

MINI-REVIEW

Hormone signaling pathways under stress combinations

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ABSTRACT

As sessile organisms, plants are continuously exposed to various environmental stresses. In contrast to the controlled conditions employed in many researches, more than one or more abiotic and/or biotic stresses simultaneously occur and highly impact growth of plants and crops in the field environments. Therefore, an urgent need to generate crops with enhanced tolerance to stress combinations exists. Researchers, however, focused on the mechanisms underlying acclimation of plants to combined stresses only in recent studies. Plant hormones might be a key regulator of the tailored responses of plants to different stress combinations. Co-ordination between different hormone signaling, or hormone signaling and other pathways such as ROS regulatory mechanisms could be flexible, being altered by timing and types of stresses, and could be different depending on plant species under the stress combinations. In this review, update on recent studies focusing on complex-mode of hormone signaling under stress combinations will be provided.

Abbreviations: ABA, abscisic acid; APX1, ascorbate peroxidase 1; AUX, auxin; BR, brassinosteroid; ET, ethylene; GSH, glutathione; JA, jasmonic acid; JAZ, Jasmonate-zim-domain protein; MBF1c, multiprotein bridging factor 1c; NCED, 9-cis epoxy-carotenoid dioxygenase; NO, nitric oxide; ROS, reactive oxygen species; SA, salicylic acid

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As sessile organisms, plants are continuously exposed to various environmental stresses. The major abiotic stresses that impact growth of plants and crops in the field have been extensively studied.¹⁻⁴ However, the field environment in nature is very different from the controlled conditions employed in many laboratory researches, and often involves the simultaneous exposure of plants to more than one abiotic and/or biotic stresses.⁵ In addition, current climate prediction models indicate that high temperature will be accompanied by other weather disasters and more detrimental effects on crop production can be expected in future.^{4,6-9} Therefore, an urgent need to generate crops with enhanced tolerance to stress combinations exists. Researchers, however, focused on the molecular and physiological mechanisms underlying acclimation of plants to stress combinations only in recent studies.^{5,10}

Recent transcriptome and proteome analyses suggested that unique signaling pathways might be tailored in plants in response to different stress combinations.¹¹⁻¹³ Unique acclimatory responses of plants to stress combinations cannot be directly deduced from that to each of the different stress applied individually.^{5,10} Plant hormones could be a key player in the regulation of such tailored responses of plants to stress combinations, because hormone signaling can be flexibly modulated depending on the types of environmental stresses.¹⁴⁻¹⁶ In addition, different types of stresses that oppositely affect the hormone synthesis and signaling can simultaneously occur in nature. Thus, precise regulation of hormone synthesis and signaling should be required for the acclimation of plants to various combinations of stresses. In this review, the complex mode of hormone signaling pathways under

different combinations of more than one abiotic and/or biotic stresses will be addressed.

Abscisic acid (ABA) has long been known to play integral role in response of plants to abiotic stresses.¹⁷ For example, ABA functions as a key regulator of stomatal closure to prevent excess water loss through transpiration under water deficiency and salt stress.¹⁸ In addition, ABA also activates signaling pathways involving LATE EMBRYOGENESIS-ABUNDANT class genes and other regulatory genes required for acclimation of plants to abiotic stresses.¹⁹ Recent studies suggested that ABA might be involved in tailored response of plants to the drought and heat stress combination as well as drought or heat stress applied individually. For example, accumulation of 9-cis epoxy-carotenoid dioxygenase (NCED) protein that is required for ABA synthesis was shown to be gradually up-regulated in poplar in response to drought or heat stress alone.²⁰ Under the drought and heat stress combination, in contrast, NCED protein accumulation initially increased, then declined. These results indicate the different regulatory functions of ABA under these single and combined stresses. Moreover, a recent study demonstrated that Arabidopsis mutants deficient in ABA synthesis (*aba1-1*) or response (*abi1-1*) were impaired in their acclimation to the drought and heat stress combination.¹⁵ Sensitivity of these mutants to this stress combination might not be due to deficiency in the regulatory mechanisms of stomatal closure. Although stomata of *abi1-1* mutant significantly more opened compared to WT plants under drought, its stomatal aperture was reduced to the similar level with WT plants when subjected to the drought and heat stress combination. These

results suggest that other signaling pathways, rather than ABA signaling, could play important role in the regulation of stomatal movement under the drought and heat stress combination. Indeed, accumulation of ROS and jasmonic acid (JA) that might be also involved in stomatal closure²¹ was higher in *abi1-1* mutant compared to WT under this stress combination. Furthermore, transcriptional responses to drought, heat and their combination were compared between 2 different wheat cultivars that are tolerant or sensitive to the stress combination.²² In the sensitive cultivar, expression of transcripts encoding phospholipase D and phosphatidylinositol kinase, key regulators of ABA-dependent stomatal closure,^{23,24} were up-regulated by all stresses with the highest level under the stress combination. In the tolerant cultivar, in contrast, the highest expression of these transcripts was detected under heat stress, not under the stress combination. Although ABA-dependent stomatal closure does not seem to be significant in tailored response of plants to the drought and heat stress combination, ABA was implicated in the regulation of ROS scavenging systems as well as heat response pathways under this stress combination. *abi1-1* mutant demonstrated lower accumulation of ascorbate peroxidase 1 (APX1) protein,²⁵ a cytosolic ROS scavenging enzyme, as well as multiprotein bridging factor 1c (MBF1c) protein,²⁶ a master regulator of heat response, compared to WT plants under the drought and heat stress combination.¹⁵ These proteins were shown to be required for the acclimation of plants to combinations of water deficit and heat stress.^{27,28}

Recent studies indicated complex mode of co-ordination between different hormone signaling in response of Arabidopsis and other crops to drought, heat and their combination. In citrus, ABA highly accumulated in response to drought applied individually.¹⁶ The drought and heat stress combination also induced increase in ABA accumulation, but much lower extent compared to drought alone. In contrast to ABA, higher level of salicylic acid (SA) that might be involved in the signaling pathway antagonizing ABA²⁹ accumulated under the stress combination compared to drought or heat stress applied individually. This pattern of ABA and SA accumulation under these single and combined stresses in citrus was different from that in Arabidopsis which showed the highest or lowest level of ABA or SA accumulation, respectively under the drought and heat stress combination.¹⁶ JA whose signaling pathway could be antagonized by SA³⁰ was also highly accumulated in Arabidopsis under the drought and heat combination as well as heat stress alone. In addition, expression of transcript homologous to Arabidopsis Rap2.6L was significantly up-regulated in wheat in response to drought or heat stress applied individually, but not to the drought and heat stress combination.³¹ Overexpression of Rap2.6L in Arabidopsis was shown to enhance tolerance to abiotic stresses via activating hormone signaling pathways involving ABA, JA, SA and ethylene.^{32,33} These results suggest that, to some extent, regulatory mechanisms of hormone signaling pathways underlying tailored responses of plants to drought, heat and their combination might be different depending on plant species.

Integration of hormone signaling pathways with ROS regulatory systems was also implicated in acclimation of plants to the drought and heat stress combination. Overexpression of cytokinin oxidase, the cytokinin degrading enzyme, resulted in

enhanced tolerance of transgenic tobacco plants to the drought and heat stress combination accompanied by the altered expression patterns of transcripts involved in ROS scavenging.³⁴ In contrast to ABA which is implicated in activation of ROS scavenging mechanism in Arabidopsis,¹⁵ down-regulation of cytokinin signaling in tobacco might be associated with regulation of antioxidant mechanisms under the combined stress. To further elucidate co-ordination between hormone signaling pathways and ROS regulatory systems, accumulation of ROS and hormones should be measured in mutants deficient in synthesis or signaling of different hormones.

Response of plants to combinations of drought and other abiotic stresses has been also addressed in recent studies. Although the drought and heat stress combination negatively affects plant growth, the drought and UV-B combination might have beneficial effects on plants compared with each of the individual stress applied individually.³⁵ Tossi et al., (2014) suggested that in Arabidopsis UV-B irradiation increased ABA synthesis as well as NO and ROS production which might lead to stomatal closure.³⁶ In contrast to the tailored response of plants to the drought and heat stress combination, ABA-dependent stomatal closure might be essential for acclimation of plants to the drought and UV-B combination.³⁵ In addition, requirement of ethylene signaling in ABA synthesis was evidenced by the finding that Arabidopsis *etr1-1* mutant, deficient in ethylene perception was impaired in ABA synthesis in response to UV-B irradiation.³⁷ Furthermore, drought can induce synthesis of flavonoids that possess antioxidant and UV-B screening functions, as well as ABA that activates proline synthesis and antioxidant systems.³⁸ Both flavonoid synthesis and ABA signaling pathway were shown to be regulated by a transcription factor MYB12 in Arabidopsis.³⁸ It should be important to reveal how ABA signaling pathway and flavonoid synthesis were integrated during the drought and UV-B stress combination in future studies. Response of plants to the osmotic and cold stress combination has been also analyzed using a glutathione (GSH) deficient mutant, *pad2.1* in Arabidopsis that showed higher sensitivity to this stress combination. Transcripts responsive to hormones such as auxin, ethylene, brassinosteroid and ABA were differentially expressed in *pad2.1* mutant compared to WT plants under the osmotic and cold stress combination.³⁹ Transcripts involved in ethylene synthesis were down-regulated in *pad2.1* mutants. The alteration of these transcripts might be due to the increase in ROS by GSH deficiency, or indicating the possibility that GSH might regulate genes and protein expression by thiol mediated modification of various regulatory proteins. In contrast to the ethylene responsive transcripts, transcription factors that are involved in regulation of brassinosteroid and auxin signaling were up-regulated. These findings indicate that hormone signaling pathways might be uniquely tailored depending on the types of stresses that simultaneously occur with drought (Fig. 1).

In addition to drought, salt stress can be also combined with other abiotic stresses and highly impacts plant growth. Involvement of hormone signaling pathway in acclimation of plants to the salt and heat stress combination has been indicated in a recent study. Transcriptome analysis of Arabidopsis plants subjected to salt, heat and their combination demonstrated that expression of 699 transcripts were specifically enhanced in

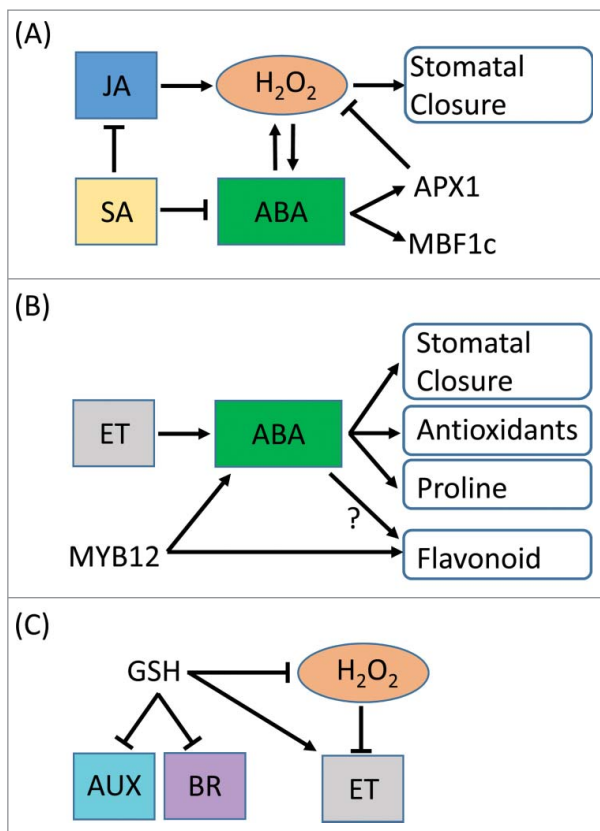


Figure 1. Simplified model of hormone signaling pathways under different abiotic stress combinations in *Arabidopsis*. The models suggest the tailored response of *Arabidopsis* to (A) drought and heat combination, (B) drought and UV-B combination, and (C) osmotic and cold combination. The models were generated based on the researches using *Arabidopsis* subjected to different stress combinations.^{15,36-39} A model of the signaling pathway under the drought and UV-B combination was also suggested in a recent review³⁵ based on the researches using different plant species. ABA; abscisic acid, AUX; auxin, BR; brassinosteroid, ET; ethylene, JA; jasmonic acid, SA; salicylic acid.

response to the salt and heat stress combination.¹⁴ Interestingly, transcripts associated with ABA signaling pathway were highly represented in these 699 transcripts. In contrast, SA- and gibberellic acid (GA)-associated transcripts that could antagonize ABA signaling pathway^{29,40} were least represented. Involvement of ABA in the acclimation of plants to the salt and heat stress combination was also supported by the finding that mutants deficient in ABA synthesis (*aba1-1*) or response (*abi1-1*) were significantly more sensitive to this stress combination compared to WT plants. ABA was implicated in tailored responses of *Arabidopsis* both to the drought and salt stress combined with heat stress. However, ABA-dependent pathways that are involved in plant's acclimation to these stress combinations could be different, because little overlap was found between the different sets of transcripts specifically up-regulated in response to the salt and heat stress combination and the drought and heat stress combination.¹⁴ Differences and similarities in ABA-dependent tailored responses of *Arabidopsis* to these stress combinations, however, still need to be investigated in future studies.

In nature, abiotic and biotic stresses can simultaneously occur and defense pathways with a high degree of complexity might be activated in plants. Complex mode of plant responses to the biotic and abiotic stress combinations has also been

addressed. A recent study demonstrated that expression of different sets of SA- and JA-associated genes were up-regulated in rice in response to biotic stress combined with drought or salt stress.⁴¹ Although both drought and salt stress are able to activate SA- and JA-dependent defense mechanisms, different signaling pathways might be up-regulated by these abiotic stresses. This hypothesis could be supported by the finding that drought and salt stress are able to enhance tolerance of plants to different types of pathogens.⁴² In some cases, ABA was also shown to be accumulated in response to pathogen infection.⁴² Higher level of ABA induced by Pst DC 3000 infection suppressed defense pathways against other pathogens.⁴³ However, recent findings demonstrated a positive effect of ABA on biotic stress resistance.^{44,45} ABA and ROS induced by drought results in stomatal closure that might inhibit penetration of pathogen as second effects, and activation of defense pathways.¹⁰ This dual effect makes ABA a controversial molecule that can regulate both positive and negative effects on pathogen responses depending on the environmental conditions.⁴⁵ Effects of ABA on defense pathways under biotic and abiotic stress combinations could be at least partially modulated via its temporal coordination with other hormone signaling pathways. Response of plants to biotic and abiotic stress combinations might be consist of 3 phases.⁴⁶ In the first phase, ABA induces stomatal closure and maintains water potential. During this phase, synthesis of SA, JA and ethylene can be antagonized. In the second phase, callose accumulation increases via the function of ABA. In the third phase, pathogen-associated molecular patterns stimulate SA, JA and ethylene signaling to activate defense pathways. In addition, hormone signaling pathways might be fine-tuned depending on the order of stress applications. In *Arabidopsis*, transcripts involved in SA and JA signaling were up-regulated in response to drought and pathogen combination, when drought application was followed by pathogen infection.⁴⁷ Under this condition, expression of ABA response transcripts was only marginally altered. In contrast, several defense genes including JA related, JASMONATE-ZIM-DOMAIN PROTEIN 10 (JAZ10) were repressed when pathogen infection was followed by drought. These results suggest that hormone-dependent defense mechanisms under the biotic and abiotic stress combinations could be flexible, being altered by timing of stress applications.

Taken together, fine-tuned co-ordination of hormone signaling pathways might be essential in the regulation of tailored responses of plants to different stress combinations (Fig. 1), and these responses to stress combinations cannot be deduced from those under corresponding individual stresses. Although ABA might be involved in responses of plants to a broad range of stress combinations, its integration with other hormones or other signaling pathways such as ROS regulatory systems seems to be different depending on types of stress combinations (Fig. 1). These findings indicate that ABA could function as a key regulators of tailored responses of plants to various stress combinations. In addition, hormone-dependent signaling pathways under the stress combinations could be flexible being altered by intensity, timing and types of stress applications, and could be different depending on plant species. Master regulators that switch on/off the different hormone signaling pathways should be revealed in future studies.

Disclosure of potential conflicts of interest

The author has declared that no competing interests exist.

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