAi-defective 1 (AVI1)/aminophospholipid transporting ATPase 2 (ALA2), ALA1, and AVI2 were identified through a robust forward genetic screen using a cucumber mosaic virus (CMV) mutant in which start codons of VSR-2b were mutated [17,93–95]. In the *ala1/ala2* or *avi2* mutant, production of secondary vsiRNAs was dramatically reduced. ALA1/ALA2 contain the typical P4-type ATPase structure (Figure 2) and may transport specific phospholipids across cellular membranes in plants. ALA1 and ALA2 could cooperate with RDR1 and RDR6 to promote secondary vsiRNA biogenesis, probably by defining the cellular localization of its substrate phospholipid [17,94]. AVI2 was also named as a New factor enhancer of *rdr6* 3 (ENOR3) since it was also identified through a genetic screen from *rdr6* background using another CMV mutant in which the 2b gene was deleted [96]. AVI2, a putative magnesium transporter in Arabidopsis, also

promoted secondary vsiRNA biogenesis-dependent RDR1 and RDR6 [93]. Interestingly, calmodulin-binding transcription activator-3 (CAMTA3) was recently found to activate Bifunctional nuclease-2 (BN2) to stabilize AGO1/2 and DICER-LIKE1 and to activate RDR6 for the amplification of vsiRNAs [97].

RDRs and new factors such as ALA1/2 and AVI2 are widely conserved in plants and worms to ensure sufficient biogenesis of vsiRNA for efficient RNAi-based antiviral innate immunity. However, RDRs are absent in *Drosophila*, mice, and humans, in which a different mechanism was recently discovered for vsiRNA amplification through extrachromosomal circular DNA [21]. Whether the new mechanism also exists in plants or worms remains to be investigated.

#### 4. Antiviral Function of RNAi Effector Argonautes

vsiRNA must be loaded to AGO effectors to form RISC, then targets complementary viral genomes to PTGS or TGS in RNAi-based antiviral innate immunity. Effector AGOs are evolutionarily conserved and widespread in eukaryotes, though absent in prokaryotes [98]. They were demonstrated to regulate a variety of biological progresses in plant development and the plant response to environmental stimuli [98–103], in addition to their functions in antiviral defense. Crystallographic studies showed canonical eukaryotic AGOs contain five domains called the N-terminal (N) domain, PIWI-ARGONAUTE-ZWILLE (PAZ) domain, middle (MID) domain, a PIWI domain, and a domain of unknown function 1785 (DUF1785) [104,105] (Figure 2). The N domain may block guide-target pairing beyond position 16, PAZ domain recognizes the 3' end of sRNA, the MID domain anchors the 5' phosphate of sRNA, PIWI domain possesses ribonuclease activity to slice target RNA [106–108], and the function of DUF1785 domains was recently shown to impair the perfect matched siRNA and miRNA duplexes [109]. Together, all domains facilitate the correct combination between sRNA and target RNA to ensure proper silencing.

Ten AGOs are encoded in *Arabidopsis* [110–113]. AGO1 and AGO2 are the main components of RNAi mediated antiviral immunity against RNA viruses [100]. AGO1 also functions as an effector of miRNA to regulate all aspects of plant development by modulating the expression of endogenous genes [114–122]. Thus *ago1* knockout mutants are lethal. Therefore, the function of AGO1 in RNAi-based antiviral innate immunity was only examined using hypomorphic AGO1 mutants, such as *ago1-27*, which still displayed severe developmental defects [123]. Unlike AGO1, AGO2 does not participate in regulating plant development, and the *ago2* mutant does not show defects in growth and development; AGO2 may solely regulate plant defense in *Arabidopsis*. It was reported that AGO2 prefers to bind vsiRNAs with 5' terminal A and AGO1 prefers to U [124]. AGO2 is required for resistance to a broad spectrum of plant viruses [56,125–128]. It was also reported that the catalytical activity of AGO2 was necessary for local and systemic antiviral activity [125,127], while the *ago1* mutant with intact catalytical activity was susceptible to viral infection [123]. AGO2 is also involved in resistance against the phytopathogenic bacterium *Pseudomonas syringae* [129], and AGO2 binds with miR393b\* and silences *MEMB12* to modulate exocytosis of antimicrobial PR proteins and increase antiviral activity [129]. Therefore, AGO1 and AGO2 may play distinct roles in antiviral defense in plants.

AGO4, AGO6, and AGO9 are the major effectors functioning in the RdDM pathway in *Arabidopsis*. AGO4, AGO6, and AGO9 were shown to bind 24 nt heterochromatic small interfering RNAs (het-siRNAs) and contribute to the RdDM pathway [130,131]. It was reported that AGO4 mainly combated the aggression of DNA viruses through modulating RdDM, as reported that *ago4* mutants was susceptible to the infection of BCTV due to the diminished hypermethylation on BCTV genome [47]. Surprisingly, *ago4* mutants are susceptible to several RNA viruses, such as *turnip crinkle virus* (TCV), *bamboo mosaic virus* (BaMV), and *plantago asiatica mosaic virus* (PIAMV) [132–135] through a mechanism independent of RdDM pathway [135].

As to other AGO effectors, AGO5 together with AGO2 participate in reducing *potato virus X* (PVX) systemic infection, while AGO5 only plays a secondary role when AGO2 is

overcome in the initially infected leaves [136]. AGO7 (also known as ZIP) was found to be a crucial factor during TCV infection by the image-based disease analysis method [132]. AGO7 can also bind with miR390 and mediate the biogenesis of endogenous tasiRNA [137]. AGO10 cooperates with AGO1 and has a redundant role in protecting inflorescence tissues from the infection of *turnip mosaic virus* (TuMV) [125], besides its function in regulating shoot apical meristem development by binding miR165/166 [138].

Interestingly, more than 10 AGO orthologs were found in some important crops such as rice and tomato, with 19 orthologs in rice and 15 in tomato. They can evolve to have differential functions in antiviral defense and development. For example, when infected with *rice stripe tenuivirus* (RSV), RSV coat protein (CP) triggers JA accumulation and upregulates JA-responsive transcription factor JAMYB to directly bind to the AGO18 promoter to activate AGO18 transcription [139]. AGO18 will bind and sequester miR168, which increase the accumulation of AGO1 for the antiviral process [140]. On the other hand, AGO18 preferentially binds miR528 to upregulate the accumulation of ROS and resists virus infection [141]. Our unpublished data also shows that some AGO orthologs in tomatoes possess differential functions compared to Arabidopsis.

### 5. Viral Suppressors of RNAi

In the defense and counter-defense arm race between host plants and viruses, viruses evolve VSR proteins to inhibit RNAi-based antiviral innate immunity. VSrs target different steps of the RNAi-based antiviral pathway to counteract the conserved antiviral immunity (Table 1) [142,143].

**Table 1.** Viral suppressors of RNA silencing (VSR) reported in plant viruses.

VSRs	Genus	Species	Viral Strategies to Suppress Antiviral RNA Silencing	Suppression of Systemic Silencing (YES/NO/Unknown)
NSs	<i>Tospovirus</i>	TSWV	<ul style="list-style-type: none"> <li>Binds with dsRNA (size-independent, long dsRNA, or dssRNA) [144,145]</li> </ul>	YES
		GBNV	<ul style="list-style-type: none"> <li>Affects miRNA biogenesis [146]</li> </ul>	NO
		RHBV	<ul style="list-style-type: none"> <li>Binds dsRNA (size-selectively) [144]</li> </ul>	Unknown
NS3	<i>Tenuivirus</i>	RSV	<ul style="list-style-type: none"> <li>Binds dsRNA (size-independent, recognizes minimum 9 bp or long dsRNA) [147]</li> <li>Interacts with DRB1 [148]</li> </ul>	YES
Rep	<i>Mastrevirus</i>	WDV	<ul style="list-style-type: none"> <li>Binds siRNA (size-selectively, 21 nt and 24 nt ds-siRNA and ss-siRNA) [149]</li> </ul>	YES
P14	<i>Aureusvirus</i>	PoLV	<ul style="list-style-type: none"> <li>Binds dsRNA (size-independent) [150,151]</li> </ul>	Unknown
P15	<i>Pecluvirus</i>	PCV	<ul style="list-style-type: none"> <li>Binds dsRNA (size-selectively) [151]</li> </ul>	Unknown
$\gamma$ B	<i>Hordeivirus</i>	BSMV	<ul style="list-style-type: none"> <li>Binds dsRNA (size-selectively) [151]</li> <li>The function of <math>\gamma</math>b phosphorylation in regulating RNA silencing [152]</li> </ul>	YES
P21	<i>Closterovirus</i>	BYV	<ul style="list-style-type: none"> <li>Binds siRNA (size-selectively) [151]</li> <li>Blocks HEN1 methyltransferase [153]</li> </ul>	Unknown
		CaMV	<ul style="list-style-type: none"> <li>Interact with DRB4 [154]</li> </ul>	NO
P6	<i>Caulimovirus</i>	RYSV	<ul style="list-style-type: none"> <li>Blocks RDR6-mediated biosynthesis of secondary vsiRNAs [155]</li> </ul>	YES

Table 1. Cont.

VSRs	Genus	Species	Viral Strategies to Suppress Antiviral RNA Silencing	Suppression of Systemic Silencing (YES/NO/Unknown)
HC-Pro	<i>Potyvirus</i>	TEV	<ul style="list-style-type: none"> <li>Binds dsRNA (size-selectively) [151]</li> <li>Inhibits AGO1 (by inducing miR168) [156]</li> <li>Interacts with RAV2 to block the activity of primary siRNAs [157]</li> </ul>	Unknown
		TuMV	<ul style="list-style-type: none"> <li>Interacts with HEN1 [158]</li> </ul>	Unknown
		ZYMV	<ul style="list-style-type: none"> <li>Interacts with the HEN1methyltransferase and inhibits its activity [159]</li> </ul>	Unknown
		PVA	<ul style="list-style-type: none"> <li>Interacts with AGO1 [160]</li> <li>Mediates HEN1 methyltransferase by inhibiting the SMA activity in the methionine cycle [160]</li> </ul>	YES
		PVY	<ul style="list-style-type: none"> <li>Binds 21 nt and 22 nt sRNA [161]</li> </ul>	Unknown
		SCMV	<ul style="list-style-type: none"> <li>Down-regulated the accumulation of RDR6 mRNA and 3' secondary siRNA [162]</li> </ul>	Unknown
CP(P38)	<i>Carmovirus</i>	TCV	<ul style="list-style-type: none"> <li>Binds dsRNA (size-independent, long dsRNA or ds-sRNA) [151]</li> <li>Inhibits DCL4 activity [55]</li> <li>Inhibits AGO1 (by inducing miR168) [156]</li> </ul>	Unknown
P19	<i>Tombusvirus</i>	CymRSV	<ul style="list-style-type: none"> <li>Binds dsRNA (size-selectively, only 21 nt ds-sRNA) [151]</li> <li>Inhibits AGO1 (by inducing miR168) [30]</li> </ul>	Unknown
		TBSV	<ul style="list-style-type: none"> <li>Interacts with miRNA and hair-pin RNA-derived siRNA [163]</li> <li>Inhibits miRNA methylation [164]</li> </ul>	Unknown
		CIRV	<ul style="list-style-type: none"> <li>Binds dsRNA (size-selectively, 20-22 nt) [165]</li> </ul>	Unknown
P1	<i>Ipomovirus</i>	CVYV	<ul style="list-style-type: none"> <li>Down-regulates dsRNA formation and suppresses local RNA silencing through its duplicated form, P1b [166]</li> </ul>	Unknown
		SPMMV	<ul style="list-style-type: none"> <li>Interacts with AGO1 [167]</li> </ul>	Unknown
P122	<i>Tobamovirus</i>	TMV	<ul style="list-style-type: none"> <li>Binds dsRNA (size-selectively, siRNA and miRNA) and mediates 3' methylation of small RNA [168]</li> <li>Inhibits AGO1 (by inducing miR168) [156,168]</li> </ul>	Unknown
P0	<i>Polerovirus</i>	PLRV	<ul style="list-style-type: none"> <li>Targets AGO1 and promotes AGO1 degradation [169]</li> </ul>	YES
		SCYLV	<ul style="list-style-type: none"> <li>Suppression of local and systemic dsGFP-PTGS [170], while the detailed mechanism is unknown</li> </ul>	YES
		CLRVD	<ul style="list-style-type: none"> <li>Mediate the decay of ARGONAUTE proteins [171]</li> </ul>	YES
		CYDV	<ul style="list-style-type: none"> <li>Effects on secondary siRNA production and AGO1 stability [172]</li> </ul>	YES
		BWYV	<ul style="list-style-type: none"> <li>Acts as an F-box and targets AGO1 to modulate gene silencing [173,174]</li> </ul>	NO
			<i>Enamovirus</i>	PEMV-1
TGBp1 (P25)	<i>Potexvirus</i>	PVX	<ul style="list-style-type: none"> <li>Interacts with AGO1 and promotes AGO1 degradation through the proteasome pathway [176]</li> </ul>	YES
		PLAMV	<ul style="list-style-type: none"> <li>Interacts with SGS3 and RDR6 [177]</li> </ul>	Unknown

Table 1. Cont.

VSRs	Genus	Species	Viral Strategies to Suppress Antiviral RNA Silencing	Suppression of Systemic Silencing (YES/NO/Unknown)
RNase III	<i>Crinivirus</i>	SPCSV	• Cleaves 21-24nt vsRNAs into 14 bp products and renders them inactive [178,179]	Unknown
$\beta$ C1	<i>Begomovirus</i>	TYLCCNV	Repress RDR6 expression to inhibit secondary siRNA production [180]	Unknown
V2	<i>Begomovirus</i>	TYLCV	• Interacts with SGS3 [181]	NO
V2	<i>Begomovirus</i>	CLCuMuV	• Disrupts the calmodulin–CAMTA3 interaction [97]	Unknown
P4	<i>Rhabdovirus</i>	RSMV	• Interacts with SGS3 [182]	Unknown
2b	<i>Cucumovirus</i>	CMV	• Binds dsRNA (size-independent) [183] • Interacts with AGO1 and AGO4 [184,185] • Inhibits AGO1 (by inducing miR168) [156,185]	YES
		TAV	• Binds dsRNA (size-dependent) [186] • Down-regulates the accumulation of RDR6 mRNA [162]	Unknown
V3	<i>Begomovirus</i>	TYLCV	• Functions in both PTGS and TGS [187]	Unknown
VPg	<i>Potyvirus</i>	PVA	• Interacts with SGS3 and mediates SGS3 degradation through the ubiquitination and autophagy pathways [188]	Unknown
P2	<i>Tenuivirus</i>	RSV	• Interacts with SGS3 [189]	Unknown
Pns10	<i>Phytoreovirus</i>	RDV	• Interferes with the perception of silencing signals in recipient tissues [190] • Binds dsRNA (with 2 nt 3' overhangs) [190,191] • Causes downregulated expression of RDR6 [190]	YES
Pns11	<i>Phytoreovirus</i>	RDV	• Dependent its nuclear localization signal [192]	No

NSS (nonstructural protein), VPg (Viral genome-linked protein), TGBp1 (the first ORF of triple-gene block proteins encoded protein), HC-Pro (helper component-proteinase), Rep (replication initiator protein), P14 (PoLV ORF5-encoded 14-kDa protein), P19 (19-kDa suppressor protein), P15 (PCV RNA-1-encoded 15-kDa protein),  $\gamma$ B (BSMV RNA $\gamma$  encodes  $\gamma$ B protein), P21 (21-kDa product of BYV ORF 8), P6 (ORF6-encoded protein), CP (coat protein), P122 (122-kDa replicase subunit), P0 (the first ORF poleroviruses), RNase III (dsRNA-specific class 1 RNase III endoribonuclease), VPg (the viral protein genome-linked). SAMS (S-adenosyl-L-methionine synthase). BSMV (*barley stripe mosaic virus*), BWYV (*beet western yellows virus*), BYV (*beet yellows virus*), CABYV (*cucurbit aphid-borne yellows virus*), CaMV (*cauliflower mosaic virus*), CIRV (*carnation Italian ringspot virus*), CLCuMuV (*cotton leaf curl Multan geminivirus*), CLRDV (*cotton leaf roll dwarf virus*), CMV (*cucumber mosaic virus*), CVYV (*cucumber vein yellowing virus*), CYDV (*cereal yellow dwarf virus*), CymRSV (*cymbidium ringspot virus*), GBNV (*groundnut bud necrosis virus*), PEMV-1 (*pea enation mosaic virus-1*), PCV (*peanut clump virus*), PIAMV (*plantago asiatica mosaic virus*), PLRV (*potato leafroll virus*), PoLV (*pothos latent virus*), PVA (*potato virus A*), PVX (*potato virus X*), PVY (*potato virus Y*), RDV (*rice dwarf virus*), RHBV (*rice hoja blanca virus*), RSMV (*rice stripe mosaic virus*), RSV (*rice stripe virus*), RYSV (*rice yellow stunt virus*), SCMV (*sugarcane mosaic virus*), SCYLV (*sugarcane yellow leaf virus*), SPCSV (*sweet potato chlorotic stunt crinivirus*), SPMNV (*sweet potato mild mottle virus*), TAV (*tomato aspermy virus*), TBSV (*tomato bushy stunt virus*), TCV (*turnip crinkle virus*), TEV (*tobacco etch virus*), TMV (*tobacco mosaic virus*), TSWV (*tomato spotted wilt virus*), TuMV (*turnip mosaic virus*), TYLCV (*tomato yellow leaf curl virus*), TYLCCNV (*tomato yellow leaf curl China virus*), WDV (*wheat dwarf virus*), ZYMV (*zucchini yellow mosaic virus*).

A very common counteraction of VSRs is to impede vsRNA amplification. For example, 2b of CMV,  $\beta$ C1 of *tomato yellow leaf curl China virus* (TYLCCNV), and P6 of *rice yellow stunt virus* (RYSV) interfere with the RDR1/6-dependent biogenesis of secondary vsRNA [155,180,185]. The V2 of *tomato yellow leaf curl geminivirus* (TYLCV), P2 of RSV and P4 of *rice stripe mosaic virus* (RMSV) interacts with SGS3 to inhibit the biogenesis of secondary vsRNA [181,182,189]. Geminivirus V2 protein was also found to disrupt the calmodulin–CAMTA3 interaction, which decreases the expression of RDR6 to reduce vsRNA biogenesis [97].

Some VSRs were found to obstruct the perception or dicing of viral dsRNA. For example, CP of TCV could inhibit the dicing activity of DCL4 [55], and P6 of *cauliflower mosaic virus* (CaMV) interacts with DRB4 to block dsRNA binding [154]. Some VSRs, such as NSs of *tomato spotted wilt virus* (TSWV) and Hc-Pro of *potato virus Y* (PVY), also bind to long viral dsRNA, which could block the sensing or processing of the viral RNAs by DCLs. Some other VSRs could directly target vsRNA to inhibit RNAi-based antiviral innate immunity. For example, P19, the well-known VSR of tombusviruses, binds and sequesters vsRNA, while RNase III of *sweet potato chlorotic stunt crinivirus* (SPCSV) binds and mediate vsRNA degradation, and HC-Pro of *zucchini yellow mosaic virus* (ZYMV) decreases vsRNA stability by disturbing vsRNA methylation by HEN1. Disturbing the antiviral function of effector AGOs is another strategy used by some VSRs. For example, P0 of *potato leafroll virus* (PLRV) can mediate AGO1 degradation, and 2b of CMV can interfere with AGO1 and AGO4 and disturb their functions.

Surprisingly, unlike the above VSRs that counteract RNAi-based antiviral innate immunity, other mechanisms were found to antagonize antiviral responses by some VSRs. Recently, a study showed that VSR p19 can interact with the receptor-like kinase (RLK) BARELY ANY MERISTEM 1 (BAM1) and BAM2 to inhibit the cell-to-cell movement of RNA silencing [193,194]. VSR C4 of *tomato leaf curl Guangdong virus* (ToLCGdV) can also interact with BAM1 to suppress PTGS and reverse methylation-mediated TGS [195]. In addition, accumulated evidence indicates autophagy-modulated plant–virus interactions [196,197]. It was reported that the cargo receptor NEIGHBOR OF BRCA1 (NBR1) could target HC-Pro to suppress the viral accumulation of TuMV [198]. However,  $\gamma$ B, the VSR of *barley stripe mosaic virus* (BSMV), targeted AUTOPHAGY PROTEIN7 (ATG7) to disrupt the ATG7–ATG8 interaction and promote viral infection [199].

Now we know that almost all plant viruses, especially pathogenic plant viruses, possess one or more VSR. The existence of VSRs contributes to the successful aggression of viruses and viral epidemics; they also seriously hinder our appreciation of the indispensable antiviral innate immunity in plants and other eukaryotes.

## 6. Question and Perspective

RNAi-based antiviral innate immunity is recognized as a fundamental antiviral innate immunity in plants and animals; some key components functioning in the antiviral pathway were found and are well characterized. However, our understanding of the exact mechanism of the antiviral pathway is far from complete since only a few novel components in the pathway were found, and some critical questions or challenges in the field are waiting to be tackled. For example, (1) whether a specific cellular structure exists for vsRNA biogenesis and amplification, and (2) whether/how vsRNAs move over long-distances to confer systematic resistance. (3) Additionally, the impact of function differentiation on the translation inhibition or slicing of different AGOs and their functional localization in cells are largely unknown. (4) The true function and mechanism of RNAi-based antiviral innate immunity in important agricultural crops are elusive and (5) the application of RNAi-based antiviral innate immunity in agricultural practice needs to be further explored. Therefore, further studies are required to dissect the vital antiviral innate immunity, and progress in the field could eventually lead to finding novel strategies or methods to prevent specific and broad-spectrum viral diseases in plants and even humans.

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## References

1. Napoli, C.; Lemieux, C.; Jorgensen, R. Introduction of a Chimeric Chalcone Synthase Gene into *Petunia* Results in Reversible Co-Suppression of Homologous Genes in trans. *Plant Cell* **1990**, *2*, 279–289. [[CrossRef](#)] [[PubMed](#)]
2. Van Der Krol, A.R.; Mur, L.A.; Beld, M.; Mol, J.N.; Stuitje, A.R. Flavonoid genes in *petunia*: Addition of a limited number of gene copies may lead to a suppression of gene expression. *Plant Cell* **1990**, *2*, 291–299. [[CrossRef](#)] [[PubMed](#)]
3. Fire, A.; Xu, S.; Montgomery, M.K.; Kostas, S.A.; Driver, S.E.; Mello, C.C. Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*. *Nature* **1998**, *391*, 806–811. [[CrossRef](#)] [[PubMed](#)]
4. Mello, C.C.; Conte, D. Revealing the world of RNA interference. *Nature* **2004**, *431*, 338–342. [[CrossRef](#)] [[PubMed](#)]
5. Bartel, D.P. MicroRNAs. *Cell* **2004**, *116*, 281–297. [[CrossRef](#)]
6. Carthew, R.W.; Sontheimer, E.J. Origins and Mechanisms of miRNAs and siRNAs. *Cell* **2009**, *136*, 642–655. [[CrossRef](#)] [[PubMed](#)]
7. Meister, G.; Tuschl, T. Mechanisms of gene silencing by double-stranded RNA. *Nature* **2004**, *431*, 343–349. [[CrossRef](#)]
8. Yu, B.; Yang, Z.; Li, J.; Minakhina, S.; Yang, M.; Padgett, R.W.; Steward, R.; Chen, X. Methylation as a Crucial Step in Plant microRNA Biogenesis. *Science* **2005**, *307*, 932–935. [[CrossRef](#)]
9. Filipowicz, W. RNAi: The Nuts and Bolts of the RISC Machine. *Cell* **2005**, *122*, 17–20. [[CrossRef](#)]
10. Huang, C.-Y.; Wang, H.; Hu, P.; Hamby, R.; Jin, H. Small RNAs—Big Players in Plant-Microbe Interactions. *Cell Host Microbe* **2019**, *26*, 173–182. [[CrossRef](#)]
11. Niu, D.; Hamby, R.; Sanchez, J.N.; Cai, Q.; Yan, Q.; Jin, H. RNAs—A new frontier in crop protection. *Curr. Opin. Biotechnol.* **2021**, *70*, 204–212. [[CrossRef](#)] [[PubMed](#)]
12. Ratcliff, F.; Harrison, B.D.; Baulcombe, D.C. A Similarity Between Viral Defense and Gene Silencing in Plants. *Science* **1997**, *276*, 1558–1560. [[CrossRef](#)] [[PubMed](#)]
13. Kasschau, K.D.; Carrington, J.C. A counter defensive strategy of plant viruses: Suppression of posttranscriptional gene silencing. *Cell* **1998**, *954*, 461–470. [[CrossRef](#)]
14. Nayak, A.; Tassetto, M.; Kunitomi, M.; Andino, R. RNA Interference-Mediated Intrinsic Antiviral Immunity in Invertebrates. *Intrinsic Immun.* **2013**, *371*, 183–200. [[CrossRef](#)]
15. Maillard, P.V.; Ciaudo, C.; Marchais, A.; Li, Y.; Jay, F.; Ding, S.W.; Voinnet, O. Antiviral RNA Interference in Mammalian Cells. *Science* **2013**, *342*, 235–238. [[CrossRef](#)] [[PubMed](#)]
16. Li, Y.; Lu, J.; Han, Y.; Fan, X.; Ding, S.-W. RNA Interference Functions as an Antiviral Immunity Mechanism in Mammals. *Science* **2013**, *342*, 231–234. [[CrossRef](#)]
17. Guo, Z.; Lu, J.; Wang, X.-B.; Zhan, B.; Li, W.; Ding, S.-W. Lipid flippases promote antiviral silencing and the biogenesis of viral and host siRNAs in *Arabidopsis*. *Proc. Natl. Acad. Sci. USA* **2017**, *114*, 1377–1382. [[CrossRef](#)]
18. Guo, Z.; Li, Y.; Ding, S.-W. Small RNA-based antimicrobial immunity. *Nat. Rev. Immunol.* **2018**, *19*, 31–44. [[CrossRef](#)]
19. Cenik, E.S.; Fukunaga, R.; Lu, G.; Dutcher, R.; Wang, Y.; Hall, T.M.T.; Zamore, P.D. Phosphate and R2D2 Restrict the Substrate Specificity of Dicer-2, an ATP-Driven Ribonuclease. *Mol. Cell* **2011**, *42*, 172–184. [[CrossRef](#)]
20. Margis, R.; Fusaro, A.; Smith, N.A.; Curtin, S.J.; Watson, J.M.; Finnegan, E.J.; Waterhouse, P. The evolution and diversification of Dicers in plants. *FEBS Lett.* **2006**, *580*, 2442–2450. [[CrossRef](#)]
21. Bologna, N.G.; Voinnet, O. The Diversity, Biogenesis, and Activities of Endogenous Silencing Small RNAs in *Arabidopsis*. *Annu. Rev. Plant Biol.* **2014**, *65*, 473–503. [[CrossRef](#)]
22. Szczepanska, A.; Wojnicka, M.; Kurzynska-Kokorniak, A. The Significance of the DUF283 Domain for the Activity of Human Ribonuclease Dicer. *Int. J. Mol. Sci.* **2021**, *22*, 8690. [[CrossRef](#)] [[PubMed](#)]
23. Qin, H.; Chen, F.; Huan, X.; Machida, S.; Song, J.; Yuan, Y.A. Structure of the *Arabidopsis thaliana* DCL4 DUF283 domain reveals a noncanonical double-stranded RNA-binding fold for protein–protein interaction. *RNA* **2010**, *16*, 474–481. [[CrossRef](#)] [[PubMed](#)]
24. Welker, N.C.; Pavelec, D.M.; Nix, D.A.; Duchaine, T.F.; Kennedy, S.; Bass, B.L. Dicer’s helicase domain is required for accumulation of some, but not all, *C. elegans* endogenous siRNAs. *RNA* **2010**, *16*, 893–903. [[CrossRef](#)] [[PubMed](#)]
25. Xie, M.; Zhang, S.; Yu, B. microRNA biogenesis, degradation and activity in plants. *Experientia* **2014**, *72*, 87–99. [[CrossRef](#)] [[PubMed](#)]
26. Wei, X.; Ke, H.; Wen, A.; Gao, B.; Shi, J.; Feng, Y. Structural basis of microRNA processing by Dicer-like 1. *Nat. Plants* **2021**, *7*, 1389–1396. [[CrossRef](#)]
27. Xie, D.; Chen, M.; Niu, J.; Wang, L.; Li, Y.; Fang, X.; Li, P.; Qi, Y. Phase separation of SERRATE drives dicing body assembly and promotes miRNA processing in *Arabidopsis*. *Nat. Cell Biol.* **2020**, *23*, 32–39. [[CrossRef](#)] [[PubMed](#)]
28. Li, M.; Yu, H.; Liu, K.; Yang, W.; Zhou, B.; Gan, L.; Li, S.; Zhang, C.; Yu, B. Serrate-Associated Protein 1, a splicing-related protein, promotes miRNA biogenesis in *Arabidopsis*. *New Phytol.* **2021**, *232*, 1959–1973. [[CrossRef](#)] [[PubMed](#)]
29. Willmann, M.R.; Mehalick, A.J.; Packer, R.L.; Jenik, P.D. MicroRNAs Regulate the Timing of Embryo Maturation in *Arabidopsis*. *Plant Physiol.* **2011**, *155*, 1871–1884. [[CrossRef](#)] [[PubMed](#)]
30. Várallyay, E.; Válcózi, A.; Agyi, A.; Burgyán, J.; Havelda, Z. Plant virus-mediated induction of miR168 is associated with repression of ARGONAUTE1 accumulation. *EMBO J.* **2010**, *29*, 3507–3519. [[CrossRef](#)]

31. Shivaprasad, P.V.; Chen, H.-M.; Patel, K.; Bond, D.; Santos, B.; Baulcombe, D.C. A MicroRNA Superfamily Regulates Nucleotide Binding Site–Leucine-Rich Repeats and Other mRNAs. *Plant Cell* **2012**, *24*, 859–874. [[CrossRef](#)]
32. Li, F.; Pignatta, D.; Bendix, C.; Brunkard, J.; Cohn, M.M.; Tung, J.; Sun, H.; Kumar, P.; Baker, B. MicroRNA regulation of plant innate immune receptors. *Proc. Natl. Acad. Sci. USA* **2012**, *109*, 1790–1795. [[CrossRef](#)] [[PubMed](#)]
33. Blevins, T.; Rajeswaran, R.; Shivaprasad, P.V.; Beknazariants, D.; Ammour, A.S.; Park, H.-S.; Vazquez, F.; Robertson, D.; Meins, F.; Hohn, T.; et al. Four plant Dicers mediate viral small RNA biogenesis and DNA virus induced silencing. *Nucleic Acids Res.* **2006**, *34*, 6233–6246. [[CrossRef](#)] [[PubMed](#)]
34. Laubinger, S.; Zeller, G.; Henz, S.R.; Buechel, S.; Sachsenberg, T.; Wang, J.-W.; Ratsch, G.; Weigel, D. Global effects of the small RNA biogenesis machinery on the Arabidopsis thaliana transcriptome. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 17466–17473. [[CrossRef](#)] [[PubMed](#)]
35. Xie, Z.; Johansen, L.K.; Gustafson, A.M.; Kasschau, K.D.; Lellis, A.D.; Zilberman, D.; Jacobsen, S.E.; Carrington, J.C. Genetic and Functional Diversification of Small RNA Pathways in Plants. *PLoS Biol.* **2004**, *2*, e104. [[CrossRef](#)] [[PubMed](#)]
36. Borsani, O.; Zhu, J.; Verslues, P.E.; Sunkar, R.; Zhu, J.-K. Endogenous siRNAs Derived from a Pair of Natural cis-Antisense Transcripts Regulate Salt Tolerance in Arabidopsis. *Cell* **2005**, *123*, 1279–1291. [[CrossRef](#)]
37. Qin, C.; Li, B.; Fan, Y.; Zhang, X.; Yu, Z.; Ryabov, E.; Zhao, M.; Wang, H.; Shi, N.; Zhang, P.; et al. Roles of Dicer-Like Proteins 2 and 4 in Intra- and Intercellular Antiviral Silencing. *Plant Physiol.* **2017**, *174*, 1067–1081. [[CrossRef](#)]
38. Zhang, X.; Zhu, Y.; Liu, X.; Hong, X.; Xu, Y.; Zhu, P.; Shen, Y.; Wu, H.; Ji, Y.; Wen, X.; et al. Suppression of endogenous gene silencing by bidirectional cytoplasmic RNA decay in Arabidopsis. *Science* **2015**, *348*, 120–123. [[CrossRef](#)]
39. Wu, H.; Li, B.; Iwakawa, H.-O.; Pan, Y.; Tang, X.; Ling-Hu, Q.; Liu, Y.; Sheng, S.; Feng, L.; Zhang, H.; et al. Plant 22-nt siRNAs mediate translational repression and stress adaptation. *Nature* **2020**, *581*, 89–93. [[CrossRef](#)]
40. Wang, T.; Deng, Z.; Zhang, X.; Wang, H.; Wang, Y.; Liu, X.; Liu, S.; Xu, F.; Li, T.; Fu, D.; et al. Tomato DCL2b is required for the biosynthesis of 22-nt small RNAs, the resulting secondary siRNAs, and the host defense against ToMV. *Hortic. Res.* **2018**, *5*, 1–14. [[CrossRef](#)]
41. Henderson, I.; Zhang, X.; Lu, C.; Johnson, L.; Meyers, B.; Green, P.J.; Jacobsen, S.E. Dissecting Arabidopsis thaliana DICER function in small RNA processing, gene silencing and DNA methylation patterning. *Nat. Genet.* **2006**, *38*, 721–725. [[CrossRef](#)] [[PubMed](#)]
42. Wang, Q.; Xue, Y.; Zhang, L.; Zhong, Z.; Feng, S.; Wang, C.; Xiao, L.; Yang, Z.; Harris, C.J.; Wu, Z.; et al. Mechanism of siRNA production by a plant Dicer-RNA complex in dicing-competent conformation. *Science* **2021**, *374*, 1152–1157. [[CrossRef](#)] [[PubMed](#)]
43. Matzke, M.; Kanno, T.; Daxinger, L.; Huettel, B.; Matzke, A.J. RNA-mediated chromatin-based silencing in plants. *Curr. Opin. Cell Biol.* **2009**, *21*, 367–376. [[CrossRef](#)]
44. Matzke, M.A.; Kanno, T.; Matzke, A.J. RNA-Directed DNA Methylation: The Evolution of a Complex Epigenetic Pathway in Flowering Plants. *Annu. Rev. Plant Biol.* **2015**, *66*, 243–267. [[CrossRef](#)]
45. Hua, X.; Berkowitz, N.; Willmann, M.; Yu, X.; Lyons, E.; Gregory, B. Global Analysis of RNA-Dependent RNA Polymerase-Dependent Small RNAs Reveals New Substrates and Functions for These Proteins and SGS3 in Arabidopsis. *Non-Coding RNA* **2021**, *7*, 28. [[CrossRef](#)] [[PubMed](#)]
46. Matzke, M.A.; Mosher, R. RNA-directed DNA methylation: An epigenetic pathway of increasing complexity. *Nat. Rev. Genet.* **2014**, *15*, 394–408. [[CrossRef](#)] [[PubMed](#)]
47. Raja, P.; Jackel, J.N.; Li, S.; Heard, I.M.; Bisaro, D.M. Arabidopsis Double-Stranded RNA Binding Protein DRB3 Participates in Methylation-Mediated Defense against Geminiviruses. *J. Virol.* **2013**, *88*, 2611–2622. [[CrossRef](#)]
48. Xie, Z.; Allen, E.; Wilken, A.; Carrington, J.C. DICER-LIKE 4 functions in trans-acting small interfering RNA biogenesis and vegetative phase change in Arabidopsis thaliana. *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 12984–12989. [[CrossRef](#)]
49. Kakiyama, S.; Tabara, M.; Nishibori, Y.; Moriyama, H.; Fukuhara, T. Long DCL4-substrate dsRNAs efficiently induce RNA interference in plant cells. *Sci. Rep.* **2019**, *9*, 6920. [[CrossRef](#)]
50. D’Ario, M.; Griffiths-Jones, S.; Kim, M. Small RNAs: Big Impact on Plant Development. *Trends Plant Sci.* **2017**, *22*, 1056–1068. [[CrossRef](#)]
51. Gascioli, V.; Mallory, A.C.; Bartel, D.P.; Vaucheret, H. Partially Redundant Functions of Arabidopsis DICER-like Enzymes and a Role for DCL4 in Producing trans-Acting siRNAs. *Curr. Biol.* **2005**, *15*, 1494–1500. [[CrossRef](#)] [[PubMed](#)]
52. Liu, B.; Chen, Z.; Song, X.; Liu, C.; Cui, X.; Zhao, X.; Fang, J.; Xu, W.; Zhang, H.; Wang, X.; et al. Oryza sativa Dicer-like4 Reveals a Key Role for Small Interfering RNA Silencing in Plant Development. *Plant Cell* **2007**, *19*, 2705–2718. [[CrossRef](#)]
53. Wu, Y.-Y.; Hou, B.H.; Lee, W.-C.; Lu, S.-H.; Yang, C.-J.; Vaucheret, H.; Chen, H.-M. DCL2- and RDR6-dependent transitive silencing of SMXL4 and SMXL5 in Arabidopsis dcl4 mutants causes defective phloem transport and carbohydrate over-accumulation. *Plant J.* **2017**, *90*, 1064–1078. [[CrossRef](#)]
54. Jiang, N.; Gutierrez-Diaz, A.; Mukundi, E.; Lee, Y.S.; Meyers, B.C.; Otegui, M.S.; Grotewold, E. Synergy between the anthocyanin and RDR6/SGS3/DCL4 siRNA pathways expose hidden features of Arabidopsis carbon metabolism. *Nat. Commun.* **2020**, *11*, 1–13. [[CrossRef](#)]
55. Deleris, A.; Gallego-Bartolome, J.; Bao, J.; Kasschau, K.D.; Carrington, J.C.; Voinnet, O. Hierarchical Action and Inhibition of Plant Dicer-Like Proteins in Antiviral Defense. *Science* **2006**, *313*, 68–71. [[CrossRef](#)] [[PubMed](#)]

56. Wang, X.-B.; Jovel, J.; Udomporn, P.; Wang, Y.; Wu, Q.; Li, W.-X.; Gascioli, V.; Vaucheret, H.; Ding, S.-W. The 21-Nucleotide, but Not 22-Nucleotide, Viral Secondary Small Interfering RNAs Direct Potent Antiviral Defense by Two Cooperative Argonautes in *Arabidopsis thaliana*. *Plant Cell* **2011**, *23*, 1625–1638. [[CrossRef](#)] [[PubMed](#)]
57. Bouché, N.; Laressergues, D.; Gascioli, V.; Vaucheret, H. An antagonistic function for *Arabidopsis* DCL2 in development and a new function for DCL4 in generating viral siRNAs. *EMBO J.* **2006**, *25*, 3347–3356. [[CrossRef](#)] [[PubMed](#)]
58. Diaz-Pendon, J.; Li, F.; Li, W.-X.; Ding, S.-W. Suppression of Antiviral Silencing by Cucumber Mosaic Virus 2b Protein in *Arabidopsis* Is Associated with Drastically Reduced Accumulation of Three Classes of Viral Small Interfering RNAs. *Plant Cell* **2007**, *19*, 2053–2063. [[CrossRef](#)]
59. Katsarou, K.; Mavrothalassiti, E.; Dermauw, W.; Van Leeuwen, T.; Kalantidis, K. Combined Activity of DCL2 and DCL3 Is Crucial in the Defense against Potato Spindle Tuber Viroid. *PLoS Pathog.* **2016**, *12*, e1005936. [[CrossRef](#)]
60. Nakazawa, Y.; Hiraguri, A.; Moriyama, H.; Fukuhara, T. The dsRNA-binding protein DRB4 interacts with the Dicer-like protein DCL4 in vivo and functions in the trans-acting siRNA pathway. *Plant Mol. Biol.* **2007**, *63*, 777–785. [[CrossRef](#)]
61. Fukudome, A.; Fukuhara, T. Plant dicer-like proteins: Double-stranded RNA-cleaving enzymes for small RNA biogenesis. *J. Plant Res.* **2016**, *130*, 33–44. [[CrossRef](#)]
62. Johnston, D.S.; Brown, N.H.; Gall, J.G.; Jantsch, M. A conserved double-stranded RNA-binding domain. *Proc. Natl. Acad. Sci. USA* **1992**, *89*, 10979–10983. [[CrossRef](#)] [[PubMed](#)]
63. Rytter, J.M.; Schultz, S.C. Molecular basis of double-stranded RNA-protein interactions: Structure of a dsRNA-binding domain complexed with dsRNA. *EMBO J.* **1998**, *17*, 7505–7513. [[CrossRef](#)] [[PubMed](#)]
64. Han, M.-H.; Goud, S.; Song, L.; Fedoroff, N. The *Arabidopsis* double-stranded RNA-binding protein HYL1 plays a role in microRNA-mediated gene regulation. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 1093–1098. [[CrossRef](#)] [[PubMed](#)]
65. Hiraguri, A.; Itoh, R.; Kondo, N.; Nomura, Y.; Aizawa, D.; Murai, Y.; Koiwa, H.; Seki, M.; Shinozaki, K.; Fukuhara, T. Specific interactions between Dicer-like proteins and HYL1/DRB- family dsRNA-binding proteins in *Arabidopsis thaliana*. *Plant Mol. Biol.* **2005**, *57*, 173–188. [[CrossRef](#)]
66. Vazquez, F.; Gascioli, V.; Crété, P.; Vaucheret, H. The Nuclear dsRNA Binding Protein HYL1 Is Required for MicroRNA Accumulation and Plant Development, but Not Posttranscriptional Transgene Silencing. *Curr. Biol.* **2004**, *14*, 346–351. [[CrossRef](#)]
67. Jakubiec, A.; Yang, S.W.; Chua, N.-H. *Arabidopsis* DRB4 protein in antiviral defense against Turnip yellow mosaic virus infection. *Plant J.* **2011**, *69*, 14–25. [[CrossRef](#)]
68. Incarbone, M.; Clavel, M.; Monsion, B.; Kuhn, L.; Scheer, H.; Vantard, É.; Poignavent, V.; Dunoyer, P.; Genschik, P.; Ritzenthaler, C. Immunocapture of dsRNA-bound proteins provides insight into Tobacco rattle virus replication complexes and reveals *Arabidopsis* DRB2 to be a wide-spectrum antiviral effector. *Plant Cell* **2021**, *33*, 3402–3420. [[CrossRef](#)]
69. Qu, F. Antiviral Role of Plant-Encoded RNA-Dependent RNA Polymerases Revisited with Deep Sequencing of Small Interfering RNAs of Virus Origin. *Mol. Plant-Microbe Interact.* **2010**, *23*, 1248–1252. [[CrossRef](#)]
70. Borges, F.; Martienssen, R.A. The expanding world of small RNAs in plants. *Nat. Rev. Mol. Cell Biol.* **2015**, *16*, 727–741. [[CrossRef](#)]
71. Wassenegger, M.; Krczal, G. Nomenclature and functions of RNA-directed RNA polymerases. *Trends Plant Sci.* **2006**, *11*, 142–151. [[CrossRef](#)] [[PubMed](#)]
72. Cao, M.; Du, P.; Wang, X.-B.; Yu, Y.-Q.; Qiu, Y.-H.; Li, W.; Gal-On, A.; Zhou, C.; Li, Y.; Ding, S.-W. Virus infection triggers widespread silencing of host genes by a distinct class of endogenous siRNAs in *Arabidopsis*. *Proc. Natl. Acad. Sci. USA* **2014**, *111*, 14613–14618. [[CrossRef](#)] [[PubMed](#)]
73. Li, S.; Zhang, Z.; Zhou, C.; Li, S. RNA-dependent RNA polymerase 1 delays the accumulation of viroids in infected plants. *Mol. Plant Pathol.* **2021**, *22*, 1195–1208. [[CrossRef](#)] [[PubMed](#)]
74. Xie, Z.; Fan, B.; Chen, C.; Chen, Z. An important role of an inducible RNA-dependent RNA polymerase in plant antiviral defense. *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 6516–6521. [[CrossRef](#)]
75. Liu, C.; Shen, Y.; Qin, B.; Wen, H.; Cheng, J.; Mao, F.; Shi, W.; Tang, D.; Du, G.; Li, Y.; et al. *Oryza sativa* RNA-Dependent RNA Polymerase 6 Contributes to Double-Strand Break Formation in Meiosis. *Plant Cell* **2020**, *32*, 3273–3289. [[CrossRef](#)]
76. Hong, W.; Qian, D.; Sun, R.; Jiang, L.; Wang, Y.; Wei, C.; Zhang, Z.; Li, Y. OsRDR6 plays role in host defense against double-stranded RNA virus, Rice Dwarf Phytoreovirus. *Sci. Rep.* **2015**, *5*, 11324. [[CrossRef](#)]
77. Mourrain, P.; Béclin, C.; Elmayan, T.; Feuerbach, F.; Godon, C.; Morel, J.-B.; Jouette, D.; Lacombe, A.-M.; Nikic, S.; Picault, N.; et al. *Arabidopsis* SGS2 and SGS3 Genes Are Required for Posttranscriptional Gene Silencing and Natural Virus Resistance. *Cell* **2000**, *101*, 533–542. [[CrossRef](#)]
78. Peragine, A.; Yoshikawa, M.; Wu, G.; Albrecht, H.L.; Poethig, R.S. SGS3 and SGS2/SDE1/RDR6 are required for juvenile development and the production of trans-acting siRNAs in *Arabidopsis*. *Genes Dev.* **2004**, *18*, 2368–2379. [[CrossRef](#)]
79. Fukunaga, R.; A Doudna, J. dsRNA with 5' overhangs contributes to endogenous and antiviral RNA silencing pathways in plants. *EMBO J.* **2009**, *28*, 545–555. [[CrossRef](#)]
80. Li, F.; Wang, Y.; Zhou, X. SGS3 Cooperates with RDR6 in Triggering Geminivirus-Induced Gene Silencing and in Suppressing Geminivirus Infection in *Nicotiana Benthamiana*. *Viruses* **2017**, *9*, 247. [[CrossRef](#)]
81. Willmann, M.R.; Endres, M.W.; Cook, R.T.; Gregory, B.D. The Functions of RNA-Dependent RNA Polymerases in *Arabidopsis*. *Arab. Book* **2011**, *9*, e0146. [[CrossRef](#)]
82. Dalmay, T.; Hamilton, A.; Rudd, S.; Angell, S.; Baulcombe, D.C. An RNA-dependent RNA polymerase gene in *Arabidopsis* is re-quired for posttranscriptional gene silencing mediated by a transgene but not by a virus. *Cell* **2000**, *101*, 543–553. [[CrossRef](#)]

83. Yoshikawa, M.; Han, Y.-W.; Fujii, H.; Aizawa, S.; Nishino, T.; Ishikawa, M. Cooperative recruitment of RDR6 by SGS3 and SDE5 during small interfering RNA amplification in Arabidopsis. *Proc. Natl. Acad. Sci. USA* **2021**, *118*. [[CrossRef](#)] [[PubMed](#)]
84. Boccarda, M.; Sarazin, A.; Thiébeauld, O.; Jay, F.; Voinnet, O.; Navarro, L.; Colot, V. The Arabidopsis miR472-RDR6 Silencing Pathway Modulates PAMP- and Effector-Triggered Immunity through the Post-transcriptional Control of Disease Resistance Genes. *PLoS Pathog.* **2014**, *10*, e1003883. [[CrossRef](#)] [[PubMed](#)]
85. Jiang, L.; Qian, D.; Zheng, H.; Meng, L.-Y.; Chen, J.; Le, W.-J.; Zhou, T.; Zhou, Y.-J.; Wei, C.-H.; Li, Y. RNA-dependent RNA polymerase 6 of rice (*Oryza sativa*) plays role in host defense against negative-strand RNA virus, Rice stripe virus. *Virus Res.* **2011**, *163*, 512–519. [[CrossRef](#)]
86. Mosher, R.; Schwach, F.; Studholme, D.; Baulcombe, D.C. PolIVb influences RNA-directed DNA methylation independently of its role in siRNA biogenesis. *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 3145–3150. [[CrossRef](#)] [[PubMed](#)]
87. Ronemus, M.; Vaughn, M.W.; Martienssen, R.A. MicroRNA-Targeted and Small Interfering RNA-Mediated mRNA Degradation Is Regulated by Argonaute, Dicer, and RNA-Dependent RNA Polymerase in Arabidopsis. *Plant Cell* **2006**, *18*, 1559–1574. [[CrossRef](#)]
88. Huang, K.; Wu, X.-X.; Fang, C.-L.; Xu, Z.-G.; Zhang, H.-W.; Gao, J.; Zhou, C.-M.; You, L.-L.; Gu, Z.-X.; Mu, W.-H.; et al. Pol IV and RDR2: A two-RNA-polymerase machine that produces double-stranded RNA. *Science* **2021**, *374*, 1579–1586. [[CrossRef](#)]
89. Li, C.F.; Pontes, O.; El-Shami, M.; Henderson, I.; Bernatavichute, Y.V.; Chan, S.W.-L.; Lagrange, T.; Pikaard, C.; Jacobsen, S.E. An ARGONAUTE4-Containing Nuclear Processing Center Colocalized with Cajal Bodies in Arabidopsis thaliana. *Cell* **2006**, *126*, 93–106. [[CrossRef](#)]
90. Chellappan, P.; Xia, J.; Zhou, X.; Gao, S.; Zhang, X.; Coutino, G.; Vazquez, F.; Zhang, W.; Jin, H. siRNAs from miRNA sites mediate DNA methylation of target genes. *Nucleic Acids Res.* **2010**, *38*, 6883–6894. [[CrossRef](#)]
91. Pontier, D.; Picart, C.; Roudier, F.; Garcia, D.; Lahmy, S.; Azevedo, J.; Alart, E.; Laudié, M.; Karlowski, W.M.; Cooke, R.; et al. NERD, a Plant-Specific GW Protein, Defines an Additional RNAi-Dependent Chromatin-Based Pathway in Arabidopsis. *Mol. Cell* **2012**, *48*, 121–132. [[CrossRef](#)] [[PubMed](#)]
92. Stroud, H.; Greenberg, M.; Feng, S.; Bernatavichute, Y.V.; Jacobsen, S.E. Comprehensive Analysis of Silencing Mutants Reveals Complex Regulation of the Arabidopsis Methylome. *Cell* **2013**, *152*, 352–364. [[CrossRef](#)] [[PubMed](#)]
93. Guo, Z.; Wang, X.-B.; Li, W.-X.; Ding, S.-W. A Sensitized Genetic Screen to Identify Novel Components and Regulators of the Host Antiviral RNA Interference Pathway. In *Antiviral Resistance in Plants*; Humana: New York, NY, USA, 2019; Volume 2028, pp. 215–229. [[CrossRef](#)]
94. Zhu, B.; Gao, H.; Xu, G.; Wu, D.; Song, S.; Jiang, H.; Zhu, S.; Qi, T.; Xie, D. Arabidopsis ALA1 and ALA2 Mediate RNAi-Based Antiviral Immunity. *Front. Plant Sci.* **2017**, *8*, 422. [[CrossRef](#)] [[PubMed](#)]
95. Guo, Z.; Wang, X.-B.; Wang, Y.; Li, W.-X.; Gal-On, A.; Ding, S.-W. Identification of a New Host Factor Required for Antiviral RNAi and Amplification of Viral siRNAs. *Plant Physiol.* **2017**, *176*, 1587–1597. [[CrossRef](#)] [[PubMed](#)]
96. Gao, H.; Yang, M.; Yang, H.; Qin, Y.; Zhu, B.; Xu, G.; Xie, C.; Wu, D.; Zhang, X.; Li, W.; et al. Arabidopsis ENOR3 regulates RNAi-mediated antiviral defense. *J. Genet. Genom.* **2017**, *45*, 33–40. [[CrossRef](#)]
97. Wang, Y.; Gong, Q.; Wu, Y.; Huang, F.; Ismayil, A.; Zhang, D.; Li, H.; Gu, H.; Ludman, M.; Fátýol, K.; et al. A calmodulin-binding transcription factor links calcium signaling to antiviral RNAi defense in plants. *Cell Host Microbe* **2021**, *29*, 1393–1406.e7. [[CrossRef](#)]
98. Fang, X.; Qi, Y. RNAi in Plants: An Argonaute-Centered View. *Plant Cell* **2016**, *28*, 272–285. [[CrossRef](#)]
99. Ramesh, S.V.; Yogindran, S.; Gnanasekaran, P.; Chakraborty, S.; Winter, S.; Pappu, H.R. Virus and Viroid-Derived Small RNAs as Modulators of Host Gene Expression: Molecular Insights Into Pathogenesis. *Front. Microbiol.* **2021**, *11*, 614231. [[CrossRef](#)]
100. Carbonell, A.; Carrington, J.C. Antiviral roles of plant ARGONAUTES. *Curr. Opin. Plant Biol.* **2015**, *27*, 111–117. [[CrossRef](#)]
101. Zhang, H.; Xia, R.; Meyers, B.C.; Walbot, V. Evolution, functions, and mysteries of plant ARGONAUTE proteins. *Curr. Opin. Plant Biol.* **2015**, *27*, 84–90. [[CrossRef](#)]
102. Carbonell, A. Plant ARGONAUTES: Features, Functions, and Unknowns. *Plant Argon. Proteins* **2017**, *1640*, 1–21. [[CrossRef](#)]
103. Ma, Z.; Zhang, X. Actions of plant Argonautes: Predictable or unpredictable? *Curr. Opin. Plant Biol.* **2018**, *45*, 59–67. [[CrossRef](#)] [[PubMed](#)]
104. Tolia, N.; Joshua-Tor, L. Slicer and the Argonautes. *Nat. Chem. Biol.* **2006**, *3*, 36–43. [[CrossRef](#)] [[PubMed](#)]
105. Silva-Martins, G.; Bolaji, A.; Moffett, P. What does it take to be antiviral? An Argonaute-centered perspective on plant antiviral defense. *J. Exp. Bot.* **2020**, *71*, 6197–6210. [[CrossRef](#)] [[PubMed](#)]
106. Wang, Y.; Juranek, S.; Li, H.; Sheng, G.; Wardle, G.S.; Tuschl, T.; Patel, D.J. Nucleation, propagation and cleavage of target RNAs in Ago silencing complexes. *Nature* **2009**, *461*, 754–761. [[CrossRef](#)]
107. Mallory, A.; Vaucheret, H. Form, Function, and Regulation of ARGONAUTE Proteins. *Plant Cell* **2010**, *22*, 3879–3889. [[CrossRef](#)] [[PubMed](#)]
108. Song, J.-J.; Smith, S.K.; Hannon, G.J.; Joshua-Tor, L. Crystal Structure of Argonaute and Its Implications for RISC Slicer Activity. *Science* **2004**, *305*, 1434–1437. [[CrossRef](#)]
109. Derrien, B.; Clavel, M.; Baumberger, N.; Iki, T.; Sarazin, A.; Hacquard, T.; Ponce, M.R.; Ziegler-Graff, V.; Vaucheret, H.; Micol, J.L.; et al. A Suppressor Screen for AGO1 Degradation by the Viral F-Box P0 Protein Uncovers a Role for AGO DUF1785 in sRNA Duplex Unwinding. *Plant Cell* **2018**, *30*, 1353–1374. [[CrossRef](#)]
110. Vaucheret, H. Plant ARGONAUTES. *Trends Plant Sci.* **2008**, *13*, 350–358. [[CrossRef](#)]

111. Bai, M.; Yang, G.-S.; Chen, W.-T.; Mao, Z.-C.; Kang, H.-X.; Chen, G.-H.; Yang, Y.-H.; Xie, B.-Y. Genome-wide identification of Dicer-like, Argonaute and RNA-dependent RNA polymerase gene families and their expression analyses in response to viral infection and abiotic stresses in *Solanum lycopersicum*. *Gene* **2012**, *501*, 52–62. [[CrossRef](#)]
112. Xian, Z.; Yang, Y.; Huang, W.; Tang, N.; Wang, X.; Li, Z. Molecular cloning and characterisation of SLAGO family in tomato. *BMC Plant Biol.* **2013**, *13*, 126. [[CrossRef](#)] [[PubMed](#)]
113. Kapoor, M.; Arora, R.; Lama, T.; Nijhawan, A.; Khurana, J.P.; Tyagi, A.K.; Kapoor, S. Genome-wide identification, organization and phylogenetic analysis of Dicer-like, Argonaute and RNA-dependent RNA Polymerase gene families and their expression analysis during reproductive development and stress in rice. *BMC Genom.* **2008**, *9*, 451. [[CrossRef](#)]
114. Baumberger, N.; Baulcombe, D.C. Arabidopsis ARGONAUTE1 is an RNA Slicer that selectively recruits microRNAs and short interfering RNAs. *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 11928–11933. [[CrossRef](#)] [[PubMed](#)]
115. Rogers, K.; Chen, X. Biogenesis, Turnover, and Mode of Action of Plant MicroRNAs. *Plant Cell* **2013**, *25*, 2383–2399. [[CrossRef](#)] [[PubMed](#)]
116. Wang, W.; Ye, R.; Xin, Y.; Fang, X.; Li, C.; Shi, H.; Zhou, X.; Qi, Y. An Importin  $\beta$  Protein Negatively Regulates MicroRNA Activity in Arabidopsis. *Plant Cell* **2011**, *23*, 3565–3576. [[CrossRef](#)] [[PubMed](#)]
117. Bologna, N.G.; Iselin, R.; Abriata, L.A.; Sarazin, A.; Pumplin, N.; Jay, F.; Grentzinger, T.; Dal Peraro, M.; Voinnet, O. Nucleocytoplasmic Shuttling of ARGONAUTE1 Prompts a Revised Model of the Plant MicroRNA Pathway. *Mol. Cell* **2018**, *69*, 709–719.e5. [[CrossRef](#)]
118. Trolet, A.; Baldrich, P.; Criqui, M.-C.; Dubois, M.; Clavel, M.; Meyers, B.C.; Genschik, P. Cell Cycle-Dependent Regulation and Function of ARGONAUTE1 in Plants. *Plant Cell* **2019**, *31*, 1734–1750. [[CrossRef](#)]
119. Li, S.; Liu, L.; Zhuang, X.; Yu, Y.; Liu, X.; Cui, X.; Ji, L.; Pan, Z.; Cao, X.; Mo, B.; et al. MicroRNAs Inhibit the Translation of Target mRNAs on the Endoplasmic Reticulum in Arabidopsis. *Cell* **2013**, *153*, 562–574. [[CrossRef](#)]
120. Michaeli, S.; Clavel, M.; Lechner, E.; Viotti, C.; Wu, J.; Dubois, M.; Hacquard, T.; Derrien, B.; Izquierdo, E.; Lecorbeiller, M.; et al. The viral F-box protein P0 induces an ER-derived autophagy degradation pathway for the clearance of membrane-bound AGO1. *Proc. Natl. Acad. Sci. USA* **2019**, *116*, 22872–22883. [[CrossRef](#)]
121. Bajczyk, M.; Bhat, S.S.; Szewc, L.; Szweykowska-Kulinska, Z.; Jarmolowski, A.; Dolata, J. Novel Nuclear Functions of Arabidopsis ARGONAUTE1: Beyond RNA Interference. *Plant Physiol.* **2019**, *179*, 1030–1039. [[CrossRef](#)]
122. Wang, T.; Zheng, Y.; Tang, Q.; Zhong, S.; Su, W.; Zheng, B. Brassinosteroids inhibit miRNA-mediated translational repression by decreasing AGO1 on the endoplasmic reticulum. *J. Integr. Plant Biol.* **2021**, *63*, 1475–1490. [[CrossRef](#)] [[PubMed](#)]
123. Morel, J.-B.; Godon, C.; Mourrain, P.; Béclin, C.; Boutet, S.; Feuerbach, F.; Proux, F.; Vaucheret, H. Fertile Hypomorphic ARGONAUTE (ago1) Mutants Impaired in Post-Transcriptional Gene Silencing and Virus Resistance. *Plant Cell* **2002**, *14*, 629–639. [[CrossRef](#)]
124. Takeda, A.; Iwasaki, S.; Watanabe, T.; Utsumi, M.; Watanabe, Y. The Mechanism Selecting the Guide Strand from Small RNA Duplexes is Different Among Argonaute Proteins. *Plant Cell Physiol.* **2008**, *49*, 493–500. [[CrossRef](#)]
125. Garcia-Ruiz, H.; Carbonell, A.; Hoyer, J.S.; Fahlgren, N.; Gilbert, K.; Takeda, A.; Giampetruzzi, A.; Ruiz, M.T.G.; McGinn, M.G.; Lowery, N.V.; et al. Roles and Programming of Arabidopsis ARGONAUTE Proteins during Turnip Mosaic Virus Infection. *PLoS Pathog.* **2015**, *11*, e1004755. [[CrossRef](#)]
126. Jaubert, M.; Bhattacharjee, S.; Mello, A.F.; Perry, K.L.; Moffett, P. ARGONAUTE2 Mediates RNA-Silencing Antiviral Defenses against Potato virus X in Arabidopsis. *Plant Physiol.* **2011**, *156*, 1556–1564. [[CrossRef](#)] [[PubMed](#)]
127. Carbonell, A.; Fahlgren, N.; Garcia-Ruiz, H.; Gilbert, K.; Montgomery, T.; Nguyen, T.; Cuperus, J.; Carrington, J.C. Functional Analysis of Three Arabidopsis ARGONAUTES Using Slicer-Defective Mutants. *Plant Cell* **2012**, *24*, 3613–3629. [[CrossRef](#)] [[PubMed](#)]
128. Brosseau, C.; Bolaji, A.; Roussin-Léveillé, C.; Zhao, Z.; Biga, S.; Moffett, P. Natural variation in the Arabidopsis AGO2 gene is associated with susceptibility to potato virus X. *New Phytol.* **2019**, *226*, 866–878. [[CrossRef](#)] [[PubMed](#)]
129. Zhang, X.; Zhao, H.; Gao, S.; Wang, W.-C.; Katiyar-Agarwal, S.; Huang, H.-D.; Raikhel, N.; Jin, H. Arabidopsis Argonaute 2 Regulates Innate Immunity via miRNA393\*-Mediated Silencing of a Golgi-Localized SNARE Gene, MEMB12. *Mol. Cell* **2011**, *42*, 356–366. [[CrossRef](#)]
130. Duan, C.-G.; Zhang, H.; Tang, K.; Zhu, X.; Qian, W.; Hou, Y.-J.; Wang, B.; Lang, Z.; Zhao, Y.; Wang, X.; et al. Specific but interdependent functions for Arabidopsis AGO 4 and AGO 6 in RNA-directed DNA methylation. *EMBO J.* **2014**, *34*, 581–592. [[CrossRef](#)]
131. Olmedo-Monfil, V.; Duran-Figueroa, N.; Arteaga-Vazquez, M.A.; Demesa-Arevalo, E.; Autran, D.; Grimanelli, D.; Slotkin, R.K.; Martienssen, R.A.; Vielle-Calzada, J.-P. Control of female gamete formation by a small RNA pathway in Arabidopsis. *Nature* **2010**, *464*, 628–632. [[CrossRef](#)]
132. Zheng, X.; Fahlgren, N.; Abbasi, A.; Berry, J.C.; Carrington, J.C. Antiviral ARGONAUTES Against Turnip Crinkle Virus Revealed by Image-Based Trait Analysis. *Plant Physiol.* **2019**, *180*, 1418–1435. [[CrossRef](#)] [[PubMed](#)]
133. Alazem, M.; He, M.-H.; Moffett, P.; Lin, N.-S. Abscisic Acid Induces Resistance against Bamboo Mosaic Virus through Argonaute2 and 3. *Plant Physiol.* **2017**, *174*, 339–355. [[CrossRef](#)] [[PubMed](#)]
134. Marie-Claude, N.; Nicole, M.-C.; Meteignier, L.-V.; Hong, N.; Wang, G.; Moffett, P. Different roles for RNA silencing and RNA processing components in virus recovery and virus-induced gene silencing in plants. *J. Exp. Bot.* **2014**, *66*, 919–932. [[CrossRef](#)]

135. Brosseau, C.; El Oirdi, M.; Adurogbangba, A.; Ma, X.; Moffett, P. Antiviral Defense Involves AGO4 in an Arabidopsis–Potexvirus Interaction. *Mol. Plant-Microbe Interact.* **2016**, *29*, 878–888. [[CrossRef](#)] [[PubMed](#)]
136. Brosseau, C.; Moffett, P. Functional and Genetic Analysis Identify a Role for Arabidopsis ARGONAUTE5 in Antiviral RNA Silencing. *Plant Cell* **2015**, *27*, 1742–1754. [[CrossRef](#)]
137. Allen, E.; Xie, Z.; Gustafson, A.M.; Carrington, J.C. microRNA-Directed Phasing during Trans-Acting siRNA Biogenesis in Plants. *Cell* **2005**, *121*, 207–221. [[CrossRef](#)]
138. Zhu, H.; Hu, F.; Wang, R.; Zhou, X.; Sze, S.-H.; Liou, L.W.; Barefoot, A.; Dickman, M.; Zhang, X. Arabidopsis Argonaute10 Specifically Sequesters miR166/165 to Regulate Shoot Apical Meristem Development. *Cell* **2011**, *145*, 242–256. [[CrossRef](#)]
139. Yang, Z.; Huang, Y.; Yang, J.; Yao, S.; Zhao, K.; Wang, D.; Qin, Q.; Bian, Z.; Li, Y.; Lan, Y.; et al. Jasmonate Signaling Enhances RNA Silencing and Antiviral Defense in Rice. *Cell Host Microbe* **2020**, *28*, 89–103.e8. [[CrossRef](#)]
140. Wu, J.; Yang, Z.; Wang, Y.; Zheng, L.; Ye, R.; Ji, Y.; Zhao, S.; Ji, S.; Liu, R.; Xu, L.; et al. Viral-inducible Argonaute18 confers broad-spectrum virus resistance in rice by sequestering a host microRNA. *eLife* **2015**, *4*, e05733. [[CrossRef](#)]
141. Wu, J.; Yang, R.; Yang, Z.; Yao, S.; Zhao, S.; Wang, Y.; Li, P.; Song, X.; Jin, L.; Zhou, T.; et al. ROS accumulation and antiviral defence control by microRNA528 in rice. *Nat. Plants* **2017**, *3*, 16203. [[CrossRef](#)]
142. Díaz-Pendón, J.A.; Ding, S.-W. Direct and Indirect Roles of Viral Suppressors of RNA Silencing in Pathogenesis. *Annu. Rev. Phytopathol.* **2008**, *46*, 303–326. [[CrossRef](#)] [[PubMed](#)]
143. Pumplin, N.; Voinnet, O. RNA silencing suppression by plant pathogens: Defence, counter-defence and counter-counter-defence. *Nat. Rev. Genet.* **2013**, *11*, 745–760. [[CrossRef](#)] [[PubMed](#)]
144. Bucher, E.; Sijen, T.; de Haan, P.; Goldbach, R.; Prins, M. Negative-Strand Tospoviruses and Tenuviruses Carry a Gene for a Suppressor of Gene Silencing at Analogous Genomic Positions. *J. Virol.* **2003**, *77*, 1329–1336. [[CrossRef](#)] [[PubMed](#)]
145. Schnettler, E.; Hemmes, H.; Huismann, R.; Goldbach, R.; Prins, M.; Kormelink, R. Diverging Affinity of Tospovirus RNA Silencing Suppressor Proteins, NSs, for Various RNA Duplex Molecules. *J. Virol.* **2010**, *84*, 11542–11554. [[CrossRef](#)]
146. Goswami, S.; Sahana, N.; Pandey, V.; Doblaz, P.; Jain, R.; Palukaitis, P.; Canto, T.; Praveen, S. Interference in plant defense and development by non-structural protein NSs of Groundnut bud necrosis virus. *Virus Res.* **2011**, *163*, 368–373. [[CrossRef](#)]
147. Shen, M.; Xu, Y.; Jia, R.; Zhou, X.; Ye, K. Size-Independent and Noncooperative Recognition of dsRNA by the Rice Stripe Virus RNA Silencing Suppressor NS3. *J. Mol. Biol.* **2010**, *404*, 665–679. [[CrossRef](#)]
148. Zheng, L.; Zhang, C.; Shi, C.; Yang, Z.; Wang, Y.; Zhou, T.; Sun, F.; Wang, H.; Zhao, S.; Qin, Q.; et al. Rice stripe virus NS3 protein regulates primary miRNA processing through association with the miRNA biogenesis factor OsDRB1 and facilitates virus infection in rice. *PLoS Pathog.* **2017**, *13*, e1006662. [[CrossRef](#)]
149. Wang, Y.; Dang, M.; Hou, H.; Mei, Y.; Qian, Y.; Zhou, X. Identification of an RNA silencing suppressor encoded by a mastrevirus. *J. Gen. Virol.* **2014**, *95*, 2082–2088. [[CrossRef](#)]
150. Merai, Z.; Kerényi, Z.; Molnár, A.; Barta, E.; Válóczy, A.; Bisztray, G.; Havelda, Z.; Burgyán, J.; Silhavy, D. Aureusvirus P14 Is an Efficient RNA Silencing Suppressor That Binds Double-Stranded RNAs without Size Specificity. *J. Virol.* **2005**, *79*, 7217–7226. [[CrossRef](#)]
151. Merai, Z.; Kerényi, Z.; Kertész, S.; Magna, M.; Lakatos, L.; Silhavy, D. Double-Stranded RNA Binding May Be a General Plant RNA Viral Strategy To Suppress RNA Silencing. *J. Virol.* **2006**, *80*, 5747–5756. [[CrossRef](#)]
152. Zhang, X.; Dong, K.; Xu, K.; Zhang, K.; Jin, X.; Yang, M.; Zhang, Y.; Wang, X.; Han, C.; Yu, J.; et al. Barley stripe mosaic virus infection requires PKA-mediated phosphorylation of  $\gamma$ b for suppression of both RNA silencing and the host cell death response. *New Phytol.* **2018**, *218*, 1570–1585. [[CrossRef](#)] [[PubMed](#)]
153. Lakatos, L.; Csorba, T.; Pantaleo, V.; Chapman, E.J.; Carrington, J.; Liu, Y.-P.; Dolja, V.V.; Calvino, L.F.; Lopez-Moya, J.J.; Burgyán, J. Small RNA binding is a common strategy to suppress RNA silencing by several viral suppressors. *EMBO J.* **2006**, *25*, 2768–2780. [[CrossRef](#)] [[PubMed](#)]
154. Haas, G.; Azevedo, J.; Moissiard, G.; Geldreich, A.; Himber, C.; Bureau, M.; Fukuhara, T.; Keller, M.; Voinnet, O. Nuclear import of CaMV P6 is required for infection and suppression of the RNA silencing factor DRB4. *EMBO J.* **2008**, *27*, 2102–2112. [[CrossRef](#)] [[PubMed](#)]
155. Guo, H.; Song, X.; Xie, C.; Huo, Y.; Zhang, F.; Chen, X.; Geng, Y.; Fang, R. Rice yellow stunt rhabdovirus Protein 6 Suppresses Systemic RNA Silencing by Blocking RDR6-Mediated Secondary siRNA Synthesis. *Mol. Plant-Microbe Interact.* **2013**, *26*, 927–936. [[CrossRef](#)]
156. Varallyay, E.; Havelda, Z. Unrelated viral suppressors of RNA silencing mediate the control of ARGONAUTE1 level. *Mol. Plant Pathol.* **2013**, *14*, 567–575. [[CrossRef](#)]
157. Endres, M.W.; Gregory, B.D.; Gao, Z.; Foreman, A.W.; Mlotshwa, S.; Ge, X.; Pruss, G.J.; Ecker, J.R.; Bowman, L.H.; Vance, V. Two Plant Viral Suppressors of Silencing Require the Ethylene-Inducible Host Transcription Factor RAV2 to Block RNA Silencing. *PLoS Pathog.* **2010**, *6*, e1000729. [[CrossRef](#)]
158. Sanobar, N.; Lin, P.-C.; Pan, Z.-J.; Fang, R.-Y.; Tjita, V.; Chen, F.-F.; Wang, H.-C.; Tsai, H.-L.; Wu, S.-H.; Shen, T.-L.; et al. Investigating the Viral Suppressor HC-Pro Inhibiting Small RNA Methylation through Functional Comparison of HEN1 in Angiosperm and Bryophyte. *Viruses* **2021**, *13*, 1837. [[CrossRef](#)]
159. Jamous, R.; Boonrod, K.; Fuellgrabe, M.W.; Ali-Shtayeh, M.S.; Krczal, G.; Wassenegger, M. The helper component-proteinase of the Zucchini yellow mosaic virus inhibits the Hua Enhancer 1 methyltransferase activity in vitro. *J. Gen. Virol.* **2011**, *92*, 2222–2226. [[CrossRef](#)]

160. Ivanov, K.; Eskelin, K.; Bašić, M.; De, S.; Löhmus, A.; Varjosalo, M.; Mäkinen, K. Molecular insights into the function of the viral RNA silencing suppressor HCPro. *Plant J.* **2015**, *85*, 30–45. [[CrossRef](#)]
161. Del Toro, F.J.; Donaire, L.; Aguilar, E.; Chung, B.-N.; Tenllado, F.; Canto, T. Potato Virus Y HCPro Suppression of Antiviral Silencing in *Nicotiana benthamiana* Plants Correlates with Its Ability To Bind In Vivo to 21- and 22-Nucleotide Small RNAs of Viral Sequence. *J. Virol.* **2017**, *91*, e00367-17. [[CrossRef](#)]
162. Zhang, X.; Du, P.; Lu, L.; Xiao, Q.; Wang, W.; Cao, X.; Ren, B.; Wei, C.; Li, Y. Contrasting effects of HC-Pro and 2b viral suppressors from Sugarcane mosaic virus and Tomato aspermy cucumovirus on the accumulation of siRNAs. *Virology* **2008**, *374*, 351–360. [[CrossRef](#)]
163. Chapman, E.J.; Prokhnevsky, A.I.; Gopinath, K.; Dolja, V.V.; Carrington, J.C. Viral RNA silencing suppressors inhibit the microRNA pathway at an intermediate step. *Genes Dev.* **2004**, *18*, 1179–1186. [[CrossRef](#)] [[PubMed](#)]
164. Yu, B.; Chapman, E.J.; Yang, Z.; Carrington, J.; Chen, X. Transgenically expressed viral RNA silencing suppressors interfere with microRNA methylation in *Arabidopsis*. *FEBS Lett.* **2006**, *580*, 3117–3120. [[CrossRef](#)] [[PubMed](#)]
165. Vargason, J.M.; Szittyá, G.; Burguán, J.; Hall, T.M. Size Selective Recognition of siRNA by an RNA Silencing Suppressor. *Cell* **2003**, *115*, 799–811. [[CrossRef](#)]
166. Valli, A.; Martín-Hernández, A.M.; López-Moya, J.J.; García, J.A. RNA Silencing Suppression by a Second Copy of the P1 Serine Protease of Cucumber Vein Yellowing Ipomovirus, a Member of the Family Potyviridae That Lacks the Cysteine Protease HCPro. *J. Virol.* **2006**, *80*, 10055–10063. [[CrossRef](#)] [[PubMed](#)]
167. Giner, A.; Lakatos, L.; García-Chapa, M.; Lopez-Moya, J.J.; Burguán, J. Viral Protein Inhibits RISC Activity by Argonaute Binding through Conserved WG/GW Motifs. *PLoS Pathog.* **2010**, *6*, e1000996. [[CrossRef](#)]
168. Csorba, T.; Bovi, A.; Dalmay, T.; Burguán, J. The p122 Subunit of Tobacco Mosaic Virus Replicase Is a Potent Silencing Suppressor and Compromises both Small Interfering RNA- and MicroRNA-Mediated Pathways. *J. Virol.* **2007**, *81*, 11768–11780. [[CrossRef](#)] [[PubMed](#)]
169. Barón, M.P.B.; Delfosse, V.C.; Agrofoglio, Y.C.; Nahirñak, V.; Almasia, N.I.; Rovere, C.V.; Distéfano, A.J. Argentinian potato leafroll virus P0 protein: Novel activities for a previously known suppressor. *Plant Pathol.* **2020**, *70*, 259–274. [[CrossRef](#)]
170. Mangwende, T.; Wang, M.-L.; Borth, W.; Hu, J.; Moore, P.H.; Mirkov, T.E.; Albert, H.H. The P0 gene of Sugarcane yellow leaf virus encodes an RNA silencing suppressor with unique activities. *Virology* **2009**, *384*, 38–50. [[CrossRef](#)]
171. Cascardo, R.S.; Arantes, I.L.G.; Silva, T.F.; Sachetto-Martins, G.; Vaslin, M.F.S.; Corrêa, R.L. Function and diversity of P0 proteins among cotton leafroll dwarf virus isolates. *Virol. J.* **2015**, *12*, 1–10. [[CrossRef](#)]
172. Almasi, R.; Miller, W.A.; Ziegler-Graff, V. Mild and severe cereal yellow dwarf viruses differ in silencing suppressor efficiency of the P0 protein. *Virus Res.* **2015**, *208*, 199–206. [[CrossRef](#)] [[PubMed](#)]
173. Pazhouhandeh, M.; Dieterle, M.; Marrocco, K.; Lechner, E.; Berry, B.; Brault, V.R.; Hemmer, O.; Kretsch, T.; Richards, K.E.; Genschik, P.; et al. F-box-like domain in the polerovirus protein P0 is required for silencing suppressor function. *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 1994–1999. [[CrossRef](#)] [[PubMed](#)]
174. Bortolamiol, D.; Pazhouhandeh, M.; Marrocco, K.; Genschik, P.; Ziegler-Graff, V. The Polerovirus F Box Protein P0 Targets ARGONAUTE1 to Suppress RNA Silencing. *Curr. Biol.* **2007**, *17*, 1615–1621. [[CrossRef](#)] [[PubMed](#)]
175. Fusaro, A.F.; Correa, R.L.; Nakasugi, K.; Jackson, C.; Kawchuk, L.M.; Vaslin, M.F.; Waterhouse, P.M. The Enamovirus P0 protein is a silencing suppressor which inhibits local and systemic RNA silencing through AGO1 degradation. *Virology* **2012**, *426*, 178–187. [[CrossRef](#)]
176. Chiu, M.-H.; Chen, I.-H.; Baulcombe, D.; Tsai, C.-H. The silencing suppressor P25 of Potato virus X interacts with Argonaute1 and mediates its degradation through the proteasome pathway. *Mol. Plant Pathol.* **2010**, *11*, 641–649. [[CrossRef](#)]
177. Okano, Y.; Senshu, H.; Hashimoto, M.; Neriya, Y.; Netsu, O.; Minato, N.; Yoshida, T.; Maejima, K.; Oshima, K.; Komatsu, K.; et al. In Planta Recognition of a Double-Stranded RNA Synthesis Protein Complex by a Potexviral RNA Silencing Suppressor. *Plant Cell* **2014**, *26*, 2168–2183. [[CrossRef](#)]
178. Cuellar, W.J.; Kreuze, J.F.; Rajamäki, M.-L.; Cruzado, K.R.; Untiveros, M.; Valkonen, J.P.T. Elimination of antiviral defense by viral RNase III. *Proc. Natl. Acad. Sci. USA* **2009**, *106*, 10354–10358. [[CrossRef](#)]
179. Kreuze, J.F.; Savenkov, E.I.; Cuellar, W.; Li, X.; Valkonen, J.P.T. Viral Class 1 RNase III Involved in Suppression of RNA Silencing. *J. Virol.* **2005**, *79*, 7227–7238. [[CrossRef](#)]
180. Li, F.; Huang, C.; Li, Z.; Zhou, X. Suppression of RNA Silencing by a Plant DNA Virus Satellite Requires a Host Calmodulin-Like Protein to Repress RDR6 Expression. *PLoS Pathog.* **2014**, *10*, e1003921. [[CrossRef](#)]
181. Glick, E.; Zrachya, A.; Levy, Y.; Mett, A.; Gidoni, D.; Belausov, E.; Citovsky, V.; Gafni, Y. Interaction with host SGS3 is required for suppression of RNA silencing by tomato yellow leaf curl virus V2 protein. *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 157–161. [[CrossRef](#)]
182. Zhang, C.; Chen, D.; Yang, G.; Yu, X.; Wu, J. Rice Stripe Mosaic Virus-Encoded P4 Is a Weak Suppressor of Viral RNA Silencing and Is Required for Disease Symptom Development. *Mol. Plant-Microbe Interact.* **2020**, *33*, 412–422. [[CrossRef](#)] [[PubMed](#)]
183. Goto, K.; Kobori, T.; Kosaka, Y.; Natsuaki, T.; Masuta, C. Characterization of Silencing Suppressor 2b of Cucumber Mosaic Virus Based on Examination of its Small RNA-Binding Abilities. *Plant Cell Physiol.* **2007**, *48*, 1050–1060. [[CrossRef](#)] [[PubMed](#)]
184. Zhang, X.; Yuan, Y.-R.; Pei, Y.; Lin, S.-S.; Tuschl, T.; Patel, D.J.; Chua, N.-H. Cucumber mosaic virus-encoded 2b suppressor inhibits *Arabidopsis* Argonaute1 cleavage activity to counter plant defense. *Genes Dev.* **2006**, *20*, 3255–3268. [[CrossRef](#)] [[PubMed](#)]

185. Fang, Y.-Y.; Zhao, J.-H.; Liu, S.-W.; Wang, S.; Duan, C.-G.; Guo, H.-S. CMV2b-AGO Interaction Is Required for the Suppression of RDR-Dependent Antiviral Silencing in Arabidopsis. *Front. Microbiol.* **2016**, *7*, 1329. [[CrossRef](#)] [[PubMed](#)]
186. Chen, H.; Yang, J.; Lin, C.; Yuan, Y.A. Structural basis for RNA-silencing suppression by Tomato aspermy virus protein 2b. *EMBO Rep.* **2008**, *9*, 754–760. [[CrossRef](#)]
187. Gong, P.; Tan, H.; Zhao, S.; Li, H.; Liu, H.; Ma, Y.; Zhang, X.; Rong, J.; Fu, X.; Lozano-Durán, R.; et al. Geminiviruses encode additional small proteins with specific subcellular localizations and virulence function. *Nat. Commun.* **2021**, *12*, 1–11. [[CrossRef](#)]
188. Cheng, X.; Wang, A. The Potyvirus Silencing Suppressor Protein VPg Mediates Degradation of SGS3 via Ubiquitination and Autophagy Pathways. *J. Virol.* **2017**, *91*. [[CrossRef](#)]
189. Du, Z.; Xiao, D.; Wu, J.; Jia, D.; Yuan, Z.; Liu, Y.; Hu, L.; Han, Z.; Wei, T.; Lin, Q.; et al. p2 of Rice stripe virus (RSV) interacts with OsSGS3 and is a silencing suppressor. *Mol. Plant Pathol.* **2011**, *12*, 808–814. [[CrossRef](#)]
190. Ren, B.; Guo, Y.; Gao, F.; Zhou, P.; Wu, F.; Meng, Z.; Wei, C.; Li, Y. Multiple Functions of Rice Dwarf Phytoevirus Pns10 in Suppressing Systemic RNA Silencing. *J. Virol.* **2010**, *84*, 12914–12923. [[CrossRef](#)]
191. Cao, X.; Zhou, P.; Zhang, X.; Zhu, S.; Zhong, X.; Xiao, Q.; Ding, B.; Li, Y. Identification of an RNA Silencing Suppressor from a Plant Double-Stranded RNA Virus. *J. Virol.* **2005**, *79*, 13018–13027. [[CrossRef](#)]
192. Gao, F.; Zhao, S.; Men, S.; Kang, Z.; Hong, J.; Wei, C.; Hong, W.; Li, Y. A non-structural protein encoded by Rice Dwarf Virus targets to the nucleus and chloroplast and inhibits local RNA silencing. *Sci. China Life Sci.* **2020**, *63*, 1703–1713. [[CrossRef](#)] [[PubMed](#)]
193. Rosas-Díaz, T.; Zhang, D.; Fan, P.; Wang, L.; Ding, X.; Jiang, Y.; Jimenez-Gongora, T.; Medina-Puche, L.; Zhao, X.; Feng, Z.; et al. A virus-targeted plant receptor-like kinase promotes cell-to-cell spread of RNAi. *Proc. Natl. Acad. Sci. USA* **2018**, *115*, 1388–1393. [[CrossRef](#)] [[PubMed](#)]
194. Gómez, B.G.; Rosas-Díaz, T.; Shi, C.; Fan, P.; Zhang, D.; Rufián, J.S.; Lozano-Durán, R. The viral silencing suppressor P19 interacts with the receptor-like kinases BAM1 and BAM2 and suppresses the cell-to-cell movement of RNA silencing independently of its ability to bind sRNA. *New Phytol.* **2020**, *229*, 1840–1843. [[CrossRef](#)] [[PubMed](#)]
195. Li, Z.; Du, Z.; Tang, Y.; She, X.; Wang, X.; Zhu, Y.; Yu, L.; Lan, G.; He, Z. C4, the Pathogenic Determinant of Tomato Leaf Curl Guangdong Virus, May Suppress Post-transcriptional Gene Silencing by Interacting With BAM1 Protein. *Front. Microbiol.* **2020**, *11*, 851. [[CrossRef](#)] [[PubMed](#)]
196. Ismayil, A.; Yang, M.; Liu, Y. Role of autophagy during plant-virus interactions. *Semin. Cell Dev. Biol.* **2019**, *101*, 36–40. [[CrossRef](#)]
197. Medina-Puche, L.; Lozano-Duran, R. Tailoring the cell: A glimpse of how plant viruses manipulate their hosts. *Curr. Opin. Plant Biol.* **2019**, *52*, 164–173. [[CrossRef](#)]
198. Hafrén, A.; Üstün, S.; Hochmuth, A.; Svenning, S.; Johansen, T.; Hofius, D. Turnip Mosaic Virus Counteracts Selective Autophagy of the Viral Silencing Suppressor HCpro. *Plant Physiol.* **2017**, *176*, 649–662. [[CrossRef](#)]
199. Yang, M.; Zhang, Y.; Xie, X.; Yue, N.; Li, J.; Wang, X.-B.; Han, C.; Yu, J.; Liu, Y.; Li, D. Barley stripe mosaic virus  $\gamma$ b Protein Subverts Autophagy to Promote Viral Infection by Disrupting the ATG7-ATG8 Interaction. *Plant Cell* **2018**, *30*, 1582–1595. [[CrossRef](#)]