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The Role of Thiamine in Plants and Current Perspectives in Crop Improvement

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<http://dx.doi.org/10.5772/intechopen.79350>

Abstract

Current research is focusing on selecting potential genes that can alleviate stress and produce disease-tolerant crop variety. The novel paradigm is to investigate the potential of thiamine as a crop protection molecule in plants. Thiamine or vitamin B₁ is important for primary metabolism for all living organisms. The active form, thiamine pyrophosphate (TPP), is a cofactor for the enzymes involved in the synthesis of amino acids, tricarboxylic acid cycle and pentose phosphate pathway. Recently, thiamine is shown to have a role in the processes underlying protection of plants against biotic and abiotic stresses. The aim of this chapter is to review the role of thiamine in plant growth and disease protection and also to highlight that TPP and its intermediates are involved in management of stress. The perspectives on its potential for manipulating the biosynthesis pathway in crop improvement will also be discussed.

Keywords: thiamine, vitamin B₁, plant protection, stress, crops

1. Introduction

Thiamine also known as vitamin B₁ was the first vitamin type B identified [1]. Free thiamine, thiamine monophosphate (TMP) and thiamine pyrophosphate (TPP) are the three most predominant forms of B₁ that exist in the cells [2]. Vitamin B₁ is a colourless, water-soluble vitamin made solely by plants and microorganisms and act as essential micronutrient in the human diet [3].

Thiamine occurrence in plants is widely distributed across organs, namely, leaves, flowers, fruits, seeds, roots, tubers and bulb [4]. Studies in *Arabidopsis* plant showed that the most abundant vitamer is TPP followed by TMP and thiamine, respectively [5]. The concentration

of thiamine vitamer can be increased by supplementation of hydroxyethyl-thiazole (HET) and hydroxy-methylpyrimidine (HMP) [3]. The highest concentration of vitamin B in plants can be secured up to μ g/g relatively [6]. Diverse B₁ sources include yeast, cereal grains, beans, nut and meat [7].

2. Role of thiamine

In plants, thiamine is known to have its role as a cofactor for important metabolic activities [8]. Thiamine is known to be an essential regulator that plays an important role in plant's primary regulatory system [9]. Living organisms require the active form of thiamine which is known as thiamine pyrophosphate (TPP) in order to play the role as an important cofactor. TPP is a crucial component required in many metabolic activities such as acetyl-CoA biosynthesis, amino acid biosynthesis, Krebs cycle and Calvin cycle [10].

3. Role of thiamine in plant protection

In plants, thiamine plays a role as a response molecule towards abiotic and biotic stresses, and data from the literature suggest that boosting thiamine content could increase resistance to stresses [11]. Biotic stress is usually involve in the damage of plants caused by living organisms, while abiotic stress is due to environmental factors which cause a series of morphological, physiological, biochemical and molecular changes to plants that will affect the plants' growth, development and productivity [12].

Previous study that the effect of the infection of *Ganoderma boninense*, a pathogenic fungus, to the expression of *ThiC* gene in oil palm suggests that thiamine may play an important role in dealing with biotic stress [13]. Comprehensive studies on the effect of abiotic stresses on the regulation of thiamine in oil palm were also done where various types of stresses, namely, oxidative, salinity and osmotic stresses, have been induced in oil palm where an increase in gene expression and also total thiamine content was observed post-stress inductions [14–17]. A study by Kamarudin et al. explored the application of an endophytic fungus, *Hendersonia toruloidea*, in elevating the expression of thiamine biosynthesis genes in oil palm post-fungal application and also in the accumulation of thiamine and its intermediates in the plant [18, 19]. It was clear that a fungal endophyte could also boost thiamine content in oil palm. Current work is providing data on thiamine accumulation in oil palm seedlings upon application of beneficial endophytic bacteria, namely, *Pseudomonas aeruginosa* and *Burkholderia cepacia*.

Besides that, a study on the impact of *ThiC* promoter as well as its riboswitch on thiamine regulation in *Arabidopsis* sp. showed that the transcript of *ThiC* gene is highest at the end of the light period and lowest at the end of dark period [20]. Other than that, the responses of thiamine biosynthesis genes under several types of abiotic stresses such as salt and osmotic stress in *Arabidopsis* were examined, and it was found that these conditions have caused the

upregulation of the expression of the genes, thus eventually causing significant changes in thiamine level [5].

A study by Croft et al. revealed the declination of *ThiC* gene expression upon exogenous application of thiamine, which suggests a feedback regulation system in thiamine biosynthesis of green alga, *Chlamydomonas reinhardtii* [21]. On the other hand, Mcrose et al. proved that the relative gene expression of prasinophyte algae, *Emiliania huxleyi*, was significantly increased when thiamine supply was exhausted [22]. It has been demonstrated in *Cassava* sp. plant that the application of exogenous thiamine led in the formation of splicing variants of *ThiC* gene suggesting the presence of TPP riboswitch [23].

Thiamine possesses an antioxidant capacity as it has O_2^-/OH^- scavenger properties [24]. Vitamin B₁ is responsible for the recycling of vitamin C through the synthesis of nicotinamide adenine dinucleotide phosphate (NADPH) [4]. The antioxidant properties of thiamine were seen in a study on *Arabidopsis* sp. where paraquat-treated plant caused reduction in protein carbonyls and dichlorofluorescein diacetate (indicator of oxidative stress) when thiamine was applied [25]. Thiamine pyrophosphate indirectly acts as antioxidant by supplying NADH and NADPH to tackle oxidative stress [25]. However, out of all the studies conducted, scientists still find difficulties to unravel the cellular mechanism of B₁ as an antioxidant either through indirect effect of cofactor or as direct effect as antioxidant [4].

Recently, it has been reported that thiamine formed an indirect role in enhancing anti-oxidative capacity in plants, which is important in defence responses [26]. In addition, systemic acquired resistance (SAR) in *Oryza sativa*, *Arabidopsis thaliana*, *Nicotiana* sp. and *Cucumis sativus* was shown to be induced when thiamine was applied to these plants [27].

4. Thiamine biosynthesis is regulated by TPP riboswitch

In the past years, we recognise DNA as the main key on every single reaction that occurs in the cellular environment. The paradigm has been shifted to RNA nowadays. Since RNA sequences can carry out diverse tasks and are amenable to engineering both *in vitro* and *in vivo*, they are particularly attractive for controlling cell behaviour [28].

5. Thiamine pyrophosphate: the dominant class of riboswitch

Riboswitch is a natural RNA sensor that allows the direct binding of small metabolites, thus regulating the expression of various metabolic genes without the needs of protein cofactor [29, 30]. Without the protein involvement, regulation of gene expression can still occur due to the direct metabolite binding at riboswitch sequence [31]. RNA can specifically recognise and bind other molecules, including low molecular weight metabolites [32]. This includes nucleobases, cofactors, amino acids, second messenger and metal ion [33]. The metabolites are usually small, non-toxic molecule which exhibits a good cell permeability [34].

To date, there are about 15 riboswitch classes reported as shown in **Table 1**, and more of it is still unknown [35]. Among all classes of riboswitches, TPP riboswitches are the most ubiquitous in three life domains [36]. Thiamine pyrophosphate (TPP) is the most abundant riboswitch and is known to be present even in eukaryotes [37]. It has an intermediate level of sequence conservation [38]. So in many organisms (prokaryotes, algae, plants and fungi), riboswitch has been found to play the role of regulating thiamine biosynthesis [39].

In all plant taxa, the TPP riboswitch is present in the *ThiC* gene, and some of the TPP riboswitches that are lost during the gymnosperm evolution are present in the *Thi1* gene of ancient plants [40]. Studies by Cheah and co-worker testified that *Thi4* and N-myristoyltransferase (*NMT*) genes in *Neurospora crassa* are controlled by TPP riboswitch by splicing mechanism of an intron located in the 5' untranslated region (UTR) [39].

From the perspective of evolution, the presence of TPP riboswitch in ancient plant taxa suggests that this mechanism is active 400 million years ago, in early emergence of vascular plants [40]. The ancient plant taxa including ancient land plants consist of supplementary TPP riboswitch which ought to be found in the *Thi1* gene and no longer found, suggesting that during gymnosperm evolution, this sequence might be lost from this family gene [40]. Apart from that, the alternative splicing of 3' UTR gene also found in lycophytes, which are an ancient vascular plant family that existed around 150–200 million years before angiosperm (i.e. *Arabidopsis* and rice) [40]. **Table 2** shows the list of the discovered TPP riboswitches in various organisms.

Generally, riboswitches in bacteria can be found on the upstream 5' region of the non-coding region of mRNA, while in plant and fungi, this regulatory element resides at the 3' end of the untranslated region of a gene [20, 40, 41]. Although the location of TPP riboswitch in prokaryotes and eukaryotes might differ, its structure reveals a high similarity. This difference in location suggests a unique mode of action for the plant riboswitch [40].

Type	Riboswitches class	Gene	Reference
Amino acid derivatives	Purine	<i>ydhL</i>	[48]
	Lysine	<i>Asd</i>	[41]
	Glycine		[49]
Carbohydrates	Glucosamine-6-phosphate	<i>glmS</i>	[50]
Enzyme cofactor	Flavin mononucleotide	<i>ThiC</i>	[29]
	Thiamine pyrophosphate	<i>BtuB</i>	[51]
	Cobalamin (B ₁₂)	<i>S-box</i>	[52]
	Tetrahydrofolate (THF)		[53]
	S-adenosyl methionine		
	S-adenosyl homocysteine		
Nucleotide precursor	Adenine, guanine	<i>pbuE</i>	[54]
	c-di-GMP	<i>tfoX</i>	[55]
	pre-queuosine (preQ1)	<i>ykv</i>	[56]

Table 1. Riboswitch classes reported across all kingdom of life.

Gene	Location	Organism	Reference
<i>ThiC</i>	3' UTR	<i>Arabidopsis thaliana</i>	[41]
	5' UTR	<i>Chlamydomonas reinhardtii</i>	[21]
	3' UTR	<i>Oryza sativa</i>	[49]
		<i>Poa secunda</i>	[49]
		<i>Solanum lycopersicon</i>	[26]
		<i>Thalassiosira pseudonana</i>	[37]
		<i>Phaeodactylum tricornutum</i>	[37]
		<i>Alishewanella</i> sp.	[36]
<i>Thi4</i>	5' UTR	Flowering plant	[58]
		<i>Neurospora crassa</i>	[39]
		<i>Volvox carteri</i>	[21]
		<i>Fusarium oxysporum</i>	[41]
<i>ThiA</i>		<i>Aspergillus oryzae</i>	[52]
<i>ThiM</i>	5' UTR	<i>Escherichia coli</i>	[49]
<i>Thi-box</i>		<i>Bacillus subtilis</i>	[29]
		<i>Rhizobium</i> sp.	[60]
<i>Thi1</i>	3' UTR	Ancient plant (bryophytes, lycophytes)	[40]
<i>ThiR</i>	5' UTR	<i>Haloferax volcanii</i>	[61]

Table 2. The list of RNA regulatory element involved in thiamine biosynthesis pathway, TPP riboswitch, in various organisms.

The biosynthesis of thiamine is uncommon from other vitamins. This is because previous study by Guan et al. revealed that the energy cost of thiamine synthesis is higher as compared to other vitamin cofactors [42]. Therefore, the location of riboswitch at the initial pathway strongly suggests that a novel riboswitch regulates the regulation of thiamine.

6. Thiamine biofortification in plants

As previously mentioned, thiamine has shown to act as cofactor and activator for plant stress and disease resistance. Furthermore, supplementation and accumulation of thiamine in plants showed no evidence of toxicity towards the plants as supported by the feeding studies [3]. However, a review by Goyer in 2010 suggested that thiamine production will be regulated in order to perfectly match the production to the demand of the cofactor. The study also stated that thiamine biosynthesis is regulated via (1) riboswitch-dependent gene regulation and (2) tissue specificity, stress dependence and post-translational regulation. Tissue-specific transcription factors have been found in *THI1* gene, and the regulation has been widely studied [43] at the promoter level. The promoter activity in the roots is not due to light regulation but rather to promoter tissue specificity. On the other hand, stress dependence can be seen in maize seedlings where under osmotic and oxidative stresses, TPK enzyme activity increased [44] but exhibited a decrease under normal condition [45]. Furthermore, post-translational regulation or feedback inhibition has been identified in *TH1* where excess of HMP-PP and ATP has shown to inhibit *TH1* activity.

Gene transcript/ enzymes/thiamine derivatives	Stress	Outcomes	References
THIC	Oxidative, osmotic, temperature (cold), biotic (colonisation by endophyte)	Increase in expression	[15, 18, 25, 62, 63]
	Exogenous thiamine	Decrease in expression	[64]
THI4	Light, oxidative, biotic (colonisation by endophyte)	Increase in expression	[18, 25, 65, 66]
	Dark	Decrease in expression	
TH1	Oxidative, biotic (colonisation by endophyte)	Increase in expression	[18, 25, 45]
TPK	Osmotic, salinity, oxidative, biotic (colonisation by endophyte)	Enzyme activity increase	[18, 44, 45]
Total thiamine	Osmotic, salinity, oxidative, biotic (colonisation by endophyte)	Increase in concentration	[18, 25, 45]
	Exogenous thiamine	Decrease in expression	[64]

Table 3. Effects of stress towards thiamine biosynthesis in plants.

Total thiamine content in wild-type plants is mainly composed of thiamine, thiamine mono-phosphate (ThMP) and thiamine diphosphate (ThDP) [27]. Overexpression of THIC and THI4 simultaneously has shown to increased thiamine levels up to sixfold and ThDP levels twofold compared to single overexpression of either THIC or THI4 which showed no elevation of total thiamine content [11]. This shows the relationship between thiamine biosynthesis genes and thiamine production. Elevation of thiamine content and also the thiamine biosynthesis gene transcripts in plants have been demonstrated quite extensively via the application of biotic and abiotic stresses. Utilisation of these stresses may aid in the fortification of thiamine in crops. **Table 3** shows the studies done in understanding the effects of the application of stress towards thiamine production in plants.

Apart from that, higher possibilities of thiamine fortification in plants could be achieved via genetic manipulation. Genetic engineering via mutation of riboswitch coding sequence in plant model organism, *Arabidopsis*, has produce an organism with deficiency in TPP riboswitch activity and enhanced accumulation of total thiamine esters [20]. However, due to increasing TPP concentrations, this condition has led to an increase of metabolic flux into the TCA cycle and pentose phosphate pathway which causes a significant increase in the organism respiratory rate, hence more CO₂ production [20]. Genetic manipulation in *Arabidopsis* and rice by overexpression of THIC and THI4 has shown to increase thiamine levels up to sixfold and ThDP levels twofold in *Arabidopsis* and increased total thiamine level up by fivefold in *Oryza sativa* [11, 46]. Furthermore, genetic manipulation of TPK via promoter enhancement in *Arabidopsis* has led to an increased expression of TPK up to 30-fold and transketolase enzyme activity by 2.5-fold [47]. The mutant plant also resulted in chlorotic and slow-growth characteristics. However, levels of total thiamine of mutant plants were significantly lower compared to control.

7. Conclusion

Overall, based on the extensive studies done, thiamine fortification in plants could be achieved via both abiotic and biotic stress and genetic engineering [20, 24, 25, 45]. Manipulation by the knowledge available on the riboswitch associated with THIC could likely be an effective strategy to manipulate thiamine levels in plants, especially in terms of biofortification. However, it is well agreed that the process on enhancing thiamine levels in plants is not as straightforward and as easy as it seems. Further understanding of the two key precursors (HMP and HET) will be required as this will lead to the accumulation of thiamine, with hopefully least side effects. These two intermediates have been shown to be not toxic to plants, and plant tolerance towards stress is expected to increase when the levels of these two intermediates are enhanced. However, the modification of this will still come with its own challenges since it involves highly complex enzymes which are regulated very tightly and there have not been much studies on the understanding of the mechanisms just yet.

Acknowledgements

Z.N. Balia Yusof gratefully acknowledges the support of the Ministry of Science, Technology and Innovation of Malaysia (MOSTI) (ScienceFund Project No. 02-01-04-SF2234) as well as funding by the Ministry of Higher Education of Malaysia (MOHE) (FRGS Vote No. 5524589) and also Geran Putra Universiti Putra Malaysia (UPM) (GP-IPM Vote No. 9425900) for the funding of the work described.

Conflict of interest

The authors declare that there is no conflict of interest.

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References

- [1] Funk C. The etiology of the deficiency. *Analytica Chimica Acta*. 1975;76:176-177

- [2] Bettendorff L, Wirtzfeld B, Makarchikov AF, Mazzucchelli G, Frédérick M, Gigliobianco T. Discovery of a natural thiamine adenine nucleotide. *Nature Chemical Biology*. 2007;3:211-212
- [3] Pourcel L, Moulin M, Fitzpatrick TB. Examining strategies to facilitate vitamin B1 biofortification of plants by genetic engineering. *Frontiers in Plant Science*. 2013;4:160
- [4] Asensi-Fabado MA, Munné-Bosch S. Vitamins in plants: Occurrence, biosynthesis and antioxidant function. *Trends in Plant Science*. 2010;15(10):582-592
- [5] Rapala-Kozik M, Wolak N, Kujda M, Banas AK. The upregulation of thiamine (vitamin B1) biosynthesis in *Arabidopsis thaliana* seedlings under salt and osmotic stress conditions is mediated by abscisic acid at the early stages of this stress response. *BMC Plant Biology*. 2012;12:2
- [6] Rodionov DA, Vitreschak AG, Mironov AA, Gelfand MS. Comparative genomics of thiamin biosynthesis in prokaryotes. *The Journal of Biological Chemistry*. 2002;277:48949-48959
- [7] Vidal-Valverde C, Frias J, Sierra I, Blazquez I, Lambein F, Kou YH. New functional legume foods by germination: Effect on the nutritive value of beans, lentils and peas. *European Food Research and Technology*. 2002;215(6):472-477
- [8] Colinas M, Fitzpatrick TB. Nature's balancing act: Examining biosynthesis de novo, recycling and processing damaged vitamin B metabolites. *Current Opinion in Plant Biology*. 2015;25:98-106
- [9] Bocobza SE, Aharoni A. Small molecules that interact with RNA: Riboswitch-based gene control and its involvement in metabolic regulation in plants and algae. *Plant Journal*. 2014;79:693-703
- [10] Du Q, Wang H, Xie J. Thiamin (vitamin B1) biosynthesis and regulation: A rich source of antimicrobial drug targets? *International Journal of Biological Sciences*. 2011;7(1):41-52
- [11] Dong W, Thomas N, Ronald PC, Goyer A. Overexpression of thiamin biosynthesis genes in rice increases leaf and unpolished grain thiamin content but not resistance to *Xanthomonas oryzae* pv. *Oryzae*. *Frontiers in Plant Science*. 2016;7:616
- [12] Boubakri H, Wahab MA, Chong J, Bertsch C, Mliki A, Soustre-Gacougnolle I. Thiamine induced resistance to *Plasmopara viticola* in grapevine and elicited host-defense responses, including HR like-cell death. *Plant Physiology and Biochemistry*. 2012;57:120-133
- [13] Balia Yusof ZN, Borhan FP, Mohamad FA, Rusli MH. The effect of *Ganoderma boninense* infection on the expressions of thiamine (vitamin B1) biosynthesis genes in oil palm. *Journal of Oil Palm Research*. 2015;27:12-18
- [14] Wong SY, Syamimi DAA, Balia, Yusof ZN. Osmotic stress upregulates the transcription of thiamine (vitamin B1) biosynthesis genes (THIC and THI4) in oil palm (*Elaeis guineensis*). *African Journal of Biotechnology*. 2016;15:1566-1574

- [15] Abidin AAZ, Yee WS, Rahman NSA, Idris ZHC, Balia Yusof ZN. Osmotic, oxidative and salinity stresses upregulate the expressions of thiamine (vitamin B1) biosynthesis genes (THIC and THI1/THI4) in oil palm (*Elaeis guineensis*). *Journal of Oil Palm Research*. 2016; **28**:308-319
- [16] Hushiarian R, Yusof NA, Dutse SW. Detection and control of *Ganoderma boninense*: Strategies and perspectives. *Springerplus*. 2013;**2**:555
- [17] Idris AS, Ahmad Kushari D, Nur Rashyeda R, Madihah AZ, Haida N, Sebran. Compositions for controlling *Ganoderma* disease in plants and method thereof by using endophytic fungus. In: *Hendersonia* Gano EF1. 2013
- [18] Kamarudin AN, Balia Yusof ZN, Kok Song L, Lamasudin DU. Enhancement of thiamine biosynthesis in oil palm seedlings by colonization of endophytic fungus *Hendersonia toruloidea*. *Frontiers in Plant Science*. 2017;**8**:1799
- [19] Kamarudin AN, Seman IA, Balia Yusof ZN. Thiamine biosynthesis gene expression analysis in *Elaeis guineensis* during interactions with *Hendersonia toruloidea*. *Journal of Oil Palm Research*. 2017;**29**:218-226
- [20] Bocobza SE, Malitsky S, Araújo WL, Nunes-Nesi A, Meir S, Shapira M, Fernie AR, Aharoni A. Orchestration of thiamin biosynthesis and central metabolism by combined action of the thiamin pyrophosphate riboswitch and the circadian clock in *Arabidopsis*. *The Plant Cell*. 2013;**25**(1):288-307
- [21] Croft MT, Moulin M, Webb ME, Smith AG. Thiamine biosynthesis in algae is regulated by riboswitches. *Proceedings of the National Academy of Sciences of the United States of America*. 2007;**104**:20770-20775
- [22] McRose D, Guo J, Monier A, Sudek S, Wilken S, Yan S, Worden AZ. Alternatives to vitamin B1 uptake revealed with discovery of riboswitches in multiple marine eukaryotic lineages. *The ISME Journal*. 2014;**8**(10):2517-2529
- [23] Mangel N, Fudge JB, Fitzpatrick TB, Gruissem W, Vanderschuren H. Vitamin B1 diversity and characterization of biosynthesis genes in cassava. *Journal of Experimental Botany*. 2017;**42**:322-327
- [24] Ahn IP, Kim S, Lee YH, Suh SC. Vitamin B1-induced priming is dependent on hydrogen peroxide and the NPR1 gene in *Arabidopsis*. *Plant Physiology*. 2007;**143**:838-848
- [25] Tunc-ozdemir M, Miller G, Song L, Kim J, Sodek A, Koussevitzky S, Misra AN, Mittler R, Shintani D. Thiamin confers enhanced tolerance to oxidative stress in *Arabidopsis*. *Plant Physiology*. 2009;**151**:421-432
- [26] Zhao W, Cheng X, Huang Z, Fan H, Wu H, Ling HQ. Tomato LeTHIC is an Fe-requiring HMP-P synthase involved in thiamine synthesis and regulated by multiple factors. *Plant and Cell Physiology*. 2011;**52**(6):967-982

- [27] Goyer A. Thiamine in plants: Aspects of its metabolism and functions. *Phytochemistry*. 2010;**71**:1615-1624
- [28] Peselis A, Serganov A. Themes and variations in riboswitch structure and function. *Biochimica et Biophysica Acta*. 2014;**1839**(10):908-918
- [29] Mironov AS, Gusarov I, Rafikov R, Lopez LE, Shatalin K, Kreneva RA, Perumov DA, Nudler E. Sensing small molecules by nascent RNA: A mechanism to control transcription in bacteria. *Cell*. 2002;**111**:747-756
- [30] Walker JM. Riboswitch methods and protocols. *Life Sciences*. 2009;**531**:588
- [31] Serganov A, Polonskaia A, Phan AT, Breaker RR, Patel DJ. Structural basis for gene regulation by a thiamine pyrophosphate-sensing riboswitch. *Nature*. 2006;**441**:1167-1171
- [32] Sudarsan N, Cohen-Chalamish S, Nakamura S, Emilsson GM, Breaker RR. Thiamine pyrophosphate riboswitches are targets for the antimicrobial compound pyrithiamine. *Chemistry and Biology*. 2005;**12**:1325-1335
- [33] Breaker RR. Prospects for riboswitch discovery and analysis. *Molecular Cell*. 2011;**43**:867-879
- [34] Bauer G, Suess B. Engineered riboswitches as novel tools in molecular biology. *Journal of Biotechnology*. 2006;**124**:4-11
- [35] Palou-Mir J, Musiari A, Sigel RKO, Barceló-Oliver M. Characterization of the full-length btuB Riboswitch from *Klebsiella pneumoniae*. *Journal of Inorganic Biochemistry*. 2016;**160**: 106-113
- [36] Aghdam EM, Sinn M, Tarhriz V, Barzegar A, Hartig JS, Hejazi MS. TPP Riboswitch characterization in *Alishewanella tabrizica* and *Alishewanella aestuarii* and comparison with other TPP riboswitches. *Microbiological Research*. 2016
- [37] Bocobza SE, Aharoni A. Switching the light on plant riboswitches. *Trends in Plant Science*. 2008;**13**:526-533
- [38] Singh P, Bandyopadhyay P, Bhattacharya S, Krishnamachari A, Sengupta S. Riboswitch detection using profile hidden Markov models. *BMC Bioinformatics*. 2009;**10**:325
- [39] Cheah MT, Wachter A, Sudarsan N, Breaker RR. Control of alternative RNA splicing and gene expression by eukaryotic riboswitches. *Nature*. 2007;**447**:497-500
- [40] Bocobza S, Adato A, Mandel T, Shapira M, Nudler E, Aharoni A. Riboswitch-dependent gene regulation and its evolution in the plant kingdom. *Genes & Development*. 2007;**21**: 2874-2879
- [41] Sudarsan N, Wickiser J, Nakamura S, Ebert MS, Breaker RR. An mRNA structure in bacteria that controls gene expression by binding lysine. *Genes and Development*. 2003;**17**:2688-2697
- [42] Guan JC, Hasnain G, Garrett TJ, Chase CD, Gregory J, Hanson AD, McCarty DR. Divisions of labor in the thiamin biosynthetic pathway among organs of maize. *Frontiers in Plant Science*. 2014;**5**:370

- [43] Belanger F, Leustek T, Chu B, Kirz A. Evidence for the thiamine biosynthetic pathway in higher plant plastids and its developmental regulation. *Plant Molecular Biology*. 1995;**29**: 809-821
- [44] Rapala-Kozik M, Golda A, Kujda M. Enzymes that control the thiamine diphosphate pool in plant tissues. Properties of thiamine pyrophosphokinase and thiamine-(di)phosphate phosphatase purified from *Zea mays* seedlings. *Plant Physiology and Biochemistry*. 2009; **47**:237-242
- [45] Rapala-Kozik M, Kowalska E, Ostrowska K. Modulation of thiamine metabolism in *Zea mays* seedlings under conditions of abiotic stress. *Journal of Experimental Botany*. 2008; **59**(15):4133-4143
- [46] Dong W, Stockwell VO, Goyer A. Enhancement of thiamin content in *Arabidopsis thaliana* by metabolic engineering. *Plant & Cell Physiology*. 2015;**56**:2285-2296
- [47] Khozaei M, Fisk S, Lawson T, Gibon Y, Sulpice R, Stitt M, Lefebvre SC, Raines CA. Overexpression of plastid transketolase in tobacco results in a thiamine auxotrophic phenotype. *The Plant Cell*. 2015;**27**(2):432-447
- [48] Mondal T, Kanduri C. Maintenance of epigenetic information: A noncoding RNA perspective. *Chromosome Research*. 2013;**21**:615-625
- [49] Winkler W, Nahvi A, Breaker RR. Thiamine derivatives bind messenger RNAs directly to regulate bacterial gene expression. *Nature*. 2002;**419**:952-956
- [50] Jansen JA, McCarthy TJ, Soukup GA, Soukup JK. Backbone and Nucleobase contacts to glucosamine-6-phosphate in the glm S ribozyme. *Nature Structural & Molecular Biology*. 2006;**13**(6):517-523
- [51] Nahvi A, Barrick JE, Breaker RR. Coenzyme B12 riboswitches are widespread genetic control elements in prokaryotes. *Nucleic Acids Research*. 2004;**32**:143-150
- [52] Trausch JJ, Ceres P, Reyes FE, Batey RT. The structure of a tetrahydrofolate-sensing riboswitch in vitro *Bacillus subtilis* reveals two ligand binding sites in a single aptamer. *Structure*. 2011;**19**:1413-1423
- [53] Batey RT. Riboswitches: Still a lot of undiscovered country. *RNA (New York, N.Y.)*. 2015; **21**(4):560-563
- [54] Lemay JF, Desnoyers G, Blouin S, Heppell B, Bastet L, St-Pierre P, Massé E, Lafontaine DA. Comparative study between transcriptionally- and translationally-acting adenine riboswitches reveals key differences in riboswitch regulatory mechanisms. *PLoS Genetics*. 2011;**7**:e1001278
- [55] Weinberg Z, Ruzzo WL. Sequence-based heuristics for faster annotation of non-coding RNA families. *Bioinformatics*. 2006;**22**:35-39
- [56] Mayer JE, Pfeiffer WH, Beyer P. Biofortified crops to alleviate micronutrient malnutrition. *Current Opinion in Plant Biology*. 2008;**11**:166-170

- [57] Wachter A, Tunc-Ozdemir M, Grove BC, Green PJ, Shintani DK, Breaker RR. Riboswitch control of gene expression in plants by splicing and alternative 3' end processing of mRNAs. *The Plant Cell*. 2007;**19**:3437-3450
- [58] Yadav S, Swati D, Chandrasekharan H. Thiamine pyrophosphate riboswitch in some representative plant species. *Journal of Computational Biology*. 2014;**21**:1-9
- [59] Kubodera T, Watanabe M, Yoshiuchi K, Yamashita N, Nishimura A, Nakai S, Gomi K, Hanamoto H. Thiamine-regulated gene expression of *Aspergillus oryzae* THIA requires splicing of the intron containing a riboswitch-like domain in 5'UTR. *Federation of European Biochemical Societies*. 2003;**555**(3):516-520
- [60] Miranda-Rios J, Navarro M, Sobero'n MA. A conserved RNA structure (thi box) is involved in regulation of thiamin biosynthetic gene expression in bacteria. *Proceedings of the National Academy of Sciences of the United States of America*. 2001;**98**:9736-9741
- [61] Hwang S, Cordova B, Abdo M, Pfeiffer F, Maupin-Furlow JA. ThiN as a versatile domain of transcriptional repressor and catalytic enzymes of thiamine biosynthesis. *Journal of Bacteriology*. 2017;**199**(7):810-816
- [62] Rizhsky L, Liang H, Shuman J, Shulaev V, Davletova S, Mittler R. When defense pathways collide. The response of *Arabidopsis* to a combination of drought and heat stress. *Plant Physiology*. 2004;**134**:1683-1696
- [63] Wong CE, Li Y, Labbe A, Guevara D, Nuin P, Whitty B, Diaz C, Golding GB, Gray GR, Weretilnyk EA, Griffith M, Moffatt BA. Transcriptional profiling implicates novel interactions between abiotic stress and hormonal responses in *Thellungiella*, a close relative of *Arabidopsis*. *Plant Physiology*. 2006;**140**:1437-1450
- [64] Subki A, Thaw SFK, Yusof ZNB. Exogenous thiamine application affects the regulation of thiamine biosynthesis in oil palm (*Elaeis guineensis*). *Journal of Oil Palm Research*. 2018
- [65] Ribeiro A, Praekelt U, Akkermans AD, Meacock PA, van Kammen A, Bisseling T, Pawlowski K. Identification of agthi1, whose product is involved in biosynthesis of the thiamine precursor thiazole, in actinorhizal nodules of *Alnus glutinosa*. *The Plant Journal*. 1996;**10**:361-368
- [66] Ribeiro DT, Farias LP, de Almeida JD, Kashiwabara PM, Ribeiro AF, Silva-Filho MC, Menck CF, Van Sluys MA. Functional characterization of the thi1 promoter region from *Arabidopsis thaliana*. *Journal of Experimental Botany*. 2005;**56**:1797-1804