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REVIEW

miRNAs: Major modulators for crop growth and development under abiotic stresses

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Abstract Cumulatively, biotic and abiotic stresses of various magnitudes can decrease the production of crops by 70%. miRNAs have emerged as a genetic tool with enormous potential that can be exploited to understand stress tolerance at the molecular level and eventually regulate stress in crops. Plant miRNA targets frequently fit into diverse families of TFs that control the expression of genes related to a certain trait. As key machinery in gene regulatory networks, it is agreed that a broad understanding of miRNAs will greatly increase our understanding of plant responses to environmental stresses. miRNA-led stress regulatory networks are being considered as novel tools for the development of abiotic stress tolerance in crops. At this time, we need to expand our knowledge about the modulatory role of miRNAs during environmental fluctuations. It has become exceedingly clear that with increased understanding of the role of miRNAs during stress, the techniques for using miRNA-mediated gene regulation to enhance plant stress tolerance will become more effective and reliable. In this review we present: (1) miRNAs as a potential avenue for the modulation of abiotic stresses, and (2) summarize the research progress regarding plant responses to stress. Current progress is explained through discussion of the identification and validation of several miRNAs that enhance crop tolerance of salinity, drought, etc., while missing links on different aspects of miRNAs related to abiotic stress tolerance are noted.

Keywords Environment · Gene expression · Growth regulators · miRNA · Plant responses · Stress tolerance

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Introduction

The finding that microRNAs (miRNAs) in plants and animals function as gene regulators has resulted in a shift in the understanding of post-transcriptional gene regulation. Now, miRNAs are considered chief regulators of plant growth and development (Zhang and

Wang 2015). miRNAs are diverse regulatory molecules of small size present in many types of plants. For any individual plant species, the identified number of miRNAs varies from many to hundreds (Griffiths-Jones et al. 2008; Ferdous et al. 2016). A study of their structures found that the majority of miRNAs are 21 nucleotides in length, with the second greatest number being 24 nucleotides. Now, 7385 mature miRNAs and 6150 precursor miRNAs (pre-miRNAs) have been identified in 72 plant species (Griffiths-Jones et al. 2008). In contrast to plants, miRNAs regulate approximately 60% of the protein-coding genes in animals. Many of the miRNAs are evolutionarily conserved across the kingdom Plantae, e.g., mosses to flowering plants. The species-specific presence and identification of miRNAs (Zhang et al. 2006a; Shriram et al. 2016) favors a probable role of these molecules in controlling some common traits, such as tissue differentiation, auxin response or the development of organs such as roots, stems, leaves and flower parts, etc. (Carthew and Sontheimer 2009; Chen et al. 2011). Due to their extensive role in plant life, miRNAs are currently regarded as the most important gene regulators negatively regulating gene expression (Barrera-Figueroa et al. 2012).

Abiotic stress-regulated miRNAs were first observed in *Arabidopsis thaliana (*Sunkar and Zhu 2004*)*. In addition, the expression profiles of the majority of miRNAs involved in plant growth and development are altered during abiotic and biotic stresses. These later observations imply that the impaired plant growth and development under stress may be governed by different stress-responsive miRNAs (Li et al. 2016). miRNAs mediate plant responses by modulating their levels, the levels of their mRNA targets or the activity of miRNA–protein complexes (Stief et al. 2014). Additionally, in *Arabidopsis*, drought caused the down-regulation of a miRNA that, in turn, mediates drought tolerance (Li et al. 2008). Therefore, the discovery of miRNAs dealing with stress regulation has expanded to model as well as other non-model plants. This has forced scientists to do more in this area (Liu et al. 2009; Gao et al. 2016). In addition to the conservation of water and land, new as well as the most feasible agricultural techniques are currently needed to ensure future food security (Ali et al. 2016). Large-scale losses in various agricultural production systems occur due to biotic and abiotic stresses during the planting season (Agarwal et al. 2006). During the period of growth and development, crops can experience erratic rainfall, floods, drought, extreme temperatures, nutrient imbalances or salinity (Zafar et al. 2016). As noted by the FAO (2004), nearly 22% of the cultivable land has a high salt content, and the rising damage triggered by drought has been noticed to limit plant growth and productivity worldwide (Shao et al. 2008).

In comparison with conventional approaches, such as targeted gene knockout, this comparatively innovative technique of using miRNA has emerged as highly effective, pragmatic and adaptable. On the other hand, the specificity and safety of this technique are regarded as unique (Ossowski et al. 2008). At the same time, the overall success rate of miRNA-based gene silencing is nearly 75%, suggesting the need for a greater number of studies in this field (Park et al. 2009). In this review, we have highlighted the significance of miRNAs specifically as an aid for the modulation of crop growth, development and productivity under different stresses. Here, we review recent developments in miRNA-mediated plant stress tolerance.

Associate managers of vegetative and developmental activities

Spermatophytes exhibit diversity in their tissue architecture that is more positively based on the genetic potential of particular plant species (Noman et al. 2012). These architectural modifications have been directly correlated with plant's morphological, physiological and agronomical traits and its ability to survive in harsh environments (Peng et al. 1999; Noman et al. 2014). Studies of the model plant *Arabidopsis thaliana* and crop plants, such as *Oryza sativa, Zea mays, Hordeum vulgare* etc., have greatly supported our understanding of the molecular genetic basis of plant responses to abiotic stresses (Song et al. 2013; Ferdous et al. 2016; Gao et al. 2016). miRNAs have paved the way to optimizing crop architecture through molecular design and has led to enhanced grain productivity. They are involved in hormone signal transduction e.g. jasmonates, auxins etc. (Liu and Chen 2009; Lima et al. 2011), and also play a diverse role in plant growth and development and the response to abiotic stresss and pathogens (Fig. 1—and see also Fig. 3 below). Against abiotic stresses, the

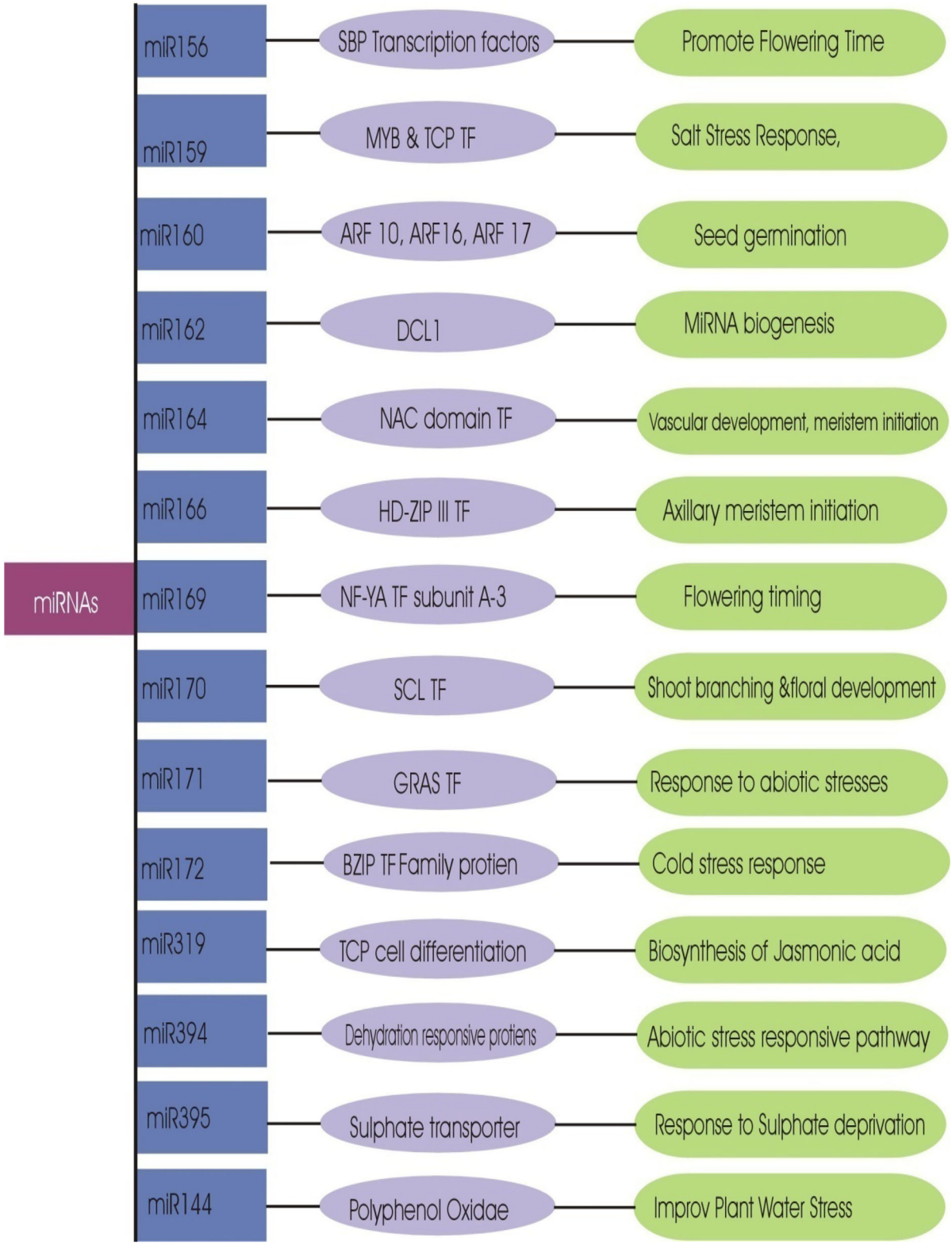

Fig. 1 miRNAs along with target transcription factors and their ultimate role for plant growth and development

change in miRNAs expression levels results in modulation of the expression patterns of target genes that are associated with stress adaptations. Such regulatory functions of miRNAs have motivated the notion of developing artificial miRNAs for silencing certain specific genes. This targeted gene silencing may perhaps allow the undeviating molecular modulation of plant traits, for application in breeding of crops.

With regard to the shoot meristem, the participation of many miRNAs, e.g., miR164 and miR165/miR166, has been identified and confirmed in shoot morphogenesis by targeting a variety of genes, i.e., NAC genes and class III HD-ZIP (homeodomain-leucine zipper) (Baker et al. 2005; Zhou et al. 2007). miR165 and miR166 regulate HD-ZIP III which later acts as a signal specifying leaf polarity. Over-expression of miRNA 165 causes a reduction in carpel size and sterility. In addition to these miRNAs, some other miRNAs i.e. miR164 have been detected due to their active involvement in other growth processes (Srivastava et al. 2012; Zeng et al. 2012; Zhou et al. 2012), such as the negative regulation of leaf senescence by controlling the level of the ORE1 transcript (Nikovics et al. 2006; Peaucelle et al. 2007; Kim et al. 2009). With special reference to leaf development, miR319 has dual functions in controlling leaf morphogenesis and senescence by regulating the plant-specific class II TCP transcription factors (Teosinte branched1/cycloidea/pcf) (Efroni et al. 2008; Schommer et al. 2008; Burklew et al. 2012). miRNAs 156 and 172 are regulators that are involved in promoting floral transitions (Wu and Poethig 2006).

According to Li et al. (2013), it is now possible to delay or advance the commencement of flowering in *Sinningia speciosa* by up- or down-regulating miR159 levels which constrains flowering by reducing the expression of the Gloxinia *GAMYB* and *LFY* homologues. In addition to regulating flowering time, miRNAs have been studied regarding their involvement in male sterility (Toppino et al. 2011; Zhou et al. 2012) and can be influentially used to create male-sterile lines for F1 hybrid production. The results prove that miR397b regulates lignin content and seed number in *Arabidopsis thaliana* (Wang et al. 2014). Similarly, studies have found a miMTD (*miRNA/MADS/TCP/D14*) regulatory network that can modulate tillering in rice (Guo et al. 2013). Varying the expression levels of specific plant miRNAs and the use of artificial miRNAs make it feasible to modulate the primary transcription factors and thus modulate downstream gene regulatory networks (Schwab et al. 2006). Furthermore, vital processes such as plant growth and development, flowering, and seed production are clear targets for the application of this technology as an attempt to improve agricultural productivity via environmental stress tolerance.

miRNA biogenesis and its role in combating environmental stresses

Biogenesis starts with the transcription of miRNA genes mediated by RNA polymerase 11. The first step is to add a cap (7-methyl GTP) and a tail (PolyA tail) to this primary transcript in order to protect it from restriction endonucleases. The product of MIR genes (pri-miRNA) then undergoes a series of enzyme-dependent post-transcriptional modifications. First it undergoes self-folding forming a stem loop structure. This stem loop structure (pri-miRNA) is then converted into pre-miRNA. The pre-miRNA stem loop structure is finally transformed into 20–22-nt miRNA/miRNA* duplex by the key enzyme, DCL1; however, HYL1 and SE assist in this conversion. The next step is methylation at the 3′-terminus by HEN1 followed by its subsequent transport to cytoplasm by HST1. In the cytoplasm, miRNA strand of the duplex becomes part of the RNA-induced silencing complex (RISC) which triggers translational inhibition of the target transcript responsible for a particular physiological function (Fig. 2) (Lu and Fedoroff 2000; Zhang et al. 2008). With advancements in genome-based investigations, it has become apparent that the expression of conserved, constitutively expressed miRNAs in plants can be modulated in a specific spatiotemporal manner in response to stress (Fig. 3; Table 1).

The gathered evidence places us in a position to infer that the regulation of miRNA expression in response to environmental stress varies between domesticated species and those that are adapted to suboptimal conditions. It is commonly believed that the regulation of stress-responsive miRNAs occurs at the transcriptional level but we should also keep in mind that potential regulation at the post-transcriptional level cannot be excluded. The stress-induced decreases in miRNAs levels due to enhanced degradation still require extensive research. It is still debatable whether plants under stress use both

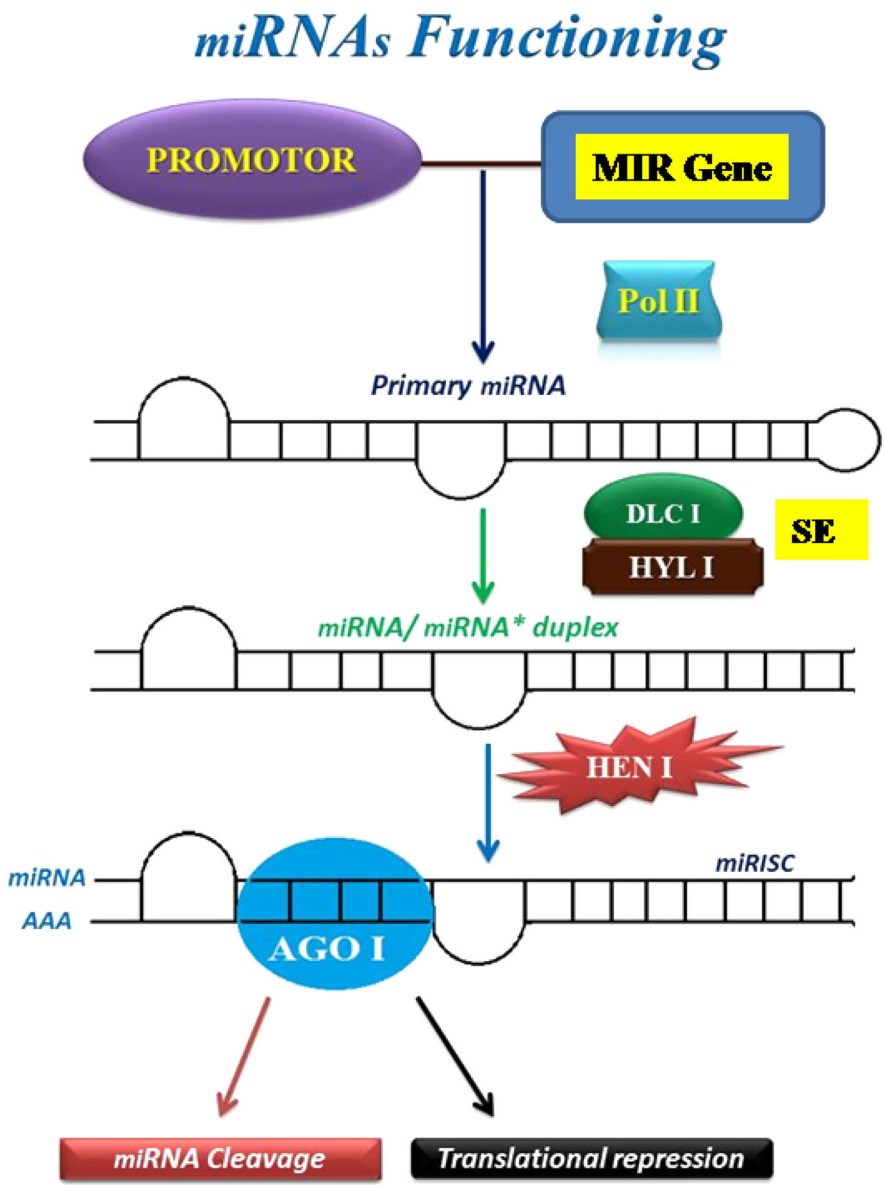

Fig. 2 miRNA biogenesis and its function in modulation of Abiotic Stresses

methods of target gene regulation or one is preferred over the other. The confirmation and characterization of stress responsive miRNAs requires the application of highly trustworthy and rigorous assays. We hypothesize that we can gain extensive insight into the miRNA target networks operating within cells or in a tissue-specific manner during stress by reviewing the expression of stress-responsive miRNAs and target genes. Now, it has become exceedingly clear that, with increased understanding of the role of miRNAs during stress, the techniques for using miRNA-mediated gene regulation to enhance plant stress tolerance will become more effective and reliable. Thus, we will review different stresses and the role of miRNAs in the modulation of these abiotic and biotic stresses.

Drought

As gene regulators, miRNAs are likely to participate in the regulation of drought-responsive genes. Drought-responsive miRNAs have been observed in different plant species, such as *Arabidopsis* (Li et al. 2016), *Oryza sativa* (Zhou et al. 2010; Gao et al. 2016),

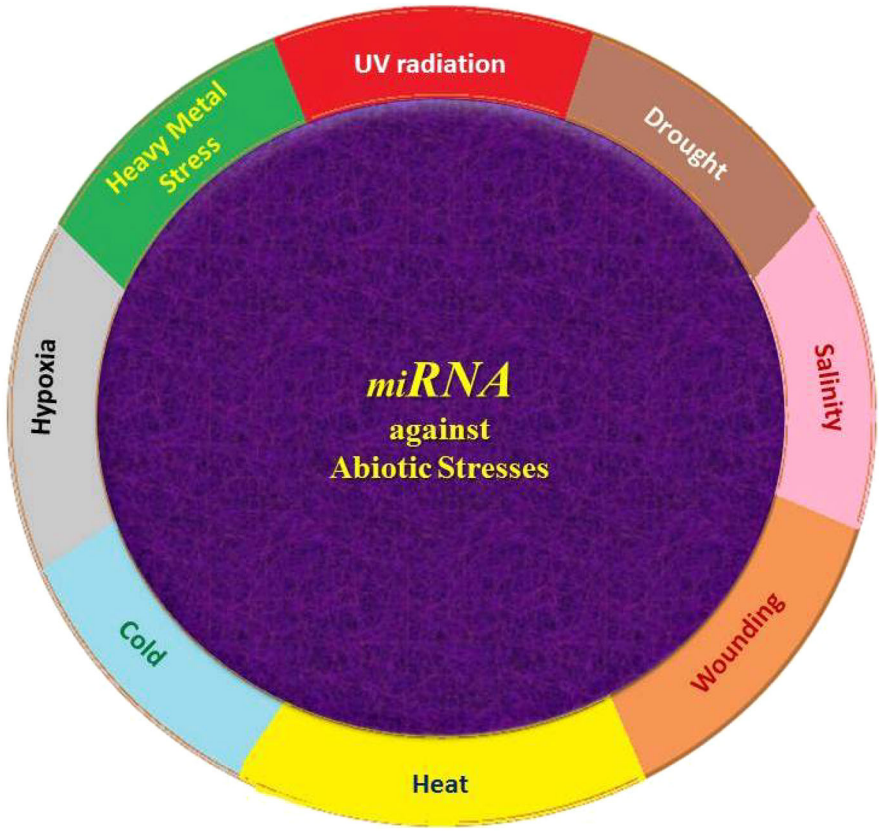

Fig. 3 General illustration of miRNA response against environmental stresses

Nicotiana tabacum (Frazier et al. 2011) and *Glycine max* (Kulcheski et al. 2011) (Table 1). In various crops, the roles of miRNAs in the response to different conditions at different growth stages have been explored during the last decade (Fig. 4). Most of the time, early growth stages were taken into special consideration while studying or evaluating miRNA activity under abiotic stresses (Huang et al. 2009). Wide-ranging studies have attempted to discover unique miRNAs and analyze their role in response to drought e.g. *Oryza sativa, Triticum aestivum* etc. (Liu et al. 2009; Li et al. 2011a, b; Gao et al. 2016). Presently, we need to expand our knowledge about the modulatory role of miRNAs in drought stress, especially during the reproductive phase and growth phase of plants.

Water scarcity during crop reproductive stages can dramatically compromise seed and grain production (Saud et al. 2013, 2014, 2016). Seed development requires a sequence of molecular events that are ultimately regulated at the transcriptional and post-transcriptional levels (Duan et al. 2005), and miRNAs are also involved in this process (Zhu et al. 2008). Barrera-Figueroa et al. (2012) have identified 227 miRNAs falling into Fig. 5.

127 families in water-stress-exposed rice plants. miRNA activity can result in both up-regulation or down regulation (Table 1). While most stress-regulated miRNAs were up-regulated by low water availability or cold stress (Fig. 4, 5), the majority of salt-stress-regulated miRNAs were down-regulated. In addition, 16 miRNAs were regulated by one of the imposed abiotic stresses (drought, cold, salt) and 12 miRNAs were regulated by two or three stresses; e.g., miR2871b was induced by all three abiotic stresses, indicating that this miRNA might be involved in a pathway that is shared in the response to different stresses (Barrera-Figueroa et al. 2012). Different miRNAs also are up- or down- regulated in different plants facing drought. For example, miR170 was down regulated in rice, miR168 was up-regulated in drought-stressed maize and tomato plants (Firdous et al. 2015), and miR171 also up- and down-regulates

Table 1 List of plants with different miRNAs activity under drought stress

Plant Species	Up-regualted	Down-regulated	References
Arabidopsis thaliana	miR156, iR159,miR167, miR168, miR171, miR172, miR319, miR393, miR394a, miR395c, miR395e, miR396, miR397	miR161, miR168a, iR168b, miR169, miR171a, miR319c	Liu et al. (2008) and Sunkar and Zhu (2004)
Oryza sativa	miR156, miR474, miR395, miR319, miR171, miR159	miR408, miR319, miR172, miR171, miR170, miR168, miR156	Zhou et al. (2010), Ren et al. (2012), Shuai et al. (2013) and Trindade et al. (2010)
Brachypodium distachyon		miR164	Shuai et al. (2013) and Wang et al. (2011)
Glycine max	miR394, miR169, miR166		Ren et al. (2012) and Shuai et al. (2013)
Hordeum vulgare	miR156		Eldem et al. (2012),
Medicago truncatula	miR2118, miR399, miR398	miR398, miR396, miR171, miR164	Jones-Rhoades and Bartel (2004) and Ren et al. (2012)
Populus euphratica	miR169, miR156		Liu et al. (2008), Ren et al. (2012), and Shuai et al. (2013)
Populus trichocarpa		miR1444, miR164,	Shuai et al. (2013)
Populus tomentosa	miR403, miR399, miR319, miR172, miR167	miR408, miR399, miR397,miR395,miR394, miR390, miR171, miR169,	Allen et al. (2005), Kantar et al. (2011), and Liu et al. (2008)
Prunus persica	miR160, miR157	miR408, miR398, miR397, m,iR396, miR395, miR393, miR169, miR167, miR165, miR159, miR157, miR156	Liu et al. (2008), Ren et al. (2012), Shuai et al. (2013), Trindade et al. (2010) and Zhou et al. (2010)
Triticum dicoccoides	miR1432, miR156	miR474, miR398, miR171, miR166	(Zhou et al. 2010)
Zea mays.	miR827	miR528	Wei et al. (2009) and Zhang et al. (2009)

genes in rice. *Populus* and *Arabidopsis* plants under stress (Zhou et al. 2010; Yu et al. 2012).

Shared upstream sequence motifs have been identified that are significant for stress-responsive miRNA genes in plants, highlighting the co-regulation of different miRNAs. Devi et al. (2013) discussed six stress-related elements (M1–M6) that were observed in the promoter regions of genes encoding three drought-responsive miRNAs, e.g., miR166k, miR393 and miR397b. In addition to this, some genes encoding drought-responsive miRNAs harbor motifs responsive to ABA, such as ABA responsive elements, MYB and MYC binding sites, Motiflib, and CE3. Thus, in our view, this indicates a strong regulatory role of miRNAs through ABA-independent or ABA-dependent pathways. However, it is clear that miRNA differential expression profiles do not solely result from motif content in all cases (Lima et al. 2011; Burklew et al. 2012; Zhou et al.2012). For example, the expression of miR408 remained steady in drought-tolerant *Oryza sativa* plants in response to water loss, while the expression of this miRNA was reduced in a sensitive cultivar (Mutam et al. 2013) NFY proteins (nuclear factor Y) have been extensively studied due to their participation in stress response. Numerous members of the *NFY* gene family are targets of miR169 in *Arabidopsis*. During water stress, *NFYA* transcript levels were up-regulated and the induction of *NFYA5* expression, due to low water availability in plants, partially depends on the down-regulation of miR169. With regard to performance, *NFYA5*-expressing transgenic plants were observed to be drought

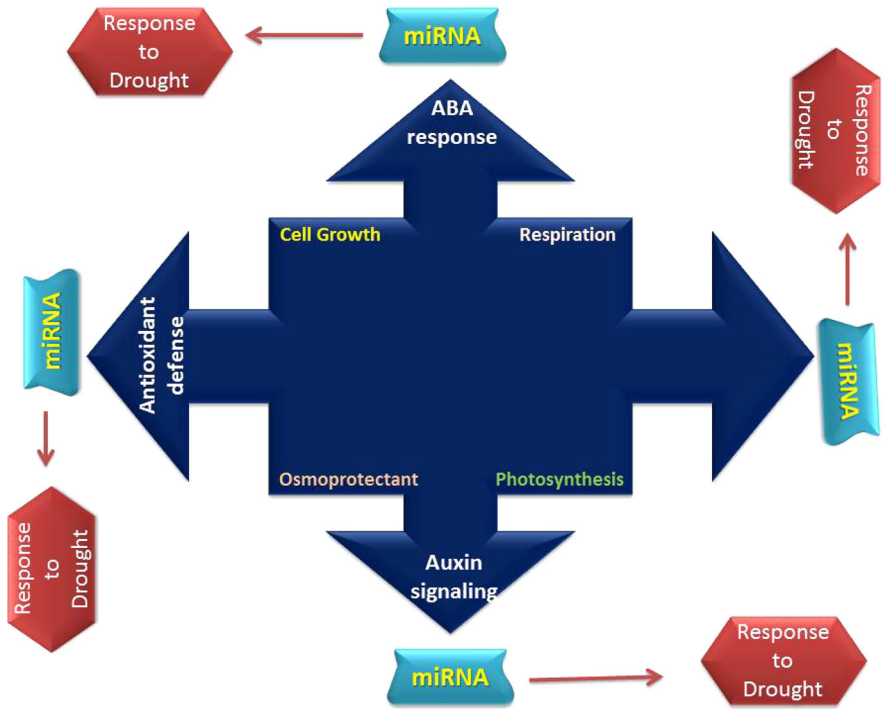

Fig. 4 Different cellular processes in association with miRNAs for drought tolerance in plants

tolerant (Li et al. 2008). The future of crop stress tolerance relies on multiple factors. From the above-quoted facts and figures, it can easily be understood that miRNAs have an important role in plants responses to drought. These molecules have emerged as genetic basins with enormous capacity that can be exploited to understand water stress tolerance at the molecular level and eventually will become very useful for regulating stress in crops.

Salt stress

Salinity stress, a major abiotic stress, modifies major metabolic processes and results in extensive damages that ranges from cell wall destruction to genomic unsteadiness (Macovei and Tuteja 2012; Fahad and Bano 2012; Fahad et al. 2014a, b, 2015c). Various genomic and proteomic studies have revealed that tolerance to salinity occurs because of effectors that directly up or down regulate the stress response or temper the effects of stress. Additionally, some key regulatory molecules were found to be involved in sensing stress, signal transduction, and the modulation of effector functions (Hasegawa et al. 2000; Bej and Basak 2014). Plant responses to saline conditions comprise a broad spectrum of processes, such as signal transduction, transcription, membrane trafficking, protein biosynthesis, etc. Additionally, the expression of several miRNAs under saline conditions has been determined (Fig. 1, 3). The expression of different miRNAs, including miR396, miR168, miR359, miR159, miR319, miR165, miR167, miR156, miR393, miR158, miR171 and miR169, was up-regulated in *Arabidopsis* under salt stress (Liu et al. 2008; Gao et al. 2016). In contrast, both the up-regulation and the down-regulation of miRNAs were observed in *Populus trichocarpa*. For example, miR530a, miR1445, miR1446a-e, miR1447 and miR1711 were down-regulated and miR482 and miR1450 were up-regulated during high-salt conditions (Lu et al. 2008; Wang et al. 2014). In *Oryza sativa,* miR169g and miR169n were strongly up-regulated. Up-regulation of miRS1 and miR159.2 was recorded in *Phaseolus vulgaris* when subjected to salt stress (Arenas-Huertero et al. 2009). Likewise, in *Arabidopsis*, miR169 was up-regulated in response to salinity (Zhao et al. 2009). The curtailed expression of miR398 due to salt stress was negatively correlate with the expression of its target genes, CSD1 and CSD2 (Cu–Zn superoxide dismutase 1&2), in *Arabidopsis* (Jagadeeswaran et al. 2009). Contrastingly, miR398

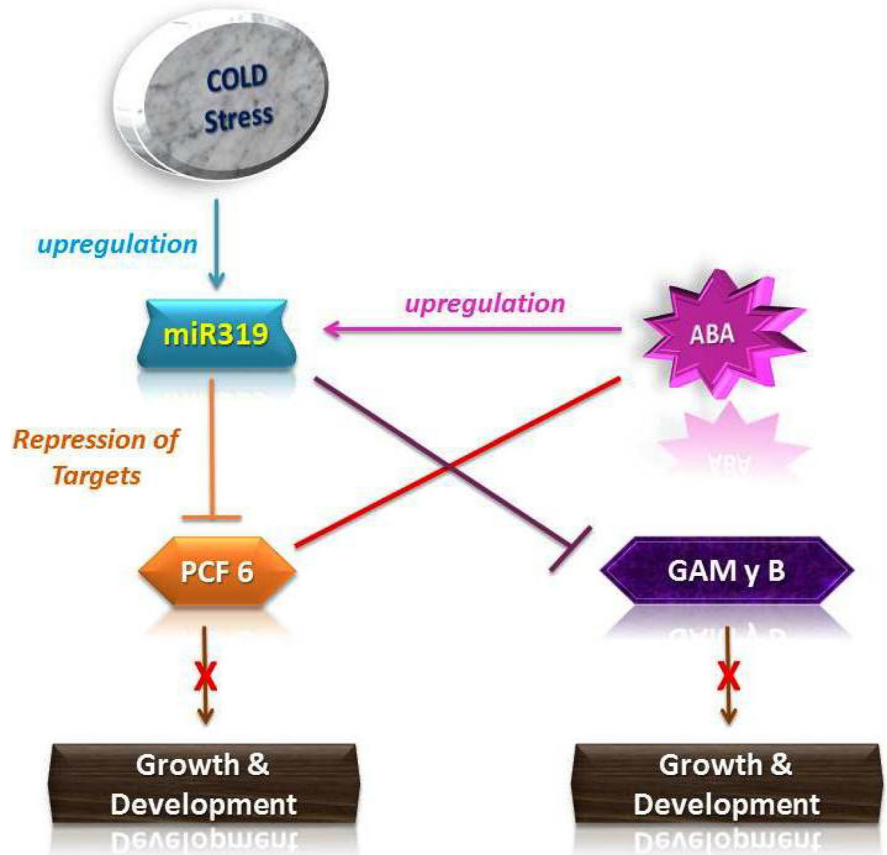

Fig. 5 Proposed model for *Sacchrum officinarum* response to cold and ABA treatment. In cold stress, upregulation of the miR319 leads to Target repression. which in turn inhibits the growth and development of the plant. In plants treated with ABA, however, it is possible that ABA treatment induces the expression of genes *PCF6* and *GAMyB*. (modified from Theibut et al. 2012)

expression is actively regulated in *P. tremula* during saline conditions, as miR398 levels initially increased but decreased after 48 h and then rose again after 72 h of salt stress; these levels were negatively correlated with CSD1 and CSD2 transcript abundance (Jia et al. 2009). Virtual miRNA profiling has been performed for two maize lines that differ in salt sensitivity. The response of miRNAs also varied greatly between these genotypes (Ding et al. 2009).

The existing information on the critical role of miRNAs in salt stress responses is extensively based on expression profiling in plant species with varying sensitivities to salinity under variable salt levels (Covarrubias and Reyes 2010). Like drought-responsive miRNAs, salt-responsive miRNAs also possess diverse stress-linked promoter elements such as ABA-responsive elements, W-box sequences, G-box sequences, MYB binding sites, etc. (Shen et al. 2010; Wang et al. 2014). Regulation is effected by various members of one miRNA family through ABA-dependent and ABA-independent pathways in response to salinity and drought (Covarrubias and Reyes 2010). *ABRE* (*cis*-acting ABA-responsive element) was recognized in the upstream region of miR169n, indicating that miR169n may be regulated by ABA. In contrast, miR169g and miR169n target nuclear factor Y subunit A (*NFYA*) mRNA, which was down-regulated in leaves of *Triticum aestivum* facing drought (Stephenson et al. 2007). Thus, we can say conclusively that the involvement of one miRNA or its sequence variants, including members of the same family, in many stress responses is a general phenomenon.

Cold stress

The molecular basis of low temperature or freezing acclimation and tolerance in different plants, chiefly in *Arabidopsis* and winter cereals (Fig. 5), has been widely studied. During cold acclimation, gene expression is reprogrammed and cell metabolism is altered

(Chinnusamy et al. 2010). Cold response is not a simple metabolic process but a combination of different genes regulation and metabolic pathways (Hannah et al. 2005; Yu et al. 2012). In certain plants, genes regulated by low-temperature/cold stress have been recognized (Gao et al. 2016). However, little data regarding the epigenetic regulation of cold stress are available (Nogueira et al. 2003, 2005).

Song et al. (2013) revealed that cold acclimation process in *Arbidopsis thaliana* is supported by miRNA417. This miRNA target C2-domain containing protein and SNF7 family protein that play crucial role in tolerating low temperature stress. In addition to this, miRNA535 is involved regulating cold responses in *Glycine max.* Cyclin B2 as well as retro-transposon protein is in direct correlation with miRNA535 levels. This relation between proteins and miRNA levels point out their credibility in plant tolerance to cold (Yu et al. 2012). Barrera-Figueroa et al. (2012) described the DUF1242 super-family of proteins as putative target of miRNA 1867 for cold tolerance in *Oryza sativa.* Furthermore, miR319 induction was much more robust in roots. These investigations were validated by earlier studies in *Arabidopsis*, in which miR319 was up-regulated in response to low temperature stress (Sunkar and Zhu 2004; Liu et al. 2008). Furthermore, this miRNA319 is involved in multiple processes in plants, including the regulation of ethylene biosynthesis and the leaf response to cold stress (Jones-Rhoades and Bartel 2004; Schwab et al. 2005; Reyes and Chua 2007). Up-regulation of miR319 is in response to both cold and ABA treatment. According to Nogueira et al. (2003), cold response pathways are both dependent on and independent of ABA in sugarcane. In *Arabidopsis* miR319 targets genes from two classes of transcription factors, *TCP*-like (*Teosinte branched 1*) and *MYB*-like, which are characterized as PGRs (Palatnik et al. 2003, 2007; Schommer et al. 2008). In addition, experiments using *Arabidopsis* have validated the involvement of many miRNAs targeting cold-responsive genes (Kantar et al. 2011; Song et al. 2013; Gao et al. 2016). In sugarcane, phylogenetic analyses of the described *TCP*- and *MYB*-like genes (regulated by cold responsive miRNA) indicated that these genes are grouped in a separate clade present only in the poaceae family, suggesting that their role is to regulate signaling pathways specific in members of this family.

Cold response regulation mediated by miR319 seems to be functional in the entire plant body as both miR319 induction and *PCF6* and *GAMyb* repression occur in both roots and shoots. In contrast, miR319 target genes were expressed differentially in plantlets treated with ABA, while direct regulation by miRNA was not recorded in sugarcane plants grown in vitro. It is possible that while both messenger RNAs are still cleaved by miR319, the genes are induced by ABA, and this induction in expression balances the destruction of mRNAs. Ding et al. (2009b) have found that genes affiliated with the *MYB* transcription factor family can be up-regulated by ABA. Otherwise, under stress conditions, reductions in target mRNA levels are not always recorded due to incremental changes in miRNA expression even when the miRNA cleaves the matching target mRNA (Joeng et al. 2009).

Thus, we can infer from the given results that the miRNA-directed, cleavage-dependent post-transcriptional regulation of target genes does not continuously restrict the accumulation of mRNA in stressful conditions. Thiebaut et al. (2012) developed a hypothetical model of miR319 regulation in *Saccharum officinarum* facing low temperature stress (Fig. 5). The exposure of sugar cane plants to cold resulted in amplified expression of miR319, which regulates the expression of its target genes, e.g., *PCF6* and *GAMyb,* by cleavage. Repression of the *PCF6* gene may result in abnormal leaf development (Koyama et al. 2007). In barley, the *GAMyb* gene controls anther development, early flowering, stem elongation and seed development (Woodger et al. 2003). Thus, it is logical that a reduction in *GAMyb* -mRNA levels in plants facing cold may lead to impaired growth and development. Additionally, miRNA319 signaling responses in barley can be regulated by ABA as in sugarcane. MiR319 regulation was also observed in plants grown in a greenhouse.

In root tips subjected to cold treatment, there is an absence of *GAMyb* transcripts. This suggests that at least one of the mechanisms leading to plant growth inhibition in response to cold stress is initiated by the miRNA319-mediated cleavage of its targets.

Nutrient deprivation

miRNAs have dynamic contributions to the regulation of nutrient homeostasis (Kharwaish et al. 2102; Shriram et al. 2016). Transcriptional regulation is the

primary plant response to nutrient deprivation (Sunkar et al. 2012) but miRNA-assisted post-transcriptional regulation also plays a vital role in this phenomenon. As a result of nutrient deficiency, different miRNAs are expressed, leading to the appropriate response to the conditions. For example, during phosphorous deprivation, the induction of miR399, miR827 and miR2111 specifically occurs. On the other hand, a change in the abundance of miR156, miR778, miR828, miR169, miR395, miR398 and miR399* becomes evident during low phosphate availability. This suggests a positive role of miRNAs in phosphate homeostasis (Bonnet et al. 2004; Sunkar and Zhu 2004).

miR399 synthesis is induced by phosphate starvation response (*PHR1*) transcription factors (Chiou 2007). Shoots are the production sites of miR399, which then moves via phloem to roots for cleavage of the targeted *PHO2* transcripts (Li et al. 2011). This cleavage results in the uptake of phosphate due to the up-regulation of phosphate transporters, namely, Pht1;8 and Pht1;9. As phosphate ions approach equilibrium, IPS1 acts as a target mimic for miR399 and stops the degradation of *PHO2* transcripts. This miR399-PHO2-IPS1 axis is therefore an important part of the P-deficiency signaling pathway for maintaining phosphate homeostasis. It is thought provoking that E3 ligases become targets of miR827 and miR2111 which are induced during phosphate deprivation, signifying that the ubiquitination-mediated protein degradation pathway is typically used during phosphate scarcity. During sulfate deficiency, miR395, which targets the sulfur transporter SULTR2;1/AST68 along with APS1, APS3, and APS4, three ATP sulfurylase genes, is induced. During sulfate deficiency, miR395 induction is negatively correlated with APS1 transcript levels but not with the levels of AST68. Conversely, in *Arabidopsis* roots, both miR395 and AST68 levels increase during sulfate deprivation (Yoshomito 2007). miR395 functions in sulfate remobilization between leaves in *Arabidopsis* during sulfate deprivation (Liang and Yu 2010) although the mechanism involved is unclear. Moreover, in *Brassica napa,* changes in the levels of miR156, miR160, miR164, miR167, miR168 and miR394 were also noticed during sulfate starvation (Huang 2010). This suggests that miRNAs may have a strong role in growth modulation and the developmental adjustments needed for adaptation to sulfate-limited conditions.

Among plants, Cu homeostasis is a firmly controlled process that comprises numerous conserved Cu-responsive miRNAs, such as miR397, miR398, miR408 and miR857 (Burkheed 2009; Liu and Zhang 2012). Interestingly, these miRNAs target transcripts encode Cu-containing proteins like Cu–Zn SODs (superoxide dismutase). The down-regulation of target gene expression by miRNAs in conditions of Cu shortage supports the hypothesis that Cu-responsive miRNAs can save Cu for other essential proteins such as cytochrome (Ghani and pilon 2008; Burklew et al. 2012). In contrast, miR398 responds to both Cu deficiency and oxidative stress. In stressful conditions, ROS (reactive oxygen species) tend to accumulate, and their detoxification requires increased CSD1 and CSD2 expression, which is ultimately mediated through reduced miR398 levels (Lima et al. 2011; Pilon 2016). On the other hand, when Cu is lacking, the induction of mi398 will result in the silencing of CSD1/CSD2/CCS1 to conserve copper. Different gene regulatory mechanisms are adopted by plants, including miRNA-mediated gene regulation, to tackle limited nitrogen availability. The miR393/AFB3 module functions in regulating root system architecture during conditions with limited N availability (Sunkar et al. 2012). In response to nitrogen treatment, AFB3 (auxin receptor) levels are regulated at the transcriptional and post-transcriptional levels, with post-transcriptional regulation depending on miR393. Up-regulation of miR393 clearly leads to the down regulation of AFB3, which controls primary and lateral root growth (Vidal et al. 2010). An additional well-known nitrogen-responsive miRNA module is miR167/ARF8 (auxin responsive factor8). Cell-specific profiling has indicated that miR167a is repressed in the pericycle and root cap, while its target, ARF8, is induced in these tissues as a result of N treatment, which in turn initiates lateral root formation in *Arabidopsis* (Huang et al. 2010; Valdés-López et al. 2010; Zhou et al. 2012; Srivastava et al. 2012). Together, studies have indicated that nitrogen availability modifies the expression of miRNAs that regulate auxin signaling by targeting AFB3 or ARF8.

UV-B radiation

UV-B radiation ultimately results in drastic responses in terms of physiological, biochemical and molecular changes (Fahad et al. 2013). Sunkar (2010) has

described the regulation of twenty-one miRNAs during UV-B radiation exposure in *Arabidopsis*. According to Jia et al. (2009), miRNA array analysis has shown a total of twenty-four microRNAs to be differentially regulated in *P. tremula* as a response to UV-B radiation; of these, 13 miRNAs were up-regulated while 11 were down-regulated. Small RNA blot analysis has confirmed the altered miRNA profile (miR169, miR395, miR472, miR168, miR398 and miR408). In *A. thaliana,* the miRNAs miR156, miR160, miR165/166, miR167 and miR398 were believed to be UV-B-responsive (Zhou et al. 2009), while similar miRNAs were confirmed as responsive to UV-B stress in *Populus tremula* (Jia et al. 2009); these results suggest conserved regulatory mechanisms in two different species.

Hypoxia and anoxia

SODs are considered crucial enzymes that convert O^{2-} into less toxic H_2O_2, which is detoxified by POD (peroxidase) and CAT (catalase) (Noman et al. 2015). Up-regulation of the two CSD genes (Cu–Zn superoxide dismutase) is dependent on miR398 levels. In *Arabidopsis,* Cu–Zn SOD1 and SOD2 levels were inversely related with the levels of miR398 during stress. The suppression of miR398 transcription ultimately suppresses the miR398-directed cleavage of CSD1 and CSD2 transcripts. Low O_2 availability to plants, e.g., plants facing water logging, interferes with respiration. The induction of changes in the transcriptome is attributed to hypoxia.

A very positive role of miRNAs has been suggested during hypoxia stress (Zhang et al. 2008). Substantial regulation of different miRNAs (miR166, miR167, miR171, miR396) occur in maize seedlings facing submergence. During the early phase, miR159, miR395, miR474 and miR528 were down-regulated. In *Arabidopsis thaliana,* low O_2 levels modified the expression profiles of 19 miRNA families. The role of miRNAs during hypoxia stress has further been confirmed in studies using a chemical that inhibits mitochondrial respiration (Moldovan et al. 2009).

Conclusion and future directions

Before 1998, miRNA technology was entirely unidentified. Though, this field has massively developed within a shorter period of time with great degree of success achieved. Here we synthesized the existing data to provide a comprehensive review of miRNAs as an incredible modulators for crop growth and development under abiotic stresses. As documented in this review, numerous miRNAs have been determined to be involved in several plant development and abiotic stress responses. They are positioned for the fine tuning of distinct regulatory networks. Computational and experimental methodologies have augmented efforts to characterize numerous miRNAs and their targets in order to control multiple plant traits. The availability of ample genomic information and NGS technologies has augmented the efforts aimed at understanding miRNA regulation during several types of abiotic stress.

Improved abiotic stress tolerance demands wide-ranging knowledge for identification as well as validation of miRNAs and association of their expression profiles with the ultimate targets. This information will allow the identification of miRNAs/targets that influence stress tolerance. Another challenge will be characterization of the cis-regulatory elements of the miRNA genes to determine the corresponding transcription factors and describe the process by which miRNAs regulate the response to different stresses. These data will provide novel insight into the functions of miRNAs and perspective for developing engineered plants with enhanced stress tolerance. By meeting this challenge, we will be able to decode novel components in plant stress tolerance and guide to interpretation of plant stress responses. Nonetheless, the understanding of miRNA evolution is in its infancy. Further work must identify and characterize the catalogue of small RNAs that display shifts in expression level upon stress conditions in crop plants and unravel the target genes of newly discovered miRNAs.

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