Review

Long Non-Coding RNAs as Endogenous Target Mimics and Exploration of Their Role in Low Nutrient Stress Tolerance in Plants

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Abstract: Long non-coding RNA (lncRNA) research in plants has recently gained momentum taking cues from studies in animals systems. The availability of next-generation sequencing has enabled genome-wide identification of lncRNA in several plant species. Some lncRNAs are inhibitors of microRNA expression and have a function known as target mimicry with the sequestered transcript known as an endogenous target mimic (eTM). The lncRNAs identified to date show diverse mechanisms of gene regulation, most of which remain poorly understood. In this review, we discuss the role of identified putative lncRNAs that may act as eTMs for nutrient-responsive microRNAs (miRNAs) in plants. If functionally validated, these putative lncRNAs would enhance current understanding of the role of lncRNAs in nutrient homeostasis in plants.

Keywords: long non-coding RNAs; endogenous target mimicry; microRNA; nitrogen and phosphorus deprivation

1. Introduction

Non-coding RNAs (ncRNAs) are functional RNAs with very low or no potential for encoding protein but are involved in controlling developmental processes or stress responses [1,2]. Non-coding RNAs are a heterogeneous group of RNA molecules that can be classified in different ways according to their location, length and biological functions [3,4]. The first ncRNAs were discovered in the early 1980s when small nuclear RNAs (snRNAs) were established as building blocks of the spliceosome [5].

The application of high throughput RNA-sequencing (hereafter RNAseq) has facilitated the identification of thousands of novel ncRNAs in a diverse range of organisms including human, animals and plants [3,6,7]. In addition to protecting genomes from the introgression of foreign nucleic acids, ncRNAs have been shown to be involved in regulating gene expression at the transcription, RNA processing, and translation levels [8]. The ncRNA-mediated regulation of gene expression at transcriptional, post-transcriptional and epigenetic levels occurs via long non-coding RNAs (lncRNAs), named based on their length relative to microRNAs (miRNAs; around 22 bp in length) [9]. Long non-coding RNAs are large RNAs of length 200 nucleotides or greater and do not code proteins. The diversity of ncRNAs offers an important insight into their dominance in gene regulation. There has been significant work on lncRNAs in the animal kingdom [6,10–23] but studies on plant lncRNA are still in their infancy. There are several intriguing similarities between lncRNAs and messenger...
RNAs (mRNAs). Similar to mRNAs, most lncRNAs are transcribed by RNA polymerase II, although they can also be transcribed by RNA polymerase III, IV or V [24,25]. A few lncRNAs have features including a 5’ cap and 3’ polyadenylated tail but lack the ability to encode proteins.

In contrast to small RNAs, lncRNA sequences show weak sequence conservation which is proposed as the result of a high rate of primary evolution as the latter may be the frequent target of positive selection [26]. The molecular mechanisms of lncRNAs can be studied by considering lncRNAs in four archetypes: (i) signal (ii) decoys (iii) guides, and (iv) scaffolds [4]. Long non-coding RNAs under the archetype ‘signal’ are transcribed by RNA polymerase II as evidenced by polymerase II occupancy, 5’ caps, histone modification associated with polymerase II transcriptional elongation and polyadenylation [7]. The incorporation of environmental signals such as temperature, light, drought, and salt are some of the well-studied examples of the ‘signal’ type mechanism. Recently reported lncRNA DROUGHT INDUCED lncRNA (DRIR) expression under drought and salt stress was observed to regulate the modulation of the activity of genes involved in abiotic stress response in Arabidopsis thaliana [27]. DROUGHT INDUCED lncRNA functions upstream of gene transcription whilst its constitutive expression does not affect the expression of other stress responsive genes under normal environmental conditions. Although the molecular mechanism of DRIR is still not clear, there is speculation that it might influence the activity or regulation of FUT4 gene encoding fucosyltransferase, or transcription factor NAC3 (NAM/ATAF/CUC family) or redox status, resulting in enhanced tolerance to drought and salt stress. Another example of an environmental signal mechanism is lncRNA LONG-DAY SPECIFIC MALE FERTILITY ASSOCIATED RNA (LDMAR), which causes photoperiod sensitive male sterility in rice, thus regulating fertility by day length [28].

The second ‘decoy’ mechanism demonstrates negative regulation of transcription. Here, the RNA acts as a molecular sink and miRNA target mimics are good examples of this archetype. Long non-coding RNAs are thought to act as a decoy and moderate the quantity of protein produced, effectively titrating away proteins and small regulatory RNAs [4]. In silico analysis of maize (Zea mays) degradome data showed that there are 86 lncRNAs which act as decoys for 58 miRNA [29]. Their work has confirmed that miRNA decoy sites are conserved across genomes of five monocot species and the putative miRNA decoys can inhibit miRNA function in a spatial or temporal manner [30]. This has been proposed as a contributing factor for maize transcript complexity. A well-studied example of the decoy mechanism is INDUCED BY PHOSPHATE STARVATION 1 (IPS1) which acts as a decoy of miRNA399 (further discussed below).

The third ‘guide’ mechanism involves the binding of RNA and positioning of the ribo-nucleo protein complex to a specific target, in either-cis or -trans, in such a way that cannot be easily predicted based on lncRNA sequences. The Nuclear Speckles RNA-binding protein (NSRs) mediates the alternative splicing of a group of genes involved in lateral root initiation in A. thaliana. However, the lncRNA ALTERNATIVE SPLICING COMPETITOR (ASCO)-RNA can bind with NSRs and alter alternative splicing resulting in weakening of lateral root initiation [31]. A recent example is ELF18-INDUCED LONG-NONCODING RNA1 (ELENA1) lncRNA which is induced by disease caused by Pseudomonas syringae and is involved in imparting plant immunity [32]. They provided evidence by using a combination of overexpressed and mutant/knockdown lines of A. thaliana showing that ELENA1 and MED19a subunit (a mediator that liaise between transcription factors and RNA Pol II) function interdependently to induce expression of PATHOGENESIS RELATED (PR1 and PR2), β-1,3-glucanases and salicylic acid induced genes. ELENA1 acts not only in cis by affecting nearby locus but also in trans by influencing PR1 and other loci not close to the ELENA1 locus.

The final archetype ‘scaffold’ mechanism serves as a central platform upon which relevant molecular components are assembled. A putative example of a scaffold mechanism is COLD ASSISTED INTRONIC NONCODING RNA (COLDAIR) involved in vegetative to reproductive transition in A. thaliana. COLDAIR recruits the polycomb repressive complex 2 (PRC2), a group of proteins that can cause histone modification [33]. During vernalization, increased enrichment of PRC2 causes mitotically stable silencing of the floral repressor gene FLOWERING LOCUS C (FLC) through chromatin
Among the ncRNAs, miRNA is the most frequently studied ncRNA [43]. It acts in a sequence specific manner to interact with targets via base pairing to complementary sites. This interaction leads to the silencing of specific protein-coding mRNAs at the post-transcriptional level (Figure 1A). This is achieved through the induction of mRNA cleavage accompanied by protein translation. By this mechanism of action, miRNA plays a key regulatory role in diverse developmental processes, stress responses and metabolism [44,45].

In addition to classical protein coding mRNAs, several ncRNAs containing competing miRNA-binding sites are included as targets for miRNAs. It is assumed in existing literature that functional endogenous target mimics (eTMs) are mainly composed of lncRNAs [30,46]. Emergence of lncRNAs as eTMs of miRNAs was first supported by the discovery of IPS1 in A. thaliana [46]. The transcripts of IPS1 and PHO2 (Phosphate 2) mRNA are key genes involved in inorganic P (Pi) homeostasis, and possess a similar 23 nucleotide (nt) binding site which competes for pairing with miR399. In contrast to the miRNA-binding sites of PHO2, the IPS1 binding site forms a three-nucleotide bulge opposite the miR399 cleavage site on miRNA binding. This bulge prevents the cleavage of IPS1 and sequesters miR399; thus, the original PHO2 target is deregulated (Figure 1B). Known as target mimicry, this mechanism of inhibition of miRNA activity results in sequestered transcripts known as competing endogenous RNAs (ceRNAs) [47,48].

![Figure 1](image-url)  
**Figure 1.** A schematic representation of (a) regular miRNA silencing, and (b) target mimicry mechanism. miRNA: Micro RNA; mRNA: Messenger RNA; MRE: miRNA recognition elements.
In plants, these ceRNAs are known as target mimics (TMs) while in mammals the terms miRNA decoys or microRNA sponges are synonymously used for TMs [49] miRNA targets and TMs have highly similar target sites, known as miRNA recognition elements (MREs). The Franco-Zorrilla method of miRNA/TM interaction is based on MRE conservation and the position of the three-nucleotide bulge [46,47] but later work demonstrated that poor central complementarity is sufficient for the inhibition of miRNA [50,51].

Target mimicry has provided an alternative method for functional studies on miRNAs. As miRNAs have been shown to be regulated up to two-thirds of a eukaryotic transcriptome [52], the relevance of TMs has increased [42,47,53,54]. Target mimicry effects can also be induced by engineered artificial miRNA TMs [30,49]. Further, Short-Tandem Target Mimicry (STTM) technology has been used to engineer artificial target mimics (aTMs) [49]. An example of aTMs designed to establish the functionality of eTMs for miR160c (ath-eTM160-1) and miR166 (ath-eTM166-1) in A. thaliana was described by Wu et al. [30] with the resultant transgenic plants overexpressing eTMs displaying distinctly altered phenotypes such as dwarf plant size, serrated leaves and accelerated flowering time as compared to the wild type. These results suggest that eTMs plays a key role in regulating plant developmental processes.

There are various computational methods currently available to help predict TMs in plants. Specifically, TAPIR [55] provides target prediction of plant miRNAs including target mimics for eleven plant genomes. Available databases of plant TMs include the Plant Endogenous Target Mimics database (PeTMbase [56]), miRSponge [57] and the Plant Competing Endogenous RNA database (PceRBase [58]). The main features and links of these databases are listed in Table 1.

| Name          | Features                                                                 | Links                                                                 | Reference |
|---------------|-------------------------------------------------------------------------|----------------------------------------------------------------------|-----------|
| TAPIR         | Only tool for the TM prediction in plants; applies Franco-Zorrilla rule for target mimicry; contains data for 10 plant species; RNA hybrid and miRBase are the data sources | http://bioinformatics.psb.ugent.be/webtools/tapir/                    | [55]      |
| miR Sponge    | 1.6% data is from plant and others are of non-plant; experimentally validated; literature mining is the data source | http://www.bio-bigdata.net/miR Sponge/                              | [57]      |
| PeTMbase      | Contains 2728 TMs for 11 species; uses Wu et al. (2013) target mimicry rule; GreeNC, PNRD, miRBase, NCBI SRA are the data sources | http://petmbase.org                                                  | [56]      |
| PceRBase      | First database for plant TMs; 167608 TMs from 26 plant species; Phytozome v10, TAIR10, MSU RGGP & miRBase and literature are the data sources | http://bis.zju.edu.cn/pceRadb/                                       | [58]      |

TAPIR: Target prediction of plant miRNAs; miR Sponge: microRNA sponge; PeTMbase: Plant endogenous target mimics database; PceRBase: Plant competing endogenous RNA database.

3. Long non-coding RNAs Expressed under Nitrogen and Phosphorus Deprivation

Understanding plant response to changes in nutrient status or concentration has advanced significantly [36,37,59–66]. Developed computational approaches can provide integrated views of networks and enhanced understanding of how plants respond to an added nutrient [67]. Additional novel experimental and computational tools in nutrient homeostasis are required to improve nutrient use efficiency in crop plant [68]. To improve N use efficiency (NUE), multiple quantitative trait loci (QTLs) have been identified in the model species A. thaliana as well as in crops such as maize, rice, barley and wheat [69,70]. Differential gene expression studies in response to N have also attempted to identify major regulators of expression differences for NUE in wheat [71], sorghum [72], barley [73], maize [40] and rice [74].

By performing ultra-deep sequencing of total RNA, Lvet al. [40] identified intergenic/intronic IncRNAs expressed in maize leaves from plants grown under N deficient and N sufficient conditions.
This is the only report in a crop species showing the role of lncRNAs in regulation of the response to N nutrition. Among the 7245 putative lncRNAs identified, approximately 9% (637) were responsive to N, of which 67% (426) were down-regulated under sufficient N, whilst the remaining 211 were upregulated. For functional prediction of differentially expressed lncRNA, co-expression module analysis was performed and functional enrichment suggested their association with processes such as oxidation-reduction, generation of precursor metabolites and energy production [39]. Chen et al. [39] reported an adaptation mechanism to low N stress in the model woody species *Populus tomentosa*. They performed genome-wide identification of functional lncRNAs on *P. tomentosa* plantlets grown with low and sufficient N, and aligned to the genome of *Populus trichocarpa*. They reported 388 unique lncRNA candidates of which seven lncRNAs belonged to seven conserved ncRNA family whilst the majority (381) were novel with no homology in Rfam ncRNA family suggesting that these were specific to *P. tomentosa* species. In response to N deficiency, 126 lncRNAs were differentially expressed, of which 8 were repressed and 118 were induced. Antisense transcripts with interaction with sense genes were found to be involved in plant response to low N stress tolerance. This work is an illustration of the role of lncRNAs and the mechanism of action under N stress tolerance in woody plants. Further identification of antisense lncRNA and their associated regulatory mechanism would increase our understanding of inherent mechanisms to combat low N stress and to determine species specificity.

In plants, P has essential roles in structural (nucleic acids, phospholipids), metabolic (energy transfer) and regulatory functions (signal transduction) [75]. Phosphorus nutrition influences crop yield by imposing significant effects on above- (leaf area, dry matter accumulation, leaf P content, photosynthesis) and below-ground (root morphological traits, root exudation, symbiosis) processes [37,61,76]. In soils with low P availability, plants adapt by altering their root system architecture [65,77–81], organic acid exudation pattern [82–85], and can bypass certain metabolic processes [86–89]. Numerous studies have assessed miRNA directed P\textsubscript{i} homeostasis in plants identifying miR399, a post-transcriptional regulator, as a major component of P\textsubscript{i} starvation tolerance [59,60,90–92]. It serves as a long-distance signal for regulation of plant P\textsubscript{i} homeostasis [59,60]. Regulation of *PHO2* by miR399 and a ribo-regulator, *At4*, have been shown to be induced by *IPSI* in *A. thaliana* [93]. The members of *IPSI* family have been shown to be ribo-regulators rather than targets of miR399 [59]. The P\textsubscript{i} starvation responsive miR399 guides the cleavage of *PHO2* RNA, which encodes an E2-ubiquitin conjugase protein that negatively influences shoot P\textsubscript{i} content and P\textsubscript{i} remobilization through an unknown mechanism [94]. In *Medicago truncatula* grown under to P stress, three lncRNAs, PHOSPHATE DEFICIENCY INDUCED lncRNA (*PDILs*), were identified and functionally characterized [95]. Of the three, *PDIL1* functions in suppression of degradation of *MiPHO2* while the other two, *PDIL2* and *PDIL3*, are involved at the transcriptional level to regulate P\textsubscript{i} transport. In addition to *PHO2* mRNA, other ncRNAs containing a region of complementarity with miR399 including TOMATO PHOSPHATE STARVATION-INDUCED 1 (*TPSI1*) gene were identified in tomato (*Solanum esculentum*) [96]. *Mi4* in *M. truncatula* [97,98]. Di et al. [99] reported that many lncRNAs have the potential to regulate mRNA levels in *A. thaliana*. Their extensive study of miR399 targets revealed the mutual interaction of miRNA, lncRNA and mRNAs. For example, under P\textsubscript{i} and iron homeostasis, At5G01591.1 and *AtFer1* (ferritin) transcripts were induced in response to P\textsubscript{i} starvation, and their promoter contains Phosphate starvation response 1-Binding Sequence (*P1BS*) motif, indicating that both are also regulated by *PHR1* during P\textsubscript{i} starvation [100].

Another study in the diatom *Phaeodactylum tricornutum* identified 1510 putative long intergenic ncRNAs (lincRNA) which were responsive to P deficiency. Among these, the same set of 202 lncRNAs was upregulated and downregulated under P stress and P resupply to the growth medium [101]. Two lncRNAs, pti-MIR5472 and pti-MIR5471, were identified as precursors of annotated miRNAs. These lncRNAs were also significantly upregulated in response to P stress in *P. tricornutum* which implies that only these two lncRNAs were common between N and P deficiency stresses. This is also an indication of specificity of lncRNA expression towards a particular stress.
4. Putative Endogenous Target Mimics under Low Nitrogen and Phosphate Stress

We used plant miRBase (http://www.mirbase.org [102]) and retrieved sequences of differentially expressed miRNAs in response to N and P stress [103,104]. These miRNAs were then used to identify their putative target lncRNAs as eTM using PeTMbase (http://www.petmbase.org). PeTMbase is an online resource for endogenous miRNA target mimics for plants which searches the eTMs by corresponding miRNA name or plant species [56]. The identified lncRNAs which may act as eTMs involved in low N and P stress in model (A. thaliana) and crop species are summarized in Table 2 along with the corresponding miRNAs. While searching for eTMs, some classes of miRNAs (miR168a, miR171c, miR315b, c, f, miR778, miR2111) had no available data, although the other classes for the same miRNAs possessed corresponding eTMs. In this case, and based on the literature surveyed, it is proposed that these particular miRNAs could have another mechanism of action such as translational inhibition [105]. Moreover, lncRNAs have also been shown to have other mechanisms of epigenetic regulations such as chromatin remodeling [35,106], genomic imprinting [4] other than target mimicry. In Table 2, we observed that for a particular miRNA, there were one to seven eTM IDs because there were different regions of complementarity on an eTM sequence on the basis of corresponding lncRNAs.

To predict the regulatory network module of 'eTM-miRNA-mRNA', we selected two miRNAs from Table 2, with one representing stress response to N in soybean and another to P in Arabidopsis (Figure 2). Computational analysis shows that the miR169 (nitrogen regulated) and miR827 (phosphorus regulated) are predicted to be sponged by three and two eTMs, respectively. In soybean, out of 13 potential targets of gma-miR169g (Figure 2A), 11 are involved in encoding different subunits of transcription factor nuclear factor-YA (NF-YA) regulating various developmental processes (GO:0006355) as well as N uptake in plants. The target Glyma.19G172700.1 is involved in regulation of GTPase activity (GO:0043547) while Glyma.02G109500.4 is a hypothetical protein of unknown function. This regulation of miR169 by three eTMs (GRNC_gma_lcl|Gmax_Glyma.19G136600.8, GRNC_gma_lcl|Gmax_Glyma.19G136600.3 and GRNC_gma_lcl|Gmax_Glyma.19G136600.2) in soybean could help the plant indirectly regulate N limiting signalling. Previous work by Zhao et al. [107] has shown that miR169 is down regulated under N starvation and one of its targets, AtNFYA is induced both in roots and shoots under limiting N. Overexpression of ath-miR169a led to decreased AtNFYA expression leading to lower expression of AtNRT1.1 and AtNRT2.1 in both root and shoot and a hypersensitive response to N starvation in the ath miR169aoverexpressing plants compared to wildtype plants [107].

In Arabidopsis, 19 potential targets of ath-miR827 (Figure 2B) were identified, the most important being AT1G63010 involved in maintaining Pi homeostasis (GO:0005062). This gene belongs to the major facilitator superfamily (MFS) and encodes for SPX (SYG1/Pho81/XPR1) domain which is a negative regulator of Pi signalling. SPX proteins repress PHR1/PHR2, thereby regulating Pi starvation induced genes under P stress as reported in rice [108] and Arabidopsis [109]. The sequestration of miR827 by eTMs (PNRD_ath_NONATHT001723 and GRNC_ath_lcl|Athaliana_AT3G02832.1) thus could regulate P starvation signaling similar to that seen by ath-miR169 and N. In rice, it has been shown that osa-miR827 is expressed under Pi starvation and targets two genes, SPX-MSF1 and SPX-MFS2, which are under the control of OsPHR1 [110]. While direct evidence of the regulatory mechanism by miR827 SPX and PHR1/PHR2 has not been shown this would suggest that the targets of eTMs are transcription factors which regulate uptake transporters and not the transporters themselves.

Other interesting predicted targets of miR827 were AT4G23030 and AT1G61890 which belong to the multidrug and toxic compound extrusion (MATE) transporter family (GO:0005215). Reports have provided evidence that MATE located at the plasma membrane is involved in organic acid transport efflux under P starvation [89,111]. However, this example predicts a direct regulatory network of eTM-miR827-MATE without involvement of any transcription factor. Other targets of atm-miR827 identified were AT4G37590 which has a role in flower development (GO:0009908) while AT5G63760 and AT2G24050 are present in the cytoplasm (GO:0005737). AT1G31760 is involved in mitochondrial DNA repair (GO:0043504) while AT4G25770 is involved in chloroplast development (GO:0009507). Target
AT3G54030 encodes a protein kinase and functions in ATP binding (GO:0005524). Thus, the miRNAs differentially expressed under low N and P stress have several target genes, but may be sequestered by the lncRNAs (predicted to be eTMs) and regulate metabolic processes and developmental processes. However, functional validation of these lncRNAs for acting as potential eTMs needs to be functionally validated further in order to add to our current understanding of the role of lncRNAs in nutrient homeostasis in plants.

**Figure 2.** Computationally predicted ‘eTM-miRNA-mRNA’ regulatory network module drawn by selecting a few endogenous target mimics (eTMs) from Table 2 representing low nitrogen (miR169g) and phosphorus (miR827) stress in soybean and Arabidopsis. The central yellow circle is the miRNA while red shows potential targets of the miRNA, and blue circles depict lncRNAs that may act as eTMs. In this gene network, the green arrow shows an interaction between a putative eTM and miRNA while the grey line shows the potential for regulation between miRNAs and their target mRNAs.
Table 2. Long non-coding RNAs identified as putative eTM involved in nitrogen and phosphorus deprivation in various plant species [55]. The differentially expressed miRNA sequences specific to nitrogen and phosphorus were retrieved from ‘miRBase’ and employed to find the putative eTMs using ‘PeTMbase’. Arrows ↑— up regulated, ↓— down regulated.

| miRNA ID   | eTM ID       | lncRNA ID            | Low N          | Low P          | References |
|------------|--------------|----------------------|----------------|----------------|------------|
| ath-miR156a-5p | ath_eTM_miR156a-5p-2 | GRNC_ath_lcl| Athaliana_AT1G52347.1 gene = AT1G52347 | A. thaliana (P↑) | [112]       |
|            | ath_eTM_miR156a-5p-1 | PNRD_ath_NONATHT000580 |                |                |            |
| ath-miR156b-5p | ath_eTM_miR156b-5p-2 | GRNC_ath_lcl| Athaliana_AT1G52347.1 gene = AT1G52347 | A. thaliana (N↑) | [113]       |
|            | ath_eTM_miR156b-5p-1 | PNRD_ath_NONATHT000580 |                |                |            |
| ath-miR156c-5p | ath_eTM_miR156c-5p-2 | GRNC_ath_lcl| Athaliana_AT1G52347.1 gene = AT1G52347 | A. thaliana (N↑) | [113]       |
|            | ath_eTM_miR156c-5p-1 | PNRD_ath_NONATHT000580 |                |                |            |
| ath-miR156d-5p | ath_eTM_miR156d-5p-2 | GRNC_ath_lcl| Athaliana_AT1G52347.1 gene = AT1G52347 | A. thaliana (N↑) | [113]       |
|            | ath_eTM_miR156d-5p-1 | PNRD_ath_NONATHT000580 |                |                |            |
| ath-miR156e  | ath_eTM_miR156e-2  | GRNC_ath_lcl| Athaliana_AT1G52347.1 gene = AT1G52347 | A. thaliana (N↑) | [113]       |
|            | ath_eTM_miR156e-1 | PNRD_ath_NONATHT000580 |                |                |            |
| gma-miR156e | gma_eTM_miR156e-3 | GRNC_gma_lcl| Gmax_Glyma.18G293400.2 | Soybean (P↑) | [114]       |
|            | gma_eTM_miR156e-2 | GRNC_gma_lcl| Gmax_Glyma.18G293400.1 |                |            |
|            | gma_eTM_miR156e-1 | GRNC_gma_lcl| Gmax_Glyma.05G242200.2 |                |            |
| ath-miR156f-5p | ath_eTM_miR156f-5p-2 | GRNC_ath_lcl| Athaliana_AT1G52347.1 gene = AT1G52347 | A. thaliana (N↑) | [113]       |
|            | ath_eTM_miR156f-5p-1 | PNRD_ath_NONATHT000580 |                |                |            |
| ath-miR156g  | ath_eTM_miR156g-2  | GRNC_ath_lcl| Athaliana_AT1G52347.1 gene = AT1G52347 | A. thaliana (N↑) | [113]       |
|            | ath_eTM_miR156g-1 | PNRD_ath_NONATHT000580 |                |                |            |
| ath-miR156h  | ath_eTM_miR156h-3  | GRNC_ath_lcl| Athaliana_AT3G18217.1 gene = AT3G18217 | A. thaliana (N↑) | [113]       |
|            | ath_eTM_miR156h-2 | PNRD_ath_NONATHT000580 |                |                |            |
|            | ath_eTM_miR156h-1 | PNRD_ath_NONATHT000580 |                |                |            |
| gma-miR159a-3p | gma_eTM_miR159a-3p-1 | GRNC_gma_lcl| Gmax_Glyma.000088249 | Soybean (P↑) | [114]       |
|             | gma_eTM_miR159a-2 | GRNC_gma_lcl| Gmax_Glyma.000088249 |                |            |
|             | tae-eTM_miR159a-2 | GRNC_tae_lcl| Taestivum_Taes_2DS_9A9CAF080.1 |                |            |
|             | tae-eTM_miR159a-1 | GRNC_tae_lcl| Taestivum_Taes_1AL_8C8E4898.1 |                |            |
| zma-miR160a-3p | zma_eTM_miR160a-3p-1 | GRNC_zma_lcl| Zmays_AC211588.3_FGT002 | Maize (N↑) | [116]       |
|             | zma_eTM_miR160a-5p-1 | GRNC_zma_lcl| Zmays_GRMZM5G494973_T01 |                |            |
|             | zma_eTM_miR160a-5p-5 | GRNC_zma_lcl| Zmays_GRMZM5G494973_T01 |                |            |
|             | zma_eTM_miR160a-5p-3 | GRNC_zma_lcl| Zmays_GRMZM5G331719_T01 |                |            |
|             | zma_eTM_miR160a-5p-4 | GRNC_zma_lcl| Zmays_GRMZM5G149698.05 |                |            |
|             | zma_eTM_miR160a-5p-2 | GRNC_zma_lcl| Zmays_GRMZM5G211007.01 |                |            |
|             | zma_eTM_miR160a-5p-5 | GRNC_zma_lcl| Zmays_GRMZM5G494973_T01 |                |            |
|             | zma_eTM_miR160b-5p-4 | GRNC_zma_lcl| Zmays_GRMZM5G331719_T01 |                |            |
|             | zma_eTM_miR160b-5p-3 | GRNC_zma_lcl| Zmays_GRMZM5G149698.05 |                |            |
|             | zma_eTM_miR160b-5p-2 | GRNC_zma_lcl| Zmays_GRMZM5G211007.01 |                |            |
|             | zma_eTM_miR160b-5p-1 | PNRD_zma_GRMZM5G494973_T01 |                |                |            |
| miRNA ID      | eTM ID                  | IncRNA ID                  | Low N    | Low P    | References |
|--------------|-------------------------|----------------------------|----------|----------|------------|
| zma-miR160c-5p | zma_eTM_miR160c-5p-5    | GRNC_zma_lcl|Zmays_GRMZM5G849473_T01 | Maize (N↑) | [116]  |
|              | zma_eTM_miR160c-5p-4    | GRNC_zma_lcl|Zmays_GRMZM5G331719_T01  |          |          |
|              | zma_eTM_miR160c-5p-3    | GRNC_zma_lcl|Zmays_GRMZM5G140698_T05  |          |          |
|              | zma_eTM_miR160c-5p-2    | GRNC_zma_lcl|Zmays_GRMZM5G011007_T01  |          |          |
|              | zma_eTM_miR160c-5p-1    | PNRD_zma_GRMZM5G849473_T01 |          |          |
| zma-miR160d-3p | zma_eTM_miR160d-3p-3    | GRNC_zma_lcl|Zmays_GRMZM5G331719_T01  | Maize (N↑) | [113] |
|              | zma_eTM_miR160d-3p-2    | GRNC_zma_lcl|Zmays_GRMZM5G054392_T01  |          |          |
|              | zma_eTM_miR160d-3p-1    | GRNC_zma_lcl|Zmays_GRMZM5G052412_T01  |          |          |
| zma-miR160d-5p | zma_eTM_miR160d-5p-5    | GRNC_zma_lcl|Zmays_GRMZM5G849473_T01  | Maize (N↑) | [116] |
|              | zma_eTM_miR160d-5p-4    | GRNC_zma_lcl|Zmays_GRMZM5G331719_T01  |          |          |
|              | zma_eTM_miR160d-5p-3    | GRNC_zma_lcl|Zmays_GRMZM5G140698_T05  |          |          |
|              | zma_eTM_miR160d-5p-2    | GRNC_zma_lcl|Zmays_GRMZM5G011007_T01  |          |          |
|              | zma_eTM_miR160d-5p-1    | PNRD_zma_GRMZM5G849473_T01 |          |          |
| zma-miR160e | zma_eTM_miR160e-5       | GRNC_zma_lcl|Zmays_GRMZM5G849473_T01  | Maize (N↑) | [116] |
|              | zma_eTM_miR160e-4       | GRNC_zma_lcl|Zmays_GRMZM5G331719_T01  |          |          |
|              | zma_eTM_miR160e-3       | GRNC_zma_lcl|Zmays_GRMZM5G140698_T05  |          |          |
|              | zma_eTM_miR160e-2       | GRNC_zma_lcl|Zmays_GRMZM5G011007_T01  |          |          |
|              | zma_eTM_miR160e-1       | PNRD_zma_GRMZM5G849473_T01 |          |          |
| zma-miR160g-5p | zma_eTM_miR160g-5p-5    | GRNC_zma_lcl|Zmays_GRMZM5G849473_T01  | Maize (N↑) | [116] |
|              | zma_eTM_miR160g-5p-4    | GRNC_zma_lcl|Zmays_GRMZM5G331719_T01  |          |          |
|              | zma_eTM_miR160g-5p-3    | GRNC_zma_lcl|Zmays_GRMZM5G140698_T05  |          |          |
|              | zma_eTM_miR160g-5p-2    | GRNC_zma_lcl|Zmays_GRMZM5G011007_T01  |          |          |
|              | zma_eTM_miR160g-5p-1    | PNRD_zma_GRMZM5G849473_T01 |          |          |
| zma-miR164f-5p | zma_eTM_miR164f-5p-1    | GRNC_zma_lcl|Zmays_GRMZM5G837428_T01  | Maize (N↑) | [116] |
|              | zma_eTM_miR164f-3p      | GRNC_zma_lcl|Zmays_GRMZM5G140698_T05  |          |          |
| zma-miR166j-3p | zma_eTM_miR166j-3p-4    | GRNC_zma_lcl|Zmays_GRMZM5G134604_T01  | Maize (N↑) | [117] |
|              | zma_eTM_miR166j-3p-3    | GRNC_zma_lcl|Zmays_GRMZM5G134604_T01  | Maize (N↑) | [117] |
|              | zma_eTM_miR166j-3p-2    | GRNC_zma_lcl|Zmays_GRMZM5G134604_T01  | Maize (N↑) | [117] |
|              | zma_eTM_miR166j-3p-1    | zma_TCONS_00089106         |          |          |
| zma-miR166k-3p | zma_eTM_miR166k-3p-4    | GRNC_zma_lcl|Zmays_GRMZM5G134604_T01  | Maize (N↑) | [117] |
|              | zma_eTM_miR166k-3p-3    | GRNC_zma_lcl|Zmays_GRMZM5G110279_T02  |          |          |
|              | zma_eTM_miR166k-3p-2    | GRNC_zma_lcl|Zmays_GRMZM5G110279_T01  |          |          |
|              | zma_eTM_miR166k-3p-1    | zma_TCONS_00089106         |          |          |
| zma-miR166n-3p | zma_eTM_miR166n-3p-4    | GRNC_zma_lcl|Zmays_GRMZM5G134604_T01  | Maize (N↑) | [117] |
|              | zma_eTM_miR166n-3p-3    | GRNC_zma_lcl|Zmays_GRMZM5G110279_T02  |          |          |
|              | zma_eTM_miR166n-3p-2    | GRNC_zma_lcl|Zmays_GRMZM5G110279_T01  |          |          |
|              | zma_eTM_miR166n-3p-1    | zma_TCONS_00089106         |          |          |
| zma-miR167g-3p | zma_eTM_miR167g-3p-1    | zma_TCONS_00089106         |          |          |
|              | zma_eTM_miR167g-3p-2    | PNRD_zma_GRMZM5G174168_T02 | Maize (N↑) | [116] |
|              | zma_eTM_miR167g-3p-1    | PNRD_zma_GRMZM5G174168_T02 | Maize (N↑) | [116] |
| zma-miR167h-3p | zma_eTM_miR167h-3p-3    | GRNC_zma_lcl|Zmays_GRMZM5G158764_T04  | Maize (N↑) | [116] |
|              | zma_eTM_miR167h-3p-2    | GRNC_zma_lcl|Zmays_GRMZM5G158764_T04  | Maize (N↑) | [116] |
|              | zma_eTM_miR167h-3p-1    | PNRD_zma_GRMZM5G175272_T03 |          |          |
|              | zma_eTM_miR167h-3p-2    | GRNC_zma_lcl|Zmays_GRMZM5G159741_T04  | Maize (N↑) | [116] |
|              | zma_eTM_miR167h-3p-3    | GRNC_zma_lcl|Zmays_GRMZM5G158764_T04  | Maize (N↑) | [116] |
|              | zma_eTM_miR167h-3p-2    | GRNC_zma_lcl|Zmays_GRMZM5G158764_T04  | Maize (N↑) | [116] |
|              | zma_eTM_miR167h-3p-1    | PNRD_zma_GRMZM5G175272_T03 |          |          |
| miRNA ID    | eTM ID                     | lncRNA ID                     | Low N    | Low P    | References       |
|------------|----------------------------|-------------------------------|----------|----------|------------------|
| zma-miR167h-5p | zma_eTM_miR167h-5p-2    | GRNC_zma_lcl|Zmys_GRMZM2G174168_T02 | Maize (N↓) | [116] |
|           | zma_eTM_miR167h-5p-1    | GRNC_zma_lcl|Zmys_GRMZM2G174168_T01 |          |        |                  |
| gma-miR169f | gma_eTM_miR169f-3       | GRNC_gma_lcl|Gmax_Glyma.19G136600.8 | Soybean (N↑) | [118] |
|           | gma_eTM_miR169f-2       | GRNC_gma_lcl|Gmax_Glyma.19G136600.3 |          |        |                  |
|           | gma_eTM_miR169f-1       | GRNC_gma_lcl|Gmax_Glyma.19G136600.2 | Soybean (N↑) | [118] |
| gma-miR169q | gma_eTM_miR169q-3       | GRNC_gma_lcl|Gmax_Glyma.19G136600.8 |          |        |                  |
|           | gma_eTM_miR169q-2       | GRNC_gma_lcl|Gmax_Glyma.19G136600.3 |          |        |                  |
|           | gma_eTM_miR169q-1       | GRNC_gma_lcl|Gmax_Glyma.19G136600.2 |          |        |                  |
| ath-miR169a-3p | ath_eTM_miR169a-3p-2   | GRNC_ath_lcl|Athaliana_AT1G44940.2 | A. thaliana (P↓) | [113] |
|           | ath_eTM_miR169a-3p-1    | GRNC_ath_lcl|Athaliana_AT1G44940.1 |          |        |                  |
| zma-miR319a-5p | zma_eTM_miR319a-5p-4  | GRNC_zma_lcl|Zmys_GRMZM2G138722_T03 | Maize (N↑) | [116] |
|           | zma_eTM_miR319a-5p-3    | zma_TCONS_00089764 |          |          |                  |
|           | zma_eTM_miR319a-5p-2    | zma_TCONS_00089763 |          |          |                  |
|           | zma_eTM_miR319a-5p-1    | zma_TCONS_00024738 |          |          |                  |
| zma-miR395d-5p | zma_eTM_miR395d-5p-1  | zma_TCONS_00091080 | Maize (N↓) |          | [116] |
|           | zma_eTM_miR395d-5p-1    | zma_TCONS_00091080 |          |          |                  |
| osa-miR444a-3p.2 | osa_eTM_miR444a-3p.2-1 | GRNC_osa_lcl|Osativa_LOC_Os12g19080.1 | Rice (N↑) | [119] |
| ath-miR827   | ath_eTM_miR827-2        | GRNC_ath_lcl|Athaliana_AT5G03545.1 | A. thaliana (N↑↓) | [113] |
|           | ath_eTM_miR827-1        | PNRD_ath_NONATHT001723 |          |          |                  |
| ath-miR828   | ath_eTM_miR828-1        | PNRD_ath_NONATH001723 |          |          |                  |
5. Conclusions and Future Prospects

Understanding the role of lncRNA in plants is still in its infancy in comparison to progress made in the animal kingdom. Future research is required to systematically identify additional lncRNAs and their role in communicating abiotic and biotic signals in plants. Due to the low expression level of lncRNAs and dependency on specific signals, future work should also focus on the identification of cell type specific lncRNAs [3]. This may be achieved by in-depth transcriptome analysis of single cell or tissue type for lncRNA identification [120]. There is also an opportunity to create a database devoted to stress-responsive lncRNAs. Understanding of the interaction of lncRNAs with other molecular elements in the cell is also an interesting area which needs to be further developed. Although in silico studies have been conducted in plant lncRNA research, functional characterization is still a challenging task, but developments such as advanced imaging for large-scale screening of mutant libraries (e.g., as developed in rice [121]) should accelerate future progress in functional studies of lncRNAs in plants.

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