Mol. Cells *34*, 109-116, August 31, 2012
DOI/10.1007/s10059-012-0121-3
pISSN: 1016-8478 eISSN: 0219-1032

Molecules and Cells
http://molcells.org

Minireview

Molecular Communications between Plant Heat Shock Responses and Disease Resistance

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As sessile, plants are continuously exposed to potential dangers including various abiotic stresses and pathogen attack. Although most studies focus on plant responses under an ideal condition to a specific stimulus, plants in nature must cope with a variety of stimuli at the same time. This indicates that it is critical for plants to fine-control distinct signaling pathways temporally and spatially for simultaneous and effective responses to various stresses. Global warming is currently a big issue threatening the future of humans. Reponses to high temperature affect many physiological processes in plants including growth and disease resistance, resulting in decrease of crop yield. Although plant heat stress and defense responses share important mediators such as calcium ions and heat shock proteins, it is thought that high temperature generally suppresses plant immunity. We therefore specifically discuss on interactions between plant heat and defense responses in this review hopefully for an integrated understanding of these responses in plants.

INTRODUCTION

Since plants cannot escape from potential biotic and abiotic stresses, they are thought to have developed complicated stress-tolerance and defense mechanisms to minimize damages from such stresses. To detect harmful microorganisms, plants use two distinct patrolling systems. Plants can detect a pathogen using a surface receptor that recognizes a pathogen species-conserved molecule called pathogen-associated molecular pattern (PAMP). FLS2, EFR and CERK1 are such receptors called pattern-recognition receptors (PRRs) that specifically interact with bacterial flagellin, elongation factor Tu and fungal chitin, respectively (Miya et al., 2007; Zipfel et al., 2004; 2006). Specific interactions between PRRs and cognate PAMPs trigger the intracellular signal relay mostly *via* the mitogen-activated protein kinase (MAPK) cascade for transcriptional reprogramming by regulating transcription factors such as TGAs and WRKYs (Kwon, 2010). This process is called the PAMP-triggered immunity (PTI). To interfere with the plant defense responses, pathogens secrete and inject molecules called effectors into plants. The second strategy for plants to sense a pathogen attack is achieved by intracellular receptors called Resistance (R) proteins that recognize the pathogen-injected effectors. The direct or indirect interaction between R proteins and effectors often results in host cell death called hypersensitive response (HR) likely to restrict the pathogen spread. This plant defense response is called the effector-triggered immunity (ETI) (Dodds and Rathjen, 2010; Jones and Dangl, 2006).

Plants are highly sensitive to temperature and can distinguish slight differences of as little as 1°C. As a minor temperature elevation results in defects in the crop cycle (Mittler and Blumwald, 2010), high temperature is one of the most threatening environmental stresses for plants (Baniwal et al., 2004). Heat stress adversely affects multiple aspects in plant cells such as loss of membrane integrity, the destabilization of RNA and proteins, alteration of cytoskeleton structure, generation of reactive oxygen species and cellular metabolic imbalance via defective enzymes (Alfonso et al., 2001; Kampinga et al., 1995; Larkindale and Knight, 2002; Sangwan et al., 2002), often leading to promotion of programmed cell death (Swidzinski et al., 2002; Vacca et al., 2004). Due to the greenhouse effect, the average surface temperature on Earth is now increasing and living organisms are exposed to higher temperatures. A slight increase of temperature can affect many aspects of the metabolism as well as plant defense responses (Mittler and Blumwald, 2010; Mittler et al., 2012). Since higher temperature is thought to be in general antagonistic to plant defense responses, we believe that the combined understanding of heat/pathogen stress responses would be critically important to open a possibility to increase crop productivity in current temperature-rising situations.

CALCIUM ION IN PLANT HEAT AND PATHOGEN STRESS RESPONSES

Perception of heat stress is highly complicated in plants: that is, several pathways in different cellular compartments. The perception of high temperature at the plasma membrane (PM) results in elevated Ca^{2+} levels in plant cells in two ways. First, the perception of heat stress seems to trigger the alteration of membrane fluidity. This alteration leads to activation of phos-

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Received April 22, 2012; revised May 17, 2012; accepted May 18, 2012; published online June 18, 2012

Keywords: calcium, calmodulin, defense responses, heat stress responses, R protein

Springer

pholipase D (PLD) and a phosphatidylinositolphosphate kinase (PIPK), and the accumulation of phosphatidic acid (PA) and phosphatidylinositol 4,5-bisphosphate (PIP_2) (Mishkind et al., 2009). Then, the increased PIP_2 may be responsible for the increase of cytosolic Ca^{2+} concentration. Second, it is thought the stress affects the opening of Ca^{2+} channels, directly or via the alteration of membrane fluidity, which causes the increase of Ca^{2+} influx. To date, the identity of the PM heat stress sensor in plants is poorly understood. However, a study in moss suggests that a slight temperature increase can be sensed by heat-induced Ca^{2+} influx (Saidi et al., 2009). Studies about the cation channels involved in heat stress in animal cells additionally suggest that putative Ca^{2+} channels at the PM reported in plants may be good candidates for primary PM heat sensors (Mittler et al., 2012; Sokabe et al., 2008; Xiao et al., 2011).

Although a responsible Ca^{2+} channel remains yet to be elucidated, Ca^{2+} plays also an important role in the regulation of plant defense responses. PAMPs (flagellin and peptidoglycan derived from bacteria; elicitin, Pep-13 and cryptogein from oomycetes; chitin from fungi) as well as pathogens have been reported to drive Ca^{2+} influx, although the detailed Ca^{2+} signatures differ (Blume et al., 2000; Gust et al., 2007; Lecourieux et al., 2002; 2005; Ma et al., 2009; Zimmermann et al., 1997). Since this PAMP-triggered elevation of intracellular Ca^{2+} levels is mediated by receptors, the PAMP-PRR interactions somehow activate inward Ca^{2+} channels. Early defense responses such as MAPK phosphorylations and defense gene expression by cryptogein are compromised by blocking Ca^{2+} influx from the extracellular medium (Lecourieux et al., 2002). This suggests that the receptor-mediated increase in intracellular Ca^{2+} levels is a significant part of defense signaling in plants.

In plants, the stress-increased intracellular Ca^{2+} levels can be sensed by calmodulins (CaMs), calmodulin-like proteins (CMLs), calcineurin B-like proteins (CBLs) and calcium-dependent protein kinases (CDPKs) (Harper and Harmon, 2005; Luan et al., 2002; McCormack et al., 2005; Reddy et al., 2011). Little is known about the decoding of elevated Ca^{2+} levels by heat stress. However, the altered resistance to heat stress and the accompanied changed expression patterns of heat shock genes by deletion or overexpression of CaM3 in Arabidopsis suggest the involvement of a common CaM in interpreting the induced Ca^{2+} influx (Zhang et al., 2009). The PP7 protein phosphatase that interacts with both CaM and a heat shock transcription factor (Hsf) is likely to mediate the signal relay from Ca^{2+}/CaM to gene expression, because its mutation impairs plant thermotolerance but overexpression results in enhanced heat resistance together with changed expression levels of heat shock proteins (Liu et al., 2007).

CaMs are also important for the Ca^{2+}-mediated signaling in defense responses (Reddy et al., 2011). The direct role of CaMs in plant defense responses has been shown by heterologous expression of soybean CaMs whose expression is induced by a fungal elicitor. Overexpression of divergent but not common CaMs soybean CaM-4 and -5 in tobacco and Arabidopsis resulted in enhanced resistance to various pathogens including bacteria, oomycetes and viruses (Heo et al., 1999; Park et al., 2004). Since NbCaM1 that is differently categorized from soybean CaM-4/5 is involved only in the resistance to tobacco mosaic virus (TMV) but not to fungal and bacterial pathogens (Yamakawa et al., 2001; Zhu et al., 2010a), this suggests that specific defense responses to distinct pathogen classes might be at least in part controlled by different CaMs. CaM was also found to be important for regulating the extracellular immune responses in plants. MLO, the seven transmembrane motif (TM)-containing negative regulator of plant disease resistance to fungal pathogens, negatively regulates two currently known secretory pathways in plant defense responses (Buschges et al., 1997; Consonni et al., 2006; Humphry et al., 2010). Interestingly, MLO was found to interact with a conventional CaM, which leads to the full activity of MLO (Kim et al., 2002). Since CaM-binding mutant versions of MLO fail to fully suppress plant resistance, it is thought that some adapted fungal pathogens manipulate MLO in part by triggering the increase of intracellular Ca^{2+} levels. A similar negative activity of CaM was recently reported in relation to salicylic acid (SA), a defense hormone against biotrophic pathogens. A CaM-binding transcription factor AtSR1 suppresses plant immune responses by repressing the expression of *Enhanced Disease Susceptibility 1* (*EDS1*) (Du et al., 2009). Since its transcription repressing activity of *EDS1* requires CaM binding, increased intracellular Ca^{2+} levels is thought to balance plant defense responses via AtSR1.

In addition to CaMs, plant-specific CDPKs were found to play an important role in plant defense responses. Production of reactive oxygen species (ROS) is one of early plant defense responses. In potato, an NADPH oxidase, StRBOHB, is phosphorylated by StCDPK4 and StCDPK5, which leads to oxidative burst (Kobayashi et al., 2007). In Arabidopsis, CDPK4, 5, 6 and 11 were shown to mediate a part of flagellin-triggered defense responses. Gene expression analyses have revealed that the recognition of flagellin by FLS2 modulates the expression patterns of defense genes distinctly or synergistically through MAPK and CDPK pathways (Boudsocq et al., 2010). The reduced and delayed HR triggered by cognate effector-R protein interactions in NtCDPK2-silenced tobacco indicates the involvement of some CDPKs in ETI (Romeis et al., 2001). Interestingly, Arabidopsis CDPKs mentioned above belong to a different subgroup from the tobacco NtCDPK2. This suggests that depending on the type of plant defense responses (PTI or ETI) distinct CDPKs might be engaged.

HEAT SHOCK PROTEINS IN PLANT HEAT AND PATHOGEN STRESS RESPONSES

Heat shock proteins (Hsps) were originally identified as proteins which are strongly increased by heat treatment. Based on protein sizes, several Hsps such as Hsp101, Hsp70, Hsp90, Hsp60 (chaperonine), Hsp40 and sHsp (small Hsp) proteins have been reported. Since orthologs in other organisms have thermal adaptive functions (Hartl and Hayer-Hartl, 2002), plant Hsps are proposed to act as molecular chaperones in protein quality control, and therefore to weaken adverse effects from heat stress (Queitsch et al., 2000; Su and Li, 2008; Yamada et al., 2007). Although it is expected that their functions are not only limited by chaperone activity, it is still difficult to precisely answer the question on how they contribute to survival of heat stress in plants, because they are also essential for normal plant growth.

Hsp101 is the most widely studied protein for the role in heat response in plants. Disaggregating chaperone Hsp101 is the AAA+ family of ATPases and plays an essential role in thermotolerance in Arabidopsis (Queitsch et al., 2000). They play an important role in resolubilizing protein aggregates via interaction with the sHsp chaperone system (Bosl et al., 2006; Lee et al., 2005). Among the various types of Arabidopsis Hsp101 proteins, a cytosolic form is crucial for heat-tolerance, but not for normal growth (Hong and Vierling, 2001). Even though the regulatory mechanisms of Hsp70 under stress conditions are poorly understood in plants, results from the ectopic expression

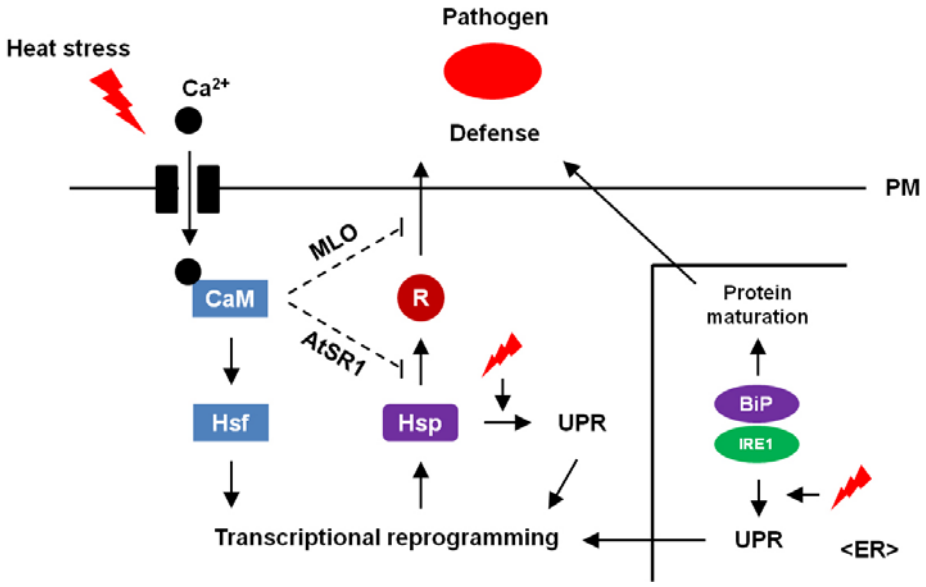

Fig. 1. Possible interactions between heat stress and defense responses in plant. The increased intracellular Ca^{2+} levels triggered by heat stress activate calmodulin (CaM), which is then thought to drive transcriptional reprogramming via the heat shock transcription factor (Hsf). Heat stress is thought to shift heat shock proteins (Hsps) that chaperone Resistance (R) proteins for effector--triggered immunity (ETI) to unfolded protein responses (UPR) in the cytoplasm, resulting in destabilized R proteins and impaired ETI (solid lines). The heat stress-activated CaM may also disrupt ETI by blocking secretory defense responses *via* MLO and/or by inhibiting transcription of EDS1 via AtSR1 (dotted lines). In the ER, high temperature is also thought to shift the BiP/IRE1-mediated protein folding pathway for heat stress responses, resulting in reduced PM delivery or secretion of defense-related molecules. The cytosolic and ER UPR also triggers transcriptional reprogramming for heat responses.

Hsp70 show that it leads to acquisition of thermotolerance and enhanced resistance in response to drought, high salt and heat stresses in plants (Alvim et al., 2001; Lee and Schoffl, 1996; Ono et al., 2001). In particular, a tobacco Hsp70 also known as an binding immunoglobulin protein (BiP) seems to be involved in the unfolded protein response (UPR), which is caused by accumulation of unfolded or misfolded proteins in the lumen of the endoplasmic reticulum (ER) under various biotic and abiotic stress conditions (Alvim et al., 2001). Besides stress-tolerance, various members of Hsp70 have been reported to be involved in ABA-dependent responses, protein import, chloroplast development, and translocation into chloroplasts and mitochondria (Clement et al., 2011; Latijnhouwers et al., 2010). Hsp90 is the most abundant proteins expressed in cells and is dependent on ATP binding and hydrolysis for its function as a molecular chaperone (Wang et al., 2004). To play its roles in cells, Hsp90 forms multichaperone complexes by associating with Hsp70 and various co-chaperones such as Hip (Hsp70 interacting protein), Hop (Hsp70/Hsp90 organizing protein), Hsp40 and p23. In addition to the role as a facilitator of signaling components maturation, it is also involved in cell-cycle control, protein degradation and protein trafficking (Richter and Buchner, 2001). The fact that *Hsp90* in Arabidopsis is highly regulated by diverse abiotic stresses including heat, cold, salt stress and heavy metals, and plant hormones indicates that Hsp90 plays an important role in plant signal-transduction networks (Krishna and Gloor, 2001). The sHsps are low-molecular-weight proteins of 12-40 kDa. They commonly possess a conserved carboxy-terminal domain of about 90 amino acids called the alpha-crystallin domain (ACD) and help in the refolding of non-native proteins performed by ATP-dependent chaperones. Each member in plants is located at a distinct cellular compartment (nuclear-cytosolic compartment, endoplasmic reticulum, peroxisomes, chloroplasts and mitochondria) and they are regulated by heat and abiotic stresses (Boston et al., 1996). Therefore, it is thought that they are related to stress signalings occurred at diverse places in plant cells.

Hsps are also critical for plant defense responses. PTI is mostly triggered by recognition of extracellular pathogen-derived nonself molecules called PAMPs, whereas ETI is activated by detection of intracellular pathogen-injected molecules called effectors (Dodds and Rathjen, 2010; Jones and Dangl, 2006). In ETI, R proteins, nucleotide-binding leucine-rich repeat (NB-LRR) intracellular immune receptors directly or indirectly recognize cognate effectors that otherwise interfere with the host defense responses by self-oligomerization through their N-terminal coiled-coil (CC) or Toll/interleukin-1 receptor (TIR) domain (Bernoux et al., 2011; Maekawa et al., 2011). Since the ETI often leads to cell death, tight regulation of R proteins is indispensable for plant life. Studies revealed that Hsp90 as a chaperone plays an important role in modulating the structure and/or stability of R proteins (Elmore et al., 2011; Sangster and Queitsch, 2005). In this process, Required for Mla12 (RAR1) and Suppressor of G2 allele of *skp1* (SGT1) function as cochaperones by interacting with Hsp90 (Azevedo et al., 2006; Bieri et al., 2004; Hubert et al., 2003; Liu et al., 2004; Lu et al., 2003; Tornero et al., 2002). Interestingly, SGT1, compared to RAR1 and Hsp90, was found to be involved in antagonistic regulation of R proteins in plant defense responses (Holt et al., 2005). However, reduced amounts of the Rx R protein by *NbSGT1* silencing in *Nicotiana benthamiana* (Azevedo et al., 2006) suggests that SGT1 is also engaged in R protein accumulation. Since SGT1 interacts with and controls the Skp1-Cul1-F-box (SCF) ubiquitin ligase complex (Azevedo et al., 2002; Liu et al., 2002) and since distinct R proteins require different levels of SGT1 (Azevedo et al., 2006), it is likely that plants fine-tune the ETI by degrading or stabilizing of R proteins depending on the levels of SGT1. Hsp90-associated chaperoning is regarded to be also important for PTI. It was recently found that the Hsp90-Hop complex is required for the transport of the rice chitin receptor (OsCERK1) that is critical for the defense against rice blast fungus from the ER to the PM (Chen et al., 2010). Suppression of the bacterial flagellin-induced PTI by a *Pseudomonas syringae* AvrB effector through RAR1 also

supports the importantce of the Hsp90 chaperoning activity in PTI (Shang et al., 2006).

In addition to Hsp90, Hsp70 is also important for plant disease resistance. Hsp70 was found to be required for resistance to *P. chicorii* in tobacco (Kanzaki et al., 2003) and to modulate Arabidopsis defense against bacterial and oomycete pathogens (Noel et al., 2007). The importance of Hsp70 in plant defense responses can be supported by a recent finding that *P. syringae* utilizes its HopI1 effector to target and interfere with the Hsp70-related immunity (Jelenska et al., 2010). The non-altered levels of an R protein by overexpression of Hsp70 (Noel et al., 2007) suggest its distinct function in plant defense responses from Hsp90. RSI2, a sHsp to interact with I-2 that is a tomato R protein, was recently found to be required for accumulation of I-2 and HR (Van Ooijen et al., 2010). Specific reduction of I-2 abundance but not another R protein Mi-1 by RSI2 depletion in plants suggests distinct modes of action between sHsp and Hsp90 in R-mediated defense responses, because silencing of Hsp90 decreases both I-2 and Mi-1(Van Ooijen et al., 2010).

HEAT STRESS TRANSCRIPTION FACTORS IN PLANT HEAT AND PATHOGEN STRESS RESPONSES

Heat stress transcription factors are the crucial regulators of the signal transduction pathways mediating the activation of HSPs and other heat shock-induced transcripts in response to heat stress. While most eukaryotes possess only a few, Hsfs in plants have unique multiplicity, with more than 20 members; 21, 23 and more than 18 members in Arabidopsis, rice and tomato, respectively (Baniwal et al., 2004; Nover and Scharf, 1997). Commonly, all plant Hsfs have DNA binding domains at the N-terminal, an oligomerization domain (HR-A/B region) and the nuclear localization signal (NLS). They are composed of three conserved evolutionary classes, A, B and C, based on their structural features (Nover et al., 2001). While the HR-A/B region of Classes A and C Hsfs possess 21 and 7 amino acid insertions between A and B parts, the HR-A/B region of class B is highly compact, similar to that of all non-plant Hsfs. Moreover, class A Hsfs have the activator modules (AHA motifs) with the consensus sequence FWxx (F/L)(F/I/L) and the NES serves in the C-terminus, as the symbol of class A. Hsf proteins utilize the heat stress element (HSE) as a common *cis*-acting element, highly conserved sequence (5′-AGAAnnTTCT-3′) within the promoters of heat-responsive genes. Several Hsfs has been reported for their cellular functions. HsfA1a has been known as a master regulator of heat response in tomato, since it cannot be replaced by any other Hsf proteins (Mishra et al., 2002). However, although the Hsf families of tomato and Arabidopsis share similar basic structure, the master regulator of heat response in Arabidopsis is not clear so far. A single *hsfA1* mutant and even the *hsfA1a hsfA1b* double mutant do not exhibit the pattern of marked thermotolerance, even though the defect of both genes impairs the HS-responsive expression of various *HSP* genes (Busch et al., 2005; Lohmann et al., 2004). This might be explained by functional redundancy caused from the two additional HsfA1 proteins in Arabidopsis. HsfA2 has been reported as a dominant form of Hsf in thermotolerant cells, because of its accumulation during repeated cycles of heat stress and recovery. Analysis of the changes in the transcriptome by heat stress in *HsfA2*-knockout Arabidopsis mutants, showed several HS-responsive genes including sHsps and individual members of the Hsp70 and Hsp100 families were largely affected by heat treatments (Schramm et al., 2006). While the HS-induced expression of HsfA2 in Arabidopsis does not seem to be regulated by HsfA1, several reports suggest the cooperative roles between HsfA1 and HsfA2 in tomato (Busch et al., 2005). Gene expression profiles mediated by HsfA1 and HsfA2 are largely overlapped with each other, and HsfA1a and HsfA2 form hetero-oligomers in tomato (Heerklotz et al., 2001; Port et al., 2004; Scharf et al., 1998). Moreover, tomato HsfA1 is required for efficient nuclear import of HsfA2 (Scharf et al., 1998). Therefore, Hsf2A2 is supposed to be a regulatory amplifier in the expression of heat stress-related genes by HsfA1.

Unlike the class A Hsfs, studies on class B and C Hsfs have not been largely conducted, and there have been no reports that they acts as a transcriptional activator. Recently, HSF4 also called HsfB1 was reported to be important for transcriptional reprogramming in response to pathogen attack (Pajerowska-Mukhtar et al., 2012). Failure to complement the yeast *hsf1* mutant, no significant effect on thermotolerance by overexpression and pathogen-inducibility of its expression suggest that HSF4 is involved in plant defense responses rather than heat stress signaling despite a sequence similarity (Boscheinen et al., 1997; Busch et al., 2005; Pajerowska-Mukhtar et al., 2012; Prandl et al., 1998). However, lower survival rate of *hsf4* mutant plants than wild-type plants in response to tunicamycin, an ER stress inducer, indicates its role in chaperoning unfolded proteins (Pajerowska-Mukhtar et al., 2012). Together with this, a study from a novel type of HS-induced HsfB1 in tomato shows the protein is able to function as a co-activator to synergistically cooperate with HsfA1a and other transcriptional activators (Bharti et al., 2004; Czarnecka-Verner et al., 2000; Kotak et al., 2004).

POSSIBLE CROSSTALKS BETWEEN PLANT DEFENSE AND HEAT STRESS RESPONSES

Little is known so far about how plant immunity and heat resistance are connected. However, it is clear that plant defense responses in many cases are modulated by higher temperature. It was reported that higher temperature suppresses resistance to TMV by N, a tobacco R protein, resistance to root-knot nematodes by Mi-1, and resistance to *Cladosporium fulvum* fungus by Cf4 and Cf9 R proteins (de Jong et al., 2002; Hwang et al., 2000; Whitham et al., 1996). This inhibition by higher temperature is accompanied by the reduced HR, suggesting that there might be a communicating point at the level of ETI between plant defense and heat responses. More bacterial growth in plant tissues but less in liquid medium at higher temperature (Wang et al., 2009) indicates increased temperature compromises plant defense responses rather than stimulates the pathogen growth.

R proteins activated by recognition of pathogen-derived effectors are stabilized and accumulated in cytosol by Hsps-associated chaperoning (Elmore et al., 2011; Sangster and Queitsch, 2005). Recent studies suggest the nuclear localization of activated R proteins is critical for ETI (Burch-Smith et al., 2007; Shen et al., 2007; Wirthmueller et al., 2007). *snc1-1* plants in which SNC1, an Arabidopsis R protein is constitutively activated show dwarfism and elevated resistance at 22°C but not at 28°C (Yang and Hua, 2004), additionally supporting the antagonism between plant immunity and higher temperature. Suppressor mutant screening of *snc1-1* at higher temperature revealed that nuclear exclusion of SNC1 is important for inhibiting plant immunity induced by increase temperature, because SNC1-4 which unlike SNC1 remains in the nuclei even at higher temperature confers retained bacterial resistance on

plants (Zhu et al., 2010b). Recently, a small molecule called [5-(3,4-dichlorophenyl)furan-2-yl]-piperidine-1-ylmethanethione (DFPM) was identified to suppress ABA responses (Kim et al., 2011). The fact that RAR1 and SGT1 are required in this inhibitory process suggests a possible crosstalk between plant defense and ABA responses via the Hsp90-associated pathway. Since ABA is the representative abiotic stress hormone, reduced ABA responses in *snc1-1* plants (Kim et al., 2011) additionally suggest that the Hsp chaperoning activity might link plant heat stress signaling and defense responses. Although direct evidence on the involvement of Hsps in the suppression of defense responses by high temperature is not revealed yet, it seems that plants prioritize heat stress responses over immunity because overexpression of Hsp70 results in heat-resistant but defense-compromised plants (Noel et al., 2007). Therefore, it is possible that higher temperature drives the allocation shift of Hsps to heat stress responses from defense responses (Fig. 1). This would lead to destabilization of R proteins resulting in impaired immunity to pathogens.

Although an increase of intracellular Ca^{2+} levels is important for both plant heat stress and defense responses, whether these processes can be crossly controlled by Ca^{2+}-mediated signaling is yet unclear. DFPM treatment inhibits the activation of S-type anion channel by intracellular Ca^{2+} increase triggered by ABA, and Phytoalexin Deficient 4 (PAD4) is required for this inhibition (Kim et al., 2011). Since PAD4 together with Senescence Associated Gene 101 (SAG101) is involved in EDS1-dependent defense responses that are mediated by R proteins (Feys et al., 2005; Lipka et al., 2005), the finding by Kim et al. indirectly suggests a possible communication at the level of Ca^{2+} signaling between plant heat responses and immunity. Since a conventional CaM is engaged in suppressing the disease resistance via MLO and/or AtSR1 (Du et al., 2009; Kim et al., 2002) and since CaM3, an additional common CaM, modulates heat stress responses (Zhang et al., 2009), it is possible that activated CaM by increased intracellular Ca^{2+} levels at least in part disrupts plant immune responses (Fig. 1).

Independent genetic approaches to understand plant immune signaling related to the bacterial elongation factor Tu recently revealed that the cyclic folding machinery in the ER is critical for plant immunity, because removal of calreticulin 3 (CRT3) and UDP-glucose:glycoprotein glucosyltransferase (UGGT) led to compromised resistance to bacterial pathogens resulted from reduced PM delivery of EFR (Li et al., 2009; Saijo et al., 2009). Genes engaging in protein modification and secretion in the ER were reported to be induced by NPR1, the key regulator of plant defense hormone SA (Wang et al., 2005). Indeed, deletion of an ER chaperone BiP and the UPR sensor inositol-requiring 1 (IRE1) impairs plant defense against bacterial pathogens, which is accompanied by reduced secretion of pathogenesis-related (PR) proteins (Moreno et al., 2012; Wang et al., 2005). This suggests that plant heat and defense responses may in part share the UPR in the ER. It is therefore possible that biased UPR to elevated temperature may weaken plant disease resistance (Fig. 1).

The gradually rising temperature on Earth by the green house effect is now endangering human life partly by reducing crop productivity due to heat stress itself and the accompanied weakening of plant immunity. However, researches on interactions between plant defense and heat stress responses are yet fragmented. Engineering plants to gain resistance to both stresses would be therefore helpful to enhance or at least maintain crop yield, because either approach cannot overcome this antagonistic dilemma.

ACKNOWLEDGMENTS

This work was supported by the Research Fund of Dankook University in 2009.

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