Review

Advances in the regulation of plant development and stress response by miR167

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1. Abstract

MicroRNAs (miRNAs) are a class of endogenous, non-coding small RNA that cleavage mRNA targets in sequence-specific manner or the inhibition of translation, which regulates gene expression at the post-transcriptional level. miRNAs are involved in the regulation of plant growth, metabolism and stress response. miR167 family is one of the highly conserved miRNA families in plants. It functions mainly by regulating the *auxin response factors* (*ARFs*) and *IAA-Ala resistant3* (*IAR3*) genes, and participates in regulating the development of roots, stems, leaves and flowers, flowering time, embryonic development, seed development and stress response. Here, we reviewed the biological functions of miR167 family and its target genes in plant growth and development and stress response, and further discussed the application prospect of miR167 in agricultural production. Furthermore, this review provides references for the further study of miR167 family in plants.

2. Introduction

MicroRNAs (miRNAs) are small endogenous noncoding RNAs with a length of 20–24 nucleotides. Plant miRNA genes (MIRs) are transcribed by RNA polymerase II into a primary transcript with stem-loop structure, after a series of cutting processes, mature miRNAs are formed [1–3]. It can regulate the target gene expression by cleaving or inhibiting the translation of mRNA [4, 5]. miRNAs play an active role in basic physiological and morphological processes and response to various stresses in plants.

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Table 1. Research progress of miR167 in recent years.

miRNA	Target gene	Function	References
miR167a	*AtARF6/AtARF8*	Promote lateral root growth and increase in number	[6, 7]
miR167c	*GmARF8a/GmARF8b*	Lateral root growth and nodule development	[8]
miR167b	*OsARF6/OsARF12/OsARF17/OsARF25*	Reduced plant height and tiller number	[9]
miR167a	*SpARF6/SpARF8*	Internodes, leaf blade reduced/petals, stamens, and style shortened	[10]
miR167	*NtARF6/NtARF8*	Leaf blade curled and wrinkled/flowering	[11]
miR167a/miR167b/miR167c	*AtARF6/AtARF8*	Ovules develop/filaments shorten/anthers elongate and do not dehisce/seeds develop/somatic embryogenesis/stomata open	[12–16]
miR167	*InARF8*	Development of shoot apices, leaf primordia and pistil organs/regulated stomatal opening	[17]
miR167a	*CsARF8*	Seed size and delayed seed maturity	[18]
miR167	*TcARF6*	Response to salt stress	[19]
miR167d	*OSARF12*	Protection against germs	[20]
miR167a	*IAR3*	Resistance to pathogen/osmotic stress	[21]
miR167	—	Regulating stomata opening	[22]

MicroRNA167 (miR167) is widely distributed in plants and plays an active role in regulating plant growth and development. According to recent studies, miR167 is involved in the regulation of plant vegetative and reproductive organ development, flowering time and stress response through the regulation of its major target genes such as *ARF6*, *ARF8* and *IAR3*. In addition, miR167 targets *ARF12*, *ARF17*, *ARF25*, ubiquitin-protein ligase *AIRP2* and *natural resistance-associated macrophage proteins* (*NRAMPs*) genes is involved in the regulation of plant growth and development. In this paper, the biological functions of miR167 and its target gene in plant growth and stress response were reviewed, the regulation mechanism of miR167 in plant growth and development was discussed, and the application prospect of miR167 in agricultural production was prospected. The research progress of miR167 in recent years is detailed in Table 1 (Ref. [6–22]).

3. miR167 family and its target gene

3.1 miR167 family

miR167 is one of the highly conserved gene family in plants. It has different stem-loop precursors and produce mature miR167 sequences. In the miR167 sequence, processing from 3'end is significantly different from that from 5'end, and primary miR167 and mature miR167 have different expression patterns in plants [23–25].

The miR167 family is found mainly in angiosperms, is more widespread in dicotyledones than in monocots, and has been identified in soybean (*Glycine max*), peanut (*Arachis hypogaea*), apple, corn (*Zea mays*), wheat, longan (*Dimocarpus longan Lour*) and sugarcane, etc. The number of miR167 precursors and mature bodies varied among different species, the number of miR167 precursors varied from 1 to 12, and the number of mature bodies varied from 1 to 22 [26]. miR167 is species-specific, such as in *Arabidopsis thaliana*, four miR167 genes (*MIR167a*, *MIR167b*, *MIR167c* and *MIR167d*), miR167a produces higher levels of miR167 maturation, and miR167a is the main miR167 gene family member that regulates the development of female and male organs [15, 27]. miR167 family of rice (*Oryza sativa*) is encoded by 10 loci, miR167a–j, there is only one nucleotide difference in the 30-end between miR167a–c and miR167d–j. Among these ten genes, *MIR167a*, *MIR167b* and *MIR167c* can produce mature miR167 more efficiently, and *miR167a–c* plays a major role in rice, affecting plant size and tiller number [9]. In soybean (*Glycine max*), miR167 family has 11 highly conserved homologous miRNAs, which can be divided into two subgroups include miR167a/b/d/e/f/g/h/i/j/k and miR167c. miR167 primary transcripts are produced by different genes, mature miR167 had only one or two nucleotide differences at the 3'end or 5'end, and miR167 mediated nodulation in soybean [8].

3.2 miR167 target gene

miR167 can target different target genes to participate in the regulation of plant growth and development, and miR167 cleavage of target genes seems to be a common way of post-transcriptional regulation. *Auxin response factor* (*ARF*) is a transcription factor that regulates the expression of auxin response genes. It can be combined with auxin response element (AUXRE) "TGTTC" in the promoter region of auxin response gene, auxin response genes are activated or inhibited and interact with the second transcription factor family, AUX/IAA repressor protein, to induce auxin response [28–30]. *ARF* transcription factors contain three domains: (1) a conserved B3 family of N-terminal DNA binding domain (DBD), and (2) a non-conserved middle region, which can activate or inhibit gene expression, (3) a conservative C-terminal domain (CTD) [31]. The C-terminal domain of *ARF* is similar to the III and IV domains of AUX IAA protein [32]. *ARF* and auxin (AUX) indole-3-acetic acid (IAA) can form dimers through this domain [33]. The number of *ARF* family members varies from species

to species, such as there are 23 and 25 *ARF* family members in *Arabidopsis thaliana* [34] and in rice [35]. *ARF* gene was also identified in tomato (*Solanum lycopersicum*) [36], *corn* [37], *rape* (*Brassica rapa*) [38], *soybean* [39] and cassava (*Manihot esculenta*) [40, 41], etc. Auxin plays an important role in the whole life process from embryogenesis to senescence, and its function is mainly mediated by ARF and AUX/IAA [42, 43]. miR167 targets *AtARF6* or *AtARF8* to regulate the normal development of anthers and ovules, and *AtARF6* and *AtARF8* are cut at the complementary site of miR167 [27]. Auxin response factors *ARF6* and *ARF8* play a conservative role in the development of vegetative and reproductive organs, regulating the development of roots and stems, the elongation of stamen filaments, the dehiscence of anthers, the maturation of gynoecium and the flowering time [10, 44, 45]. *ARF8* an *ARF* gene affected by environmental conditions. Light signal molecules strongly induce *ARF8* gene expression in hypocotyl, but *ARF8* is not induced in darkness [46]. Due to the functional conservativeness of ARF gene, it remains to be further studied that *ARF6* and *ARF8* are mediated by miR167 in the various processes of plant growth. In addition, *OsARF6*, *OsARF12*, *OsARF17*, *OsARF25* genes and miR167 exhibited high sequence complementarity in almost the same manner. The 5'RACE technology proved that four *OsARFs* transcripts are cleaved by miR167, confirming that *OsARF12*, *OsARF17* and *OsARF25* are the target genes of miR167 in rice [9]. *OsARF12* and *ARF8* have high homology, and found that the 2467-2494 region of *OsARF12* gene may be the target site of miR167d. In order to prove this, semiquantitative RT-PCR (sqRT-PCR) and quantitative RT-PCR (qRT-PCR) techniques were used to analyze the expression of *OSARF12* in tobacco and rice callus, and it was found that Osa-miRNA167d inhibited *OsARF12* [47]. It shows that *OsARF12* is regulated by miR167d and is a post-transcriptional event. Researchers constructed the target mimetic expression of *Osa-miR167d* (*MIM167d*) and established a reporting system based on yellow fluorescent protein (YFP), further indicating that *OsARF12* is the target site of Osa-miR167d [20].

IAR3 is the target gene of miR167 [48], *IAR3* is a member of the amide hydrolase family, and the IAA amide hydrolase family of *Arabidopsis thaliana* contains seven genes, including *IAR3*, *ILL1*, *ILL2*, *ILL3*, *ILL5*, *ILL6* and *ILR1* [49]. *IAR3*, a hydrolase encoding IAA-Ala, can release a biologically active auxin (IAA) from inactive IAA-Ala, regulate auxin balance in plants, and is induced by jasmonic acid (JA) [50]. It is most strongly expressed in roots, stems and flowers. *IAR3* is a regulator of root structure under osmotic stress and drought stress. miR167 targets *IAR3* on root development and stress defense response. In addition, *AIRP2* may be the target gene of miR167 [26]. *AIRP2* is a circular E3 ubiquitin ligase [51]. In the early stage of somatic embryogenesis in longan, miR167 may regulate the morphology of early somatic embryogenesis by regulating *AIRP2*. *Brassica napus* miR167 cleaves *BnNRAMP1b* transcripts [25]. NRAMPs are membrane transporters responsible for the distribution of metals in plants [52, 53]. Cadmium stress promotes the effects of *BnNRAMP1b* and miR167. The differential expression pattern verifies that *BnNRAMP1b* is the target gene of miR167.

4. Biological functions of miR167 family

4.1 miR167 regulates the development of roots, stems and leaves

In the process of plant growth and development, lateral roots are crucial for plants to absorb water and mineral elements, and the development of lateral roots is affected by many factors, auxin can integrate intrinsic and extrinsic environmental signals to regulate lateral root development [54]. miR167 is involved in auxin signaling. *GH3* is a member of the auxin responsive gene family, and GH3 protein has the adenylation function of IAA, salicylic acid or jasmonic acid (JA), regulation of cell free IAA by binding with IAA [55]. miR167 participates in the miR167-ARF8-OsGH3-2 signaling pathway, and regulates GH3 family members in the downstream by targeting *ARF8* [46, 56]. miR167-ARF8 circuit mediates plant lateral root initiation and morphogenesis, regulates plant response to nitrogen [6]. High nitrogen treatment before Arabidopsis thaliana lateral root germination inhibited the expression of miR167a, and promotes *ARF8* transcription accumulation after nitrogen treatment. In addition, miR167 interacts with other miRNAs, helping to fine tune the number of adventitious roots in plants. *ARF6* and *ARF8* interacted with *ARF17* as positive and negative regulators of adventitious root initiation, and regulated each other's expression at transcriptional and posttranscriptional levels by regulating miR160 and miR167 [7]. At the same time, based on the cucumber mosaic virus strain ZMBJ (ZMBJ-CMV), the ZMBJ-CMV-2bN81-STTM vector was newly developed to express a short tandem target mimic (STTM). Researchers used ZMBJ-CMV-STTM167 to down-regulate Zma-miR167 in corn, resulting in a significant reduction in the number and length of lateral roots [57].

The root development of leguminous plants has special function, because of the invasion and specialization of rhizobia, the lateral root nodules are produced, and the symbiotic nitrogen fixation is used to obtain the nitrogen nutrient elements needed for the growth and development of plants [58], increasing the growth of lateral roots and the number of nodules by molecular techniques can affect the nitrogen fixation ability of legumes. Rhizobium induces the expression of miR167c in the endothelial cells of soybean nodules, and can control multiple nodulation genes (*ENOD40*, *NIN*, *NSP1*, *HAP2-1*, *HAP2-2*) to actively regulate nodules. Overexpression of miR167c inhibits the activity of *GmARF8*, weakens the auxin sensitivity of root cortex cells, and promotes the development of root nodules

through downstream signals of NF signaling pathway [8]. miR167 may control nodule formation and root morphological structure by inhibiting auxin signal, the nodulation efficiency under low rhizobia has not been verified. It is suggested that miR167 mainly regulates root development through auxin transduction pathway, and miR167-ARF6/8 circuit may be a highly conservative regulatory mechanism in auxin-mediated biological processes during plant root development.

In addition, miR167 is involved in regulating the development of other vegetative organs in plants, such as the overexpression of miR167 in transgenic rice, the transcriptional levels of *OsARF6*, *OsARF12*, *OsARF17* and *OsARF25* will be significantly reduced, resulting in dwarfing of transgenic rice plants and a significant reduction in tiller number [9]. Overexpression of miR167a reduced the length of cells, but the number of cells increased, but the final internodes and leaves shrank [10]. The reduction of miR167 expression had little effect on the number of cells and the size of leaves, but resulted in leaf curling and wrinkling [11]. Studies of miR167's involvement in plant stems and leaves have been few and far between. miR167 still has many unknown functions to discover.

4.2 miR167 regulates flower development

4.2.1 miR167 regulates plant flowering time

Flowering is the transition from infancy to adulthood of vascular plant, and is the key to plant growth and development and the sustainable development of future generations, which are affected by plant growth and environmental conditions [59, 60]. miR167 (*MIM167*) target mimic was first obtained from *Arabidopsis thaliana* by artificial miRNA target mimic technology, which led to *ARF* gene expression disorder and late flowering phenotype [61]. It was confirmed that miR167 can regulate flowering time of plants. To test this idea, researchers obtained *Arabidopsis thaliana* miR16a deletion mutant, which also showed late flowering [15]. The expression of miRNA related to flowering and its target genes in *35S-MIM167* tobacco lines with different miR167 expression levels was proportional to the reduction of miR167 [11]. The low level expression of miR167 increased the expression of GA transcription factor *MYB*, when the expression of *MYB* was higher than that of *AP2*, the expression of *LFY* increased and the expression of *AP2* decreased significantly. In the contrary, the high expression of *AP2* inhibited the expression of *LFY*, which led to late flowering [11]. miR319 targets *TCP* transcription factors involved in plant biological process [62], *MYB* and *TCP* regulate miR167 to form miR159-miR167-miR319 network pattern to regulate *ARF* gene activity, and then play a role in sepals, petals and anthers [63]. Therefore, miR167 directly or with plant flowering time related miRNA co-regulate flowering gene transcription to regulate plant flowering time.

4.2.2 miR167 regulates floral organ development

The normal development of floral organs is essential to the sexual reproduction of flowering plants. There are 5 types of floral organs: sepals, petals, stamens, gynoecium (carpels) and ovules [64, 65]. The deletion of miR167a mutant leads to ovule arrest and anther do not dehiscence in *Arabidopsis thaliana*. miR167 mainly regulates *ARF* genes such as *ARF6* and *ARF8* involved in the development of female and male floral organs [27].

During flower development, anther dehiscence and pollen release are essential for sexual reproduction in flowering plants. *ARF* genes are essential for cell elongation and anther dehiscence. Too much or too little *ARF* gene expression will lead to dehiscence defects and male sterility. miR167 was partially complementary to the c-terminal conserved domain of *ARF6* and *ARF8*, and that *ARF* gene expression was mainly regulated by cutting, and miR167b overexpression was similar to *arf6/arf8* double mutant phenotype, the length of filaments became shorter, the anther did not dehisce and the germination rate of pollen decreased [13]. miR167 in terms of anther dehiscence, the miR167a mutant allows *ARF6* and *ARF8* to promote excessive cell elongation through the auxin signal transduction pathway. Eventually, the overgrowth of anthers affects the drying time of the anthers and causes them to fail to crack [14]. In addition, obtained by gene editing technology to obtain miR167a mutant, further confirming that the anthers become larger and cannot crack, but they produced normal pollen [15].

In addition to *Arabidopsis thaliana*, the role of miR167 in regulating floral organ development has also been demonstrated in other plants. miR167 targets *InARF8* to regulate the pistil development of morning glory (*Ipomoea nil*) [17]. *InARF8* gene has the strongest signal in the vascular bundle region of the cotyledons, further suggesting that *ARF* gene may be involved in flower organ development by controlling cell elongation. By in situ hybridization of tomato flower buds with *SpARF6A* and *SpARF8B* probes, it was found that the *ARF* gene was strongly expressed in pistil. Overexpression of miR167a resulted in the decrease of *SpARF6* and *SpARF8* transcripts, possibly down-regulating the termination of *Style2.1* delayed inflorescence meristems [10]. In the end, the anthers produce viable pollen, but the stamens and styles of plants are shortened, the pollen can not germinate on the surface of stigma or grow through the style, resulting in female sterility. This is different from the female sterility of *Arabidopsis thaliana* miR167a mutant and *mARF6*, which results from the ovule tegument defect and affects the pollen tube to guide the ovule and embryo development [15, 27]. The function of miR167 in floral organ morphogenesis needs further study (Fig. 1).

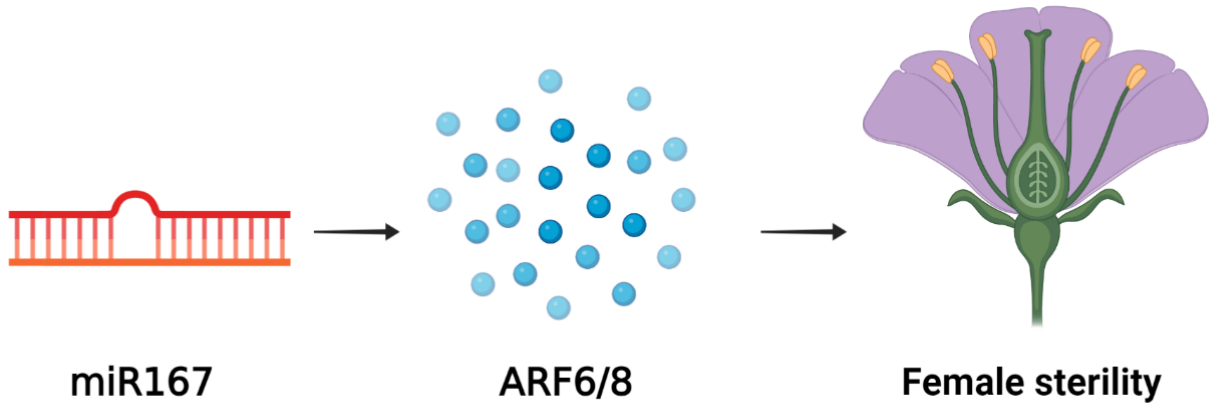

Fig. 1. miR167 regulates pistil development.

4.3 miR167 regulates plant embryo and seed development

Seeds are the descendants of seed plants. High quality seeds promote good economic returns for Cash crop, while seed size is determined by the interaction of the seed coat, embryo, and endosperm [66–68]. It has been reported that auxin biosynthesis increases in the seed coat early in embryogenesis, and that auxin produced by the mother is essential for embryonic development, and miR167a and miR167b have also been detected in globular embryos[69]. Serendipitously, researchers found that the *Arabidopsis thaliana mir167a* (♀) with Wild *Arabidopsis thaliana* (♂) to produce seed coat and endosperm defects, which further proved that miR167a played a role in regulating embryo development [15]. In order to further verify whether the developmental defects of *mir167a* mutant were caused by overexpression of *ARF6* and *ARF8*. Researchers hybridized the *mir167a* mutant with *arf6* and *arf8* double mutant can improve pollen viability and the anther dehiscence defects of *mir167a* plants were largely rescued. Furthermore, miR167a overexpression suppresses the expression of *CsF8* gene in camelina (*Camelina sativa*) plants, thereby inhibiting *CsFAD3* expression and ultimately slightly delaying seed maturation, but increasing seed size [18]. miR167 is highly expressed during seed development in maize and barley (*Hordeum vulgare*) and may be involved in the metabolic regulation of seed maturation [70, 71]. In addition, the researchers identified a candidate gene, OsAUX3, which controls grain length and grain weight, and identified OsARF6 as an upstream transcription factor for *OsAUX3*. OsAF6 can directly bind to the auxin response element on the promoter of *OsAUX3* to control grain length by changing the longitudinal expansion of grain cells and the distribution and content of auxin [72]. The revealed *miR167a-OsARF6-OsAUX3* module plays a key role in regulating rice grain length and grain weight traits.

Somatic embryogenesis (SEG) is regulated by miRNA via plant hormone signaling pathway [73]. At the early stage of somatic embryogenesis, the expression of miR167 decreased significantly at the initial dedifferentiation stage and increased at the late dedifferentiation stage, and was significantly higher in non-embryonic callus than in embryonic callus [74, 75]. miR167 was highly expressed in the late stage of SEG of larch (*Larix leptolepis*) and longan [76, 77]. miR167 reached the highest level in *Citrus reticulata Blanco* cotyledonary embryogenesis [78]. The reduction of miR167 activity promoted the formation of corpus callosum and somatic embryogenesis [79]. Auxin is essential for somatic embryogenesis, *ARF6* and *ARF*8 are necessary for auxin gradient reaction, and auxin gradient related expression is activated by selenium [80]. *LEC2* is a positive regulator of selenium-induced YUC-mediated auxin biosynthesis in *Arabidopsis thaliana* somatic embryogenesis [81, 82]. The overexpression of miR167c inhibited the formation of selenium and increases the expression of *LEC2* [12], and at the same time interfered with PIN-FORMED1 (PIN1) in cell membrane of embryogenic callus affected auxin transport [83–85]. miR167 targeted *ARF6* and *ARF8*, effects on auxin synthesis and local auxin transport in embryogenic callus, thus regulating *Arabidopsis thaliana* somatic embryogenesis.

4.4 miR167 is involved in the regulation of plant stress response

Environmental factors can affect the growth and development of plants. When plants are stimulated by adversity, growth and development are inhibited. Plants coordinate their growth and development to cope with stress through external morphological changes or internal physiological responses. The stress responses of plants mainly include biotic stress such as virus, pathogen, pest, and abiotic stress such as high salt, drought and low temperature. miR167 plays an active role in plant stress response.

4.4.1 miR167 Regulates Plant Biotic Stress

miR167 was differentially expressed in response to biotic stresses, plants may respond to various stresses by regulating miR167. Hibiscus chlorosis ringspot virus [86], cucumber mosaic virus (CMV) and tomato aspergillosis virus (TAV) [87] can all increase the expression of miR167. Cyst nematodes [88] and root knot nematodes (RKN) [89] induced significant down-regulation of miR167. The same stress had different effects on the expression of miR167 at different growth stages, and the expression of miR167 increased firstly and then decreased under the stress of wheat rust [90]. miR167 targets ARF to reduce the influence of soybean mosaic virus (SMV) infection on the growth of soybean [91]. *Arabidopsis thaliana* miR167a targets ARF6/ARF8, which results in relatively closed leaf stomata to prevent the entry of *Pseudomonas syringae* [16]. *Osa-miR167d* deletion mutant promotes the expression of defense and cell death related genes (*KS4*, *PAL*, *NAC4*, *PR1a*, *PBZ1* and *PR10b*) and increased JA content [92, 93], thereby enhancing the immunity of rice to *Magnaporthe oryzae* [20]. Solanaceae plant miR167 promotes changes in the expression of *IAR3* leading to changes in auxin homeostasis and enhances the defense of plants against pathogens [21]. Fungal or viral infections increase the expression of tomato miR167a and activate the miR167a regulatory mechanism in response to stress [94]. miR167 is differentially expressed under different stress conditions and can respond to biological stress by regulating stoma opening or inducing the expression of downstream defense genes and auxin homeostasis.

4.4.2 miR167 regulates abiotic stresses in plants

miR167 plays a role in abiotic stress and is induced under high salinity and drought stress [95]. UV-B radiation caused an up-regulation of miR167 expression in *Populus tremula* [96], and miR167 targeted *TcARF6* in *Tamarix chinensis* under salt stress [19]. The expression of miR167 under salt stress was analyzed by microarray hybridization, which was caused by different salt sensitivity of different species, it was found that the expression of miR167 in salt-tolerant cotton was up-regulated compared with that in salt-sensitive cotton [97]. Seven members of the *Osa-miR167* gene family were identified to be inhibited by salt stress, which upregulates the expression of *OsARF6*, promotes lateral root elongation and accumulates more energy to enhance plant stress resistance [98]. Researchers also confirmed this view in salt-tolerant maize. At the early stage of salt stress, the down-regulation of miR167 in salt-tolerant maize resulted in *ARF* transcription accumulation and regulated the root and stem development to accumulate more biomass to offset the damage caused by salt stress [99]. In addition, under salt stress, miR393, miR167 and *ARF* formed a network mechanism in response to stress, which stimulated the up-regulation of miR393 and inhibited the release of AUX/IAA, and the up-regulation of miR167 expression induced the decrease of *ARF* expression, thus, the development of the plant is weakened and the stress tolerance is enhanced [100, 101]. In addition, the expression of miR167 was down-regulated by drought and high temperature, and the expression of miR167 was up-regulated by cold stress [102]. In wheat (*Triticum aestivum*), the decrease of miR167 induced stomatal closure and increased leaf water content in response to water stress [22]. High osmotic stress stimulated the down-regulation of miR167, and the expression of *IAR3* increased. miR167 targets *ARF* to promote the production of jasmonic acid [92], which is a strong inducer of *IAR3*. *IAR3* regulates the expression of *ARF* by feedback of IAA content and promotes the interaction between miR167-IAR3 moudle and miR167-ARF6/8 circuit, to enhance the tolerance of plants to osmotic stress [44, 47].

miR167 is expressed differently in different species and under stress stimulation. Plant response to abiotic stress is mainly regulated by auxin signaling pathway. Plants can reduce miR167 expression and increase their energy accumulation to resist adversity, or increasing the expression of miR167 could weaken the development of plants and enhance the tolerance to stress.

5. Application prospect of miR167 in agricultural production

miR167 also has a broad application prospect in agricultural production. It regulates the development of plant reproductive organs, flowering time, seed and fruit development, and stress tolerance, all of which are beneficial to crop production. miR167 is highly expressed in elongation and maturation stage, and may play a role in cell elongation and differentiation [103]. miR167 was abundant in meiotic cells of *Arabidopsis thaliana*, soybean and cucumber (*Cucumis sativus*) [104]. miR167-ARF regulates the seed development of *Arabidopsis thaliana*, camellia, maize, barley [15, 18, 70, 71]. It also regulates the number of tillers in rice and determines the grain yield by auxin pathway or by regulating grain filling [9, 105]. And the *miR167a-OsARF6-OsAUX3* module plays a key role in regulating rice grain length and grain weight traits and improving rice yield [72]. miR167 plays an important role in the fruit development of peach (*Prunus persica*) and the pod development of peanut [106, 107]. The reproductive organ development and flowering time of crops are important for production and breeding. miR167 is involved in regulating flower organ development and flowering time, helping plants transition from vegetative growth stage to reproductive development stage [11, 15].

6. Conclusions and outlook

In recent years, miR167 has been widely studied for its role in regulating plant growth and development and biotic stress. miR167 directly or together with other miRNAs regulates plant growth and development in *Arabidopsis thaliana*, tobacco, rice, soybean, corn, camellia, longan, wheat. miR167 has been found to regulate many plant development processes, including lateral root, leaf, flowering, reproductive organs, embryo and seed development and response to stress. Therefore, according to the function summary of miR167 in *Arabidopsis thaliana* and rice, it is helpful to explore the function of miR167 in other crops. However, due to the diversity of plant species, miR167 has not been fully studied in different species. The potential function of miR167 remains to be explored.

6.1 miR167 increases crop yields

Auxin affects all aspects of plant growth and development. The miR167-*ARF* model is involved in regulating crop seed and fruit development and plant morphology through auxin pathway.

However, miR167 has not been studied in depth in soybean. Whether miR167 regulates peanut pod development can regulate soybean pod is worth studying. Soybeans convert atmospheric nitrogen to ammonia by forming nodules with nitrogen-fixing rhizobia [108]. Nitrogen is an important factor affecting seed yield. Applying nitrogen fertilizer after flowering can promote plant growth and increase nitrogen content and size of single seed significantly [109]. Studies have shown that when Rhizobium does not exist, miR167 members remain at a low level, while rhizobium induces a strong expression of miR167 [8, 110]. miR167c-GmARF8 may be an effective method to improve the nodulation efficiency of soybean in the absence of rhizobia. Inoculating rhizobia to increase the number of soybean nodules and thus improve soybean yield has become a conventional way of soybean cultivation [111–113]. Editing miR167 by molecular techniques to increase the number of lateral roots and nodules of soybean plants, to promote plant growth and yield through symbiotic nitrogen fixation. It is beneficial to reduce the use of nitrogen fertilizer to protect the environment has good economic benefits. Could this method also be applied to other legumes to increase crop yields? Therefore, in-depth study of the regulation mechanism between miR167 and crop yield, and breeding of fine varieties through biological breeding will help to play an active role in agricultural production of miR167.

6.2 miR167 and its prospect in disease resistance research

In agricultural production, the impact of pests and diseases on crops is huge, and the main way to resist crop pests and diseases is through spraying pesticides. However, now people are increasingly pursuing organic green products, it has become the trend of the times to strengthen the defense ability of plants against diseases and insect pests by biotechnology. miR167-*ARF* pattern is known to enhance the immunity of soybean, wheat, rice and other important crops against diseases and pests, or miR167-IAR3 can enhance the defense ability of solanaceous plants against pathogens and pests. Whether miR167 can be applied to other important crops, such as peanuts and corn, to enhance the defense against pests and diseases and obtain economic benefits. It is still needs further exploration and research.

6.3 Future application of miR167 in plant stress resistance

The expression of miR167 was increased or decreased under different adversity conditions. *ARF* or *IAR3* could accumulate energy by auxin pathway or weaken the development of plants to enhance the tolerance to stress. miR167 is responsive to high salinity, drought and low temperature stress, and these environmental factors are the main environmental factors that limit crop yield and affect food security. For saline-alkali land, planting halophytes can improve different types of saline soil [114]. Therefore, it is significant to obtain stress-resistant crops. It has been reported that miR167 targets *ARF* in response to salt stress in *Tamarix ramosissima* and salt-tolerant maize, which means that the miR167-*ARF* model can be established to enhance the salt tolerance of plants. It is possible to obtain more salt-tolerant crops, such as rice and soybeans, to expand the planting area of cash crops, and to effectively use saline land.

6.4 Effects of plant hormones on miR167

Plant hormones are a group of small molecules with various structures, including jasmonates, salicylates, abscisates, auxin, gibberellins, and cytokinin, in which auxin is involved in many processes of plant growth. ARF interacts with AUX/IAA gene in signal transduction pathway and participates in plant hormone signaling pathway [115, 116]. miR167-targeted *ARFs* participates in the miR167-ARF8-OSGH3-2 signaling pathway, which affects the level of IAA and responds to the presence of exogenous auxin. Exogenous auxin rapidly promotes the expression of miR167, thereby affects the expression of downstream genes. However, it seems that other plant hormones, such as Cytokinin, abscisic acid and gibberellin, have no obvious effect on miR167. Whether auxin's effect on miR167 expression is direct still needs further investigation.

6.5 Study on miR167 target gene mechanism model by gene editing technique

Genome editing technology is a powerful tool for studying gene function and crop improvement. Among them, CRISPR/Cas9 and base editing (BE) are widely used in functional genomics and precise molecular breeding of crops. CRISPR/Cas9 is a genome-directed editing technique mediated by guide RNA [117–119]. The technique has been widely used in biology and crop ge-

netics and breeding, and the CRISPR/Cas9 technique has unique advantages. It has simple operation and high editing efficiency and has become the main gene editing technique at present. The improved base-editing technology of CRISPR-Cas9 system can achieve high-precision target gene editing without double-stranded DNA cleavage. The conversion of pyrimidine-pyrimidine (CBE), purine-purine (ABE), pyrimidine-purine (CGBE1 or miniCGBE1) can be realized by base editing tools [120–122]. Considering that with the development of CRISPR/Cas9 and base editing technology, miR167 and downstream target genes are edited to explore and improve the understanding of interaction mechanism between miR167 and target genes, thereby obtain high quality or high resistance germplasm resources. This will be a big step forward in agricultural production.

7. Author contributions

XL wrote this manuscript; SH participated in the writing and modification of this manuscript; HTX conceptualized the idea. All authors have read and agreed to the published version of the manuscript.

8. Ethics approval and consent to participate

Not applicable.

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11. Conflict of interest

The authors declare no conflict of interest, and the Bellagen Biotechnology Co., Ltd has no conflict of interest with this paper.

12. References

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