microRNAs and Their Roles in Plant Development

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Small RNAs are short non-coding RNAs with a length ranging between 20 and 24 nucleotides. Of these, microRNAs (miRNAs) play a distinct role in plant development. miRNAs control target gene expression at the post-transcriptional level, either through direct cleavage or inhibition of translation. miRNAs participate in nearly all the developmental processes in plants, such as juvenile-to-adult transition, shoot apical meristem development, leaf morphogenesis, floral organ formation, and flowering time determination. This review summarizes the research progress in miRNA-mediated gene regulation and its role in plant development, to provide the basis for further in-depth exploration regarding the function of miRNAs and the elucidation of the molecular mechanism underlying the interaction of miRNAs and other pathways.

Keywords: microRNA, plant development, microRNA movement, hormone, crop yield

INTRODUCTION

RNA is one of the four major macromolecules of life and is essential in the regulation and expression of genes. RNA can be divided into two groups: coding and non-coding RNAs. In plants, 24 nt small interfering RNAs (siRNA) and 21 nt microRNAs (miRNA) have the highest expression abundance of small non-coding RNAs. siRNAs were first discovered in plants and are involved in the transcriptional gene silencing and post-transcriptional gene silencing (PTGS) pathway in plants (Hamilton and Baulcombe, 1999; Sijen et al., 2001; Pal-Bhadra et al., 2002) and RNA interfering pathway in animals (Elbashir et al., 2001).

miRNAs were first identified from nematodes (*Caenorhabditis elegans*) by Victor Ambros lab in collaboration with Gary Ruvkun lab, who confirmed that a miRNA (Lin-4) has a role in regulating the temporal developmental of nematode larvae (Lee et al., 1993; Wightman et al., 1993; Fire et al., 1998; Stricklin et al., 2005). Since then, miRNAs have been reported in *Drosophila*, nematodes, mammals, and plants. In plants, 22 nt miRNA is able to cut the target mRNA and the cleavage product can be further processed by RNA-DEPENDENT RNA POLYMERASE 6 (RDR6) and DICER-LIKE 4 to produce secondary 21 nt siRNA. In addition, the symmetric miRNA/miRNA* can be processed by DCL2 and generate secondary 22 nt miRNAs. These siRNAs are called phased siRNAs (PhasiRNAs) because they are the endogenous plant siRNAs with phase arrangement structure characteristics (Borges and Martienssen, 2015). PhasiRNA can be divided into cis-acting siRNA and trans-acting siRNA (ta-siRNA; Chen et al., 2010; Zhai et al., 2011; Arikit et al., 2014; Deng et al., 2018).

miRNAs are demonstrated to be vital in plant development. They are usually transcribed by RNA Polymerase II (Pol II) into pri-miRNAs. These pri-miRNAs are cleaved by a class of RNase-III nucleases called Dicer-like proteins, after which they combine with ARGONAUTE

(AGO) family proteins to form the RNA-induced silencing complexes (RISCs). RISCs are then involved in the expression and regulation of target genes (Song et al., 2019). miRNAs act in the regulation of meristem characteristics, leaf polarity, flowering patterns. etc. Mutations in miRNA transcription or processing complexes usually have multiple effects on plant from and function, indicating that miRNAs are important to coordinate plant development. For example, the roles of HD-ZIP III-miR165/166 pathway are important in the development of vascular, meristem, and leaf polarity, and the roles of miR156/miR172 are important in flowering time and flower pattern (D'Ario et al., 2017; Ramachandran et al., 2017; Du et al., 2020; Ma et al., 2020; Lian et al., 2021; Yadav et al., 2021). During plant development, endogenous miRNAs play an important role in gene regulation by targeting related target genes. Several miRNAs function through interactions with hormones. Many components in hormone signaling are targets of miRNAs, and the interactions of these components and the miRNAs enable plants to regulate their growth, development, and differentiation rapidly and effectively. This signaling is done by selecting miRNAs as intermediates to control hormone responses or, conversely, by using hormones to regulate specific miRNA levels (Jodder, 2020; Li et al., 2020; Yu and Wang, 2020). There is evidence indicating that miRNAs can diffuse in tissues as inhibitor signals, so they play an elaborate role in tissue differentiation (Chen and Rechavi, 2021). Here we will summarize the role of miRNAs in the aspects of biogenesis, action mechanism, function in specific tissues, interaction with hormones, and movement to understand how they regulate plant development. miRNAs and their targets involved in plant development are listed in **Table 1**.

BIOSYNTHESIS AND ACTION MECHANISM OF miRNAs IN PLANTS

Most of miRNAs are a kind of conserved endogenous small RNA, which plays an important regulatory role after eukaryotic gene transcription (Rodriguez et al., 2010). Most metazoan miRNA genes exist in thousands of introns or exons, whereas plant miRNA genes exist between genes. In addition to this, the secondary structures and lengths of miRNA are greatly different among plant species (Voinnet, 2009). Animal miRNAs exist in clusters along the genome, and they can be co-transcribed in the form of poly-cistrons (Ha and Kim, 2014). In contrast, plant miRNA genes are rarely arranged in series (Kim, 2005; Zhang et al., 2008). Like protein-coding genes, miRNAs start by being transcribed in the nucleus by Pol II to form pri-miRNAs, which range in length from several hundred to several thousand nucleotides and have a 5′ cap and a 3′ poly-A tail (Jones-Rhoades and Bartel, 2004; Lee et al., 2004; Jones-Rhoades et al., 2006). Under the action of DCL1, pri-miRNAs are cleaved into pre-miRNAs, which are ~70 nt – 350 nt. These pre-miRNAs are further formed by the interaction of the DCL1 enzyme, RNA-binding protein HYL1 (Hyponastic Leaves 1), and C2H2 zinc finger protein SE (Serrate) on pre-miRNA (Kurihara and Watanabe, 2004; Jones-Rhoades et al., 2006) into

mature miRNAs. The mature miRNAs have 2 bases protruding at the 3′ end (miRNA double-stranded complex). This miRNA complex is methylated at the 2′-OH position of its 3′ end under the action of HUAENHANCER1 protein to prevent degradation (Li et al., 2005). Most of the methylated miRNA complexes are transported into the cytoplasm with the help of plant homolog of exportin-5, HASTY (HST; Park et al., 2005; Brioudes et al., 2021). The RNA-induced RISC, generated by miRNA, is eventually produced in the cytoplasm (Park et al., 2005; Jones-Rhoades et al., 2006). Recent studies showed that RISC can be assembled in the nucleus and exported to the cytosol by EXPO1 (Bologna et al., 2018), and HST also regulates pri-miRNA transcription and processing (Cambiagno et al., 2021). In the RISC complex, the AGO protein is the most important structural protein. It contains four domains: the N-terminal domain (N), the PIWI/Argonaute/Zwille (PAZ) domain, the MID domain, and the P-element-induced wimpy tested (PIWI) domain. The PAZ domain can bind to RNA and the PIWI domain with RNase H activity. 10 different types of AGO proteins have been found in *Arabidopsis thaliana*; most of them contain catalytic reaction residues. Of these different AGO proteins, ARGONAUTE1 (AGO1; Baumberger and Baulcombe, 2005; Qi et al., 2005), AGO2 (Carbonell et al., 2012), AGO4 (Qi et al., 2006), AGO7 (Montgomery et al., 2008), and AGO10 (Ji et al., 2011; Zhu et al., 2011) have been demonstrated in the gene silencing pathway of target RNAs. AGO1 protein is involved in PTGS as the main component of RISC that binds to a short guide RNA such as miRNA or siRNA. AGO4 and AGO6 are mainly involved in the repeat-associated siRNA pathway, and AGO7 plays a role in the formation of ta-siRNA (Vaucheret, 2008; Duan et al., 2015; Singh et al., 2015; Fang and Qi, 2016).

Studies have shown that mature miRNAs inhibit the translation of target genes, regulate the expression of plant genes by complementary pairing with coding region, some binding to 3′UTR and 5′UTR of the target mRNA, or regulate the expression of genes by cutting target gene mRNA at the post-transcriptional level. This inhibition by mature miRNAs alters the morphogenesis of plant organs, growth, development, hormone secretion, signal transduction, and the ability of plants to respond to external stress and environmental factors (Liu et al., 2009a; Yokotani et al., 2009; Naqvi et al., 2012). miRNA in plants is highly complementary to its target mRNA, so its main mode of action is cleavage. The translation inhibition pathways in plants have only been found in recent years. The cleavage and inhibition mechanisms are mostly coordinated depending on the complementarity between miRNAs and their targets (Brodersen et al., 2008; Yu et al., 2017; O'Brien et al., 2018).

THE FUNCTION OF miRNAs IN PLANT GROWTH AND DEVELOPMENT

The regulation of plant growth and development is very precise and is influenced by both internal genetic information and the external environmental factors. Normal expression of miRNAs is necessary for the growth and development of plants. Previous studies have shown that miRNA widely regulates plant growth and development.

TABLE 1 | miRNAs, the targets, and their roles in plant development.

miRNA	Target	Target function	Species	References
miR156	SPL family	Plastochron length, promoting flowering; Leaf development, root development, secondary metabolism and abiotic stress; tillering and corn development in *Zea mays*	*Arabidopsis* and *Zea mays*	Aukerman and Sakai, 2003; Chuck et al., 2007a, 2010; Wang et al., 2008; Xu et al., 2016b; Dai et al., 2018
miR159	GAMYB or GAMYB-like gene	Male reproductive development, seed development, vegetative tissues and reproductive development	*Arabidopsis*	Allen et al., 2007; Millar et al., 2019
miR160	ARFs	Embryo, leaf and root development, hypocotyl elongation	*Arabidopsis*, Medicago truncatula and *Zea mays*	Bustos-Sanmamed et al., 2013; Lopez-Ruiz et al., 2019; Yang et al., 2019; Dai et al., 2021
miR164	NAC family	Meristem boundary identity, Auxiliary meristem formation, leaf and flower development, lateral root initiation	*Arabidopsis*, *Zea mays* and *Oryza*	Li et al., 2003; Laufs et al., 2004; Hibara et al., 2006; Raman et al., 2008; Zheng et al., 2019; Wang et al., 2021b
miR165/166	HD-ZIP III	Maintaining meristematic cells, adaxial identity of leaves, lateral root growth, and procambium identity	*Arabidopsis*	Williams et al., 2005; Jia et al., 2015; Merelo et al., 2016; Yan et al., 2016
miR167	ARFs	Development of male organ、roots、stems、leaves and flowers, flowering time, embryonic development, seed development and stress response, defense against pathogens	*Arabidopsis* and *Oryza*	Wu et al., 2006; Liu et al., 2012; Yao et al., 2019; Caruana et al., 2020
miR169	CBF and NF-YA family	Enhancer of C homeotic gene transcription and root architecture	*Arabidopsis*, *Antirrhinum majus* and *Zea mays*	Cartolano et al., 2007; Sorin et al., 2014; Xu et al., 2014; Xing et al., 2021
miR171	SCL	Chlorophyll biosynthesis, phase transitions and floral meristem determinacy	*Arabidopsis*，barley	Curaba et al., 2013; Ma et al., 2014; Li et al., 2021
miR172	AP2 family	Represses flowering, flower meristem identity and patterning; vegetative phase change, carpel and stamen development; flower opening, tuberization and *salt tolerance*	*Arabidopsis*, *Z. mays*, *Oryza*,*H. vulgare*, and *S. tuberosum*	Chuck et al., 2007b; Martin et al., 2009; Wu et al., 2009; Nair et al., 2010; Wollmann et al., 2010; Zhu and Helliwell, 2011; Cheng et al., 2021a; Lian et al., 2021; Werner et al., 2021
miR319	TCP family	Leaf development and senescence, organ curvature, and hormone biosynthesis and signaling.	*Arabidopsis* and *Solanum lycopersicum*	Ori et al., 2007; Schommer et al., 2014; Koyama et al., 2017; Bresso et al., 2018
miR390	TAS3	ta-siRNA biogenesis for ARF repression and indirect miR165/166 regulation，lateral root growth，leaf patterning	*Arabidopsis*	Fahlgren et al., 2006; Marin et al., 2010; Endo et al., 2013; Dastidar et al., 2019
miR393	TIR1 and AFB	Auxin homeostasis, lateral root growth, leaf shape/number	*Arabidopsis* and *Oryza*	Parry et al., 2009; Chen et al., 2011; Windels and Vazquez, 2011; Lu et al., 2018; Wang et al., 2018
miR394	LCR	Meristematic identity suppression *via* WUS downregulation, leaf inclination and architecture,	*Arabidopsis*	Baumann, 2013; Knauer et al., 2013; Qu et al., 2019
miR396	GRF	Cell proliferation in leaves, disease-resistance, somatic embryogenesis, grain size and panicle branching	*Arabidopsis*, *Medicago*, and *Oryza*	Debernardi et al., 2012; Bazin et al., 2013; Liu et al., 2014a; Chandran et al., 2018; Szczygiel-Sommer and Gaj, 2019; Liebsch and Palatnik, 2020; Zhang et al., 2020
mir397	OsLAC	Grain yield, panicle branches	*Oryza*	Zhang et al., 2013
miR824	AGL16	Stomatal patterning	*Arabidopsis*	Bergmann and Sack, 2007
miR828 and miR858	MYBs	Fiber development, anthocyanin, and flavonol accumulation	Cotton, grapes	Guan et al., 2014; Tirumalai et al., 2019
miR847	IAA28	Lateral root formation	*Arabidopsis*	Wang and Guo, 2015
miR857	LACCASE7	Secondary growth	*Arabidopsis*	Abdel-Ghany and Pilon, 2008; Zhao et al., 2015
TAS3	ARF3/4 and (only in mosses) AP2-like	Vasculature development, Leaf polarity / phase transition	All land plants	Fahlgren et al., 2006; Jing et al., 2017

The Role of miRNAs in the Shoot Meristem

Unlike animals, plants can continuously produce new organs throughout their life cycle. Their apical meristem forms in embryo and has a group of stem cells with multidirectional differentiation potential and the ability to self-replicate. During the development of a plant, the shoot apical meristem (SAM) plays a central role in the formation and development of its aboveground organs. The STM (shoot meristemless)-WUS (Wuschel)-CLV (Clavata) pathway plays a key role in the maintenance of meristem activity (Schoof et al., 2000; Gaillochet and Lohmann, 2015; Somssich et al., 2016). To some extent, the same mechanisms are also demonstrated in flower meristems.

miRNA plays a central role in the regulation of gene expression networks, orchestrating the establishment and the maintenance

of the SAM by targeting and regulating multiple genes in the STM-WUS-CLV signaling pathway (**Figure 1**). miR394 is generated in the L1 layer on the surface of the SAM and diffuses down to the Organizing Center (OC; **Figure 1**). In the OC, expression of Leaf Curling Responsiveness (*LCR*) is inhibited (Knauer et al., 2013) and directly results in the downregulation of *WUS*, a SAM-specific gene (Song et al., 2012). Although the concentration of miR394 in the L1 layer is higher than that in the OC layer, the inhibitory effect of miR394 on LCR only occurs in OC, implying that an exact concentration of miR394 is of great importance to its function in *A. thaliana* (Knauer et al., 2013). Meanwhile, there are diversified functions for stem cell regulation mediated by miR394-LCR (Kumar et al., 2019). AGO10 can specifically bind to miR165/166 and ultimately promote the expression of *HD-ZIP III*. *HD-ZIP III* is an important transcription factor family that regulates SAM in *A. thaliana* and is a target of miR165/166. When miR166/165 does not bind to AGO10 or the *AGO10* gene is knocked out, the meristematic tissue of plants is destroyed. AGO1 antagonizes AGO10 in the binding of miR166/165. When miR166/165 binds to AGO1, plants will decrease the expression of the *HD-ZIP III* genes and terminate SAM development. Recent studies indicate that the interaction between AGO10 and miR165/166 depends solely on the structure of miR165/166 and is independent of the catalytic activity of AGO10 (Zhu et al., 2011).

The Role of miRNAs in Leaf Development

Leaf development includes the differentiation of leaf primordium from the SAM and the subsequent development of leaf blades. In these processes, various regulatory factors are involved. Organogenesis in the SAM is determined by the distribution and polar transport of auxin (Veit, 2009). The target genes of miR160, namely *ARF10*, *ARF16*, and *ARF17* in the auxin response factors (ARF) family affect leaf development by regulating auxin response. Mutants *arf10* and *arf17* of *A. thaliana* which are resistant to miR160 cleavage, have an abnormal number of cotyledons, and the edge of the leaves was serrated and curled upward (Liu et al., 2007). At the same time, leaf genesis is regulated by several transcription factors, such as the expression of *MYB DOMAIN PROTEIN* (*MYB*) transcription factor, in leaf primordium. These specific ASYMMETRIC LEAVES1/ROUGH SHEATH2/PHANTASTICA gene families can be used as a transcription suppressor to turn off the meristematic specific gene *KNOX1* to promote growth and differentiation (Hay et al., 2004; Piazza et al., 2005). In the process of establishing dorsal–ventral polarity in plant leaves, expression of *HD-ZIP III* and the MYB protein ASYMMETRIC LEAVES1 are the determinants of the ventral axis, while expression of *KANADI* (*KAN*), *ARF3*, and *ARF4* determine the fate of the dorsal axis. The *YABBY* gene acts downstream of the *KAN* gene in *A. thaliana* and is a decisive gene for leaf dorsal development. The function of *HD-ZIP III* genes in leaf polarization is relatively clear (**Figure 2**). The expression of *HD-ZIP III* was maintained only on the adaxial side, as members of *HD-ZIP III* family, are inhibited by miR165/166 on the abaxial side (Zhong and Ye, 2004).
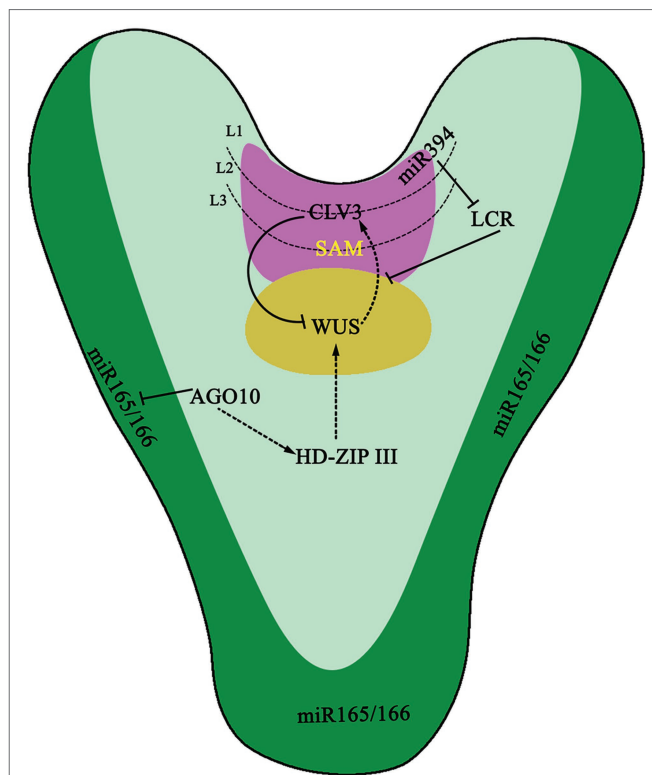

FIGURE 1 | The function of miRNAs in embryo. miR394 expresses in the L1 layer of shoot apical meristem (SAM) and then moves to L3 layer to target *Leaf Curling Responsiveness* (*LCR*) gene. LCR further regulates CLAVATA-WUSCHEL (CLV-WUS) negative feedback loop for proper SAM development and specification. ARGONAUTE10 (AGO10) specifically sequesters miR166/165 to upregulate Class III homeodomain leucine zipper transcription factors (HD-ZIP III TFs) to maintain SAM development. The dotted arrows represent a proposed positive regulation, whereas lines with perpendicular end bars indicate negative regulation.

AGO1 is necessary for targeting miR165/166 to *HD-ZIP III* transcripts in leaves and is required for miR165/166 to regulate and restrict *PHBOLUSA* (*PHB*) to the adaxial side (Kidner and Martienssen, 2004). Like AGO1, the localization of AGO10 on the adaxial side of the leaf is necessary to inhibit the acellular autonomous miR165/166 activity and maintain the accumulation of *HD-ZIP III* mRNA in this region (Liu et al., 2009c).

At the same time, miR390 and its effector AGO7 are required to be involved in leaf polarization (**Figure 2**). TAS3 ta-siRNA determines the adaxial side by inhibiting the expression of *ARF3* and *ARF4* on the abaxial side of leaves (Chitwood et al., 2009). In *Zea maize* and *A. thaliana*, the ventral ta-siARF pathway interacts with the dorsal regulatory factors to some extent. Additionally, the ta-siARF pathway is also required to inhibit the expression of miR165/miR166, which allows for the proliferation of HD-ZIP III. Interference with ta-siARF pathway in maize will obviously affect leaf polarity. Wang et al. reported that miR396 also participated in leaf polarity formation by regulating the proliferation of leaf cells by targeting growth-regulating factors (GRFs), thus affecting the formation of dorsal–ventral axis polarity in leaves (Wang et al., 2011).

miRNAs also regulate leaf size and structure. The balance between miR396 and GRFs ultimately controls the number of cells in leaves and regulates the size of the meristem (Kim et al., 2003; Liu et al., 2009b; Rodriguez et al., 2010; Wang et al., 2011; Baucher et al., 2013; Debernardi et al., 2014). In addition, miR396 can also regulate leaf size through targeting *basic Helix–Loop–Helix 74* (Debernardi et al., 2012) and *CUC2*, which is necessary for the formation of the organ primordial boundary. miR319 regulates the growth and development of *A. thaliana* leaves by degrading the mRNA of the *TCP-like* transcription factor family which can regulate *CUC2* (Palatnik et al., 2007). In addition, *CUC2* expression is also regulated by the repressor miR164 (Koyama et al., 2010). The CUC2-miR164 system plays a key role in the evolution of composite leaves (Blein et al., 2008).

Meanwhile, miR319-TCP4 controls leaf senescence (Sun et al., 2017). The sequences of miR159 and miR319 are very similar, and the leaves of the miR159a miR159b double mutant are curled upward, indicating that miR159 also works on leaf development (Allen et al., 2007). miR393 and its target genes *TRANSPORT INHIBITOR RESPONSE 1* and *AUXIN SIGNALING F-BOX PROTEIN 1/2/3* can affect the shape and size of leaves by regulating the auxin response (Chen et al., 2011).

Stomata are special structures in the plant epidermis. miR824 and its target gene *Agamous Like 16* (*AGL16*) are involved in stomatal development. Overexpression of miR824 led to a decrease in stomatal density, similar to *agl16* mutant plants. However, when the regulation of miR824 on *AGL16* is destroyed, stomatal density will increase (Kutter et al., 2007). In maize, an increase of *GLl5* (*Glossy5*) activity can increase the number of young leaves and delay the reproductive development. miRl72 can also promote the transformation from young leaves to mature leaves of maize through the negative regulation of *GLl5* mRNAs (Lauter et al., 2005). In tomato (*Solanum lycopersicum*), the *LANCEOLATE* gene encodes a *TCP* transcription factor. Its mutation or downregulation can cause compound leaves of plants to become single leaves. miR319 can target the *LANCEOLATE* (*LA*) gene and cause the formation of single leaves from multiple leaflets (Ori et al., 2007). Yanai et al. found that miR319 in tomato affects the differentiation and leaf shape by inhibiting the expression of the *SlGA20 oxidase1* gene, which is an enzyme involved in the GA synthesis pathway (Yanai et al., 2011). miR396 of the legume *Medicago truncatula* negatively regulates the expression of not only six *MtGRF* genes but also two *bHLH79*-like target genes and thus influences root growth and mycorrhizal associations (Bazin et al., 2013).

The Role of miRNAs in Vascular Development

Vascular plants use xylem to transport water and nutrients absorbed by roots upward and the phloem to transport the carbohydrate assimilated by leaves downward. The vascular bundle consists of three neatly arranged tissues: xylem, procambium/cambium, and phloem (**Figure 3**). In *A. thaliana*, the *HD-ZIP III* gene family is strongly expressed in vascular bundles of roots, stems, and leaves. Overexpression of miR165 in
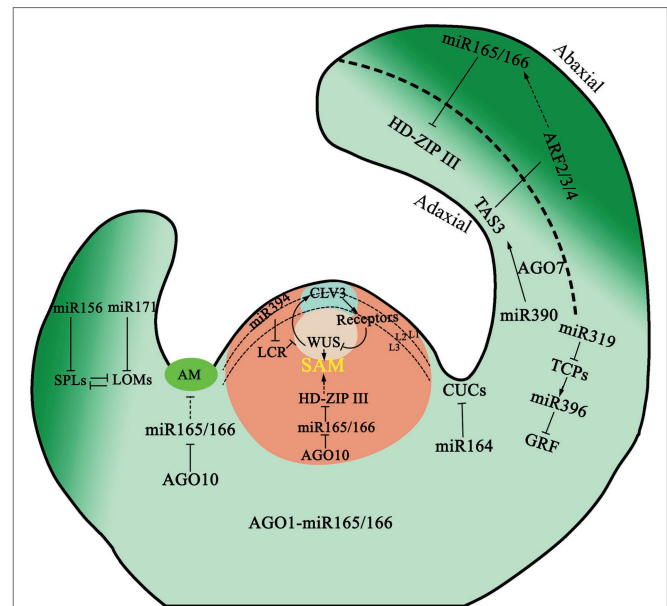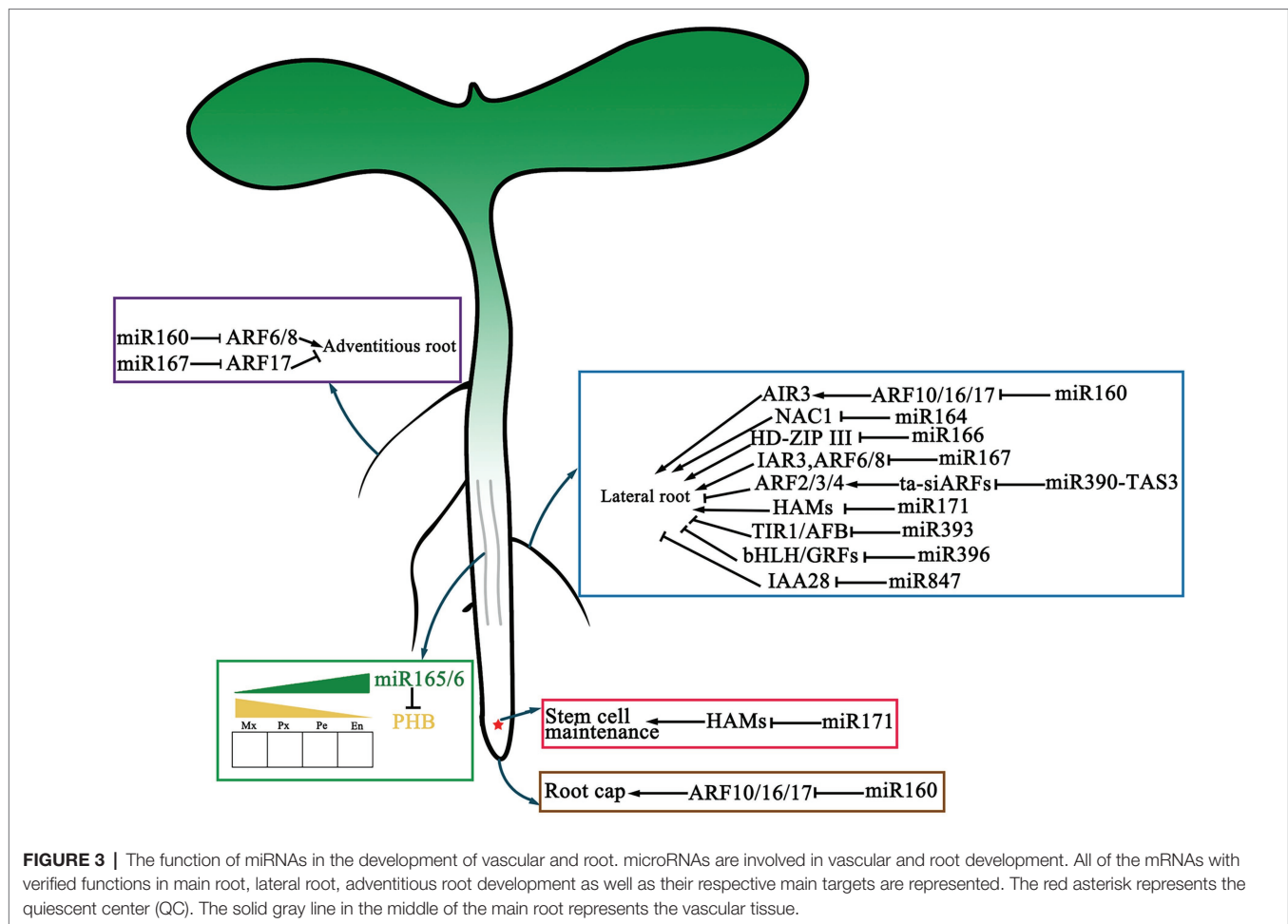

FIGURE 2 | Model for the role of miRNAs in shoot apex. miR394 synthesized at the protoderm represses *LCR* in subtending cells, which leads to the activation of the WUSCHEL (WUS) transcription factor to maintain stem cell identity and *CLAVATA3 (CLV3) peptide* expression. ARGONAUTE10 (AGO10) specifically sequesters miR165/166 and antagonizes its activity in the meristematic cells, thus regulating SAM and AM development. ARGONAUTE1 (AGO1) is expressed ubiquitously in the apex, recruit miR165/166 to form RNA-induced silencing complex (RISC). The adaxial and abaxial domains of leaves are established during leaf primordia emergence. HD-ZIP III transcription factors are restricted to the adaxial side by the action of miR165/166. In turn, AUXIN RESPONSE FACTOR 2/3/4 are restricted to the abaxial side by the action of TAS3 ta-siRNA. Two NAC-domain transcription factors are post-transcriptionally regulated by miR164 in embryonic meristem initiation, boundary size control, and cotyledon establishment. miR319 and miR396 target several *TEOSINTE BRANCHED1/CYCLOIDEA/PROLIFERATING CELL FACTOR* (*TCP*) and *Growth-Regulating Factor* (*GRF*) genes, respectively, and act coordinately to control leaf cell proliferation and differentiation. miR156 and miR171 synergistically regulate trichome initiation by targeting *SQUAMOSA PROMOTER BINDING PROTEIN-LIKE* (*SPL*) and *LOST MERISTEMS* (*LOM*), respectively. Arrows indicate positive regulation, whereas the dotted lines with perpendicular end bars represents a hypothesized negative regulation.

A. thaliana can reduce the transcription level of all members of the *HD-ZIP III* family, thus regulating the polar differentiation of vascular tissue cells and affecting plant morphogenesis (Zhong and Ye, 1999; Kang and Dengler, 2002; Zhou et al., 2007; Muraro et al., 2014; Du and Wang, 2015; Jia et al., 2015). It was reported that miR166 controls the development of vascular cells and phloem cells by regulating the Homeobox 15 protein (*ATHB15*) in *A. thaliana* (Kim et al., 2005). In almost all plant species, it is found that the target site of miR165/166 in class *HD-ZIP III* genes is highly conserved suggesting that this module is necessary in plant development and evolution (Floyd and Bowman, 2004).

Some miRNAs are also related to cell wall synthesis and fiber development in plants (Kim, 2005). It has been reported that a new miRNA (miR857), is decisive in the formation of secondary walls of vascular in a copper ion-dependent manner.

FIGURE 3 | The function of miRNAs in the development of vascular and root. microRNAs are involved in vascular and root development. All of the mRNAs with verified functions in main root, lateral root, adventitious root development as well as their respective main targets are represented. The red asterisk represents the quiescent center (QC). The solid gray line in the middle of the main root represents the vascular tissue.

miR857 regulates the expression of the putative laccase *LACCASE7*, a member of laccase family of genes, at transcriptional level and affects lignin content (Zhao et al., 2015). A recent study highlighted that some components related to leaf polarity and vascular development, such as miR390, TAS3, and ARF, are conserved across all terrestrial plants. For example, in liverworts, TAS3 ta-siRNA targets ARF as it does in angiosperms (Xia et al., 2017). In *Nicotiana tabacum*, the semi-dominant *phv* (*phavoluta*) mutant without miRl65 regulation has abnormal radial growth of stem and leaf vascular systems, and the vascular tissue of stem nodes is discontinuous, showing that miRl65 controls the growth of vascular cambium suggesting that the function of miR165/166 in vascular development is also conserved in plants (Yu et al., 2005).

The Role of miRNAs in Flower Development

Flower development is divided into three stages: flowering induction, flowering initiation, and floral organ development. It is a very complicated process involving multiple genes and is also an important event in development of higher plants. Many studies have shown that miRNA plays an important role in flowering.

In *A. thaliana*, the vegetative phase transition is promoted by a group of plant-specific transcription factors (SBP/SPL proteins).

Their expression is inhibited by miR156 and miR157 in the juvenile developmental stage. When the level of miR156/miR157 decreases, the abundance of SBP/SPL proteins increases and the plant changes from vegetative phase to reproductive phase (Xu et al., 2016a; He et al., 2018; Fouracre et al., 2021). miR156 is the main regulatory gene for plant growth cycle transformation, which affects plant phase transformation by targeting *SPL* (*Squamosa Promoter binding protein-Like*) transcription factors (He et al., 2018; **Figure 4**). Overexpression of miR156 and subsequent downregulation of *SPL3/5* resulted in delayed flowering period of *A. thaliana*; downregulation of *SPL9* and *SPL15* resulted in shortened leaf plastochrons, slower growth, and extremely abundant leaves of *A. thaliana* (Schwab et al., 2005; Wu and Poethig, 2006; Xu et al., 2016b; Zhang et al., 2019). The role of miR156 and SPLs in flower development was also reported in rice (Xie et al., 2006). Studies have shown that the fine negative regulation of miR156 on *SPL3* ultimately affects the flowering phase transition process of *A. thaliana* by changing the expression of the *FT* gene in *A. thaliana* leaves leading to delayed flowering (Kim et al., 2012). Similar to the function of juvenile hormones in insects, high concentrations of miR156 keeps plants in the juvenile developmental stage. As development progresses, the amount of miR156 decreases gradually, which promotes the
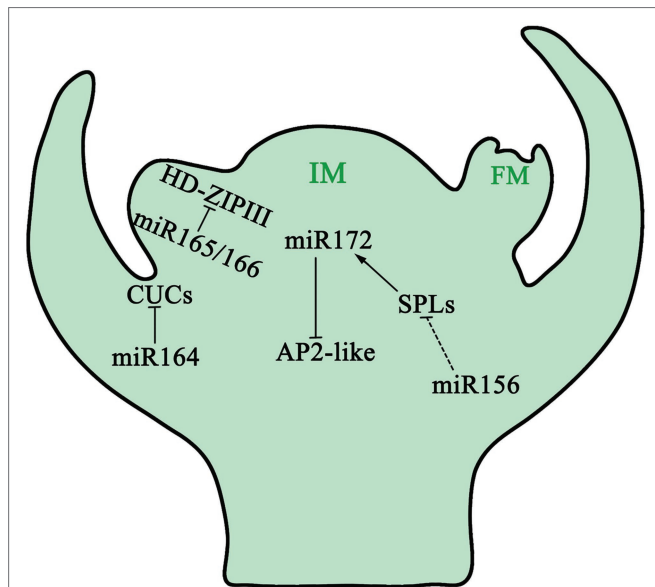
FIGURE 4 | The function of miRNAs in inflorescence meristem. As plants change growing phases from juveniles to adults, downregulation of miR156 dampens the inhibition of *SPL* expression, which in turn promotes miR172 transcription. miR172 triggers the development of inflorescence meristem by reducing the mRNA level of *AP2-like* genes. Spatiotemporal functions of miR165/166 and their targets *HD-ZIP III* genes, together with miR164, restrict the functions of *CUCs* in specific regions of the boundary to maintain the inflorescence meristem. miR156 decreases during IM development, whereas miR172 increases. IM: Inflorescence Meristem; FM: Floral Meristem.

juvenile-to-adult transition. Further studies showed that the decrease of miR156 content was not related to the absolute age (i.e., absolute time) of plants, but associated with the physiological age of plants (Cheng et al., 2021b).

miR172 is similar to miR156: namely, both are involved in controlling flowering time and the formation of floral organs by degrading and inhibiting target mRNA (Jung et al., 2007). miR172 regulates the transformation of plant development from the juvenile to flowering stage by regulating AP2-like genes including *SM-LIKE 2, SCHNARCHZAPFEN*, and *TARGET OF EARLY ACTIVATION TAGGED 1/2/3*. miR172 regulates plant flowering time, flower organ determination, flower morpho-genesis, and plant development by controlling *AP2* transcription factors (Aukerman and Sakai, 2003). Overexpression of miR172 in *A. thaliana* will promote early flowering, while overexpression of *AP2* genes will delay flowering.

In addition, miR156 and miR172 interact together in some parts of the plant growth cycle that are regulated by miRNA. miR156 inhibited the expression of the *SPL* family, while some SPLs promoted the expression of miR172. Previous studies have shown that the miR156-SPL-miR172 pathway in *A. thaliana* is the decisive factor in controlling the juvenile-to-adult transition. The miR156-SPL-miR172 pathway can be divided into two modules: the leaf module and the apical meristem module, both of which have different combinations of SPL and miR172 encoding gene modules. In leaves, the SPL9-miR172b/c modules regulate flowering time by regulating the expression of the *FT*

gene; while in apical meristem, the SPL15-miR172d modulus promotes flowering by activating the expression of *MADS-box* genes. In addition, the expression of the *MIR172* gene can be regulated by ambient temperature and photoperiod, and different *MIR172* genes have different response patterns (Lian et al., 2021).

Other miRNAs, such as miR159 and miR319, also function in flowering development. Their target genes are *MYB* and *TCP (TCP FAMILY TRANSCRIPTION FACTOR)* transcription factors, respectively. Overexpression of miR159 and miR319 will cause floral development disorders, such as delayed flowering (Palatnik et al., 2007). miR159 can regulate the expression of *MYB33* and *MYB65*, and a loss-of-function miR159 displays strong pleiotropic defects, stunted growth, curled leaves, defective sepals, petals, and anthers in *A. thaliana* (Achard et al., 2004; Millar and Gubler, 2005; Tsuji et al., 2006; Yu et al., 2012). At the same time, miR159 can prevent the over-activation of miR156, thus regulating the phase transition of *A. thaliana* in vegetative developmental period (Guo et al., 2017). *MYB33*, the target of miR159, promotes the transcription of *ABA INSENSITIVE 5 (ABI5)* by binding directly to its promoter, then *ABI5* plays a role in the upstream of miR156 and regulates the juvenile-to-adult transition in *Arabidopsis* by affecting the gene expression in the miR156-SPL pathway (Guo et al., 2021).

In *A. thaliana*, miR164 regulates the number of petals and the differentiation of floral organ marginal cells and apical meristem cells by increasing the accumulation of CUC transcription factors in the boundary. Meanwhile, overexpression of miR164 leads to sepal fusion and reduction of petal number, suggesting that miR164 is related to the activity of flower meristem and the specific boundary division of the meristem region (Laufs et al., 2004; Jung et al., 2009).

miR165/166 also regulates flower morphogenesis. miR166/165 gene showed tissue-specific expression patterns in different flower organs. miR166a was mainly expressed in stamens, while miR166b was highly expressed in ovule and stigma. miR166d and miR165a were highly expressed in ovule. In contrast, miR166g had a broad expression in the stigma, stamen, and receptacle, but not in the ovule (Jung and Park, 2007). In terms of meristem activity regulation, miR165/166 is closely related to meristem formation in floral organs (Zhang et al., 2007). In the *Arabidopsis* mutants with miR165/166 overexpression, the flower structure was seriously damaged. For example, when miR166 is overproduced in *mum enhancer 1* and *jabba* mutants, and the pistil population is very small and the number of carpels is also reduced.

The significant increase of miR396 expression can cause the bending of the stigma in flowers, which demonstrated that miR396 also participates in the regulation of flower development. In *A. thaliana*, excessive production of miR167 displays floral defects resulting to that filaments were abnormally short, anthers could not properly release pollen, and pollen grains did not germinate (Ru et al., 2006). *ARF6* and *ARF8*, the target genes of miR167, play a meaningful role in the regulation of pistil and stamen population. miR167 also controls the fertility of male and female flowers of *A. thaliana* (Wu et al., 2006).

In addition to regulating reproductive organ morphology in the model organism *A. thaliana,* miRNAs have also been shown to regulate these organs in other plants. Tomato miR156b performs a key role in controlling flower and fruit morphology by regulating meristem activity and the initial stage of fruit development. Also, in tomato, overexpression of *A, thaliana* miR167a causes the downregulation of *ARF6* and *ARF8*, resulting in serious disorders in floral organ development and female gamete fertility (Liu et al., 2014b). In *Petunia* and *Antirrhinum* species, researchers found that miR169 can partially replace AP2, which results from the fact miR169 can regulate transcription factor *NF-YA*, thus affecting the development of flower organs (Chen, 2004; Cartolano et al., 2007; Zhao et al., 2009; Waheed and Zeng, 2020).

miRNAs also regulate flower and seed production in monocots. In rice, Zhu et al. found that overexpression of miR172 can cause spikelet deletion, floral organ development malformation, and fertility reduction (Zhu et al., 2009). OsmiR397 is a miRNA that is expressed at a high level in the young panicles and grains of rice, which increases grain yield by downregulating its target gene *OsLAC*. Overexpression of OsmiR397 can increase grain size and promote panicle branching (Zhang et al., 2013). In maize, Chuck et al. showed that miRNA-targeting SBP-box transcription factor *tasselsheath4* plays a critical role in the development of maize bracts and the establishment of meristem boundaries in inflorescences (Chuck et al., 2010, 2014) auxin.

Other Processes Involving miRNAs

miRNA also plays an essential regulatory role in other developmental processes. In *A. thaliana*, auxin response factors *ARF10*, *ARF16*, and *ARF17* are targeted by miR160. Studies have shown that miR160 plays a very important role in the negative regulation of *ARF10* to promote seed germination (Liu et al., 2007). Llave et al. found that during *Arabidopsis* root growth, root cap cell formation is related to miR160, which controls stem cell differentiation at the end of the root meristematic region and determines root growth direction by regulating the expression of *ARF10* (**Figure 3**; Llave et al., 2002).

In addition, miR164 and miR390 greatly influence the development of plant root organs, including root cap formation, lateral root development, and adventitious root formation (Yoon et al., 2010). The process of lateral root growth of *A. thaliana* is regulated by miR164. Guo et al. found that miR164 can mediate *NAC1* expression after being induced by auxin, thus affecting auxin transmission and regulating lateral root growth (**Figure 3**; Guo et al., 2005).

miR165/166 is related to the formation of xylem and cell arrangement in plants. The regulation of miRNA on plant tissue development is a complex molecular process (**Figure 3**; Carlsbecker et al., 2010). The same miRNA may have the multiple functions in different tissues. For example, miR165/miR166 is also related to leaf polarization in addition to xylem and cell arrangement as mentioned in a previous section (Tatematsu et al., 2015; Manuela and Xu, 2020).

Furthermore, miRNA is involved in regulating plant morphological structure and yield, which is important in crop plants. In soybean, the miR156-SPL gene module plays a key role in regulating the morphological structure and yield of soybean. In transgenic soybean overexpressing miR156b, axillary bud formation and branching are regulated by reducing the expression amount of *SPL9d* (Wang and Wang, 2015). In rice, inhibiting the expression of miR1432 or overexpressing *OsACOT* (*Acyl-CoA Thioesterase*) can cause the grain weight to be significantly boosted by increasing the grain filling rate, which can improve crop yield (Zhao et al., 2019). Genetic analysis shows that *OsSPL7* is the target of miR156f, which regulates plant morphological structure, namely tillering and height of rice (Dai et al., 2018). At the same time, *OsSPL7* directly binds to the *OsGH3.8* promoter to regulate its transcription, indicating that the miR156f-OsSPL7-OsGH3.8 is the complete regulatory pathway for these traits in rice.

miRNA is widely connected to plant diseases and environmental stress responses. Virus infections can greatly influence plant morphology and productivity. More and more evidence has shown that miRNA is related to virus-mediated diseases and virus-induced gene silencing (Chapman et al., 2004). More than 30 RNA silencing suppressors, also known as pathogenic factors, have been identified from plant viruses, including p19, p21, p25, and p69. Pathogenic factors can usually hinder the formation of siRNA, affect the stability of siRNA, or interfere with the combination of siRNA and RISC complexes, and can also lead to the generation of other diseases in plants and cause developmental malformation. Excessive HC-Pro protease (helper-component proteinase) in plants will reduce miR171 level and produce developmental deletion plants associated with miR171 which included branching defects, an increased number of short vegetative phytomers and late flowering. Through the overexpression of the *Hc-Pro* gene in *A. thaliana*, it was found that most miR171 target mRNAs are increased which results in virus-mediated diseases in plants (Kasschau et al., 2003).

Under abiotic stress, plants can directly synthesize some miRNAs and induce low or excessive expression of other miRNAs. These miRNAs act on transcription factors related to stress resistance, *Plant Growth Regulator 9* response protein genes, stress tolerance protein genes, and other target genes, which enables plants to quickly respond to environmental changes. In plants, miRNA responding to stress was first found in *A. thaliana* (Jones-Rhoades and Bartel, 2004). The expression of miR393 in *A. thaliana* was significantly upregulated after low temperature, drought, salt, or hormone (ABA) treatment. However, no responses to drought or NaCl were observed when miR310 and miR319 were upregulated after low-temperature stress indicating that these two miRNAs only function in low-temperature response. miR389a was downregulated after the above stress was induced (Sunkar and Zhu, 2004). miR393, miR397, miR402 (Sunkar and Zhu, 2004), miR165/miR166, miR169, and miR172 (Zhou et al., 2008) were all found to be induced by low temperature to enhance the plant resistance. In *A. thaliana*, the expression level of miR395 increased in the absence of sulfate, while the expression level of miR399 was upregulated, and the mRNA level of its target gene *PHO2/UBC24* (*PHOSPHATE 2*) was lower

(Chiou et al., 2006). miR169 is downregulated in a drought environment. Compared to wild-type plants, plants overexpressing miR169a or plants with *Nuclear transcription factor Y subunit A-5* deletion of miR169's target gene are more likely to lose leaf water and are more sensitive to drought (Li et al., 2008). In *grapevine*, miR398 participates in plant biotic stress, heavy metals, high salt, drought, ultraviolet radiation, and other abiotic stresses through the targeted regulation of two superoxide dismutases, *COPPER/ZINC SUPEROXIDE DISMUTASE 1/2* (Leng et al., 2017).

As mentioned above, studies in *Arabidopsis thaliana* and other plants have showed that miRNAs participate in many biological processes. Compared with the plant-wide action of hormones, miRNAs are crucial in precise regulation of gene expression in a tissue-specific pattern. How the plants integrate miRNAs fine regulation into hormonal system pathway to modulate tissue formation deserves more attention. Study the role and mechanism of miRNA movement between cells and tissues are vital to understand miRNA function.

THE INTERACTION BETWEEN miRNAs AND PLANT HORMONES

Plant hormones are important regulatory factors synthesized in plants. They regulate plant growth, development, and differentiation either individually or together. Plant hormones mainly include auxin (AUX), cytokinin (CK), abscisic acid (ABA), gibberellic acid (GA), ethylene (ET), brassinosteroid (BR), and jasmonic acid (JA). As signaling molecules regulating plant growth and development, these hormones have absolutely necessary function in controlling development timing, metabolism, and stress response through the whole plant growth cycle. Specific stages of development often involve the participation of multiple hormones; this enables plant cells to respond adaptively to development signals and changes in their internal and external environment (Li et al., 2020). miRNAs coordinate with hormones by negatively regulating target genes in hormonal pathways. It was found that in the seedlings, the overall miRNA accumulation level decreased after *HYL1* mutation, which displayed a variety of developmental defect phenotypes and abnormal sensitivity to ABA, AUX, and CK, indicating that miRNA is related to the signal responses of these hormones (Han et al., 2004). Many miRNA gene promoters contain hormone response elements as well as cis-elements response to stresses, indicating that the regulation of miRNA gene transcription may be a way of hormone and stress response (Ding et al., 2013).

miRNAs regulate auxin receptors and several transcription factors in plants. In *Arabidopsis*, when the expression of miR160 was silenced, the expression levels of *ARF16* and *ARF17* genes increased, which led to abnormal germ development, cotyledon shape defect, slow inflorescence development, stamen reduction, root shortening, and other adverse developmental symptoms. However, overexpression of miR160 in *Arabidopsis* inhibited the development of root cap and increased the number of

lateral roots (**Figure 3**; Mallory et al., 2005; Wang et al., 2005). These results indicate that precise accumulation of miR160 is crucial to auxin-related plant development. miR167 and ARF6/8 co-regulate adventitious root formation (Gutierrez et al., 2009). miR847 targets and silences IAA28, the AUX/IAA inhibitory protein, to activate the auxin signaling pathway. The ubiquitination-mediated degradation of the IAA28 protein combined with miR847/IAA28 mRNA regulatory module to achieve the rapid disinhibition of the auxin signaling pathway (Wang and Guo, 2015). At the same time, miR165/166 directly targets *PHB*, an activator of *ARF5*, and then triggers the expression of miR390, which directly lead to the accumulation of ta-siRNAs (tasiR-ARF3/4; Marin et al., 2010; Muller et al., 2016; Dastidar et al., 2019). In addition, the miR165/166-tasiR-ARFs module also establishes the paraxial/distal polarity of the blade.

miR159 and miR319 inhibit the expression of *SHOOT-MERISTEMLESS* and *BREVIPEDICELLUS*, and then enhance the expression of *IPT* (*ISOPENTENYL TRANSFERASE*) and promote the biosynthesis of CK in SAM (Rubio-Somoza and Weigel, 2013; Scofield et al., 2014). At the cytokinin signal transduction level, the miR156-SPL9 complex modulates cytokinin-related plant regeneration by inhibiting the *B-type ARR genes9* [*type B Arabidopsis Response Regulators* (*ARRs*)], which are transcription factors that act as positive regulators in the two-component cytokinin signaling pathway (Zhang et al., 2015).

miRNAs also affect the biosynthesis and signal transduction of cytokinin through auxin, and then continue to maintain the dynamic balance between auxin and cytokinin, such as miR160 and miR165/6 (Dello et al., 2012; Liu et al., 2016). Another signaling molecule, gibberellin, can regulate the levels of various miRNAs through DELLA (aspartic acid–glutamic acid–leucine–leucine–alanine) protein and its interacting proteins, such as IDD2 (indeterminate (ID)-domain 2), PHYTOCHROME-INTERACTING FACTOR 4, or SCARECROW-LIKE (SCL; Han et al., 2014; Fan et al., 2018). Conversely, miRNAs can directly regulate GA biosynthesis and signal transduction through different complexes such as miR156-SPL, miR171-SCL, and miR159-GAMYB(L)s modules (Yu et al., 2012; Ma et al., 2014; Sun et al., 2018; Millar et al., 2019). Brassinosteroids (BR) negatively regulate miRNA-mediated translation inhibition of target genes by interfering with the distribution and localization pattern of AGO1, the miRNA effector protein, in the endoplasmic reticulum (Wang et al., 2021d).

miRNAs can regulate seed germination and leaf senescence by affecting the levels of ABA and ethylene. ABA, the signaling hormone, and SnRK2 (SNF1-related protein kinase 2) protein kinase, the core component of the osmotic stress response pathway, can regulate miRNA synthesis (Yan et al., 2017). At the same time, the ABA and ethylene signaling pathway can cause feedback on the level of sRNA by affecting the core protein in sRNA synthesis pathway, such as CBP20 (CAP-BINDING PROTEIN 20; Kim et al., 2008; Li et al., 2012, 2013; Zhang et al., 2016). Therefore, miRNAs coordinate with hormone responses in many ways and play an important role in plant development.

ROLE OF SMALL RNA MOVEMENT IN PLANT DEVELOPMENT

Plant small RNAs can spread silencing signals by moving in plants to participate in plant development regulation and respond to environmental stresses. Usually, mobile small RNAs generate sharply defined domains of target gene expression through an intrinsic and direct threshold-based readouts of their mobility gradients to drive developmental patterning (Skopelitis et al., 2017). There are two main types of small RNA movement in plants: one is short-distance (cell-to-cell) movement between neighboring cells, the other is long-distance (such as shoot to root or root to shoot) movement in plants. Currently, there is a hypothesis that 21 nt-siRNA are mainly involved in short-distance transport and 23–24 nt small RNAs are mainly involved in long-distance transport. The mechanisms of these two types of small RNA movement may be different (Tamiru et al., 2018), and will be explored in the following sections.

Short-Distance Movement

The short-distance movement of plant small RNAs is was thought to be mainly conferred *via* plasmodesmata between adjacent cells (Vaten et al., 2011). However, using a type of miR-GFP sensor system, it has been found that small RNAs are an independent mobile unit, and their mechanisms of movement between cells are different from that of proteins (Skopelitis et al., 2018). Some small RNAs have been discovered that can move in short distances of up to ten files of cells. For example, mature miR165/166 can move from the endoderm of the root to the vasculature, thereby forming a gradient-like distribution of miR165/166 to regulate the expression pattern of its target gene *PHB* and finally complete the establishment of proto- and metaxylem (Carlsbecker et al., 2010). In leaves, miR165/166 can be moved from the abaxial surface to the adaxial side, also forming a gradient to regulate the expression pattern of *HD-ZIP III* genes and ultimately form leaf polarity. In the SAM, miR394 moves to the cells in the L2 and L3 layers to repress its target gene *LCR* as a mobile signal produced by L1 layer cell. Repression of *LCR* signal in the underneath stem cells is used to maintain stem cell pluripotency by influencing the WUS-CLV loop (Knauer et al., 2013). In addition to miRNAs, PhasiRNAs have also been found to be able to move from cell to cell. For example, tasiR-ARF is produced from long non-coding RNAs transcribed at the TAS3 loci by the processing of the miR390-AGO7 complex on the adaxial side of leaves (Allen et al., 2005; Endo et al., 2013). These tasiR-ARFs can move to the abaxial side of leaves and form a gradient of to inhibit the expression of *ARF3* on adaxial side. Inhibition of *ARF3* expression ensures the establishment of leaf polarity patterns (Chitwood et al., 2009). Recent experiments show that processed tasiR-ARFs in the apical epidermal cells can move to hypodermal cells in the nucellar region to repress *ARF3* expression and suppress ectopic megaspore mother cell (MMC) fate (Su et al., 2020).

Long-Distance Movement

The long-distance movement of plant small RNA is mainly mediated through the phloem following source–sink relationships (Melnyk et al., 2011; Tamiru et al., 2018). In line with this, miRNAs have been found in the phloem saps of multiple plants (Tamiru et al., 2018). For example, miR172 was found in the vascular bundles of potatoes, indicating that miR172 might be mobile or that it regulates long-distance signals to induce tuberization(Marin et al., 2010). In *Brassica napus*, using small RNA sequencing, it was discovered that levels of miR395, miR398, and miR399 in the phloem are strongly increased in response to sulphate, copper, or phosphate starvation, respectively (Buhtz et al., 2008).

In *Arabidopsis*, miR399 moves from shoot to root to inhibit the expression of its target gene *PHO2* in response to phosphate homeostasis (Lin et al., 2008; Pant et al., 2008). During phosphate starvation, miR827 and miR2112a can also move from shoot to root (Huen et al., 2017). miR2112 can move from shoot to root to inhibit the expression of symbiosis suppressor TOO MUCH LOVE, thereby controlling rhizobial infection (Tsikou et al., 2018).

FUTURE PERSPECTIVES

Understanding the elaborate regulation of plant development by miRNAs is crucial for crop breeding. Knocking out dominant genes in development often causes lethality in plants, while miRNAs can safely modify gene expression to some extent and improve plant development. In rice, the number of branches (including tiller and inflorescence branches) determines grain yield. It was found that the genes regulating rice tillering and panicle branching consisted of miR156/miR529/SPL and miR172/AP2 modules. The *SPL* gene negatively controls tillering, but positively regulates the transformation of inflorescence meristem and spikelet. Changes in *SPL* expression will reduce panicle branching (Wang and Wang, 2015). In the regulation of seed size and grain yield, OsmiR397 can increase grain size, promote panicle branching, and increase grain yield by downregulating its target gene *OsLAC* (Zhang et al., 2013). miR1432-OsACOT modules are involved in fatty acid metabolism and plant hormone biosynthesis, and crucial for rice (Zhao et al., 2019). miR319s negatively affects tiller number and grain yield by targeting *OsTCP21* and *OsGAmyb* (Wang et al., 2021c). Changes of "miR168-AGO1" regulatory pathway influence several "miRNA-target gene" loops, which regulate the immunity and growth of rice, respectively. Among these, the "miR535-SPL14" loop regulates the yield and immunity of rice, the "miR164-NAC11" loop regulates the growth period and immunity of rice, and miR1320 regulates the immunity of rice (Wang et al., 2021a). In maize, *TASSELSEED4* encodes miR172 to control sex determination and meristem cell fate by targeting *IDS1* (*Indeterminate Spikelet1*). Moreover, miR156a-l acts on several SPL genes during the transition from young to mature ear, and indirectly activates miR172 through *SPLs* (Lauter et al., 2005; Chuck et al., 2007b; Salvi et al., 2007). In agriculture, epigenetic variations account for a great proportion for change

in crop yield. SNPs located in non-coding regions are paid more and more attention by breeders in population genetic analysis and traditional hybrid breeding. New strategies such as Short Tandem Target Mimic (STTM), a specific miRNA targeting method which is effective in blocking small RNA functions in plants (Tang et al., 2012), are adapted and utilized in generating transgenic crops. As *MIR* genes are usually short, EMS mutation and T-DNA inserted mutation are difficult to achieve ideal mutants for *MIR* genes. However, the advances of genome editing technologies make modification of miRNA expression to increase crop yield become easier.

Modes of miRNA function need to be further explored. miRNAs also act as environmental response factors, endowing plants with corresponding phenotypes and promoting plant evolution and adaptation. For example, the essential role of HD-ZIP III-miR165/166 signaling pathway in meristematic tissues and the dual regulatory role of miR156/miR172 in flower determination are conserved in plant kingdom. The function of miRNAs and their specific mechanisms need to be further studied. It is still not clearly understood how miRNAs specifically regulate a biological process in certain temporal and spatial patterns. Many miRNA gene promoters contain plant hormones and cis-elements of stress response, indicating that regulation of miRNA gene transcription may be a way to respond to plant hormone and stresses. The expression of *AGO10* is precisely regulated by auxin, brassinolide, and light to initiate axillary meristem in certain leaf axils. This provides a way to modify gene expression in a tissue-specific pattern and potentiate modulation of organ development at certain stages.

Recently, great importance has been attached to small RNA movement between cells, tissues as well as organisms by plant researchers. Much effort is made to uncover the role and mechanism of small RNA movement. So far, it is evidenced that miRNA can move to form gradient distribution between different tissues. After biogenesis, miRNA is protected from degradation and is transported to destination cells. It is noteworthy that miRNA needs to reach a certain threshold level before it can function in a non-cellular autonomous way. How intermediate steps influence miRNA movement and its non-cellular autonomous function need more studies. To understand and prime plants for abiotic stresses, it is also worth further studies to elaborate the correlation between hormone concentration and miRNA movement.

In addition, biotic and abiotic stresses can induce plants to produce new sRNA. For example, *A. thaliana* can produce a large number of 22 nt siRNAs dependent on DCL2 and RDR6 under stresses such as nitrogen deficiency. However, it is still a puzzle as to why only a small number of gene loci in *A. thaliana* can produce 22 nt siRNAs. Meanwhile, there is also a big gap in knowledge of the synthesis of 22 nt siRNAs to their biological function. More evidence is needed to verify whether 22 nt siRNAs can also regulate target genes in distal organs due to the cellular non-autonomy of sRNA. Therefore, the improvement of sequencing technology and miRNA research methods are highly recommended here. With the help of various single-cell omics and nanopore sequencing, more miRNAs, their action mechanisms, and their regulatory pathways will be discovered in model plants, which will provide important theoretical basis for understanding how miRNA regulates plant growth and development and can then be applied to agriculturally important plants.

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