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Plant Noncoding RNAs: Hidden Players in Development and Stress Responses

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Abstract

A large and significant portion of eukaryotic transcriptomes consists of noncoding RNAs (ncRNAs) that have minimal or no protein-coding capacity but are functional. Diverse ncRNAs, including both small RNAs and long ncRNAs (lncRNAs), play essential regulatory roles in almost all biological processes by modulating gene expression at the transcriptional and post-transcriptional levels. In this review, we summarize the current knowledge of plant small RNAs and lncRNAs, with a focus on their biogenesis, modes of action, local and systemic movement, and functions at the nexus of plant development and environmental responses. The complex connections among small RNAs, lncRNAs, and small peptides in plants are also discussed, along with the challenges of identifying and investigating new classes of ncRNAs.

Contents

1. INTRODUCTION

Although up to 90% of the eukaryotic genome is transcribed into RNA, only approximately 2% of transcribed RNAs give rise to protein products (Pauli et al. 2011, Rai et al. 2018). The remaining transcriptome comprises noncoding RNAs (ncRNAs) arising from what were previously considered silent regions, such as intergenic regions, repetitive sequences, transposons, and pseudogenes. Moreover, transcripts from these regions were initially regarded as transcriptional noise due to their lack of or minimal protein-coding capacity and due to poorly conserved sequences (Ariel et al. 2015, Pauli et al. 2011). However, computational analysis and experimental validation in 15 diverse flowering plant species predict approximately 40% of intergenic transcribed regions and ncRNAs to be similar in features to protein-coding or RNA genes and to likely be functional (Lloyd et al. 2018).

ncRNAs can be classified into small RNAs [18–30 nucleotides (nt)], medium-sized ncRNAs (31–200 nt), and long ncRNAs (lncRNAs) (>200 nt). The vital roles of small RNAs, particularly microRNAs (miRNAs), in diverse biological processes such as plant growth, development, and hormone and stress responses are now being elucidated in detail (Chen 2009, D'Ario et al. 2017, Martinez & Köhler 2017, Tang & Chu 2017). Studies have also shed light on the essential regulatory functions exerted by lncRNAs (Böhmdorfer & Wierzbicki 2015, Pauli et al. 2011, Zhang & Chen 2013). In this review, we summarize recent progress on plant small RNAs and lncRNAs, with an emphasis on their biogenesis, modes of action, non–cell autonomy, and conserved and diverse functions in different plant species.

2. SMALL RNAS

To date, hundreds of thousands of small RNAs have been identified in diverse plant species. Small RNAs, despite their tiny size, play important roles in myriad intracellular processes by regulating the expression of target genes at either the transcriptional or the posttranscriptional level

(Chen 2009, D'Ario et al. 2017, Martinez & Köhler 2017, Tang & Chu 2017). Three major types of small RNAs are present in plants: miRNAs, transposable element (TE)-derived small interfering RNAs (siRNAs), and phased siRNAs (phasiRNAs). These small RNAs differ in terms of their precursors, biogenesis, and modes of action.

2.1. MicroRNAs

miRNAs constitute a major class of small RNAs in plants and impact various aspects of plant development and stress responses by posttranscriptionally regulating gene expression.

2.1.1. Biogenesis of microRNAs.

miRNA biogenesis is a multistep process including transcription, processing, modification, and assembly of the RNA-induced silencing complex (RISC) (Rogers & Chen 2013, Yu et al. 2017) (**Figure 1**). miRNAs are encoded by *MIR* genes, which are mainly located in intergenic regions and transcribed by RNA POLYMERASE II (Pol II) to give rise to long, single-stranded, 5′-capped and 3′-polyadenylated primary miRNAs (pri-miRNAs). An RNase III family DICER-LIKE (DCL) enzyme, usually DCL1, assisted by HYPONASTIC LEAVES 1 (HYL1) and SERRATE (SE), sequentially processes a pri-miRNA first into a precursor miRNA (pre-miRNA) and then into a short miRNA/miRNA* duplex. The miRNA/miRNA* duplex undergoes 2′-*O*-methylation on both 3′ terminal riboses catalyzed by the methyltransferase HUA ENHANCER 1 (HEN1). In most cases, miRNAs are stabilized by the 3′ methylation. Loss of the protective methyl group usually leads to 3′ uridylation (i.e., the addition of one to several U residues to the 3′ end) and subsequent degradation (Sanei & Chen 2015). Nevertheless, some unmethylated and uridylated miRNAs acquire the ability to trigger the generation of secondary siRNAs; examples include miR171 in *Arabidopsis* and miR1510 in soybean (Fei et al. 2018, Tu et al. 2015).

Most mature miRNA strands are incorporated into ARGONAUTE 1 (AGO1) in the nucleus, followed by the removal of the miRNA* strand and the export of the miRNA-AGO1 complex to the cytoplasm, where miRNAs guide posttranscriptional gene silencing (Baumberger & Baulcombe 2005, Bologna et al. 2018). Beyond the core components mentioned above, many other miRNA biogenesis pathway factors have been identified (Yu et al. 2017), underscoring that the biogenesis of miRNAs is precisely controlled.

2.1.2. Modes of action of plant microRNAs.

Plant miRNAs repress target gene expression through two major modes of action: transcript cleavage and translation repression (Chen 2009, Yu et al. 2017) (**Figure 1**). miRNAs recognize target mRNAs via sequence complementarity and direct AGO1 to cleave the target mRNA at the phosphodiester bond corresponding to nucleotides 10 and 11 of the miRNA. miRNAs also inhibit the translation of target mRNAs with the aid of the endoplasmic reticulum (ER)-associated protein ALTERED MERISTEM PROGRAM 1 (AMP1) (Li et al. 2013). Transcript cleavage was originally thought to be the predominant mode of action for plant miRNAs due to the high degree of sequence complementarity between miRNAs and targets (Chen 2009). However, sequence complementarity is not the factor dictating the mode of action of plant miRNAs, as supported by evidence that miRNA targets with nearly perfect sequence complementarity to the corresponding miRNAs are regulated by cleavage and translation repression. For example, *SQUAMOSA PROMOTER BINDING PROTEIN-LIKE 3* (*SPL3*) (targeted by miR156), *PHABULOSA* (*PHB*) and *REVOLUTA* (targeted by miR165/166), *SCARECROW-LIKE PROTEIN 4* (*SCL4*) (targeted by miR171), *APETALA 2* (*AP2*) (targeted by miR172), and *COPPER/ZINC SUPEROXIDE DISMUTASE 1* (*CSD1*) and *CSD2* (targeted by miR398) are subjected to both transcript cleavage and translation repression (Yu et al. 2017). Moreover, most
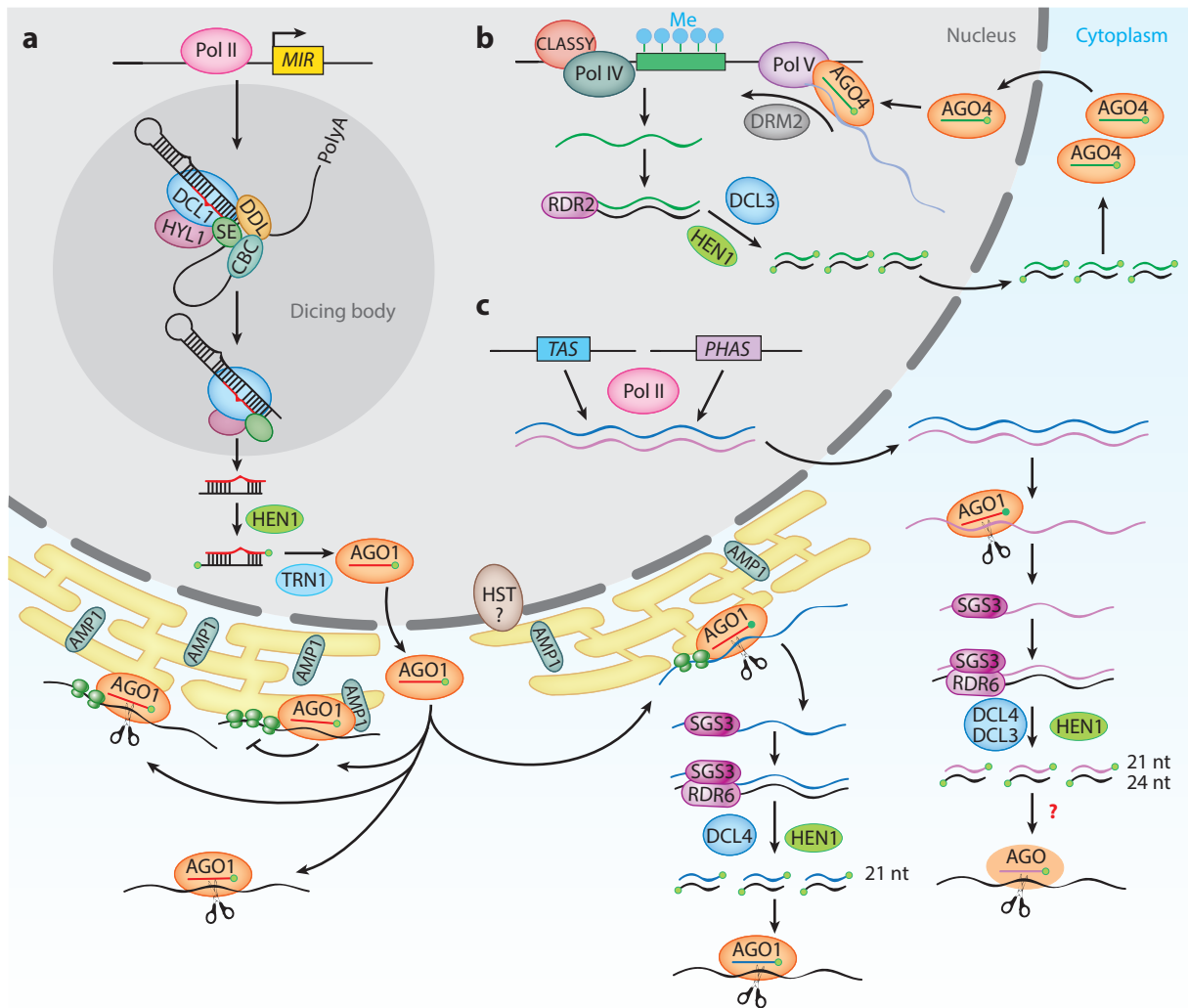
Figure 1

Biogenesis and modes of action of plant small RNAs. (*a*) A *MIR* gene is transcribed into a pri-miRNA, which is sequentially processed first into a pre-miRNA and then into a miRNA/miRNA* duplex. The duplex is methylated by HEN1, and the miRNA strand is loaded into AGO1 in the nucleus. The miRNA-AGO1 complex is transported to the cytoplasm and regulates target gene expression through transcript cleavage and/or translation repression. (*b*) Pol IV generates single-stranded siRNA precursors, which are converted into dsRNAs and processed into 24-nt siRNA duplexes. Methylated siRNAs are loaded into AGO4 in the cytoplasm and are transported to the nucleus, followed by the recruitment of these siRNA-AGO4 complexes to Pol V transcripts. The subsequent recruitment of DRM2 catalyzes DNA methylation at RdDM target loci. (*c*) *TAS* or *PHAS* loci are transcribed into single-stranded RNAs that are targeted by an miRNA-AGO1/7 complex. The 5′ or 3′ cleavage fragment is protected by SGS3 and converted into dsRNA by RDR6. DCL proteins process these dsRNAs into 21- or 24-nt phasiRNAs. The 21-nt tasiRNAs, which are phasiRNAs from *TAS* loci, are primarily loaded into AGO1 and guide transcript cleavage of their targets. Abbreviations: AGO, ARGONAUTE; AMP1, ALTERED MERISTEM PROGRAM 1; CBC, CAP-BINDING COMPLEX; DCL, DICER-LIKE; DDL, DAWDLE; DRM2, DOMAINS REARRANGED METHYLASE 2; dsRNA, double-stranded RNA; HEN1, HUA ENHANCER 1; HST, HASTY; HYL1, HYPONASTIC LEAVES 1; Me, methylated; phasiRNA, phased siRNA; Pol, RNA polymerase; pre-miRNA, precursor miRNA; pri-miRNA, primary miRNA; RdDM, RNA-directed DNA methylation; RDR2/6, RNA-DEPENDENT RNA POLYMERASE 2/6; SE, SERRATE; SGS3, SUPPRESSOR OF GENE SILENCING 3; siRNA, small interfering RNA; tasiRNA, *trans*-acting siRNA; TRN1, TRANSPORTIN 1.

miRNAs are enriched on membrane-bound polysomes (Li et al. 2016), suggesting that miRNA-mediated transcript cleavage and translation repression take place on the ER. Nevertheless, transcript cleavage may also occur independently of polysomes in the cytosol.

2.1.3. Functions of microRNAs in plant development.

Plant miRNAs target many transcription factors that participate in various regulatory pathways (**Figure 2**). A single miRNA or an miRNA family often targets multiple members of a gene family, and evolutionarily conserved miRNAs among related plant species also tend to have conserved targets. For example, members of the conserved miR156 family regulate vegetative phase transition by modulating the expression of *SPL* genes in diverse flowering plants (Wang 2014). miR172 regulates floral development and flowering time in *Arabidopsis* through the repression of *AP2* genes (Aukerman & Sakai 2003, Chen 2004). miR172's role in flowering control has been reported in a variety of plant species, including maize, barley, soybean, and rice (Tang & Chu 2017). In *Arabidopsis* and maize, miR164 and its target, plant-specific transcription factor *NAC DOMAIN CONTAINING PROTEIN 1* (*NAC1*), are involved in the formation of lateral roots (Guo et al. 2005, J. Li et al. 2012). Similarly, overexpressing miR164 in potato under osmotic stress causes reduced expression of *NAC262* and limits the number of lateral roots (Zhang et al. 2018).

In addition to conserved functions, distinct roles of the same miRNA-target modules have been uncovered. For instance, the miR156-*SPL* module regulates tillering in switchgrass, controls ear development and grain formation in maize, and participates in grain size control and panicle branching in rice (D'Ario et al. 2017, Tang & Chu 2017). Thus, miR156-*SPL* has a diversified regulatory function in axillary meristem initiation in monocots. Vegetative phase transition in barley requires the miR171-*SCL* module to activate the miR156-*SPL* pathway, and this appears to be a monocot-specific function of miR171-*SCL* (Curaba et al. 2013).

The functions of different miRNAs can also converge on one biological event. In *Arabidopsis*, the shoot apical meristem (SAM) is maintained by the miR165/166 and miR394 families, which restrict the expression of the *HOMEODOMAIN LEUCINE ZIPPER III* (*HD-ZIP III*) and *LEAF CURLING RESPONSIVENESS* (*LCR*) genes, respectively (D'Ario et al. 2017). miR165/166 also regulates leaf polarity together with miR390, which triggers the production of siRNAs that target several *AUXIN RESPONSE FACTOR* (*ARF*) genes (Chitwood & Timmermans 2010, Liu et al. 2009). Two miRNA families, miR156/157 and miR172, cooperate to control the juvenile-to-adult transition and flowering (Wang et al. 2009, Wu et al. 2009). In tomato, both miR156 and miR319 regulate the floral transition in response to gibberellin signaling (Silva et al. 2018). In rice, grain size is regulated by miR156, miR396, and miR397, and tillering is controlled by miR156, miR393, and miR444 (Tang & Chu 2017). Collectively, these findings demonstrate the integrated functionalities of unrelated miRNAs.

Aside from conserved miRNAs, species-specific miRNAs constitute a large proportion of plant miRNAs. miR528, a monocot-specific miRNA, is induced by nitrogen luxury conditions in maize and regulates lodging resistance by targeting the lignin biosynthesis genes *ZmLACCASE 3* (*ZmLAC3*) and *ZmLAC5* (Sun et al. 2018). In rice, the monocot-specific miR444 controls tillering (Guo et al. 2013) and participates in antiviral defense (H. Wang et al. 2016) by targeting the three MIKCC-type MADS-box genes *OsMADS23*, *OsMADS27a*, and *OsMADS57*; these genes repress the expression of *RNA-DEPENDENT RNA POLYMERASE 1* (*RDR1*), a key component of the antiviral RNA silencing pathway (Garcia-Ruiz et al. 2010, H. Wang et al. 2016).

2.2. Transposable Element–Derived Small Interfering RNAs

Most endogenous siRNAs in plants are heterochromatic siRNAs derived from repeats and TEs. They are involved in transcriptional gene silencing by directing DNA methylation and/or histone
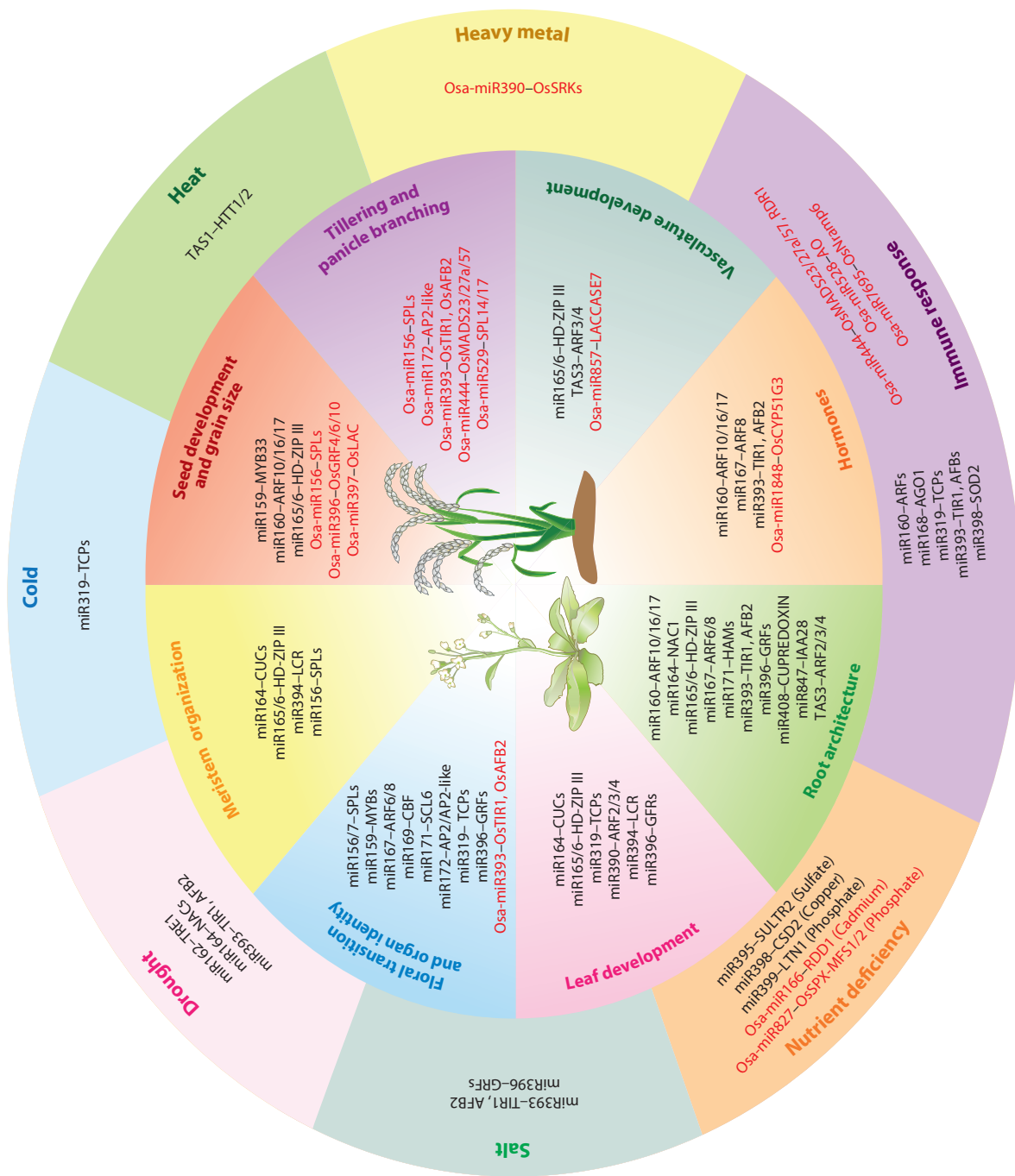
(Caption appears on following page)

Figure 2 (*Figure appears on preceding page*)

Functions of miRNAs in plant development and stress responses and an overview of the current understanding of miRNA-mediated regulation during development (*inner circle*) and responses to biotic and abiotic stresses (*outer circle*) in *Arabidopsis* and rice. Red font indicates miRNA-target modules that act in rice, but not in *Arabidopsis*.

methylation through a process known as RNA-directed DNA methylation (RdDM) (Du et al. 2015, Matzke et al. 2015) (**Figure 1**).

2.2.1. Transposable element–derived small interfering RNAs in genome stability control.
RdDM involves siRNA biogenesis from TEs and repeats as well as siRNA-guided DNA methylation at the source loci and homologous sites. The plant-specific RNA polymerase IV (Pol IV) is recruited by CLASSY chromatin remodeling factors to RdDM loci to generate single-stranded siRNA precursors (Blevins et al. 2015, S. Li et al. 2015, Zhai et al. 2015a, Zhou et al. 2018). RNA-DEPENDENT RNA POLYMERASE 2 (RDR2) converts these precursors into double-stranded RNAs (dsRNAs) that are subsequently processed by DCL3, producing 24-nt mature siRNAs that are preferentially loaded into AGO4 (Law & Jacobsen 2010). RNA polymerase V (Pol V), another plant-specific RNA polymerase, generates noncoding transcripts at the same RdDM loci, thereby recruiting the siRNA-AGO4 complex through sequence complementarity (Du et al. 2015). This activity promotes the recruitment of DNA REARRANGED METHYLASE 2 (DRM2) to trigger DNA methylation at RdDM loci (Du et al. 2015, Law & Jacobsen 2010).

The recruitment of Pol IV and Pol V to DNA is enhanced by existing repressive chromatin features such as histone H3 lysine 9 methylation and DNA methylation (Du et al. 2015). Thus, the above-described RdDM mechanism likely maintains existing heterochromatic features. Non-canonical RdDM, which involves 21–22-nt siRNAs likely generated by Pol II, may be responsible for the initiation of DNA methylation (Cuerda-Gil & Slotkin 2016).

RdDM (including noncanonical RdDM) is responsible for de novo methylation in all sequence contexts (CG, CHG, and CHH) as well as for methylation maintenance at CHH contexts in short TEs and at the edges of long TEs. In *Arabidopsis*, transposon derepression is commonly observed in RdDM-defective mutants, but transposition occurs only at a few loci (Ito et al. 2011). In maize, with a genome of approximately 85% TEs, methylated CHH islands often occur at the boundaries between active genes and nearby silent TEs. Loss of CHH methylation is often accompanied by CG and CHG hypomethylation at the adjacent TEs, suggesting that methylated CHH islands reinforce TE silencing by preventing the spread of active euchromatin to heterochromatin (Q. Li et al. 2015).

2.2.2. Functions of transposable element–derived small interfering RNAs in reproduction and hybridization.
Reproduction is a key period when TE-derived siRNAs monitor genome compatibility and dosage. In developing pollen, certain TEs are demethylated and reactivated in the vegetative nucleus and produce 21-, 22-, and 24-nt siRNAs that are thought to move into sperm cells (Calarco et al. 2012, Martínez et al. 2016, Slotkin et al. 2009). However, overall levels of CHH methylation are greatly reduced in sperm cells, probably owing to the low levels of expression of the RdDM machinery (Calarco et al. 2012). In the female gametophyte, the central cell and the egg cell are fertilized by sperm cells to produce the endosperm and the embryo, respectively. CHH methylation levels increase during embryogenesis (Bouyer et al. 2017, Jullien et al. 2012, Martínez et al. 2016), suggesting that the paternal genome gains CHH methylation after fertilization. The siRNAs that guide CHH methylation in the embryo may come from two sources: sperm and endosperm. The maternal genome in the endosperm is undermethylated at numerous loci, probably due to active demethylation in the central cell (Ibarra et al. 2012,

Martinez & Köhler 2017). The demethylation leads to reactivation of TEs from the maternal genome in the endosperm and the production of 24-nt siRNAs. The siRNAs are thought to move into the embryo to guide DNA methylation (Martinez & Köhler 2017). In contrast, 21–22-nt siRNAs in the sperm serve as a quantitative output of paternal genome dosage in the endosperm. Such siRNAs from some loci interfere with RdDM in the endosperm, perhaps by competing with 24-nt siRNAs for Pol V–derived scaffold transcripts (Martinez et al. 2018). Thus, TE-derived siRNAs likely mediate interactions between maternal and paternal genomes. Surprisingly, a recent study identified a group of 23–24-nt meiocyte-specific siRNAs (ms-sRNAs) that were significantly enriched in genic regions rather than TEs. Moreover, unlike siRNAs in somatic cells, these ms-sRNAs are positively correlated with gene expression during reproductive development in a fashion unrelated to DNA methylation, implying a novel role of siRNAs in meiocytes (Huang et al. 2019).

Perhaps owing to the central role of TE-derived siRNAs in genome interactions, these siRNAs contribute to the transgressive phenotypes of plant hybrids, i.e., hybrid vigor and novel phenotypes that transgress the parental range and are inherited stably in subsequent generations. For example, in tomato introgression lines generated from *Solanum lycopersicum* (cultivated tomato) and *Solanum pennellii* (wild tomato), several differentially expressed siRNA loci (DSR loci) were identified at locations where the siRNA abundance was either higher or lower than in the parental lines, along with corresponding hypermethylation or hypomethylation of their target DNAs (Shivaprasad et al. 2014). In addition, RdDM mediated by siRNAs at the DSR loci seems to contribute to the paramutation-like phenotype in tomato hybrids, wherein the epigenetic modification associated with a silent allele is transferred to an active allele (Gouil & Baulcombe 2018). Similarly, nonadditive expression of siRNAs and consequent DNA methylation result in transgressive phenotypes in interspecific hybrids or allotetraploids of cotton (Song et al. 2017).

2.3. Phased Small Interfering RNAs

PhasiRNAs constitute another class of endogenous siRNAs. PhasiRNAs are generated from miRNA target transcripts and may have their own targets in *trans*.

2.3.1. Models of phased small interfering RNA biogenesis.

Although mRNA cleavage fragments generated by miRISCs are typically subjected to rapid degradation, a small proportion of them are further processed into secondary siRNAs in a phenomenon that is widespread and mechanistically conserved in plants (Chen 2009, Rogers & Chen 2013, Yu et al. 2017). After AGO-mediated slicing, SUPPRESSOR OF GENE SILENCING 3 (SGS3) associates with the 5′ or 3′ cleavage fragments and recruits RDR6, which converts the single-stranded cleavage fragments into dsRNAs (**Figure 1**). DCL proteins then dice these dsRNAs into a series of 21- or 24-nt siRNAs, termed phasiRNAs, which are arranged head to tail and are in phase relative to the miRNA cleavage sites.

Trans-acting siRNAs (tasiRNAs) are a class of DCL4-dependent 21-nt phasiRNAs generated from noncoding *TAS* transcripts (Chen 2009, Fei et al. 2013). In addition to *TAS* loci, phasiRNAs are produced from protein-coding genes, such as *NUCLEOTIDE-BINDING LEUCINE-RICH REPEAT* (*NB-LRR*) and *PENTATRICOPEPTIDE REPEAT* (*PPR*) genes in dicots and lncRNAs from *PHAS* (phasiRNA-generating) loci in monocots (Chen 2009, Fei et al. 2013, Yang et al. 2018). In most cases, phasiRNAs are trigged by a 22-nt miRNA with only one binding site in the target transcript—the so-called one-hit model (Chen et al. 2010, Fei et al. 2013). In contrast, the two-hit model entails two miRNA binding sites present in the target transcript, as exemplified by *TAS3* (Axtell et al. 2006). Besides the number of miRNA binding sites and the length of the

miRNA trigger, the following factors also influence phasiRNA biogenesis: AGO1 slicer activity, the asymmetric bulge within the miRNA/miRNA* duplex, the degree of complementarity of the miRNA/target duplex, and the position of the miRNA binding site relative to the short open reading frame (ORF) of *TAS* transcripts (Yu et al. 2017). Recently, *TAS* transcripts were found to be associated with membrane-bound polysomes (Li et al. 2016), suggesting that phasiRNA biogenesis from *TAS* may be initiated on the rough ER. The finding further implies a potential relationship between translation and phasiRNA biogenesis.

2.3.2. Biological functions of phased small interfering RNAs.

tasiRNAs are the best characterized phasiRNAs in terms of biological functions. In *Arabidopsis*, *TAS1* and *TAS2* are targeted by miR173 to produce tasiRNAs, some of which can target *PPR* transcripts to cause further production of phasiRNAs (Chen et al. 2010, Fei et al. 2013). *TAS1* tasiRNAs also target the heat stress transcription factor genes *HEAT-INDUCED TAS1 TARGET 1* (*HTT1*) and *HTT2* to regulate plant thermotolerance (Li & He 2014). *TAS3* tasiRNAs are triggered by the miR390-AGO7 complex (Axtell et al. 2006) and target *ARF* family members to regulate diverse biological processes, including embryo development, developmental transitions, leaf morphology, flower and root architecture, stress responses, and phytohormone cross talk (D'Ario et al. 2017, Xia et al. 2016). *TAS4* tasiRNAs are induced by miR828 from the *TAS4* locus and repress *MYB* genes, including *MYB113*, *PRODUCTION OF ANTHOCYANIN PIGMENT 1* (*PAP1*), and *PAP2*, which regulate anthocyanin biogenesis (Luo et al. 2012). In contrast to *TAS1–TAS4* in *Arabidopsis*, the biogenesis and functions of *TAS5–TAS10* are ill defined. *TAS5* was reported in tomato and does not exhibit all of the characteristics of a *TAS* locus; specifically, it resembles a protein-coding transcript, and the tasiRNAs may function in *cis* (F. Li et al. 2012). *TAS6* from moss was found adjacent to *TAS3* loci, and the production of tasiRNAs is triggered by miR156 or miR529 (Arif et al. 2012, Cho et al. 2012). Interestingly, *TAS6A* and *TAS3A* share the same primary transcript, and the two tasiRNA-generating regions are separated by only a small central intron (Cho et al. 2012), indicating linked biogenesis of *TAS6A* and *TAS3A* tasiRNAs. *TAS7–TAS10* were identified in grapevine and tomato (Zhang et al. 2012, Zuo et al. 2017), but their biogenesis pathways and functions have not been described.

In dicots, *NB-LRR* genes exist widely in diverse plant species and represent the largest gene family that produces phasiRNAs (Fei et al. 2015, Zhai et al. 2011). *NB-LRR* genes are targeted by 22-nt miRNAs, such as miR2118 in *Medicago truncatula* and miR472 in *Arabidopsis*, and give rise to 21-nt DCL4-dependent phasiRNAs that may in turn regulate *NB-LRR* transcripts at the posttranscriptional level, perhaps both in *cis* and in *trans* (Cai et al. 2018, Zhai et al. 2011). In soybean, many *NB-LRR* genes are preferentially expressed in nodules and targeted by miR482, miR1507, and miR1510 (Fei et al. 2013). *PPR* genes are another large phasiRNA-generating gene family. In addition to being regulated by *TAS1/2* tasiRNAs, some *PPR* transcripts are directly targeted by miRNAs such as miR7122 and miR161 (Hou et al. 2018, Xia et al. 2013). *PPR* phasiRNAs contribute to pathogen defense by potentially silencing *Phytophthora* transcripts during infection (Hou et al. 2018).

In monocots, miR2118 targets noncoding transcripts arising from *PHAS* loci and generates 21-nt phasiRNAs during anther development (Fei et al. 2013, Zhai et al. 2015b). In rice, 21-nt phasiRNAs derived from more than 700 *PHAS* loci are associated with the germline-specific AGO protein MEIOSIS ARRESTED AT LEPTOTENE 1 (MEL1), which has key functions in the development of premeiotic germ cells and the progression of meiosis (Komiya et al. 2014). In maize, mutation of *OUTER CELL LAYER 4* (*OCL4*) leads to anther defects and male sterility, accompanied by a lack of 21-nt phasiRNAs (Zhai et al. 2015b). In addition to 21-nt phasiRNAs, a class of 24-nt meiotic phasiRNAs triggered by miR2275 and processed by DCL5 is present in

both male and female reproductive organs in rice and maize, suggesting that they may be involved in male and female germinal development (Kakrana et al. 2018, Zhai et al. 2015b). The grass phasiRNAs resemble mammalian PIWI-interacting RNAs (piRNAs) in that they lack sequence conservation in related species and that they are specifically found in the germline (Kakrana et al. 2018, Patel et al. 2018).

3. PLANT LONG NONCODING RNAS

RNA transcripts longer than 200 nt that have no coding potential or lack an ORF encoding >100 amino acids are classified as lncRNAs. Numerous lncRNAs have been identified in a variety of eukaryotes, including plants. There is increasing evidence that lncRNAs are essential modulators of a wide range of biological processes and function through diverse mechanisms.

3.1. Processing and Regulatory Features of Plant Long Noncoding RNAs

lncRNAs are characterized by their wide-ranging types and origins. They arise from intergenic regions [long intergenic ncRNAs (lincRNAs)], intronic regions [intronic ncRNAs (incRNAs)], and coding regions [natural antisense transcripts (NATs)] and can be subdivided according to their processing mechanisms (Chekanova 2015). lincRNAs, incRNAs, and NATs are conventional linear lncRNAs. Circular RNAs (circRNAs) are another class of lncRNAs and mostly arise from coding regions or intronic regions. Each lncRNA type is produced via specific mechanisms and has distinct regulatory features in *cis* or in *trans*.

3.1.1. Linear long noncoding RNAs. lincRNAs, incRNAs, and NATs are linear lncRNAs that constitute the majority of annotated lncRNAs, most of which are transcribed by Pol II. They also have typical mRNA-like features, with a 5′ m⁷G cap and a 3′ poly (A) tail; thus, they are processed as mRNA mimics (Wu et al. 2017). However, these molecules have a lower degree of conservation, lower abundance, more tissue-specific expression, and lower splicing efficiency than mRNAs (Ulitsky & Bartel 2013).

lncRNAs may regulate the expression of neighboring genes in *cis* and that of distant genes in *trans* (Liu et al. 2015, Yang et al. 2014). The in *cis*–regulatory feature of NATs was first globally implicated by a study that examined transcriptomic responses to light in *Arabidopsis* (H. Wang et al. 2014). This study discovered the widespread existence of NATs (approximately 70% of annotated mRNAs in *Arabidopsis* have NATs) and the potential roles of NATs in mediating histone modifications at the corresponding gene loci. It was subsequently reported that NAT expression is often positively correlated with that of their cognate sense genes (Zhao et al. 2018). For example, the NAT *MAS* regulates *MADS AFFECTING FLOWERING 4* (*MAF4*) in *cis* (Zhao et al. 2018) (**Figure 3**). Other examples include the *cis* regulation of *PHOSPHATE1;2* (*PHO1;2*) by *NAT_{pho1;2}* (Jabnoune et al. 2013), *CYCLING DOF FACTOR 5* (*CDF5*) by *FLORE* (Henriques et al. 2017), *FLOWERING LOCUS C* (*FLC*) by *COOLAIR* (Chen & Penfield 2018, Marquardt et al. 2014), and *LEUCINE-RICH REPEAT RECEPTOR KINASE* (*LRK*) by *LAIR* (Y. Wang et al. 2018) (**Figure 3**). NATs may also suppress the expression of their cognate sense genes. For example, Pol II read-through of the lncRNA *SVALKA* (*SVK*) generates a NAT transcript of *C-repeat/dehydration-responsive element binding factor 1* (*CBF1*), and Pol II collision is thought to suppress *CBF1* expression (Kindgren et al. 2018).

In contrast to NAT expression, lincRNA expression is not significantly correlated with that of their neighboring genes (Y.C. Zhang et al. 2014). In fact, a number of lincRNAs function in *trans* in plants. For example, the lincRNA *HIDDEN TREASURE 1* (*HID1*) modulates the transcription of *PHYTOCHROME-INTERACTING FACTOR 3* (*PIF3*) in *trans* (Y. Wang et al. 2014). Nuclear
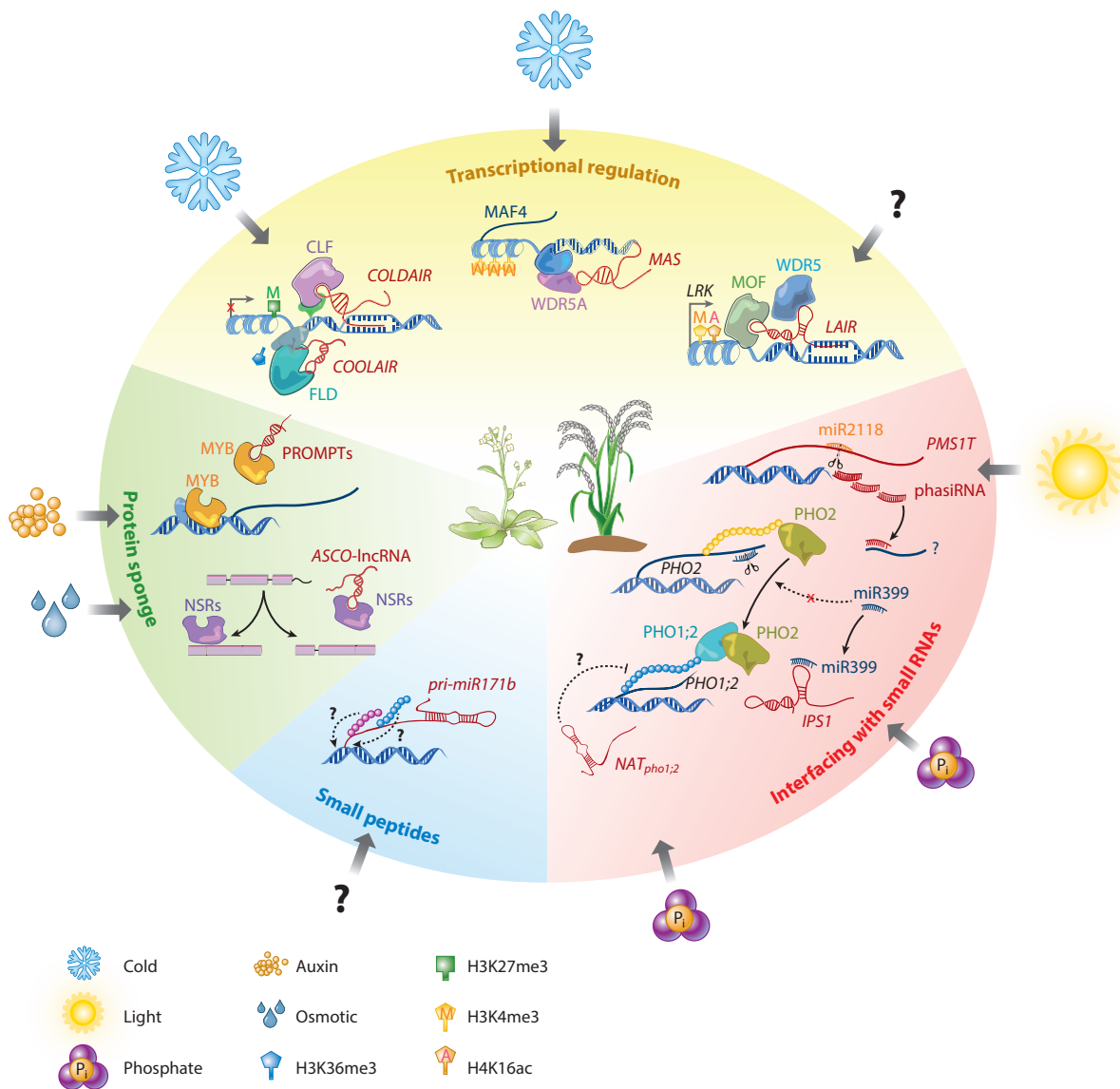
Figure 3

Representative models for the roles of plant long noncoding RNAs (lncRNAs). lncRNAs can serve as scaffolds, molecular mimics and sponges, and small interfering RNA precursors. They can also be translated into small peptides to regulate target genes in *cis* or in *trans* during plant development. The expression of most reported plant lncRNAs is induced by diverse environmental conditions. *COLDAIR*, *COOLAIR*, *MAS*, and *LAIR* are lncRNAs regulating mRNA transcription in *cis*. *PMS1T* is a lncRNA acting as a phasiRNA precursor. *IPS1* regulates PHO2 by acting as the endogenous target mimic of miR399 and affects phosphate homeostasis together with another lncRNA, *NAT_{pho1;2}*. *Pri-miR171b* is a peptide-encoding lncRNA. PROMPTs and *ASCO*-lncRNA are protein-binding lncRNAs that suppress the function of target proteins.

alternative splicing regulators (NSRs) are *trans* regulated by lincRNAs in *M. truncatula* and *Arabidopsis* (Bardou et al. 2014, Campalans et al. 2004). The *Arabidopsis* lincRNA *ELF18-INDUCED LONG-NONCODING RNA 1* (*ELENA1*) interacts with MEDIATOR SUBUNIT 19a (MED19a) in *trans* and affects MED19a enrichment at the *PATHOGENESIS-RELATED 1* (*PR1*) promoter to enhance resistance to pathogens (Seo et al. 2017).

Few functional incRNAs have been identified in plants. The incRNA *COLDAIR* is transcribed in the sense direction from the first intron of *FLC* in *Arabidopsis* and regulates *FLC* transcription in *cis* (De Lucia et al. 2008, Kim & Sung 2013, Sung & Amasino 2004) (**Figure 3**). Finally, linear lincRNAs named promoter upstream transcripts (PROMPTs) are transcribed approximately 0.5–2.5 kb upstream of transcription start sites of protein-coding genes (Wu et al. 2017). PROMPTs have rapid turnover rates and regulate target genes both in *cis* and in *trans* (Song et al. 2018) (**Figure 3**).

Given the limited number of studies on plant lncRNAs, the above-described *cis* or *trans* regulatory preferences revealed by recent studies may not reflect general rules of lncRNA activities. Functional studies such as in situ activation/inactivation of lncRNAs will be useful for identifying their targets and uncovering their regulatory functions.

3.1.2. Circular long noncoding RNAs.

Although circRNAs are present in many species, they cannot be detected by transcriptome profiling using polyadenylated RNAs owing to their non-polyadenylated loop structures, and they were only recently identified by specific RNA sequencing approaches (X.O. Zhang et al. 2014). Most circRNAs are produced from back-splicing reactions of internal exons in pre-mRNAs and are exported to the cytoplasm (Wu et al. 2017). Other circRNAs are produced from excised intron lariats that fail to be debranched, and these circRNAs are preferentially localized in the nucleus (Wu et al. 2017).

A large number of circRNAs have been identified from *Arabidopsis* (Chen et al. 2017, Pan et al. 2018), rice (*Oryza sativa*) (Lu et al. 2015, Ye et al. 2017), tomato (*S. lycopersicum*) (Tan et al. 2017), sea buckthorn fruit (*Hippophae rhamnoides* Linn.) (Zhang et al. 2017), kiwifruit (*Actinidia* Lindl.) (Wang et al. 2017), barley (*Hordeum vulgare*) (Darbani et al. 2016), cotton (several *Gossypium* species) (Xiang et al. 2018, T. Zhao et al. 2017), soybean (*Glycine max*) (Chen et al. 2018a, W. Zhao et al. 2017), maize (*Zea mays*) (Chen et al. 2018b, Tang et al. 2018), and wheat (*Triticum aestivum*) (Y. Wang et al. 2016). circRNAs are expressed in a tissue-specific manner in different plants and exhibit a much higher degree of conservation than linear lncRNAs, but their abundance is extremely low (Chu et al. 2018, Lai et al. 2018). In animals, most circRNAs have complementary sequences such as repetitive elements in the introns flanking circularized exons; these sequences are essential for efficient exon circularization by RNA pairing across the flanking introns (Aktaş et al. 2017). In plants, however, intron pairing–driven circularization appears not to be the main mechanism of circRNA biogenesis. Instead, the production of most plant circRNAs may depend on noncanonical (non-GT/AG) splicing signals (Chu et al. 2018, Ye et al. 2017).

Few functional studies have been performed on plant circRNAs. One *Arabidopsis* circRNA from exon 6 of *SEPALLATA 3* (*SEP3*) negatively regulates its parental gene in *cis* (Conn et al. 2017). The *SEP3* exon 6 circRNA binds to its cognate DNA locus to form an R-loop, which results in transcriptional pausing and increases the abundance of the exon-skipped alternative splicing variant of *SEP3*, in turn driving floral homeotic phenotypes (Conn et al. 2017). Beyond this example, further studies are needed to reveal the regulatory functions of circRNAs.

3.2. Modes of Action of Long Noncoding RNAs

The modes of action of plant lncRNAs are diverse and complex. lncRNAs can act with different molecules to modulate transcription, translation, or epigenetic modification of their target genes.

Interestingly, a subset of lncRNAs encodes peptides (<100 amino acids) necessary for a variety of cellular processes (Plaza et al. 2017).

3.2.1. Long noncoding RNAs partner with different molecules.
lncRNAs influence gene expression by acting as molecular scaffolds or decoys. As molecular scaffolds, lncRNAs influence gene expression by targeting regulatory factors such as chromatin remodelers to specific gene loci. As decoys, lncRNAs sequester proteins from their targets of action to regulate gene expression.

Plant lncRNAs regulate transcription through chromatin modifications, they may bind both DNA and protein, and they probably act as scaffolds. For example, *COLDAIR* and *COOLAIR*, both transcribed from the *FLC* locus in *Arabidopsis*, physically associate with *FLC* chromatin and recruit chromatin remodelers. This activity affects histone marks such as H3K36me3, H3K4me3, and H3K27me3 to regulate vernalization and seed dormancy (Chen & Penfield 2018, Kim & Sung 2013, Marquardt et al. 2014) (**Figure 3**). Similarly, the rice NAT *LAIR* localizes to the *LRK* genomic region and recruits chromatin-modifying complexes (*MALES-ABSENT-ON-THE-FIRST* and *WD REPEAT DOMAIN 5*) to increase H3K4me3 and H4K16ac levels at this gene (Y. Wang et al. 2018) (**Figure 3**). Although not confirmed, this mechanism may also underlie the function of the lincRNA *HID1*, which promotes photomorphogenesis and suppresses cotyledon greening in *Arabidopsis* (Y. Wang et al. 2014).

In addition to regulating transcription, some lncRNAs function as decoys that alter the behavior of target proteins. *ASCO*-lncRNA is an *Arabidopsis* lincRNA that binds NSRs, which are splicing factors, and competes with the alternative splicing targets of NSRs to modulate alternative splicing and gene expression during developmental transitions (Bardou et al. 2014) (**Figure 3**). Interestingly, NSRs also bind to the lncRNA *ENOD40*, inducing its relocalization from nuclear speckles to the cytoplasm in both *Arabidopsis* and *M. truncatula* (Campalans et al. 2004). PROMPTs can also act as decoy lncRNAs. For example, *PROMPT_1281* binds MYB transcription factors to prevent them from interacting with DNA to induce target gene expression (Song et al. 2018) (**Figure 3**). It remains to be determined whether the decoy mechanism is universal for PROMPTs.

3.2.2. Long noncoding RNAs may encode small peptides.
Although lncRNAs by definition do not encode proteins or harbor ORFs for proteins greater than 100 amino acids, some lncRNAs are translated into small polypeptides of less than 100 amino acids (Matsumoto & Nakayama 2018). In some cases, these small peptides are necessary for a variety of cellular processes.

ENOD40 was the first lncRNA shown to encode functional peptides in *Medicago sativa* and soybean (Rohrig et al. 2002, Sousa et al. 2001). Two small peptides of 12 and 24 amino acids are synthesized from soybean *ENOD40* RNA; both bind to the nodulin100 protein (a subunit of sucrose synthase), regulate sucrose use in nodules, and contribute to root nodule organogenesis (Rohrig et al. 2002). However, the *ENOD40* RNA molecule also plays a role independent of peptides, such as binding the *M. truncatula RNA BINDING PROTEIN 1* and *SMALL NODULIN ACIDIC RNA-BINDING PROTEIN* peptides (Campalans et al. 2004, Laporte et al. 2010). This role suggests that peptides encoded by lncRNAs are sometimes required for lncRNA function. Pri-miRNAs also encode peptides in *M. truncatula* and *Arabidopsis* (Lauressergues et al. 2015) (**Figure 3**). circRNAs are localized mainly in the cytosol, raising the possibility of their being translated. In animals, peptides are produced from circRNAs in a cap-independent manner and are functional (Pamudurti et al. 2017). Translation of circRNAs has not been demonstrated in plants.

Not all small ORFs present in lncRNAs encode peptides in vivo, or even if small peptides are made, they may not be functional. *LAIR*, discussed above, has the potential to encode short peptides, but mutations in the stop or start codons of the predicted small peptides do not affect

LAIR function, indicating that *LAIR* more likely functions as a lncRNA (Y. Wang et al. 2018). A priori, it may not be clear whether lncRNA function is mediated by the RNA or the small peptide it encodes. It is therefore necessary to predict small ORFs when studying the function of lncRNAs and to generate transgenic plants that eliminate the ORFs to ascertain the potential functional contribution of the small peptides.

3.3. Plant Long Noncoding RNAs in Stress Responses and Development

Plants are often exposed to biotic or abiotic stresses harmful for development and survival, such as pathogen infection, extreme temperature, drought, and salt. Reproductive development is especially sensitive to certain stresses, which may cause sterility or reduced yield (Begcy & Dresselhaus 2018). To counter such stresses, plants have evolved survival strategies that involve lncRNAs, which tend to be stress responsive as well as spatially and temporally specific in expression. Therefore, lncRNAs are thought to function as effectors during stress responses.

3.3.1. Long noncoding RNAs that respond to various stresses. Numerous plant lncRNAs are regulated by abiotic stresses. In *Arabidopsis*, differentially expressed lncRNAs have been identified under drought, cold, salinity, heat, and abscisic acid stresses (Di et al. 2014). lncRNAs responsive to various abiotic stresses have also been identified in other plant species (Ding et al. 2019, Pang et al. 2019, Qi et al. 2013, A. Wang et al. 2019, P. Wang et al. 2019, T.Z. Wang et al. 2015, W. Zhang et al. 2014). Biotic stress-responsive lncRNAs have been identified in wheat, *Arabidopsis*, grapevine, *Hevea brasiliensis*, and tomato (J. Wang et al. 2015, Xin et al. 2011, Xing et al. 2019, Yin et al. 2019, Zhang et al. 2013, Zhu et al. 2014). Several stress-responsive lncRNAs have been functionally analyzed, including the *Arabidopsis* drought- and salt-responsive lncRNA *DRIR*, whose elevated expression increases tolerance to drought and salt stresses (Qin et al. 2017). Tomato *lncRNA16397* responsive to *Phytophthora infestans* infection is a NAT of *GLUTAREDOXIN 22* and functions in *cis* to induce *GLUTAREDOXIN 22* expression, resulting in enhanced pathogen resistance (Cui et al. 2017).

Some conditions that lead to stress-specific expression patterns of circRNAs in plants include dehydration stress in wheat (Y. Wang et al. 2016), chilling in tomato (Zuo et al. 2016), nutrient depletion in rice (Ye et al. 2015) and barley (Darbani et al. 2016), and *Pseudomonas syringae* pv. *actinidiae* infection in kiwifruit (Wang et al. 2017). Differential expression of circRNAs usually does not correlate with the expression of their precursor mRNAs, suggesting that circRNAs are not simply by-products of host gene expression but rather may be functional molecules in environmental and stress responses.

Functional studies of plant stress-responsive lncRNAs are at an early stage. Given that plant lncRNAs are extremely responsive to stresses in their expression and that they evolve rapidly compared with protein-coding genes, they make suitable environmental sensors or effectors to help plants adapt to changing environments.

3.3.2. Regulatory roles of long noncoding RNAs at the nexus of plant development and environmental responses. Interestingly, lncRNAs involved in plant developmental regulation are often also regulated by environmental conditions, indicating their potential impacts on both plant development and environmental responses. The most representative examples are *COLDAIR* and *COOLAIR*, which promote flowering when plants are exposed to cold (Whittaker & Dean 2017) (**Figure 3**). Another example is *long-day-specific male-fertility-associated RNA* (*LDMAR*), which is highly and specifically expressed under long days and is required for normal pollen development under long-day conditions (Ding et al. 2012a). A single-nucleotide polymorphism

(SNP) at the *LDMAR* locus increases RdDM at its promoter region, reducing *LDMAR* transcription specifically under long-day conditions and resulting in premature programmed cell death in developing anthers (Ding et al. 2012a,b). The *photoperiod-sensitive genic male sterility 1* (*Pms1*) locus encodes another lncRNA, *PMS1T*, which is associated with photoperiod-sensitive male sterility (Fan et al. 2016) (**Figure 3**). An example of a salinity-responsive lncRNA is *npc536*, and its overexpression in *Arabidopsis* increases salt tolerance as well as primary and secondary root growth (Ben Amor et al. 2009). Recent studies have identified transcription factors that regulate lncRNA expression under biotic and abiotic stresses (Di et al. 2014, Nejat & Mantri 2018, Zhu et al. 2014).

The expression of stress resistance genes is often associated with reduced fitness, reflecting the inherent trade-off between stress responses and growth. The involvement of lncRNAs in both stress responses and plant growth makes them potential balancing factors in plants grown under different environmental conditions. Thus, lncRNAs may be good targets for the genetic engineering of crops aimed at increasing broad-spectrum disease resistance or stress resistance while mitigating yield loss.

4. LINKS BETWEEN LONG NONCODING RNAS AND SMALL RNAS

Long or medium-sized ncRNAs can be related to small RNAs in that they serve as precursors to siRNAs and miRNAs, as scaffolds to recruit siRNAs, or as sponges to sequester miRNAs. By definition, precursors to miRNAs and phasiRNAs lack long ORFs and are lncRNAs. So far, there has been no evidence of these lncRNAs having functions other than producing small RNAs. For example, *PMS1T* is a precursor to phasiRNAs. *PMS1T* is targeted by miR2118 to produce 21-nt phasiRNAs that preferentially accumulate in a photoperiod-sensitive male sterile mutant under long-day conditions (Fan et al. 2016). A SNP near the miR2118 recognition site leads to differential accumulation of phasiRNAs and underlies variations in fertility (Fan et al. 2016) (**Figure 3**). The abovementioned *LDMAR* locus was reported to generate siRNAs (Ding et al. 2012b), and our inspection of the locus suggested that *LDMAR* is likely a *PHAS* locus producing phasiRNAs. This implicates lncRNA-phasiRNAs as playing critical roles in sexual reproductive development in grasses (Yu et al. 2018). Pol V–generated transcripts are lncRNAs that serve as scaffolds to recruit siRNAs to chromatin (Wierzbicki et al. 2008). These relationships between lncRNAs and siRNAs are discussed in Sections 1 and 2.

A commonly observed function of lncRNAs in animals and plants is binding miRNAs as target mimics. In *Arabidopsis*, rice, and tomato, lncRNAs acting as potential target mimics have been identified on a large scale through RNA sequencing and bioinformatic prediction (Jiang et al. 2019, Wu et al. 2013). However, only a small number of endogenous target mimics (eTMs) are known to be functional. *INDUCED BY PHOSPHATE STARVATION 1* (*IPS1*) was the first confirmed eTM lncRNA in plants (Franco-Zorrilla et al. 2007) (**Figure 3**). *Arabidopsis IPS1* and its close paralog *At4* are target mimics of miR399 and are involved in phosphate (P_i) accumulation; *Pi-deficiency-induced long-noncoding RNA1* has a similar function in maize (Du et al. 2018, Khan et al. 2014) (**Figure 3**). In animals, a small number of circRNAs have been shown to sequester miRNAs to upregulate expression of their targets (Li et al. 2018). However, plant circRNAs are not known to act through miRNAs. Harboring of an miRNA binding site by a lncRNA does not necessarily impart an eTM function. The levels of the lncRNA need to be comparable to those of the miRNA for the lncRNA to be a functional eTM. In plants, miRNAs can cause the cleavage of target RNAs. Thus, a functional eTM needs to be able to bind the miRNA but also avoid cleavage, as in the case of *IPS1*.

Why do plants and animals employ eTMs to repress miRNA function? Other mechanisms for repressing miRNA functions include inhibiting miRNA biogenesis and enhancing miRNA

turnover. We speculate that eTMs offer a faster way to repress miRNA activity than repressing miRNA abundance. miRNAs tend to have long half-lives, which makes it difficult to quickly reduce the abundance of miRNAs when necessary (such as when plants are under stress). In fact, artificial target mimic RNAs cause the degradation of cognate miRNAs (Todesco et al. 2010, Yan et al. 2012), and eTMs may thus trigger miRNA turnover in addition to blocking miRNA activity.

5. CELL-TO-CELL AND SYSTEMIC MOVEMENT OF NONCODING RNAS

5.1. Trafficking of microRNAs

Plant small RNAs can move locally between adjacent cells or over long distances, serving as functional molecules to spread silencing signals (Chitwood & Timmermans 2010, Gursanscky et al. 2011). miRNAs are better known for short-range intercellular trafficking, largely through plasmodesmata. For proper leaf patterning, miR165/166 movement from the abaxial (lower) to the adaxial (upper) leaf region results in a gradient distribution that helps establish adaxial domain–specific expression of *HD-ZIP III* genes (Benkovics & Timmermans 2014). In roots, miR165/166 moves from the endodermis to the vasculature to control protoxylem and metaxylem patterning by forming an expression gradient of *PHB* in the vasculature (Carlsbecker et al. 2010, Miyashima et al. 2011). In shoot meristems, the movement of L1 layer–expressed miR394 to the underlying L2 and L3 layers, where its target gene *LCR* is expressed, is essential for stem cell maintenance (Knauer et al. 2013). In maize, miR2118 is specifically expressed in the epidermis of developing anthers and moves to the subepidermal cell layers, where it targets noncoding transcripts for the biogenesis of phasiRNAs (Zhai et al. 2015b). The cell-to-cell trafficking of miRNAs probably occurs through passive diffusion through the plasmodesmata (Carlsbecker et al. 2010). However, miRNA movement is likely regulated, as the capacity for and the directionality of trafficking are different at different cell-to-cell interfaces and different from that of mobile proteins (Skopelitis et al. 2018). In addition to these examples of local cell-to-cell movement, some miRNAs spread over long distances via phloem. For example, miR399 moves from shoots to roots in response to phosphate deficiency in *Arabidopsis* (Lin et al. 2008, Pant et al. 2008). Similarly, the levels of miR395 and miR398 are significantly increased in phloem sap (PS) when *Brassica rapa* plants undergo sulfate and copper deficiency, respectively (Buhtz et al. 2008, Yoo et al. 2004), suggesting that these miRNAs function as systemic silencing signals to regulate their target genes. Under conditions of nutrient stress in *Arabidopsis*, miR395 and miR399 translocate from wild-type scions to *hen1-1* mutant rootstocks, accompanied by reduced levels of their targets in the roots (Buhtz et al. 2010). Moreover, the shoot-to-root translocation of miR2111 in *Lotus japonicus* contributes to balancing bacterial infection and nodule organogenesis through repressing the symbiosis suppressor *TOO MUCH LOVE* (*TML*) (Tsikou et al. 2018).

5.2. Systemic Movement of Transposable Element–Derived Small Interfering RNAs

Almost all plant siRNAs are capable of moving locally or over long distances, as evidenced by studies using grafting and agroinfiltration strategies (Bai et al. 2011, Tamiru et al. 2018). In *Arabidopsis*, grafting experiments were performed combining wild type with the *dcl2/3/4* triple mutant, in which the production of 21–24-nt siRNAs is compromised. The experiments show that 24-nt mobile siRNAs translocate from shoot to root across graft unions and mediate DNA methylation in recipient cells at thousands of loci associated with transgenes or endogenous TEs (Lewsey et al. 2016; Melnyk et al. 2011a,b). Furthermore, mobile siRNA-directed DNA methylation primarily

occurs in non-CG contexts and largely depends on DRM1/DRM2 (Lewsey et al. 2016). However, it remains unclear whether TE-derived siRNAs also move from root to shoot and affect DNA methylation in the shoot. Although mobile siRNAs target many TE loci, they have few effects on gene expression, probably due to the low density and transposition activity of TEs in *Arabidopsis*.

5.3. Trafficking of Phased Small Interfering RNAs Between Cells

Similar to miRNAs and TE-derived siRNAs, phasiRNAs are also mobile, and the best example is the cell-to-cell trafficking of tasiRNA-ARFs. The biogenesis of tasiRNA-ARFs is thought to occur in the adaxial-most cell layers of leaves, where *AGO7* (a gene required for tasiRNA-ARF biogenesis) and *TAS3A* (a gene from which tasiRNA-ARFs are generated) are expressed. But mature tasiRNA-ARFs form an adaxial-abaxial gradient to restrict *ARF3* expression to the abaxial side, which ensures proper leaf patterning. Additionally, tasiRNA-ARFs are generated in the cells beneath the SAM, where *AGO7* is expressed, and act non–cell autonomously within the SAM region (Chitwood et al. 2009). The intercellular mobilization of 24-nt reproductive phasiRNAs in rice and maize anthers has also been proposed, although decisive evidence is lacking (Ono et al. 2018, Zhai et al. 2015b).

5.4. Movements of Long Noncoding RNAs Through the Phloem

It was recently reported that lncRNAs are enriched in the PS and respond to imposed phosphate stress (Zhang et al. 2019). Specifically, hundreds of lncRNAs were detected in source tissues, sink tissues, and PS in cucumber. Among these PS lncRNAs are those encoding IPS1 and 24 other potential eTMs. As with the PS mRNAs, a CU-rich polypyrimidine-tract-binding motif was identified in the mobile lncRNAs (Zhang et al. 2019). These findings raise the possibility that lncRNAs are transported to distant tissues and may even act in systemic signaling. Future studies investigating long-distance RNA movement in plants will need to address how RNAs are selected for phloem access, whether they are unloaded into recipient tissues, and whether and how they function in recipient tissues. Viroid circRNAs have been reported to move cell-to-cell and long distances in plants (Ding et al. 2005, Wang & Ding 2010). circRNAs have also been found in animal exosomes, which can be released into the extracellular microenvironment (Fanale et al. 2018). Further work will elucidate whether plant circRNAs are mobile and serve as signaling molecules.

6. FUTURE PERSPECTIVES

While miRNAs have long been recognized as key components of cellular regulatory networks, siRNAs as well as lncRNAs are also emerging as regulatory molecules. However, studies of plant phasiRNAs, lncRNAs, and circRNAs are at a relatively early stage, with many outstanding questions awaiting further investigation. Thus, unraveling the complexity, biogenesis, and action of plant ncRNAs, especially lncRNAs, remains an important challenge. Furthermore, new classes of ncRNAs in plants likely await discovery. For example, novel lncRNA species that have recently been identified in mammals—such as small nucleolar RNA (snoRNA)-ended and tRNA-ended lncRNAs, which are processed by noncanonical mechanisms—have not yet been reported in plants (Wu et al. 2017). Although not discussed in this review, snoRNAs are key regulators of the transcriptome and translatome by guiding RNA methylation and/or pseudouridylation (Kiss 2002). Plant snoRNAs are poorly understood in terms of their targets and biological functions.

The functions of small RNAs, lncRNAs, and small peptides overlap in many cases, and revealing these functions during plant development or stress responses is one major challenge. The

CRISPR-Cas system will enable new strategies for further identifying and analyzing components of the plant ncRNA network. Crop breeding aims to select plant varieties with disease resistance and desired growth characteristics such as high yield; however, plant growth is usually repressed by an active immune response (J. Wang et al. 2018). As molecules involved in both development and immunity, lncRNAs may be a good resource for balancing growth and immunity in crops.

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