Biotechnology Advances xxx (2013) xxx–xxx

Contents lists available at ScienceDirect

Biotechnology Advances

journal homepage: www.elsevier.com/locate/biotechadv

The role of ABA and MAPK signaling pathways in plant abiotic stress responses

Agyemang Danquah [1], Axel de Zelicourt, Jean Colcombet, Heribert Hirt *

URGV Plant Genomics, INRA-CNRS-UEVE, Saclay Plant Sciences, 2 rue Gaston Cremieux, 91000 Evry, France

ARTICLE INFO

Available online xxxx

Keywords:
Abscisic acid
Abiotic stress
MAP kinases
Signal transduction
ABA
Mitogen-activated protein kinases

ABSTRACT

As sessile organisms, plants have developed specific mechanisms that allow them to rapidly perceive and respond to stresses in the environment. Among the evolutionarily conserved pathways, the ABA (abscisic acid) signaling pathway has been identified as a central regulator of abiotic stress response in plants, triggering major changes in gene expression and adaptive physiological responses. ABA induces protein kinases of the SnRK family to mediate a number of its responses. Recently, MAPK (mitogen activated protein kinase) cascades have also been shown to be implicated in ABA signaling. Therefore, besides discussing the role of ABA in abiotic stress signaling, we will also summarize the evidence for a role of MAPKs in the context of abiotic stress and ABA signaling.

© 2013 Elsevier Inc. All rights reserved.

1. Introduction

Abiotic stresses such as drought, high salinity, heat, cold, freezing, limited nutrient availability, heavy metals and hypoxia are severe environmental stresses that impair productivity in crop systems (Qin et al., 2011; Tuteja, 2007; Wang et al., 2003). Together, these stresses constitute the primary causes of crop losses worldwide, reducing average yields of most major crop plants by more than 50% (Boyer, 1982; Bray et al., 2000; Wang et al., 2003). Current climate change scenarios predict an increase in mean surface temperatures and aridity that will drastically affect global agriculture in the near future (Le Treut et al., 2007). Together with the decline in arable farmland due to soil degradation and human activities, an immense pressure is put on crop production to feed the burgeoning human population in the next decades. For these reasons, a major goal in plant science is to understand how plants respond to and withstand environmental stresses successfully. This understanding is crucial in providing us with the basis for effective engineering strategies to increase stress tolerance.

Abiotic stresses trigger many biochemical, molecular, and physiological changes and responses that influence various cellular and whole plant processes (Wang et al., 2001, 2003). For example, drought, salinity and low temperature stress lead to reduced availability of water (also known as dehydration/osmotic stress) characterized by a decreased turgor pressure and water loss (Boudsocq and Lauriere, 2005; Dhariwal et al., 1998). Osmotic stress promotes the synthesis of the phytohormone abscisic acid (ABA) which then triggers a major change in gene expression and adaptive physiological responses (Seki et al., 2002; Shinozaki and Yamaguchi-Shinozaki, 2007; Yamaguchi-Shinozaki and Shinozaki, 2006). Recently, the core signaling complexes that perceive ABA and transmit cues to downstream events have been deciphered (Fujii et al., 2009; Ma et al., 2009; Park et al., 2009). This discovery has not only provided new avenues to test existing research hypotheses on ABA signaling but has also helped in shaping new ideas. Currently, the link between the core ABA complex and other known regulatory pathways of stress signaling in plants, such as the MAPK pathways, are beginning to unfold. This manuscript aims to review our current knowledge on the connection between ABA and MAPK pathways in the context of abiotic stress responses in plants.

2. ABA signaling in plants

ABA belongs to the class of isoprenoids (terpenoids) (Nambara and Marion-Poll, 2005) and also belongs to the most important phytohormones involved in plant growth, development and adaptation to various stress conditions (Schroeder et al., 2001a; Shinozaki and Yamaguchi-Shinozaki, 2000; Verslues et al., 2006). ABA is reported in all kingdoms of life with the exception of Archea (Hauser et al., 2011). A dynamic balance of biosynthesis and degradation determines the amount of available cellular ABA. In plants, these two processes are influenced by developmental and environmental factors such as light, salinity and water stress (Cutler and Krochko, 1999).

The functions of ABA in plants are multiple. High cellular ABA levels lead to synthesis of storage proteins in seeds, promote seed desiccation tolerance and dormancy (Finkelstein et al., 2002, 2008) and inhibit seed germination. ABA is also involved in the control of lateral root formation and seedling growth (Xiong et al., 2006) as well as in the reduction of water transpiration through promotion of stomatal pore closure

* Corresponding author.
[1] Present address: The Biotechnology Centre, College of Agriculture and Consumer Sciences, University of Ghana, P.O. Box LG66, Legon, Ghana.

0734-9750/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.biotechadv.2013.09.006

(Hetherington, 2001; Kim et al., 2010). Moreover, ABA controls the expression of a large set of stress-responsive genes (Hoth et al., 2002; Nemhauser et al., 2006; Seki et al., 2002).

2.1. ABA biosynthesis, catabolism and transport

2.1.1. ABA biosynthesis

With the exception of the conversion of xanthoxin to ABA in the cytoplasm, all the steps for the de novo ABA synthesis occur in plastids (Seo and Koshiba, 2002). The early C_5 precursor of ABA, Isopentenyl pyrophosphate (IPP) is produced primarily in plastids via 1-deoxy-D-xylulose-5-phosphate (DXP) from pyruvate and glyceraldehydes-3-phosphate (Cutler and Krochko, 1999; Nambara and Marion-Poll, 2005; Seo and Koshiba, 2002; Wasilewska et al., 2008). This leads to the sequential production of farnesyl pyrophosphate, geranylgeranyl pyrophosphate (GGPP), phytoene, ζ-carotene, lycopene and β-carotene. β-carotene is converted to a xanthophyll, zeaxanthin, which is the first oxygenated carotenoid (Seo and Koshiba, 2002). Subsequent steps involve the synthesis of *cis*-isomers of violaxanthin and neoxanthin that are cleaved to form xanthoxin (the C_{15} precursor of ABA). This cleavage is catalyzed by the 9-*cis*-epoxycarotenoid dioxygenase (NCED) enzymes (Schwartz et al., 1997, 2003; Tan et al., 1997). Xanthoxin is presumed to migrate from the plastid to the cytosol (Nambara and Marion-Poll, 2005), where it is converted to ABA by three possible pathways: via abscisic aldehyde, xanthoxic acid or abscisic alcohol (Seo and Koshiba, 2002).

2.1.2. ABA catabolism

Cellular ABA levels can be lowered via two pathways: hydroxylation and conjugation (Nambara and Marion-Poll, 2005).

ABA hydroxylation — ABA is hydroxylated via oxidation of the methyl groups of the ring structure at three positions, C-7′, C-8′, and C-9′, of which C-8′ is the primary site (Cutler and Krochko, 1999; Zeevaart and Creelman, 1988). The three forms of hydroxylated ABA exert significant biological activity (Zhou et al., 2004; Zou et al., 1995), but hydroxylation triggers further inactivation steps (Nambara and Marion-Poll, 2005). Cytochrome P450 monooxygenase (CYP707A) catalyzes the hydroxylation of ABA at the C-8′ to form unstable 8′-hydroxy ABA, which is subsequently converted to phaseic acid (PA) by spontaneous isomerization (Kushiro et al., 2004; Nambara and Marion-Poll, 2005; Saito et al., 2004). PA is then converted to dihydrophaseic acid (DPA) by a soluble PA reductase (Gillard and Walton, 1976). Other oxidation products of ABA hydroxylation include 7′-hydroxy ABA, 9′-hydroxy ABA, and neo-phaseic acid (neo-PA) (Hampson et al., 1992; Zhou et al., 2004).

ABA conjugation — Apart from de novo biosynthesis, ABA conjugation/deconjugation plays a critical role in the regulation of cellular ABA amounts under both normal and dehydration conditions (Dietz et al., 2000; Lee et al., 2006; Xu et al., 2012). ABA and hydroxy ABA are conjugated with glucose for inactivation. ABA can be inactivated at the C-1 hydroxyl group by forming different conjugates. Of these conjugates, ABA glucosyl ester (ABA-GE) is the predominant form, which is produced by ABA glycosyltransferase (Cutler and Krochko, 1999; Koshimizu et al., 1968). The corresponding gene was first isolated from adzuki bean and named *AOG* (Xu et al., 2002). Recombinant AOG can conjugate ABA with UDP-D-glucose (Xu et al., 2002). The Arabidopsis genome encodes 8 glycosyltransferases (Lim et al., 2005). While all 8 glycosyltransferases can glucosylate ABA in vitro, only one of them (UGT71B6) shows enantioselective glucosylation towards (+)-ABA (Lim et al., 2005). Over-expression of *UGT71B6* leads to an increased ABA-GE content in Arabidopsis (Priest et al., 2006). However neither the knockout mutant nor overexpression of *UGT71B6* displayed any significant ABA-related phenotypes (Priest et al., 2006).

ABA-GE is stored in vacuoles and the apoplast (Dietz et al., 2000). The low membrane permeability makes ABA-GE suitable for long-distance translocation and storage in vacuoles and the apoplastic space (Jiang and Hartung, 2008). Under dehydration conditions, ABA is released from the glucosyl ester form by β-glucosidases (Dietz et al., 2000; Jiang and Hartung, 2008; Lee et al., 2006; Xu et al., 2012). The enzymatic activity of β-glucosidases to catalyze the hydrolysis of ABA-GE for releasing free ABA was first demonstrated in barley (Dietz et al., 2000). Recently, two β-glucosidases (*BG1* and *BG2*) were isolated in Arabidopsis (Lee et al., 2006; Xu et al., 2012). Abiotic stresses such as dehydration and NaCl induce *BG1* and *BG2* expression. Knockout mutants of these genes are hypersensitive to abiotic stresses while over-expression lines were tolerant and contained more ABA. Interestingly, the two β-glucosidases localize to different compartments in the cell; BG1 is localized to the endoplasmic reticulum while BG2 is found in the vacuole. The authors of these studies suggested an organelle-specific hydrolysis of ABA-GE in response to specific developmental or environmental signals (Xu et al., 2012).

2.1.3. ABA transport

Stress-induced biosynthesis of ABA primarily occurs in vascular tissues but ABA exerts its responses in various cells, including distant guard cells (Kuromori et al., 2010). Thus, ABA responses require translocation from ABA-producing cells via intercellular transport to allow rapid distribution into neighboring tissues. Recently, cell-to-cell ABA transport was shown to be mediated by two plasma membrane-bound ATP-binding cassette (ABC) transporters (Kang et al., 2010; Kuromori et al., 2010) and a family of low-affinity nitrate transporters (Kanno et al., 2012). Most ABC transporters are integral membrane proteins and act as ATP-driven transporters for a very wide range of substrates, including lipids, drugs, heavy metals, and auxin (Rea, 2007). Kuromori et al. (2010) isolated *AtABCG25* (also known as *AtWBC26*), which encodes a half size ABC transporter protein and which is responsible for ABA transport and responses in Arabidopsis. The *atabcg25* mutant was isolated by genetic screening for ABA sensitivity during the greening of cotyledons. AtABCG25 is a membrane protein and is predominantly expressed in vascular tissues. Efflux of ABA was detected in membrane vesicles derived from Sf9 insect cells that expressed *AtABCG25*. Moreover, *AtABCG25*-overexpressing plants showed higher leaf temperatures implying an influence of AtABCG25 on stomatal regulation.

AtBCG40 (also known as *AtPDR12*) encodes a full-size ABC transporter and was reported to function as an ABA importer in plant cells (Kang et al., 2010). The *atabcg40* mutant was isolated in a screen for seed germination and stomatal movement in 13 out of 15 ABC transporter gene knockout mutants (*atabcg29–atbcg41*). AtABCG40 is also a plasma membrane protein and expressed primarily in leaves of young plantlets and in primary and lateral roots. In leaves, expression was the highest in guard cells. The stomata of *atabcg40* mutants close more slowly in response to ABA, resulting in reduced drought tolerance. Uptake of ABA into yeast and BY2 cells expressing *AtBCG40* showed a time-dependent increment, whereas ABA uptake into protoplasts of *atabcg40* plants decreased when compared with control cells. The delay in ABA uptake in *atabcg40* mutant correlated with the delayed expression of several ABA-inducible genes, indicating that AtABCG40 is necessary for the timely response to ABA.

Recently, Kanno et al. (2012) isolated ABA-IMPORTING TRANSPORTER 1 (AIT1) (which is also known as low-affinity nitrate transporter; NRT1.2) from a modified yeast-2-hybrid screen in which positive clones are capable of inducing interactions between the ABA receptor PYR/PYL/RCAR and PP2C protein phosphatase at low ABA concentrations. AIT1 preferentially localized to the plasma membrane of plant cells and was mainly expressed in vascular tissues in cotyledons, true leaves, hypocotyls, roots and inflorescence stems. Yeast and insect cells that expressed *AIT1* showed enhanced uptake of exogenously applied ABA but did not import GA_3, IAA or JA. The *ait1* mutants were less sensitive to ABA during germination and post-germination growth, and the inflorescence stems displayed a lower surface temperature than that of wild-type due to excess water loss from open stomata. Overexpression of *AIT1* resulted in

Please cite this article as: Danquah A, et al, The role of ABA and MAPK signaling pathways in plant abiotic stress responses, Biotechnol Adv (2013), http://dx.doi.org/10.1016/j.biotechadv.2013.09.006

ABA hypersensitivity. Together, these data demonstrate that AIT1 functions as an ABA importer mediating cellular ABA uptake.

2.2. ABA perception and signal transduction

Recent progress in our understanding of ABA signal transduction indicates that the earliest events occur via a central signaling module made up of proteins belonging to three protein classes: Pyracbactin Resistance/Pyracbactin resistance-like/Regulatory Component of ABA Receptor (PYR/PYL/RCARs) proposed to be the ABA receptors, Protein Phosphatase 2Cs (PP2Cs) which act as negative regulators, and SNF1-related protein kinase 2 s (SnRKs) which are positive regulators (Mustilli et al., 2002; Park et al., 2009; Schweighofer et al., 2004; Umezawa et al., 2009; Yoshida et al., 2006a). In the presence of ABA, the PYR/PYL/RCAR-PP2C complex formation leads to inhibition of PP2C activity (Fujii et al., 2009; Ma et al., 2009; Park et al., 2009; Santiago et al., 2009a), thus allowing activation of SnRKs which target membrane proteins, ion channels and transcription factors, and facilitate transcription of ABA-responsive genes (Fig. 1) (Sheard and Zheng, 2009; Soon et al., 2012; Umezawa et al., 2010).

2.2.1. The PYR/PYL/RCAR ABA receptors

In Arabidopsis, structural and molecular studies have shown that members of the PYR/PYL/RCAR family play a central role in ABA perception (Ma et al., 2009; Melcher et al., 2010; Miyazono et al., 2009; Nishimura et al., 2009, 2010; Park et al., 2009; Santiago et al., 2009a,b; Yin et al., 2009). Members of this soluble ABA receptor family were first discovered in an elegant chemical genetic approach consisting to screen for mutants able to germinate in the presence of pyrabactin, an agonist of ABA (Park et al., 2009), and independently in a yeast two hybrid screen using the PP2C ABI2 as a bait (Ma et al., 2009). The Arabidopsis genome encodes 14 PYR/PYL/RCAR proteins that are highly conserved at the amino acid sequence level. All members encode small proteins, ranging between 159 and 211 amino acid residues (Santiago et al., 2009a). Several of them, including PYR1, PYL1, and PYL2 were biochemically shown to directly bind ABA (Miyazono et al., 2009; Nishimura et al., 2009; Santiago et al., 2009b; Yin et al., 2009).

Genetic evidence of the role of PYR/PYL/RCARs in ABA signaling comes from the fact that the triple *pyr1/pyl1/pyl4* or quadruple *pyr1/pyl1/pyl2/pyl4* (and more recently the sextuple *pyr1/pyl1/pyl2/pyl4/pyl5/pyl8*) mutants show hyposensitivity in germination and root growth responses to ABA (Gonzalez-Guzman et al., 2012; Park et al., 2009), although single mutants displayed normal ABA responses, suggesting a high level of functional redundancy in this gene family. The quadruple mutant also exhibited impaired ABA-induced stomatal closure, reduced activation of SnRKs and an ABA-insensitive transcriptome profile (Gonzalez-Guzman et al., 2012; Nishimura et al., 2010; Park et al., 2009). Again, over-expression of *PYL5*, *PYL8* or *PYL9* produced enhanced ABA responses or conferred drought resistance to Arabidopsis (Ma et al., 2009; Saavedra et al., 2010; Santiago et al., 2009a). The entire PYR/PYL/RCAR family in Arabidopsis (with the exception of PYL13) is capable of activating ABA signaling responses indicating that nearly all members can function as ABA receptors (Fujii et al., 2009).

2.2.2. PP2Cs are major negative regulators of ABA signaling

ABA binding to PYR/PYL/RCARs induces a conformational change that exposes the interaction surface allowing for favorable binding of some PP2Cs (Cutler et al., 2010). In yeast and mammals, PP2Cs act as general negative regulators of stress signaling through the regulation of the stress-activated MAPK pathway, DNA damage signaling, or the dephosphorylation of AMP-activated kinase (AMPK), the mammalian counter-part of yeast SNF1 kinase (Lammers and Lavi, 2007; Vlad et al., 2009). The Arabidopsis genome encodes 76 PP2Cs that have been clustered into 10 groups (Schweighofer et al., 2004). The first two PP2C group A genes to be studied in plants, ABA-INSENSITIVE 1 (ABI1) and ABI2 were identified in genetic screens for ABA-insensitive mutants (Koornneef et al., 1984; Leung et al., 1994, 1997; Meyer et al., 1994; Rodriguez et al., 1998). Later, HOMOLOGY TO ABI1 (HAB1) and HABI2 were isolated based on their sequence similarity to ABI1 (Saez et al., 2004). Other members of clade A PP2Cs, such as ABA-HYPERSENSITIVE GERMINATION 1 (AHG1) and AHG3/PP2CA were identified in genetic screens of Arabidopsis and a yeast complementation test (Antoni et al., 2012; Kuhn et al., 2006; Kuromori and Yamamoto, 1994; Nishimura et al., 2007; Yoshida et al., 2006b).

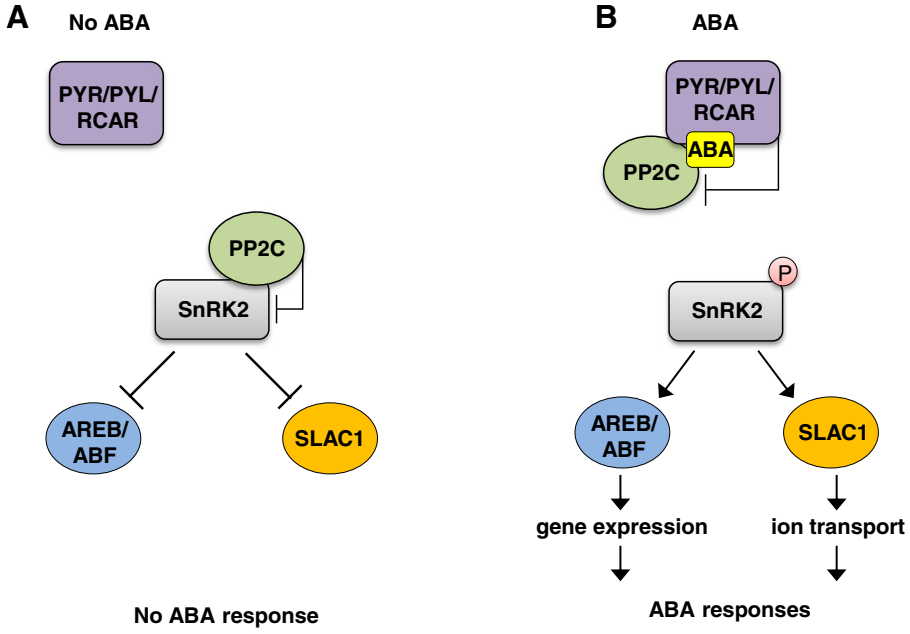

Fig. 1. A simplified model of the early events in the ABA signaling pathway. A: In the absence of ABA, PP2Cs constitutively inactivates SnRK2s by physically interacting with and dephosphorylating serine residues in the kinase activation loop. Without activation, SnRK2s are unable to transmit signal to downstream targets. B: ABA-bound PYR/PYL/RCAR receptors bind and inhibit PPC2s, thereby allowing activation of SnRK2s. Active SnRK2 kinases phosphorylate downstream target proteins, including AREB/ABF transcription factors, anion channels and NADPH oxidases, to induce ABA responses.

Please cite this article as: Danquah A, et al, The role of ABA and MAPK signaling pathways in plant abiotic stress responses, Biotechnol Adv (2013), http://dx.doi.org/10.1016/j.biotechadv.2013.09.006

Genetic evidence revealed that group A PP2Cs are negative regulators of ABA signaling in Arabidopsis. Plants carrying the dominant mutations *abi1-1* (*abi1*^{G180D}) or *abi2-1* (*abi2*^{G168D}) or plants expressing the mutant HAB1^{G246D} protein are strongly insensitive to ABA including reduced seed dormancy, ABA-resistant seed germination and seedling growth, abnormal stomatal regulation, and defects in various responses to drought (Finkelstein and Somerville, 1990; Hoth et al., 2002; Koornneef et al., 1984; Leung et al., 1994, 1997; Meyer et al., 1994; Robert et al., 2006; Rodriguez et al., 1998). The mutations have the same single amino acid substitution (Gly to Asp) in the highly conserved phosphatase catalytic domain, and are capable of blocking ABA responses (Gosti et al., 1999; Leung et al., 1994, 1997; Meyer et al., 1994; Robert et al., 2006). Isolation of intragenic suppressor alleles of *abi1-1* and *abi2-1* provided vital evidence that these proteins act as negative regulators of the ABA signaling pathway (Gosti et al., 1999). Conversely, loss-of-function and knockout mutants in ABI1, ABI2 and HAB1 are hypersensitive to ABA, providing further proof that PP2Cs are major negative regulators of ABA signaling in plants (Gosti et al., 1999; Hirayama and Shinozaki, 2007; Leonhardt et al., 2004; Merlot et al., 2001; Saez et al., 2004).

2.2.3. SnRK2s are major positive regulators of ABA signaling

The SnRK2 family of protein kinases are plant-specific Ser/Thr kinases involved in plant responses to abiotic stresses and in ABA-dependent plant development (Hrabak et al., 2003). In Arabidopsis, the SnRK2 family consists of 10 members that are categorized into three subclasses (Hrabak et al., 2003; Yoshida et al., 2002). Members of subclass I are rapidly activated by osmotic stress but not ABA. In contrast, subclass II and III members are activated by both ABA and osmotic stress, albeit subclass II is weakly activated by ABA (Boudsocq et al., 2004). The first reports of an involvement of SnRK2s in ABA signaling was found in wheat (PKABA1) and *Vicia faba* (AAPK), indicating their high conservation throughout the plant kingdom (Gomez-Cadenas et al., 1999; Li et al., 2000). The putative ortholog of AAPK in Arabidopsis, SnRK2.3/OPEN STOMATA 1 (OST1) was identified independently by different experimental approaches aimed at identifying key regulatory elements in osmotic stress adaptation (Boudsocq et al., 2004; Merlot et al., 2002; Mustilli et al., 2002; Wasilewska et al., 2008; Xie et al., 2006; Yoshida et al., 2002). *snrk2.3* mutations blocked stomatal responses to ABA and to mild drought conditions (Mustilli et al., 2002; Yoshida et al., 2002). Later on, SnRK2.3/OST1 was shown to interact with ABI1 in yeast-two-hybrid assays (Yoshida et al., 2006a). A conserved domain II motif in the C-terminus constitutes the binding site for ABI1 (Yoshida et al., 2006a). In in vitro assays, Group A PP2Cs dephosphorylated SnRK2s (Umezawa et al., 2009; Vlad et al., 2009). Compared to wild type, the ABA-activated kinase activity is significantly reduced in quadruple *pry1/pyl1/pyl2/pyl4* or dominant PP2C mutants, while higher kinase activities are observed in PP2C loss-of-function or knockout mutants (Umezawa et al., 2009; Vlad et al., 2009). Boudsocq et al. (2004) reported that the subclass III kinases, SnRK2.2, SnRK2.3 and SnRK2.6, exhibit strongest activation by ABA and thus have to be considered as major regulators of ABA. Recently, the importance of subclass III SnRK2s was genetically highlighted by the analysis of a triple knockout mutant in Arabidopsis. The *snrk2.2/snrk2.3/snrk2.6* triple mutant is extremely sensitive to low humidity and highly resilient to ABA in all the elementary phenotypic responses (Fujita et al., 2009; Nakashima et al., 2009). These 3 SnRK2s, along with 9 of the 14 members of PYR/PYL/RCARs, co-immunoprecipitated with ABI in Arabidopsis protein extracts. Though the composition of co-purified proteins was ABA-independent, these data suggest that at least ABI1, the 3 SnRK2s and at least 9 of the 14 receptor proteins may constitute a core ABA signaling complex (Fujii and Zhu, 2009; Joshi-Saha et al., 2011; Nishimura et al., 2010).

In a recent study, Soon et al. (Soon et al., 2012) reported the 3D structure of the SnRK2-PP2C protein complex which helped to solve the question of how SnRK2 activation is orchestrated with ABA binding and PP2C inhibition. In the absence of ABA, PP2Cs dephosphorylate SnRK2 in a serine residue in the kinase activation loop (Ser175 in SnRK2.6/OST1) whose phosphorylation is necessary for kinase activity (Ma et al., 2009; Park et al., 2009; Soon et al., 2012; Umezawa et al., 2009; Vlad et al., 2009; Yin et al., 2009; Yoshida et al., 2006a). The kinase activation loop of SnRK2s docks into the active site of PP2Cs, while the conserved ABA-sensing tryptophan of PP2Cs inserts into the kinase catalytic cleft. This SnRK2–PP2C complex structure also mimics a receptor–PP2C interaction (Soon et al., 2012). Binding of ABA to PYR/PYL/RCAR receptors promotes the receptors to bind to the catalytic site of PP2Cs and inhibit their enzymatic activity (Melcher et al., 2010; Miyazono et al., 2009; Nishimura et al., 2009; Santiago et al., 2009b). In turn, ABA-induced inhibition of PP2Cs leads to SnRK2 activation by activation loop autophosphorylation (Boudsocq et al., 2007), which allows the SnRK2s to relay the ABA signal to downstream effectors (Cutler et al., 2010; Hubbard et al., 2010; Umezawa et al., 2010). In plants, SnRK2 activation loop phosphorylation may also involve unidentified upstream kinases (Boudsocq et al., 2007; Burza et al., 2006).

2.2.4. Additional ABA signal perception and transduction modules

The existence of intracellular ABA receptors as well as extracellular receptors has been proposed by several laboratories. Earlier studies suggested the presence of ABA transmembrane receptors. For example, when ABA is negatively charged at high pH, it was shown that ABA can no longer cross the plasma membrane and thereby loses its potential to promote stomatal closure in *Valerianella locusta* (Hartung, 1983). Moreover, ABA failed to inhibit stomatal opening when microinjected directly in the cytosol of *Commelina* guard cells (Anderson et al., 1994). Another piece of evidence comes from experiments with barley aleurone protoplasts when externally applied ABA reversed the stimulation of α-amylase synthesis by gibberellic acid (GA), whereas microinjection of up to 250 μM ABA was ineffective (Gilroy and Jones, 1994). Several candidate proteins were proposed as potential ABA receptors including the G-protein coupled receptor (GCPR)-type G proteins (GTG1 and GTG2) and ABA binding protein (ABAR)/Mg-chelatase H subunit (CHLH)/Genomes uncoupled 5 (GUN5).

GTG1 and GTG2 are plasma membrane proteins that share sequence similarity to the mammalian Golgi pH regulator membrane protein (Pandey et al., 2009). These GPCRs were shown to genetically and physically interact with the G-protein α-subunit GPA1 to mediate all known ABA responses (Liu et al., 2007; Pandey et al., 2009). Previous studies have shown that the *gpa1* mutant causes ABA insensitivity in guard cells and ABA hypersensitivity in seeds (Chen et al., 2006; Pandey et al., 2009). ABA binds to a fraction (~1%) of GTG1 and GTG2 recombinant proteins. The *gtg1/gtg2* double mutant displayed reduced sensitivity to ABA in seed germination, seedling and root growth, stomatal closure and gene expression. However, *gtg1/gtg2* was only partially insensitive to ABA, suggesting the likely existence of additional independent ABA receptors.

ABAR/CHLH/GUN5 is a chloroplast protein involved in chlorophyll biosynthesis (Shen et al., 2006; Walker and Willows, 1997; Wu et al., 2009) and plastid-to-nucleus retrograde signaling (Mochizuki et al., 2001; Nott et al., 2006; Strand et al., 2003; Surpin et al., 2002). ABAR/CHLH/GUN5 was identified through homology with an ABA-specific binding protein from *V. faba* (Zhang et al., 2002). ABAR/CHLH/GUN5 specifically binds ABA and mediates ABA signaling as a positive regulator in seed germination, post-germination growth and stomatal movement (Shen et al., 2006). However, mutants of the homologous ABAR/CHLH/GUN5 protein in barley, XanF, did not bind ABA or show similar ABA-related phenotypes as found in *V. faba* (Müller and Hansson, 2009). Moreover, the mechanism by which CHLH as an ABA receptor transmits a signal upon ABA binding remains unanswered (Klingler et al., 2010; Wu et al., 2009). ABAR/CHLH/GUN5 localizes to the chloroplast envelope, raising the question of how it transduces ABA to effect ABA-mediated transcriptional regulation in the nucleus. Recent studies identified

Please cite this article as: Danquah A, et al, The role of ABA and MAPK signaling pathways in plant abiotic stress responses, Biotechnol Adv (2013), http://dx.doi.org/10.1016/j.biotechadv.2013.09.006

ARTICLE IN PRESS

WRKY40, WRKY18 and WRKY60 transcription factors that could interact with the cytosolic C-terminus of ABAR/CHLH/GUN5 (Liu et al., 2012; Shang et al., 2010). In the absence of ABA, the WRKYs bind to the promoters (W-Box *cis*-elements) of ABI4 and ABI5, thus acting as negative regulators of ABA signaling in Arabidopsis. Shang et al. (2010) proposed a model in which ABA recruited the WRKYs from the nucleus to the cytosol and also promoted the interaction with ABAR/CHLH/GUN5. Sequestration of the WRKYs thus relieves inhibition of ABI4 and ABI5. Overall, these data suggest that there exist multiple ABA receptors and signal transduction cascades and more research will be required to clarify these mechanisms.

2.3. ABA signaling responses

2.3.1. Phosphorylation of bZIPs by SnRK2s activate ABA-induced gene expression

ABA signaling leads to large changes in gene expression, which may involve changes in transcription, transcript processing, and stability (Cutler et al., 2010). In Arabidopsis, about 10% of all genes are regulated by ABA (Hoth et al., 2002; Nemhauser et al., 2006; Seki et al., 2002). Analysis of the promoters of ABA-inducible genes showed that ABA gene expression requires multiple *cis*-elements (also called ABA-responsive elements; ABREs — PyACGTGG/TC), or combinations of an ABRE with a coupling element such as CE1, CE3 and DRE/CRT (Giraudat et al., 1994; Gomez-Porras et al., 2007; Umezawa et al., 2010; Zhang et al., 2005). Proteins that bind to ABRE, called ABRE-binding (AREB) or ABRE-binding factors (ABFs), were first isolated using ABRE sequences as bait in yeast one hybrid screens (Choi et al., 2000; Uno et al., 2000). AREB/ABFs are group-A subfamily basic-domain leucine zipper (bZIP) transcription factors with 13 members in Arabidopsis (Bensmihen et al., 2002; Correa et al., 2008; Jakoby et al., 2002; Yamaguchi-Shinozaki and Shinozaki, 2006).

Expression of *AREB1/ABF2*, *AREB2/ABF4*, and *ABF3/DPBD5* in Arabidopsis was up-regulated by ABA, dehydration and high salinity stresses (Fujita et al., 2005). Over-expression of these factors in transgenic plants resulted in ABA hypersensitivity in germination and seedling growth, and also enhanced drought tolerance (Abdeen et al., 2010; Fujita et al., 2005; Furihata et al., 2006; Kang et al., 2002; Kim et al., 2004). Recently, Yoshida et al. (2010) generated triple mutants of *areb1/areb2/abf3*, which were more resistant to ABA than the single and double mutants with respect to primary root growth and reduced drought tolerance. Transcriptome analysis revealed that stress-responsive gene expression was remarkably impaired in this triple mutant. Another group-A bZIP factor, ABI5, was isolated by genetic screening of γ-irradiated seeds for ABA-insensitivity during germination (Finkelstein, 1994; Finkelstein et al., 2002; Lopez-Molina and Chua, 2000).

Phosphorylation/dephosphorylation events play important roles in ABA signaling (Yamaguchi-Shinozaki and Shinozaki, 2006). Several studies have shown that AREB/ABF proteins are phosphorylated in multiple conserved RxxS/T regions, and this phosphorylation is necessary for their activation (Furihata et al., 2006; Kagaya et al., 2002; Uno et al., 2000). Substitution of the five serine/threonine residues in the putative phosphorylation sites by aspartic acid mimicked constitutive activation, and plants over-expressing the resulting dominant active form of AREB1/ABF2 activated ABA-responsive gene expression under non-stressed conditions (Furihata et al., 2006). AREB/ABFs co-localized and interacted with SnRK2.2, SnRK2.3 and SnRK2.6 in plant cell nuclei (Fujita et al., 2009; Yoshida et al., 2010). Furihata et al. (Furihata et al., 2006) showed that SnRK2s can phosphorylate AREB/ABF polypeptides in vitro. Also, a large part of ABA-activated protein kinase activities were eliminated in the *snrk2.2/snrk2.3/snrk2.6* triple mutant, and the expression of examined ABA-induced genes was completely blocked (Fujii and Zhu, 2009; Umezawa et al., 2010). In a recent study, a substantial number of ABA-responsive AREB/ABF target genes showed reduced expression levels in a *snrk2.2/snrk2.3/snrk2.6* triple mutant in response to ABA (Fujita et al., 2009). Together, these results indicate that the SnRK2s regulate AREB/ABFs in ABA signaling.

2.3.2. ABA induces stomatal closure in guard cells

Light induces stomatal ostiole opening, while ABA and elevated CO_2 levels promote closure (Kim et al., 2010; Mäser et al., 2003; Wasilewska et al., 2008). This aperture regulation is under the control of guard cell turgor. Closing stimuli, including ABA, were shown to inhibit the uptake cellular machinery and trigger ion and water efflux. Those fluxes are under the control of channel transporters.

Rapid production of ROS is one of the early detectable events following ABA perception (Kwak et al., 2003; Pei et al., 2000). Genetic studies suggest a role of NADPH oxidases as key regulators of ROS production in ABA signaling (Kwak et al., 2003). The ABA-activated SnRK2.3/OST1 protein kinase was shown to directly interact with and phosphorylate the RBOHF NADPH oxidase at Ser13 and Ser174 (Sirichandra et al., 2009), which is consistent with the findings that NADPH oxidases function in early ABA-mediated ROS signaling (Kim et al., 2010; Kwak et al., 2003). ROS act as a second messenger in activating Ca^{2+}-permeable channels and thus stimulate Ca^{2+} release from internal stores and influx across the plasma membrane (Cho et al., 2009; Hamilton et al., 2000; Köhler et al., 2003; Kwak et al., 2003; Pei et al., 2000; Zhang et al., 2001). Other second messengers regulating ABA signaling include nitric oxide (NO), phosphatidic acid (PA), phosphatidyl-inositol-3-phosphate (PIP3), inositol-3-phosphate (IP3), inositol-6-phosphate (IP6), and sphingolipids (Garcia-Mata et al., 2003; Jung et al., 2002; Kim et al., 2010; Park et al., 2003).

Elevated cytosolic Ca^{2+} levels activate two types of anion channels that mediate anion release from guard cells; slow-acting sustained (S-type) or rapid transient (R-type) anion channels (Roelfsema et al., 2004; Schroeder and Keller, 1992; Schroeder et al., 2001a). It was proposed that the S-type, and not the R-type, channel is responsible for ABA-mediated stomatal closure (Joshi-Saha et al., 2011). Two independent studies reported SLOW ANION CHANNEL-ASSOCIATED 1 (*SLAC1*) as the most likely S-type anion channel that triggers membrane depolarization required for stomatal closure (Negi et al., 2008; Vahisalu et al., 2008). SLAC1 is phosphorylated by OST1 at both the N- and C-terminal cytosolic tails, which may alter its gating properties, although the precise mechanism is not clear (Geiger et al., 2009; Lee et al., 2009). The membrane depolarization caused by anion efflux via ion channels activates outward-rectifying K^+ (K^+_{out}) channels and results in K^+ efflux from guard cells (Schroeder et al., 2001a). The sustained efflux of both anions and K^+ from guard cells drives water efflux and contributes to the loss of guard cell turgor, leading to stomatal closure (Fan et al., 2004; Mäser et al., 2003; Schroeder et al., 2001a).

ABA also inhibits ion uptake, which is required to initiate hyperpolarization of guard cell plasma membranes to induce stomatal opening (Schroeder et al., 2001a). Ion uptake requires the activation of plasma membrane H^+-ATPases (Kim et al., 2010). Genetic evidence for the role of H^+-ATPases in stomatal movements comes from the isolation of two dominant alleles of the Arabidopsis H^+ ATPase 1/OPEN STOMATA 2 (AHA1/OST2). The dominant *ost2-1* and *ost2-2* mutants produce constitutively active H^+-ATPases, persistent stomatal opening, and thus ABA insensitivity (Kim et al., 2010; Merlot et al., 2002). The defect found in stomatal closure in the dominant *ost2* correlates with ABA-inhibition of H^+-ATPases (Kim et al., 2010; Shimazaki et al., 1986). It was also shown that SnRK2.3 inhibited K^+-inward rectifying channel (KAT1) activity in an ABA-mediated manner to promote stomatal closure (Sato et al., 2009).

3. MAPK cascades and signal transduction

MAPKs constitute one of the most studied signaling mechanisms in plants, comprising a class of proteins that plays an essential role in linking perception of stimuli with several cellular and adaptive responses. The MAPK signal transduction pathways are evolutionarily

Please cite this article as: Danquah A, et al, The role of ABA and MAPK signaling pathways in plant abiotic stress responses, Biotechnol Adv (2013), http://dx.doi.org/10.1016/j.biotechadv.2013.09.006

conserved in all eukaryotic organisms, and have been found in plants, yeast, fungi, insects, nematodes and mammals (Hamel et al., 2012; Kelkar et al., 2000). A MAPK cascade is minimally composed of distinct combinations of at least three protein kinases: a MAPKKK (MAP3K/MEKK/MKKK), a MAPKK (MKK/MEK), and a MAPK (MPK) which activate each other in a sequential manner via phosphorylation (Fig. 2) (Colcombet and Hirt, 2008; Ichimura et al., 2002). An activated MAPKKK first phosphorylates two serine and/or threonine residues (S/T-X_{3-5}-S/T) located within the activation loop of the MAPKK. Activated MAPKKs in turn trigger MAPK activation through dual phosphorylation of a highly conserved T-X-Y motif in the activation loop (Hamel et al., 2012). The sequential activation of the MAPK cascade results in the phosphorylation of specific targets and the modulation of activity of transcription factors, phospholipases, cytoskeletal proteins, microtubule-associated proteins and the expression of specific sets of genes in response to environmental stimuli (Neill et al., 2002; Popescu et al., 2009; Taj et al., 2010). A fourth level of kinases, named MAP4Ks (MAP3K kinases), may act as adaptors linking upstream signaling steps to the core MAPK cascades (Colcombet and Hirt, 2008). Available data have shown that MAPKs are involved in plant signal transduction in response to pathogens, drought, salinity, cold, wounding, ozone, ROS, and hormone stimuli (Berriri et al., 2012; Gao et al., 2008; Jonak et al., 2002; Lu et al., 2002; Mittler, 2002; Moon et al., 2003; Samuel and Ellis, 2002; Tena et al., 2001; Xiong and Yang, 2003; Zhang and Klessig, 2001).

3.1. The MAPK family in Arabidopsis

Sequence and functional analyses of the Arabidopsis genome have revealed that there are 20 MAPKs, 10 MAPKKs and 80 MAPKKKs, with a similar repertoire of genes observed in other plant genomes (Colcombet and Hirt, 2008; Hamel et al., 2006; Ichimura et al., 2002). Based on structural motifs and sequence similarities, Arabidopsis MAPKs can be divided into four groups (A–D). Except for members of the most distant D group, which carry a T-D-Y phosphorylation motif, all other MAPKs (A, B and C groups) are activated in the T-E-Y motif (Ichimura et al., 2002). The best studied MAPKs, MPK3, MPK4 and MPK6 have been implicated in plant innate immunity (Asai et al., 2002; Droillard et al., 2004; Petersen et al., 2000), cytokinesis and microtubule organization (Beck et al., 2010, 2011; Kosetsu et al., 2010; Zeng et al., 2011), epidermal patterning (Wang et al., 2007), ovule development (Wang et al., 2008), and also activation by abiotic stresses and ABA (Ahlfors et al., 2004; Droillard et al., 2002, 2004; Gudesblat et al., 2007; Ichimura et al., 2000; Teige et al., 2004). MPK7 and MPK11 also appear to play a role in innate immunity (Bethke et al., 2012; Doczi et al., 2007; Eschen-Lippold et al., 2012). The functions of the other MAPKs are less well understood, but several appear to also function in abiotic stress signaling and ABA (see below).

Arabidopsis MAPKKs can similarly be divided into four groups (A–D). Plant MAPKKs usually carry five amino acids separating the Ser/Thr residues (S/TxxxxxS/T), which distinguish them from mammalian MAPKKs (that bear the consensus sequence S/TxxxS/T in the activation loop) (Ichimura et al., 2002). Two members of group A, MKK1 and MKK2, have been shown to function upstream of MPK4/MPK6 in stress response (Gao et al., 2008; Ichimura et al., 2006; Meszaros et al., 2006; Nakagami et al., 2006; Qiu et al., 2008; Suarez-Rodriguez et al., 2007). MKK4/MKK5 of group C function upstream of MPK3/MPK6 in positively regulating PAMP responses and some important developmental processes (Asai et al., 2002; Bush and Krysan, 2007; Kovtun et al., 2000; Ren et al., 2002; Wang et al., 2007). Other MAPKKs that have been analyzed include MKK3, MKK6, MKK7 and MKK9 (Beck et al., 2010, 2011; Dai et al., 2006; Kosetsu et al., 2010; Melikant et al., 2004; Takahashi et al., 2007, 2010, 2011; Yoo et al., 2008; Zhang et al., 2007a). MKK3 is the only member of Group B, and has an unusual C-terminal extension

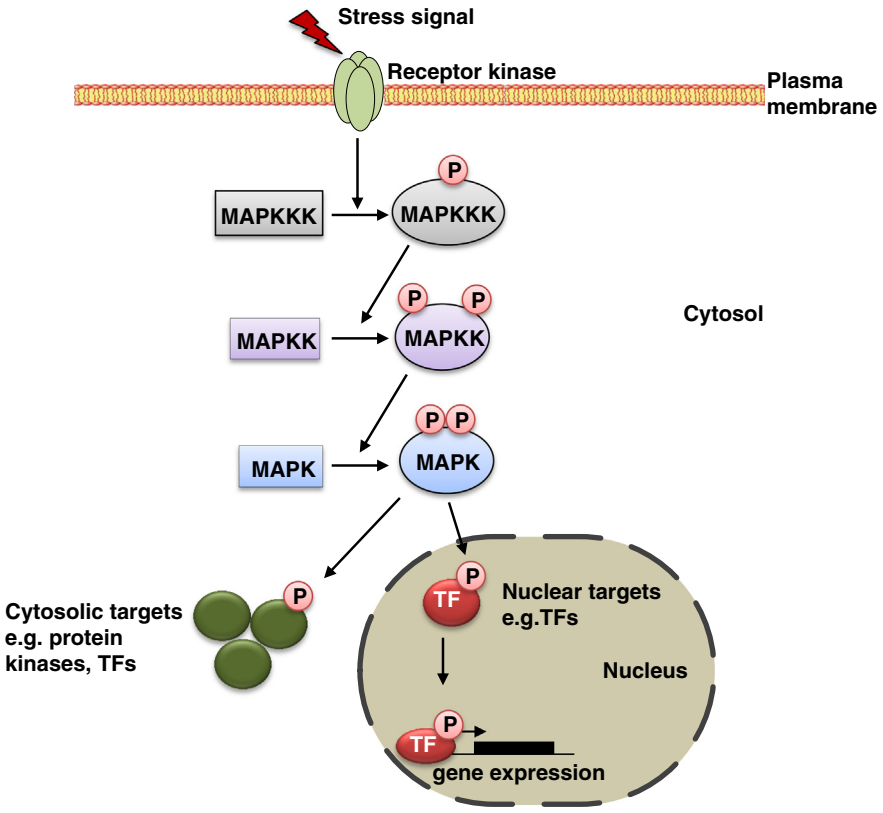

Fig. 2. A typical MAPK cascade. The MAPK cascades are generally organized as modular pathways in which the activation of upstream MAPKKKs leads to the sequential phosphorylation and subsequent activation of downstream MAPKKs and MAPKs. Through their kinase activity, MAPK cascades translate incoming environmental cues into post-translational modifications of target proteins, e.g., transcription factors, to ultimately reorganize gene expression and stress adaptation.

Please cite this article as: Danquah A, et al, The role of ABA and MAPK signaling pathways in plant abiotic stress responses, Biotechnol Adv (2013), http://dx.doi.org/10.1016/j.biotechadv.2013.09.006

ARTICLE IN PRESS

encoding a nuclear transfer factor (NTF2) domain (Hamel et al., 2006; Ichimura et al., 2002). MKK3 was implicated in jasmonic acid (JA)-mediated developmental responses and pathogen defense (Doczi et al., 2007; Takahashi et al., 2007). Recently, Takahashi et al. (2011) reported a possible role of MKK3 in ROS homeostasis in Arabidopsis.

Compared with our current knowledge on the MAPKs and MAPKKs, much less is known on the function of the much larger and heterogeneous family of MAPKKKs. Arabidopsis MAPKKKs can be divided into three main classes: MEKK-like, Raf-like and ZIK-like. To date, no evidence exists that proves Raf-like and ZIK-like kinases to encode functional MAPKKKs in plants (Colcombet and Hirt, 2008). The two best-characterized Raf-like kinases, CONSTITUTIVE TRIPLE RESPONSE 1 (CTR1) and ENHANCED DISEASE RESISTANCE 1 (EDR1), were shown to participate in ethylene-mediated signaling and defense responses (Frye and Innes, 1998; Frye et al., 2001; Huang et al., 2003; Kieber et al., 1993). Nonetheless, neither CTR1 nor EDR1 have been confirmed to participate in a canonical MAPK cascade, and thus the biochemical functions of these proteins remain uncertain (Rodriguez et al., 2010).

The MEKK-like class of MAPKKKs consists of 20 members that can further be divided into 6 subgroups A1–A6. Currently, only members of subgroups A1–A4 have been functionally characterized to some extent. Subgroup A1 comprises four proteins (MEKK1–MEKK4). MEKK1, the best-studied Arabidopsis MAPKKK, is involved in plant innate immunity (Asai et al., 2002; Gao et al., 2008; Rodriguez et al., 2010), salt and cold stress responses (Teige et al., 2004). Recently, MEKK1 was shown to negatively regulate its closest homologue, MEKK2, whose activation triggers the R protein SUMM2 (suppressor of *mkk1 mkk2*)-mediated immune responses (Kong et al., 2012). Interestingly, MEKK1, MEKK2 and MEKK3 form a tandemly arranged gene locus. Recently, it was shown that deletion of MEKK2 and MEKK3 together reverts the phenotype of mutants of the MPK4 pathway. Moreover, activated MPK4 appears to be responsible for regulating MEKK2 RNA abundance levels, an increase of which triggers defense response activation (Su et al., 2013). Therefore, the MPK4 pathway constitutes a cellular surveillance mechanism to decide between growth and cell death. The functions of MEKK3 and MEKK4 still remain unknown. Subgroup A2 consists of three proteins MAPKKKα, MAPKKKγ and YODA. The functions of MAPKKKα and MAPKKKγ remain to be determined. YODA, however, was shown to function upstream of MKK4/MKK5-MPK3/MPK6 in the regulation of embryonic cell fate and stomatal patterning (Bergmann et al., 2004; Bush and Krysan, 2007; Lukowitz et al., 2004; Wang et al., 2007). Members of subgroup A3 have been implicated in cytokinesis (Krysan et al., 2002). MAPKKKε1 and MAPKKKε2 are members of subgroup A4, which are also involved in cell division (Jouannic et al., 2001) and pollen development (Chaiwongsar et al., 2012). To date, the biological and molecular functions of the members of subgroup A5 and A6 remain unknown.

3.2. The role of MAPK pathways in abiotic stress signaling

In Arabidopsis, the most complete MAPK cascade functioning in abiotic stresses consists of the MEKK1-MKK2-MPK4/MPK6 module (Teige et al., 2004). In a previous study, mRNA levels of *MEKK1* highly accumulated in response to various environmental stresses such as low temperature, high salinity and mechanical stresses (Mizoguchi et al., 1996). Directed yeast two hybrid analyses also showed protein–protein interactions between MEKK1 and MKK1/MKK2, between MKK1/MKK2 and MPK4, and between MEKK1 and MPK4 (Ichimura et al., 1998). Further studies by Ichimura et al. (2000) demonstrated the rapid and transient activation of MPK4 and MPK6 by low temperature, low humidity, hyper-osmolarity, touch and wounding. Using yeast functional complementation assays and reverse genetics analysis, Teige et al. (2004) showed that MKK2-MPK4/MPK6 functions downstream of MEKK1 in salt and cold stress. Additionally, MKK1 is activated by salt, drought and wounding and can phosphorylate MPK4, suggesting a role in abiotic stress signaling (Teige et al., 2004; Xing et al., 2008).

Abiotic stresses can induce the production of ROS which leads to oxidative stress (Pitzschke and Hirt, 2006). In Arabidopsis, oxidative stress by exogenous H_2O_2 can activate MPK1 and MPK2 (Ortiz-Masia et al., 2007), MPK3 and MPK6 (Kovtun et al., 2000), MPK4 (Nakagami et al., 2006) and MPK7 (Doczi et al., 2007). In protoplasts, Kovtun et al. (2000) showed the H_2O_2-dependent activation of ANP1. Overexpression of the *Nicotiana* ANP1 homolog *NPK1*, enhanced abiotic stress tolerance in transgenic tobacco (Kovtun et al., 2000) and maize (Shou et al., 2004a,b). Overexpression of *DSM1*, a Raf-Like MAPKKK in rice, increased tolerance to dehydration and oxidative stress at the seedling stage (Ning et al., 2010). Overexpression of a maize MAPK gene, *ZmMPK7*, in transgenic tobacco enhanced protection provided by the peroxidase (POX) defense systems against ROS-mediated injury during osmotic stress (Zong et al., 2009). Together, these results demonstrate important roles of MAPKs in abiotic stress signaling in plants.

3.3. The role of MAPK cascades in ABA signaling

Treating plants with ABA induces the transcriptional regulation, protein accumulation and stability, and kinase activity of several components of distinct MAPK signaling cascades in many plant species, suggesting an important function of MAPK pathways in ABA signaling. The available evidence suggests that MAPK cascades are involved in several ABA responses, including antioxidant defense, guard cell signaling and seed germination (Jammes et al., 2009; Xing et al., 2008; Zhang et al., 2010; Zong et al., 2009).

3.3.1. ABA differentially regulates expression of components of the MAPK cascades

Gene expression is often indicative of gene function. Treatment with ABA induced the transcriptional regulation of *MPK3*, *MPK5*, *MPK7*, *MPK18*, *MPK20*, *MKK9*, *MAPKKK1* (*ANP1*), *MAPKKK10* (*MEKK3*), *MAPKKK14*, *MAPKKK15*, *MAPKKK16*, *MAPKKK17*, *MAPKKK18*, *MAPKKK19*, *Raf6*, *Raf12* and *Raf35* in Arabidopsis (Menges et al., 2008; Wang et al., 2011) suggesting a possible role in ABA signaling. However, the function of most of these ABA-inducible MAPK pathway genes in ABA signaling pathway remains to be determined.

In other plant species including rice, several MAPKs have also been reported to be transcriptionally activated by ABA; *OsMAPK5* (*OsMAP1*), *OsMAPK2*, *OsMSRMK2*, *OsMSRMK3*, *OsBIMK1*, *DMS1*, *OsEDR1*, *OsMAPK44*, *OsSIPK*, *OsWJUMK1*, and *OmMKK1* (Agrawal et al., 2002, 2003; De Vleesschauwer et al., 2010; Huang et al., 2002; Jeong et al., 2006; Kim et al., 2003; Lee et al., 2008; Ning et al., 2010; Song and Goodman, 2002; Wen et al., 2002; Xiong and Yang, 2003; You et al., 2007). The ABA-inducible *OsMAPK5* was shown to act as a positive regulator in abiotic stress tolerance and as a negative regulator of PR gene expression and broad-spectrum disease resistance (Xiong and Yang, 2003). A recent study in maize has implicated *ZmMKK3* in osmotic stress and ABA responses (Zhang et al., 2012). Other MAPKs in maize induced by ABA include *ZmMPK7*, *ZmMPK17*, *ZmSIMK1*, and *ZmMPK3* (Gu et al., 2010; Pan et al., 2012; Wang et al., 2010a; Zong et al., 2009). ABA has also been shown to induce transcription of MAPK genes in other plant species: *CbMAPK3*, *CsNMAPK*, *AhMPK3*, *BnOIPK*, *BnMPK3*, *RaMPK1*, *RaMPK2*, *RsMPK2*, and *StMPK1* (Blanco et al., 2006; Ghawana et al., 2010; Kumar et al., 2009; Liu et al., 2010; Wang et al., 2010b; Xu et al., 2008; Yin et al., 2010; Zhang et al., 2006a).

3.3.2. ABA-induced activation of MAPKs

Particular members of the MAPK family in plants have been reported to be activated by ABA to perform diverse functions (Jammes et al., 2009; Lu et al., 2002; Xing et al., 2008; Zhang et al., 2006b). ABA activated several MAPK isoforms of 40–43 kDa in barley aleurone protoplasts (Knetsch et al., 1996), p38MAPK in moss (D'Souza and Johri, 2002), p46MAPK and ZmMPK5 in maize (Ding et al., 2009; Zhang et al., 2006b, 2007b). In pea, an ABA-activated MAPK (p45MAPK) was implicated in guard cell signaling (Burnett et al., 2000; Schroeder et al.,

Please cite this article as: Danquah A, et al, The role of ABA and MAPK signaling pathways in plant abiotic stress responses, Biotechnol Adv (2013), http://dx.doi.org/10.1016/j.biotechadv.2013.09.006

2001b). An ABA-stimulated MAPK in rice, OsMAPK5, was shown to be involved in disease resistance and abiotic stress tolerance (Xiong and Yang, 2003). In Arabidopsis, MPK3 is activated by both H_2O_2 and ABA in seedlings, and over-expression of MPK3 increased ABA sensitivity in ABA-induced post germination arrest of growth (Lu et al., 2002). MPK4 and MPK6 are also transiently activated by ABA (Ichimura et al., 2000). Xing et al. (2008) demonstrated the ABA-dependent MKK1-mediated activation of MPK6 to regulate catalase 1 (CAT1) expression in ROS homeostasis. MPK9 and MPK12, two MAPKs that are preferentially expressed in guard cells, are also activated by ABA and have been shown to mediate ABA guard cell signaling (Xing et al., 2008). In another study, a double knockout mutant of the MAPK-interacting phosphatases, *pp2c5*/*ap2c1*, showed enhanced ABA-dependent activation of MPK3 and MPK6, resulting in ABA insensitivity, and thus suggesting that a MAPK cascade involving MPK3/MPK6 negatively regulates ABA signaling in plants (Brock et al., 2010).

Immunokinase assays showed that MPK1 and MPK2 can be activated by ABA treatment of plants (Hwa and Yang, 2008; Ortiz-Masia et al., 2007). These results are supported by an independent phosphoproteomic study in response to ABA, showing ABA-triggered phosphorylation of the activation loops of MPK1 and MPK2 (Umezawa et al., 2013).

3.3.3. MAPK-mediated ABA signaling in guard cells

ROS mediate ABA signaling in guard cells (Jammes et al., 2009; Pei et al., 2000; Zhang and Klessig, 2001). Interestingly, components of the ABA-activated MAPKs are also activated by ROS (Desikan et al., 2004; Lu et al., 2002), suggesting that ABA and ROS may converge at the MAPK level in regulating stomatal closure. Evidence of a MAPK-mediated ABA regulation of guard cell signaling came from the fact that MAPK specific inhibitors strongly impaired the ABA- or H_2O_2-mediated stomatal closure (Burnett et al., 2000; Jiang et al., 2008). In pea epidermal peels, the selective MAPKK inhibitor PD98059 significantly decreased ABA-induced stomatal closure and dehydrin gene expression (Burnett et al., 2000). Similarly, a specific inhibitor of p38 MAPK of mammals (SB203580) could block the ABA- and H_2O_2-mediated stomatal closure, ABA-induced H_2O_2 generation and decreased the K^+ flux across plasma membrane in *V. faba* (Jiang et al., 2008). Together, these data suggested that MAPKs could function in ABA signaling. Further studies using guard cell-specific silencing of MPK3 has revealed more insight into MAPK-mediated ABA signaling in stomatal closure (Gudesblat et al., 2007). Transgenic lines with reduced MPK3 expression were impaired in ABA inhibition of stomatal opening and H_2O_2-induced stomatal closure but not ABA-induced stomatal closure. Knock-out mutants of *mkk1* and *mpk6* were similarly impaired in ABA-induced H_2O_2 production in guard cells (Xing et al., 2008).

Recently, using a cell type-specific functional genomics approach, Jammes et al. (2009) identified the MAPKs *MPK9* and *MPK12* to be preferentially expressed in guard cells. MPK12 was activated by ABA and H_2O_2. Double mutants of *mpk9*/*mpk12*, but not the single mutants of *mpk9* and *mpk12*, exhibited enhanced transpirational water loss and ABA- and H_2O_2-insensitivity in both stomatal opening and closure. These data suggest that MPK9 and MPK12 are positive regulators of ABA signaling in guard cells (Fig. 3). Interestingly, recent evidence indicates that two independent MAPK pathways mediate ABA and pathogen signals in guard cells. Whereas MPK9 and MPK12 were found to mediate ABA signaling, pathogen signals were revealed to be mediated by MPK3 and MPK6 (Montillet et al., 2013). Although ROS produced by the NADPH oxidases RBOHD and RBOHF seems to be involved in both pathways, RBOHD only mediates pathogen and RBOHF only ABA signals (Mersmann et al., 2010). How guard cells can differentiate between ROS generated by the different RBOHs and couple to distinct MAPK pathways is presently unclear. Nonetheless, pathogen and ABA guard cell signaling pathways converge again at the level of the activation of the SLAC 1 anion channel (Montillet et al., 2013). Taken together, it appears that the closure/opening machinery of stomates is regulated by at least two pathways that both use distinct sets of MAPKs (Montillet and Hirt, in press). Neither the upstream MAPKKKs, MAPKKs nor the downstream targets of the MAPKs of the pathogen and ABA pathways have been unraveled yet but their identification should help to understand the underlying regulatory mechanisms of guard cell movement.

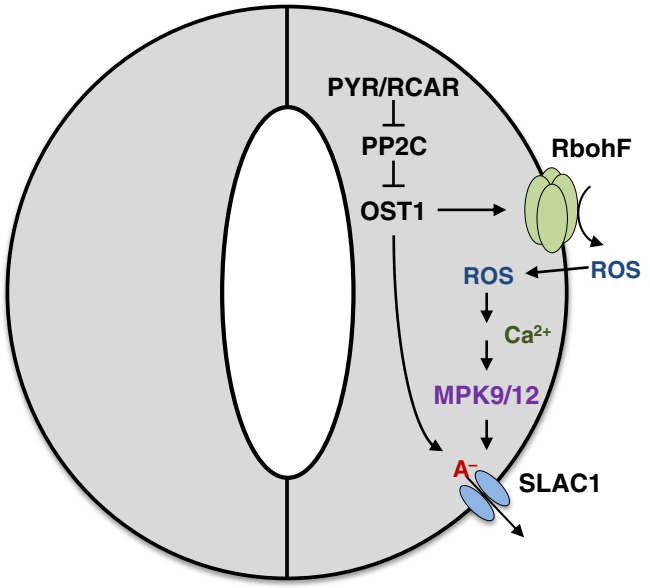

Fig. 3. MAP kinases are involved in ABA-mediated stomatal closure. Following ABA perception in guard cells, active SnRK2 kinases such as OST1 (released from inhibition by PYR/PYL/RCAR-mediated sequestration of PP2Cs) phosphorylate the NADPH oxidase RbohF, leading to ROS accumulation. ROS activate two MAPKs, MPK9 and MPK12, which function positively to regulate ABA-mediated stomatal closure. The double mutant of *mpk9/12* is impaired in S-type anion channel (SLAC1) activation by both ABA and Ca^{2+}. Consistent with this result, *mpk9/12* showed enhanced transpirational water loss, indicating that MPK9 and MPK12 are positive regulators of ABA signaling in guard cells.

4. Conclusions

ABA is a central regulator of many plant responses to environmental stresses, including drought, low temperature and salinity. The molecular mechanisms of ABA synthesis, transport, and signaling have received enormous attention and are now fairly well understood. The various physiological reactions that ABA regulates, such as stomatal closure, changes in gene expression and accumulation of osmoprotectants have also been characterized at the molecular level. Emerging evidence links ABA to another set of highly conserved environmental signaling cascades, the MAPK pathways. Although most of the links between ABA and MAPKs are only poorly understood, it is evident that these pathways are part of the complex cellular signaling network of plants to integrate various environmental cues, such as pathogen challenges, nutrient status or developmental programs. Future work will unravel the details of these signaling chains, where and how the cascades interact. Considering that ABA is a key hormone in inducing abiotic stress responses, an understanding of the molecular logic of the ABA network will considerably improve our capacity to generate plants with improved stress tolerance and many academic and industrial efforts are underway to generate such crop plants without a penalty in growth or yield.

References

Abdeen A, Schnell J, Miki B. Transcriptome analysis reveals absence of unintended effects in drought-tolerant transgenic plants overexpressing the transcription factor ABF3. BMC Genomics 2010;11:69.

Agrawal GK, Rakwal R, Iwahashi H. Isolation of novel rice (*Oryza sativa* L.) multiple stress responsive MAP kinase gene, OsMSRMK2, whose mRNA accumulates rapidly in response to environmental cues. Biochem Biophys Res Commun 2002;294:1009–16.

Please cite this article as: Danquah A, et al, The role of ABA and MAPK signaling pathways in plant abiotic stress responses, Biotechnol Adv (2013), http://dx.doi.org/10.1016/j.biotechadv.2013.09.006

ARTICLE IN PRESS

Agrawal GK, Tamogami S, Iwahashi H, Agrawal VP, Rakwal R. Transient regulation of jasmonic acid-inducible rice MAP kinase gene (OsBWMK1) by diverse biotic and abiotic stresses. Plant Physiol Biochem 2003;41:355–61.

Ahlfors R, Macioszek V, Rudd J, Brosche M, Schlichting R, Scheel D, et al. Stress hormone-independent activation and nuclear translocation of mitogen-activated protein kinases in Arabidopsis thaliana during ozone exposure. Plant J 2004;40:512–22.

Anderson BE, Ward JM, Schroeder JI. Evidence for an extracellular reception site for abscisic acid in Commelina guard cells. Plant Physiol 1994;104:1177–83.

Antoni R, Gonzalez-Guzman M, Rodriguez L, Rodrigues A, Pizzio GA, Rodriguez PL. Selective inhibition of clade A phosphatases type 2C by PYR/PYL/RCAR abscisic acid receptors. Plant Physiol 2012;158:970–80.

Asai T, Tena G, Plotnikova J, Willmann MR, Chiu WL, Gomez-Gomez L, et al. MAP kinase signalling cascade in Arabidopsis innate immunity. Nature 2002;415:977–83.

Beck M, Komis G, Muller J, Menzel D, Samaj J. Arabidopsis homologs of nucleus- and phragmoplast-localized kinase 2 and 3 and mitogen-activated protein kinase 4 are essential for microtubule organization. Plant Cell 2010;22:755–71.

Beck M, Komis G, Ziemann A, Menzel D, Samaj J. Mitogen-activated protein kinase 4 is involved in the regulation of mitotic and cytokinetic microtubule transitions in Arabidopsis thaliana. New Phytol 2011;189:1069–83.

Bensmihen S, Rippa S, Lambert G, Jublot D, Pautot V, Granier F, et al. The homologous ABI5 and EEL transcription factors function antagonistically to fine-tune gene expression during late embryogenesis. Plant Cell 2002;14:1391–403.

Bergmann DC, Lukowitz W, Somerville CR. Stomatal development and pattern controlled by a MAPKK kinase. Science 2004;304:1494–7.

Berriri S, Garcia AV, Dit Frey NF, Rozhon W, Pateyron S, Leonhardt N, et al. Constitutively active mitogen-activated protein kinase versions reveal functions of Arabidopsis MPK4 in pathogen defense signaling. Plant Cell 2012;24:4281–93.

Bethke G, Pecher P, Eschen-Lippold L, Tsuda K, Katagiri F, Glazebrook J, et al. Activation of the Arabidopsis thaliana mitogen-activated protein kinase MPK11 by the flagellin-derived elicitor peptide, flg22. Mol Plant Microbe Interact 2012;25:471–80.

Blanco FA, Zanetti ME, Casalongue CA, Daleo GR. Molecular characterization of a potato MAP kinase transcriptionally regulated by multiple environmental stresses. Plant Physiol Biochem 2006;44:315–22.

Boudsocq M, Lauriere C. Osmotic signaling in plants: multiple pathways mediated by emerging kinase families. Plant Physiol 2005;138:1185–94.

Boudsocq M, Barbier-Brygoo H, Lauriere C. Identification of nine sucrose nonfermenting 1-related protein kinases 2 activated by hyperosmotic and saline stresses in Arabidopsis thaliana. J Biol Chem 2004;279:41758–66.

Boudsocq M, Droillard MJ, Barbier-Brygoo H, Lauriere C. Different phosphorylation mechanisms are involved in the activation of sucrose non-fermenting 1 related protein kinases 2 by osmotic stresses and abscisic acid. Plant Mol Biol 2007;63:491–503.

Boyer JS. Plant productivity and environment. Science 1982;218:443–8.

Bray EA, Bailey-Serres J, Weretilnyk E. Responses to abiotic stresses. In: Buchannan BB, Gruissem W, Jones RL, editors. Biochemistry and molecular biology of plants. Rockville, MD: ASPB; 2000. p. 1158–249.

Brock AK, Willmann R, Kolb D, Grefen L, Lajunen HM, Bethke G, et al. The Arabidopsis mitogen-activated protein kinase phosphatase PP2C5 affects seed germination, stomatal aperture, and abscisic acid-inducible gene expression. Plant Physiol 2010;153:1098–111.

Burnett EC, Desikan R, Moser RC, Neill SJ. ABA activation of an MBP kinase in *Pisum sativum* epidermal peels correlates with stomatal responses to ABA. J Exp Bot 2000;51:197–205.

Burza AM, Pekala I, Sikora J, Siedlecki P, Malagocki P, Bucholc M, et al. Nicotiana tabacum osmotic stress-activated kinase is regulated by phosphorylation on Ser-154 and Ser-158 in the kinase activation loop. J Biol Chem 2006;281:34299–311.

Bush SM, Krysan PJ. Mutational evidence that the Arabidopsis MAP kinase MPK6 is involved in anther, inflorescence, and embryo development. J Exp Bot 2007;58:2181–91.

Chaiwongsar S, Strohm AK, Su SH, Krysan PJ. Genetic analysis of the Arabidopsis protein kinases MAP3Kepsilon1 and MAP3Kepsilon2 indicates roles in cell expansion and embryo development. Front Plant Sci 2012;3:228.

Chen J-G, Gao Y, Jones AM. Differential roles of Arabidopsis heterotrimeric G-protein subunits in modulating cell division in roots. Plant Physiol 2006;141:887–97.

Cho D, Kim SA, Murata Y, Lee S, Jae SK, Nam HG, et al. De-regulated expression of the plant glutamate receptor homolog AtGLR3.1 impairs long-term Ca^{2+}-programmed stomatal closure. Plant J 2009;58:437–49.

Choi H, Hong J, Ha J, Kang J, Kim SY. ABFs, a family of ABA-responsive element binding factors. J Biol Chem 2000;275:1723–30.

Colcombet J, Hirt H. Arabidopsis MAPKs: a complex signalling network involved in multiple biological processes. Biochem J 2008;413:217–26.

Correa LG, Riano-Pachon DM, Schrago CG, dos Santos RV, Mueller-Roeber B, Vincentz M. The role of bZIP transcription factors in green plant evolution: adaptive features emerging from four founder genes. PLoS One 2008;3:e2944.

Cutler AJ, Krochko JE. Formation and breakdown of ABA. Trends Plant Sci 1999;4:472–8.

Cutler SR, Rodriguez PL, Finkelstein RR, Abrams SR. Abscisic acid: emergence of a core signaling network. Annu Rev Plant Biol 2010;61:651–79.

D'Souza JS, Johri MM. ABA and NaCl activate myelin basic protein kinase in the chloronema cells of the moss *Funaria hygrometrica*. Plant Physiol Biochem 2002;40:17–24.

Dai Y, Wang H, Li B, Huang J, Liu X, Zhou Y, et al. Increased expression of MAP KINASE KINASE7 causes deficiency in polar auxin transport and leads to plant architectural abnormality in Arabidopsis. Plant Cell 2006;18:308–20.

De Vleesschauwer D, Yang Y, Cruz CV, Hofte M. Abscisic acid-induced resistance against the brown spot pathogen *Cochliobolus miyabeanus* in rice involves MAP kinase-mediated repression of ethylene signaling. Plant Physiol 2010;152:2036–52.

Desikan R, Cheung M, Bright J, Henson D, Hancock J, Neill S. ABA, hydrogen peroxide and nitric oxide signalling in stomatal guard cells. J Exp Bot 2004;55:205–12.

Dhariwal HS, Kwai M, Uchimiya H. Genetic engineering for abiotic stress tolerance in plants. Plant Biotechnol 1998;15:1–10.

Dietz KJ, Sauter A, Wichert K, Messdaghi D, Hartung W. Extracellular beta-glucosidase activity in barley involved in the hydrolysis of ABA glucose conjugate in leaves. J Exp Bot 2000;51:937–44.

Ding H, Zhang A, Wang J, Lu R, Zhang H, Zhang J, et al. Identity of an ABA-activated 46 kDa mitogen-activated protein kinase from *Zea mays* leaves: partial purification, identification and characterization. Planta 2009;230:239–51.

Doczi R, Brader G, Pettko-Szandtner A, Rajh I, Djamei A, Pitzschke A, et al. The Arabidopsis mitogen-activated protein kinase kinase MKK3 is upstream of group C mitogen-activated protein kinases and participates in pathogen signaling. Plant Cell 2007;19:3266–79.

Droillard M, Boudsocq M, Barbier-Brygoo H, Lauriere C. Different protein kinase families are activated by osmotic stresses in *Arabidopsis thaliana* cell suspensions. Involvement of the MAP kinases AtMPK3 and AtMPK6. FEBS Lett 2002;527:43–50.

Droillard MJ, Boudsocq M, Barbier-Brygoo H, Lauriere C. Involvement of MPK4 in osmotic stress response pathways in cell suspensions and plantlets of Arabidopsis thaliana: activation by hypoosmolarity and negative role in hyperosmolarity tolerance. FEBS Lett 2004;574:42–8.

Eschen-Lippold L, Bethke G, Palm-Forster MA, Pecher P, Bauer N, Glazebrook J, et al. MPK11 — a fourth elicitor-responsive mitogen-activated protein kinase in Arabidopsis thaliana. Plant Signal Behav 2012;7:1203–5.

Fan LM, Zhao Z, Assmann SM. Guard cells: a dynamic signaling model. Curr Opin Plant Biol 2004;7:537–46.

Finkelstein RR. Mutations at two new Arabidopsis ABA response loci are similar to the abi3 mutations. Plant J 1994;5:765–71.

Finkelstein RR, Somerville CR. Three classes of Abscisic Acid (ABA)-insensitive mutations of Arabidopsis define genes that control overlapping subsets of ABA responses. Plant Physiol 1990;94:1172–9.

Finkelstein RR, Gampala SSL, Rock CD. Abscisic acid signaling in seeds and seedlings. The Plant Cell Online 2002;14:S15–45.

Finkelstein R, Reeves W, Ariizumi T, Steber C. Molecular aspects of seed dormancy. Annu Rev Plant Biol 2008;59:387–415.

Frye CA, Innes RW. An Arabidopsis mutant with enhanced resistance to powdery mildew. Plant Cell 1998;10:947–56.

Frye CA, Tang D, Innes RW. Negative regulation of defense responses in plants by a conserved MAPKK kinase. Proc Natl Acad Sci U S A 2001;98:373–8.

Fujii H, Zhu J-K. Arabidopsis mutant deficient in 3 abscisic acid-activated protein kinases reveals critical roles in growth, reproduction, and stress. Proc Natl Acad Sci U S A 2009;106:8380–5.

Fujii H, Chinnusamy V, Rodrigues A, Rubio S, Antoni R, Park S-Y, et al. In vitro reconstitution of an abscisic acid signalling pathway. Nature 2009;462:660–4.

Fujita Y, Fujita M, Satoh R, Maruyama K, Parvez MM, Seki M, et al. AREB1 is a transcription activator of novel ABRE-dependent ABA signaling that enhances drought stress tolerance in Arabidopsis. The Plant Cell Online 2005;17:3470–88.

Fujita Y, Nakashima K, Yoshida T, Katagiri T, Kidokoro S, Kanamori N, et al. Three SnRK2 protein kinases are the main positive regulators of abscisic acid signaling in response to water stress in Arabidopsis. Plant Cell Physiol 2009;50:2123–32.

Furihata T, Maruyama K, Fujita Y, Umezawa T, Yoshida R, Shinozaki K, et al. Abscisic acid-dependent multisite phosphorylation regulates the activity of a transcription activator AREB1. Proc Natl Acad Sci U S A 2006;103:1988–93.

Gao M, Liu J, Bi D, Zhang Z, Cheng F, Chen S, et al. MEKK1, MKK1/MKK2 and MPK4 function together in a mitogen-activated protein kinase cascade to regulate innate immunity in plants. Cell Res 2008;18:1190–8.

Garcia-Mata C, Gay R, Sokolovski S, Hills A, Lamattina L, Blatt MR. Nitric oxide regulates K^+ and Cl^- channels in guard cells through a subset of abscisic acid-evoked signaling pathways. Proc Natl Acad Sci U S A 2003;100:11116–21.

Geiger D, Scherzer S, Mumm P, Stange A, Marten I, Bauer H, et al. Activity of guard cell anion channel SLAC1 is controlled by drought-stress signaling kinase-phosphatase pair. Proc Natl Acad Sci U S A 2009;106:21425–30.

Ghawana S, Kumar S, Ahuja PS. Early low-temperature responsive mitogen activated protein kinases RaMPK1 and RaMPK2 from *Rheum australe* D. Don respond differentially to diverse stresses. Mol Biol Rep 2010;37:933–8.

Gillard DF, Walton DC. Abscisic acid metabolism by a cell-free preparation from *Echinocystis lobata* liquid endoserum. Plant Physiol 1976;58:790–5.

Gilroy S, Jones RL. Perception of gibberellin and abscisic acid at the external face of the plasma membrane of barley (*Hordeum vulgare* L.) aleurone protoplasts. Plant Physiol 1994;104:1185–92.

Giraudat J, Parcy F, Bertauche N, Gosti F, Leung J, Morris PC, et al. Current advances in abscisic acid action and signalling. Plant Mol Biol 1994;26:1557–77.

Gomez-Cadenas A, Verhey SD, Holappa LD, Shen Q, Ho T-HD, Walker-Simmons MK. An abscisic acid-induced protein kinase, PKABA1, mediates abscisic acid-suppressed gene expression in barley aleurone layers. Proc Natl Acad Sci U S A 1999;96:1767–72.

Gomez-Porras JL, Riano-Pachon DM, Dreyer I, Mayer JE, Mueller-Roeber B. Genome-wide analysis of ABA-responsive elements ABRE and CE3 reveals divergent patterns in Arabidopsis and rice. BMC Genomics 2007;8:260.

Gonzalez-Guzman M, Pizzio GA, Antoni R, Vera-Sirera F, Merilo E, Bassel GW, et al. Arabidopsis PYR/PYL/RCAR receptors play a major role in quantitative regulation of stomatal aperture and transcriptional response to abscisic acid. Plant Cell 2012;24:2483–96.

Gosti F, Beaudoin N, Serizet C, Webb AAR, Vartanian N, Giraudat J. ABI1 protein phosphatase 2C is a negative regulator of abscisic acid signaling. Plant Cell 1999;11:1897–909.

Gu L, Liu Y, Zong X, Liu L, Li DP, Li DQ. Overexpression of maize mitogen-activated protein kinase gene, ZmSIMK1 in Arabidopsis increases tolerance to salt stress. Mol Biol Rep 2010;37:4067–73.

Please cite this article as: Danquah A, et al, The role of ABA and MAPK signaling pathways in plant abiotic stress responses, Biotechnol Adv (2013), http://dx.doi.org/10.1016/j.biotechadv.2013.09.006

ARTICLE IN PRESS

Gudesblat GE, Iusem ND, Morris PC. Guard cell-specific inhibition of Arabidopsis MPK3 expression causes abnormal stomatal responses to abscisic acid and hydrogen peroxide. New Phytol 2007;173:713–21.

Hamel LP, Nicole MC, Sritubtim S, Morency MJ, Ellis M, Ehlting J, et al. Ancient signals: comparative genomics of plant MAPK and MAPKK gene families. Trends Plant Sci 2006;11:192–8.

Hamel LP, Nicole MC, Duplessis S, Ellis BE. Mitogen-activated protein kinase signaling in plant-interacting fungi: distinct messages from conserved messengers. Plant Cell 2012;24:1327–51.

Hamilton DWA, Hills A, Köhler B, Blatt MR. Ca2+ channels at the plasma membrane of stomatal guard cells are activated by hyperpolarization and abscisic acid. Proc Natl Acad Sci U S A 2000;97:4967–72.

Hampson CR, Reaney MJT, Abrams GD, Abrams SR, Gusta LV. Metabolism of (+)-abscisic acid to (+)-7′-hydroxyabscisic acid by bromegrass cell cultures. Phytochemistry 1992;31:2645–8.

Hartung W. The site of action of abscisic acid at the guard cell plasmalemma of *Valerianella locusta*. Plant Cell Environ 1983;6:427–8.

Hauser F, Waadt R, Schroeder JI. Evolution of abscisic acid synthesis and signaling mechanisms. Curr Biol 2011;21:R346–55.

Hetherington AM. Guard cell signaling. Cell 2001;107:711–4.

Hirayama T, Shinozaki K. Perception and transduction of abscisic acid signals: keys to the function of the versatile plant hormone ABA. Trends Plant Sci 2007;12:343–51.

Hoth S, Morgante M, Sanchez JP, Hanafey MK, Tingey SV, Chua NH. Genome-wide gene expression profiling in Arabidopsis thaliana reveals new targets of abscisic acid and largely impaired gene regulation in the abi1-1 mutant. J Cell Sci 2002;115:4891–900.

Hrabak EM, Chan CW, Gribskov M, Harper JF, Choi JH, Halford N, et al. The Arabidopsis CDPK-SnRK superfamily of protein kinases. Plant Physiol 2003;132:666–80.

Huang HJ, Fu SF, Tai YH, Chou WC, Huang DD. Expression of Oryza sativa MAP kinase gene is developmentally regulated and stress-responsive. Physiol Plant 2002;114:572–80.

Huang Y, Li H, Hutchison CE, Laskey J, Kieber JJ. Biochemical and functional analysis of CTR1, a protein kinase that negatively regulates ethylene signaling in Arabidopsis. Plant J 2003;33:221–33.

Hubbard KE, Nishimura N, Hitomi K, Getzoff ED, Schroeder JI. Early abscisic acid signal transduction mechanisms: newly discovered components and newly emerging questions. Genes Dev 2010;24:1695–708.

Hwa C-M, Yang X-C. The AtMKK3 pathway mediates ABA and salt signaling in Arabidopsis. Acta Physiol Plant 2008;30:277–86.

Ichimura K, Mizoguchi T, Irie K, Morris P, Giraudat J, Matsumoto K, et al. Isolation of ATMEKK1 (a MAP kinase kinase kinase)-interacting proteins and analysis of a MAP kinase cascade in Arabidopsis. Biochem Biophys Res Commun 1998;253:532–43.

Ichimura K, Mizoguchi T, Yoshida R, Yuasa T, Shinozaki K. Various abiotic stresses rapidly activate Arabidopsis MAP kinases ATMPK4 and ATMPK6. Plant J 2000;24:655–65.

Ichimura K, Shinozaki K, Tena G, Sheen J, Henry Y, Champion A, et al. Mitogen-activated protein kinase cascades in plants: a new nomenclature. Tends Plant Sci 2002;7:301–8.

Ichimura K, Casais C, Peck SC, Shinozaki K, Shirasu K. MEKK1 is required for MPK4 activation and regulates tissue-specific and temperature-dependent cell death in Arabidopsis. J Biol Chem 2006;281:36969–76.

Jakoby M, Weisshaar B, Droge-Laser W, Vicente-Carbajosa J, Tiedemann J, Kroj T, et al. bZIP transcription factors in Arabidopsis. Trends Plant Sci 2002;7:106–11.

Jammes F, Song C, Shin D, Munemasa S, Takeda K, Gu D, et al. MAP kinases MPK9 and MPK12 are preferentially expressed in guard cells and positively regulate ROS-mediated ABA signaling. Proc Natl Acad Sci U S A 2009;106:20520–5.

Jeong M-J, Lee S-K, Kim B-G, Kwon T-R, Cho W-S, Park Y-T, et al. A rice (*Oryza sativa* L.) MAP kinase gene, OsMAPK44, is involved in response to abiotic stresses. Plant Cell Tissue Organ Cult 2006;85:151–60.

Jiang F, Hartung W. Long-distance signalling of abscisic acid (ABA): the factors regulating the intensity of the ABA signal. J Exp Bot 2008;59:37–43.

Jiang J, Wang P, An G, Wang P, Song CP. The involvement of a P38-like MAP kinase in ABA-induced and H_2O_2-mediated stomatal closure in *Vicia faba* L. Plant Cell Rep 2008;27:377–85.

Jonak C, Okresz L, Bogre L, Hirt H. Complexity, cross talk and integration of plant MAP kinase signalling. Curr Opin Plant Biol 2002;5:415–24.

Joshi-Saha A, Valon C, Leung J. A brand new START: abscisic acid perception and transduction in the guard cell. Sci Signal 2011;4:re4.

Jouannic S, Champion A, Segui-Simarro JM, Salimova E, Picaud A, Tregear J, et al. The protein kinases AtMAP3Kepsilon1 and BnMAP3Kepsilon1 are functional homologues of *S. pombe* cdc7p and may be involved in cell division. Plant J 2001;26:637–49.

Jung JY, Kim YW, Kwak JM, Hwang JU, Young J, Schroeder JI, et al. Phosphatidylinositol 3- and 4-phosphate are required for normal stomatal movements. Plant Cell 2002;14:2399–412.

Kagaya Y, Hobo T, Murata M, Ban A, Hattori T. Abscisic acid-induced transcription is mediated by phosphorylation of an abscisic acid response element binding factor, TRAB1. Plant Cell 2002;14:3177–89.

Kang J-y, Choi H-i, Im M-y, Kim SY. Arabidopsis basic leucine zipper proteins that mediate stress-responsive abscisic acid signaling. The Plant Cell Online 2002;14:343–57.

Kang J, Hwang JU, Lee M, Kim YY, Assmann SM, Martinoia E, et al. PDR-type ABC transporter mediates cellular uptake of the phytohormone abscisic acid. Proc Natl Acad Sci U S A 2010;107:2355–60.

Kanno Y, Hanada A, Chiba Y, Ichikawa T, Nakazawa M, Matsui M, et al. Identification of an abscisic acid transporter by functional screening using the receptor complex as a sensor. Proc Natl Acad Sci U S A 2012;109:9653–8.

Kelkar N, Gupta S, Dickens M, Davis RJ. Interaction of a mitogen-activated protein kinase signaling module with the neuronal protein JIP3. Mol Cell Biol 2000;20:1030–43.

Kieber JJ, Rothenberg M, Roman G, Feldmann KA, Ecker JR. CTR1, a negative regulator of the ethylene response pathway in Arabidopsis, encodes a member of the raf family of protein kinases. Cell 1993;72:427–41.

Kim JA, Agrawal GK, Rakwal R, Han KS, Kim KN, Yun CH, et al. Molecular cloning and mRNA expression analysis of a novel rice (*Oryza sativa* L.) MAPK kinase kinase, OsEDR1, an ortholog of Arabidopsis AtEDR1, reveal its role in defense/stress signalling pathways and development. Biochem Biophys Res Commun 2003;300:868–76.

Kim S, Kang JY, Cho DI, Park JH, Kim SY. ABF2, an ABRE-binding bZIP factor, is an essential component of glucose signaling and its overexpression affects multiple stress tolerance. Plant J 2004;40:75–87.

Kim TH, Bohmer M, Hu H, Nishimura N, Schroeder JI. Guard cell signal transduction network: advances in understanding abscisic acid, CO_2, and Ca^{2+} signaling. Annu Rev Plant Biol 2010;61:561–91.

Klingler JP, Batelli G, Zhu JK. ABA receptors: the START of a new paradigm in phytohormone signalling. J Exp Bot 2010;61:3199–210.

Knetsch M, Wang M, Snaar-Jagalska BE, Heimovaara-Dijkstra S. Abscisic acid induces mitogen-activated protein kinase activation in barley aleurone protoplasts. Plant Cell 1996;8:1061–7.

Köhler B, Hills A, Blatt MR. Control of guard cell ion channels by hydrogen peroxide and abscisic acid indicates their action through alternate signaling pathways. Plant Physiol 2003;131:385–8.

Kong Q, Qu N, Gao M, Zhang Z, Ding X, Yang F, et al. The MEKK1-MKK1/MKK2-MPK4 kinase cascade negatively regulates immunity mediated by a mitogen-activated protein kinase kinase kinase in Arabidopsis. Plant Cell 2012;24:2225–36.

Koornneef M, Reuling G, Karssen CM. The isolation and characterization of abscisic acid-insensitive mutants of *Arabidopsis thaliana*. Physiol Plant 1984;61:377–83.

Kosetsu K, Matsunaga S, Nakagami H, Colcombet J, Sasabe M, Soyano T, et al. The MAP kinase MPK4 is required for cytokinesis in *Arabidopsis thaliana*. Plant Cell 2010;22:3778–90.

Koshimizu K, Inui M, Kukui H, Mitsui T. Isolation of (+)-abscisyl-ß-D-glucopyranoside from immature fruit of *Lupinus luteus*. Agric Biol Chem 1968;32:789–91.

Kovtun Y, Chiu WL, Tena G, Sheen J. Functional analysis of oxidative stress-activated mitogen-activated protein kinase cascade in plants. Proc Natl Acad Sci U S A 2000;97:2940–5.

Krysan PJ, Jester PJ, Gottwald JR, Sussman MR. An Arabidopsis mitogen-activated protein kinase kinase gene family encodes essential positive regulators of cytokinesis. Plant Cell 2002;14:1109–20.

Kuhn JM, Boisson-Dernier A, Dizon MB, Maktabi MH, Schroeder JI. The protein phosphatase AtPP2CA negatively regulates abscisic acid signal transduction in arabidopsis, and effects of abh1 on AtPP2CA mRNA. Plant Physiol 2006;140:127–39.

Kumar KR, Srinivasan T, Kirti PB. A mitogen-activated protein kinase gene, AhMPK3 of peanut: molecular cloning, genomic organization, and heterologous expression conferring resistance against *Spodoptera litura* in tobacco. Mol Genet Genomics 2009;282:65–81.

Kuromori T, Yamamoto M. Cloning of cDNAs from *Arabidopsis thaliana* that encode putative protein phosphatase 2C and a human DM-like protein by transformation of a fission yeast mutant. Nucleic Acids Res 1994;22:5296–301.

Kuromori T, Miyaji T, Yabuuchi H, Shimizu H, Sugimoto E, Kamiya A, et al. ABC transporter AtABCG25 is involved in abscisic acid transport and responses. Proc Natl Acad Sci U S A 2010;107:2361–6.

Kushiro T, Okamoto M, Nakabayashi K, Yamagishi K, Kitamura S, Asami T, et al. The Arabidopsis cytochrome P450 CYP707A encodes ABA 8′-hydroxylases: key enzymes in ABA catabolism. EMBO J. 2004;23:1647–56.

Kwak JM, Mori IC, Pei ZM, Leonhardt N, Torres MA, Dangl JL, et al. NADPH oxidase AtrbohD and AtrbohF genes function in ROS-dependent ABA signaling in Arabidopsis. EMBO J. 2003;22:2623–33.

Lammers T, Lavi S. Role of type 2C protein phosphatases in growth regulation and in cellular stress signaling. Crit Rev Biochem Mol Biol 2007;42:437–61.

Le Treut H, Somerville R, Cubasch U, Ding Y, Mauritzen C, Mokssit A, et al. Historical overview of climate change. In: Solomon S, Qin D, Manning M, Chen Z, Marquis M, Averyt KB, Tignor M, Miller HL, editors. Climate Change 2007: The physical science basis. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge and New York: Cambridge University Press; 2007. p. 96–127.

Lee KH, Piao HL, Kim HY, Choi SM, Jiang F, Hartung W, et al. Activation of glucosidase via stress-induced polymerization rapidly increases active pools of abscisic acid. Cell 2006;126:1109–20.

Lee MO, Cho K, Kim SH, Jeong SH, Kim JA, Jung YH, et al. Novel rice OsSIPK is a multiple stress responsive MAPK family member showing rhythmic expression at mRNA level. Planta 2008;227:981–90.

Lee SC, Lan W, Buchanan BB, Luan S. A protein kinase-phosphatase pair interacts with an ion channel to regulate ABA signaling in plant guard cells. Proc Natl Acad Sci U S A 2009;106:21419–24.

Leonhardt N, Kwak JM, Robert N, Waner D, Leonhardt G, Schroeder JI. Microarray expression analyses of Arabidopsis guard cells and isolation of a recessive abscisic acid hypersensitive protein phosphatase 2C mutant. Plant Cell 2004;16:596–615.

Leung J, Bouvier-Durand M, Morris PC, Guerrier D, Chefdor F, Giraudat J. Arabidopsis ABA response gene ABI1: features of a calcium-modulated protein phosphatase. Science 1994;264:1448–52.

Leung J, Merlot S, Giraudat J. The Arabidopsis ABSCISIC ACID-INSENSITIVE2 (ABI2) and ABI1 genes encode homologous protein phosphatases 2C involved in abscisic acid signal transduction. Plant Cell 1997;9:759–71.

Li J, Wang XQ, Watson MB, Assmann SM. Regulation of abscisic acid-induced stomatal closure and anion channels by guard cell AAPK kinase. Science 2000;287:300–3.

Lim E-K, Doucet CJ, Hou B, Jackson RG, Abrams SR, Bowles DJ. Resolution of (+)-abscisic acid using an Arabidopsis glycosyltransferase. Tetrahedron Asymmetry 2005;16:143–7.

Please cite this article as: Danquah A, et al, The role of ABA and MAPK signaling pathways in plant abiotic stress responses, Biotechnol Adv (2013), http://dx.doi.org/10.1016/j.biotechadv.2013.09.006

ARTICLE IN PRESS

Liu X, Yue Y, Li B, Nie Y, Li W, Wu W-H, et al. A G protein-coupled receptor is a plasma membrane receptor for the plant hormone abscisic acid. Science 2007;315:1712–6.

Liu Y, Li X, Tan H, Liu M, Zhao X, Wang J. Molecular characterization of RsMPK2, a C1 subgroup mitogen-activated protein kinase in the desert plant *Reaumuria soongorica*. Plant Physiol Biochem 2010;48:836–44.

Liu Z-Q, Yan L, Wu Z, Mei C, Lu K, Yu Y-T, et al. Cooperation of three WRKY-domain transcription factors WRKY18, WRKY40, and WRKY60 in repressing two ABA-responsive genes ABI4 and ABI5 in Arabidopsis. J Exp Bot 2012;63:6371–92.

Lopez-Molina L, Chua NH. A null mutation in a bZIP factor confers ABA-insensitivity in *Arabidopsis thaliana*. Plant Cell Physiol 2000;41:541–7.

Lu C, Han MH, Guevara-Garcia A, Fedoroff NV. Mitogen-activated protein kinase signaling in postgermination arrest of development by abscisic acid. Proc Natl Acad Sci U S A 2002;99:15812–7.

Lukowitz W, Roeder A, Parmenter D, Somerville C. A MAPKK kinase gene regulates extra-embryonic cell fate in Arabidopsis. Cell 2004;116:109–19.

Ma Y, Szostkiewicz I, Korte A, Moes D, Yang Y, Christmann A, et al. Regulators of PP2C phosphatase activity function as abscisic acid sensors. Science 2009;324:1064–8.

Mäser P, Leonhardt N, Schroeder JI. The clickable guard cell: electronically linked model of guard cell signal transduction pathways. The Arabidopsis Book; 2003. http://www-biology.ucsd.edu/labs/schroeder/clickablegc.html.

Melcher K, Zhou XE, Xu HE. Thirsty plants and beyond: structural mechanisms of abscisic acid perception and signaling. Curr Opin Struct Biol 2010;20:722–9.

Melikant B, Giuliani C, Halbmayer-Watzina S, Limmongkon A, Heberle-Bors E, Wilson C. The *Arabidopsis thaliana* MEK AtMKK6 activates the MAP kinase AtMPK13. FEBS Lett 2004;576:5–8.

Menges M, Doczi R, Okresz L, Morandini P, Mizzi L, Soloviev M, et al. Comprehensive gene expression atlas for the Arabidopsis MAP kinase signalling pathways. New Phytol 2008;179:643–62.

Merlot S, Gosti F, Guerrier D, Vavasseur A, Giraudat J. The ABI1 and ABI2 protein phosphatases 2C act in a negative feedback regulatory loop of the abscisic acid signalling pathway. Plant J 2001;25:295.

Merlot S, Mustilli AC, Genty B, North H, Lefebvre V, Sotta B, et al. Use of infrared thermal imaging to isolate Arabidopsis mutants defective in stomatal regulation. Plant J 2002;30:601–9.

Mersmann S, Bourdais G, Rietz S, Robatzek S. Ethylene signaling regulates accumulation of the FLS2 receptor and is required for the oxidative burst contributing to plant immunity. Plant Physiol 2010;154:391–400.

Meszaros T, Helfer A, Hatzimasoura E, Magyar Z, Serazetdinova L, Rios G, et al. The Arabidopsis MAP kinase kinase MKK1 participates in defence responses to the bacterial elicitor flagellin. Plant J 2006;48:485–98.

Meyer K, Leube MP, Grill E. A protein phosphatase 2C involved in ABA signal transduction in Arabidopsis thaliana. Science 1994;264:1452.

Mittler R. Oxidative stress, antioxidants and stress tolerance. Trends Plant Sci 2002;7:405–10.

Miyazono K, Miyakawa T, Sawano Y, Kubota K, Kang HJ, Asano A, et al. Structural basis of abscisic acid signalling. Nature 2009;462:609–14.

Mizoguchi T, Irie K, Hirayama T, Hayashida N, Yamaguchi-Shinozaki K, Matsumoto K, et al. A gene encoding a mitogen-activated protein kinase kinase kinase is induced simultaneously with genes for a mitogen-activated protein kinase and an S6 ribosomal protein kinase by touch, cold, and water stress in Arabidopsis thaliana. Proc Natl Acad Sci U S A 1996;93:765–9.

Mochizuki N, Brusslan JA, Larkin R, Nagatani A, Chory J. Arabidopsis genomes uncoupled 5 (GUN5) mutant reveals the involvement of Mg-chelatase H subunit in plastid-to-nucleus signal transduction. Proc Natl Acad Sci U S A 2001;98:2053–8.

Montillet J-L, Hirt H. New checkpoints in stomatal defense. Trends Plant Sci 2013;6:295–7.

Montillet JL, Leonhardt N, Mondy S, Tranchimand S, Rumeau D, Boudsocq M, et al. An abscisic Acid-independent oxylipin pathway controls stomatal closure and immune defense in Arabidopsis. PLoS Biol 2013;11:e1001513.

Moon H, Lee B, Choi G, Shin D, Prasad DT, Lee O, et al. NDP kinase 2 interacts with two oxidative stress-activated MAPKs to regulate cellular redox state and enhances multiple stress tolerance in transgenic plants. Proc Natl Acad Sci U S A 2003;100:358–63.

Müller AH, Hansson M. The barley magnesium chelatase 150-kD subunit is not an abscisic acid receptor. Plant Physiol 2009;150:157–66.

Mustilli AC, Merlot S, Vavasseur A, Fenzi F, Giraudat J. Arabidopsis OST1 protein kinase mediates the regulation of stomatal aperture by abscisic acid and acts upstream of reactive oxygen species production. Plant Cell 2002;14:3089–99.

Nakagami H, Soukupova H, Schikora A, Zarsky V, Hirt H. A Mitogen-activated protein kinase kinase kinase mediates reactive oxygen species homeostasis in Arabidopsis. J Biol Chem 2006;281:38697–704.

Nakashima K, Fujita Y, Kanamori N, Katagiri T, Umezawa T, Kidokoro S, et al. Three Arabidopsis SnRK2 protein kinases, SRK2D/SnRK2.2, SRK2E/SnRK2.6/OST1 and SRK2I/SnRK2.3, involved in ABA signaling are essential for the control of seed development and dormancy. Plant Cell Physiol 2009;50:1345–63.

Nambara E, Marion-Poll A. Abscisic acid biosynthesis and catabolism. Annu Rev Plant Biol 2005;56:165–85.

Negi J, Matsuda O, Nagasawa T, Oba Y, Takahashi H, Kawai-Yamada M, et al. CO2 regulator SLAC1 and its homologues are essential for anion homeostasis in plant cells. Nature 2008;452:483–6.

Neill S, Desikan R, Hancock J. Hydrogen peroxide signalling. Curr Opin Plant Biol 2002;5:388–95.

Nemhauser JL, Hong F, Chory J. Different plant hormones regulate similar processes through largely nonoverlapping transcriptional responses. Cell 2006;126:467–75.

Ning J, Li X, Hicks LM, Xiong L. A Raf-like MAPKKK gene DSM1 mediates drought resistance through reactive oxygen species scavenging in rice. Plant Physiol 2010;152:876–90.

Nishimura N, Yoshida T, Kitahata N, Asami T, Shinozaki K, Hirayama T. ABA-Hypersensitive Germination1 encodes a protein phosphatase 2C, an essential component of abscisic acid signaling in Arabidopsis seed. Plant J 2007;50:935–49.

Nishimura N, Hitomi K, Arvai AS, Rambo RP, Hitomi C, Cutler SR, et al. Structural mechanism of abscisic acid binding and signaling by dimeric PYR1. Science 2009;326:1373–9.

Nishimura N, Sarkeshik A, Nito K, Park SY, Wang A, Carvalho PC, et al. PYR/PYL/RCAR family members are major in-vivo ABI1 protein phosphatase 2C-interacting proteins in Arabidopsis. Plant J 2010;61:290–9.

Nott A, Jung HS, Koussevitzky S, Chory J. Plastid-to-nucleus retrograde signaling. Annu Rev Plant Biol 2006;57:739–59.

Ortiz-Masia D, Perez-Amador MA, Carbonell J, Marcote MJ. Diverse stress signals activate the C1 subgroup MAP kinases of Arabidopsis. FEBS Lett 2007;581:1834–40.

Pan J, Zhang M, Kong X, Xing X, Liu Y, Zhou Y, et al. ZmMPK17, a novel maize group D MAP kinase gene, is involved in multiple stress responses. Planta 2012;235:661–76.

Pandey S, Nelson DC, Assmann SM. Two novel GPCR-type G proteins are abscisic acid receptors in Arabidopsis. Cell 2009;136:136–48.

Park KY, Jung JY, Park J, Hwang JU, Kim YW, Hwang I, et al. A role for phosphatidylinositol 3-phosphate in abscisic acid-induced reactive oxygen species generation in guard cells. Plant Physiol 2003;132:92–8.

Park S-Y, Fung P, Nishimura N, Jensen DR, Fujii H, Zhao Y, et al. Abscisic acid inhibits Type 2C protein phosphatases via the PYR/PYL family of START proteins. Science 2009;324:1068–71.

Pei Z-M, Murata Y, Benning G, Thomine S, Klusener B, Allen GJ, et al. Calcium channels activated by hydrogen peroxide mediate abscisic acid signalling in guard cells. Nature 2000;406:731–4.

Petersen M, Brodersen P, Naested H, Andreasson E, Lindhart U, Johansen B, et al. Arabidopsis map kinase 4 negatively regulates systemic acquired resistance. Cell 2000;103:1111–20.

Pitzschke A, Hirt H. Mitogen-activated protein kinases and reactive oxygen species signaling in plants. Plant Physiol 2006;141:351–6.

Popescu SC, Popescu GV, Bachan S, Zhang Z, Gerstein M, Snyder M, et al. MAPK target networks in *Arabidopsis thaliana* revealed using functional protein microarrays. Genes Dev 2009;23:80–92.

Priest DM, Ambrose SJ, Vaistij FE, Elias L, Higgins GS, Ross AR, et al. Use of the glucosyltransferase UGT71B6 to disturb abscisic acid homeostasis in Arabidopsis thaliana. Plant J 2006;46:492–502.

Qin F, Shinozaki K, Yamaguchi-Shinozaki K. Achievements and challenges in understanding plant abiotic stress responses and tolerance. Plant Cell Physiol 2011;52:1569–82.

Qiu JL, Zhou L, Yun BW, Nielsen HB, Fiil BK, Petersen K, et al. Arabidopsis mitogen-activated protein kinase kinases MKK1 and MKK2 have overlapping functions in defense signaling mediated by MEKK1, MPK4, and MKS1. Plant Physiol 2008;148:212–22.

Rea PA. Plant ATP-binding cassette transporters. Annu Rev Plant Physiol Plant Mol Biol 2007;58:347–75.

Ren D, Yang H, Zhang S. Cell death mediated by MAPK is associated with hydrogen peroxide production in Arabidopsis. J Biol Chem 2002;277:559–65.

Robert N, Merlot S, N'Guyen V, Boisson-Dernier A, Schroeder JI. A hypermorphic mutation in the protein phosphatase 2C HAB1 strongly affects ABA signaling in Arabidopsis. FEBS Lett 2006;580:4691–6.

Rodriguez PL, Benning G, Grill E. ABI2, a second protein phosphatase 2C involved in abscisic acid signal transduction in Arabidopsis. FEBS Lett 1998;421:185–90.

Rodriguez MCS, Petersen M, Mundy J. Mitogen-activated protein kinase signaling in plants. Annu Rev Plant Biol 2010;61:621–49.

Roelfsema MR, Levchenko V, Hedrich R. ABA depolarizes guard cells in intact plants, through a transient activation of R- and S-type anion channels. Plant J 2004;37:578–88.

Saavedra X, Modrego A, Rodriguez D, Gonzalez-Garcia MP, Sanz L, Nicolas G, et al. The nuclear interactor PYL8/RCAR3 of *Fagus sylvatica* FsPP2C1 is a positive regulator of abscisic acid signaling in seeds and stress. Plant Physiol 2010;152:133–50.

Saez A, Apostolova N, Gonzalez-Guzman M, Gonzalez-Garcia MP, Nicolas C, Lorenzo O, et al. Gain-of-function and loss-of-function phenotypes of the protein phosphatase 2C HAB1 reveal its role as a negative regulator of abscisic acid signalling. Plant J 2004;37:354–69.

Saito S, Hirai N, Matsumoto C, Ohigashi H, Ohta D, Sakata K, et al. Arabidopsis CYP707As encode (+)-abscisic acid 8′-hydroxylase, a key enzyme in the oxidative catabolism of abscisic acid. Plant Physiol 2004;134:1439–49.

Samuel MA, Ellis BE. Double jeopardy: both overexpression and suppression of a redox-activated plant mitogen-activated protein kinase render tobacco plants ozone sensitive. Plant Cell 2002;14:2059–69.

Santiago J, Rodrigues A, Saez A, Rubio S, Antoni R, Dupeux F, et al. Modulation of drought resistance by the abscisic acid receptor PYL5 through inhibition of clade A PP2Cs. Plant J 2009a;60:575–88.

Santiago J, Dupeux F, Round A, Antoni R, Park SY, Jamin M, et al. The abscisic acid receptor PYR1 in complex with abscisic acid. Nature 2009b;462:665–8.

Sato A, Sato Y, Fukao Y, Fujiwara M, Umezawa T, Shinozaki K, et al. Threonine at position 306 of the KAT1 potassium channel is essential for channel activity and is a target site for ABA-activated SnRK2/OST1/SnRK2.6 protein kinase. Biochem J 2009;424:439–48.

Schroeder JI, Keller BU. Two types of anion channel currents in guard cells with distinct voltage regulation. Proc Natl Acad Sci U S A 1992;89:5025–9.

Schroeder JI, Kwak JM, Allen GJ. Guard cell abscisic acid signalling and engineering drought hardiness in plants. Nature 2001a;410:327–30.

Schroeder JI, Allen GJ, Hugouvieux V, Kwak JM, Waner D. Guard cell signal transduction. Annu Rev Plant Physiol Plant Mol Biol 2001b;52:627–58.

Schwartz SH, Tan BC, Gage DA, Zeevaart JAD, McCarty DR. Specific oxidative cleavage of carotenoids by VP14 of maize. Science 1997;276:1872–4.

Schwartz SH, Qin X, Zeevaart JA. Elucidation of the indirect pathway of abscisic acid biosynthesis by mutants, genes, and enzymes. Plant Physiol 2003;131:1591–601.

Please cite this article as: Danquah A, et al, The role of ABA and MAPK signaling pathways in plant abiotic stress responses, Biotechnol Adv (2013), http://dx.doi.org/10.1016/j.biotechadv.2013.09.006

ARTICLE IN PRESS

Schweighofer A, Hirt H, Meskiene I. Plant PP2C phosphatases: emerging functions in stress signaling. Trends Plant Sci 2004;9:236–43.

Seki M, Ishida J, Narusaka M, Fujita M, Nanjo T, Umezawa T, et al. Monitoring the expression pattern of around 7,000 Arabidopsis genes under ABA treatments using a full-length cDNA microarray. Funct Integr Genomics 2002;2:282–91.

Seo M, Koshiba T. Complex regulation of ABA biosynthesis in plants. Trends Plant Sci 2002;7:41–8.

Shang Y, Yan L, Liu ZQ, Cao Z, Mei C, Xin Q, et al. The Mg-chelatase H subunit of Arabidopsis antagonizes a group of WRKY transcription repressors to relieve ABA-responsive genes of inhibition. Plant Cell 2010;22:1909–35.

Sheard LB, Zheng N. Plant biology: signal advance for abscisic acid. Nature 2009;462:575–6.

Shen Y-Y, Wang X-F, Wu F-Q, Du S-Y, Cao Z, Shang Y, et al. The Mg-chelatase H subunit is an abscisic acid receptor. Nature 2006;443:823–6.

Shimazaki K, Iino M, Zeiger E. Blue light-dependent proton extrusion by guard-cell protoplasts of Vicia faba. Nature 1986;319:324–6.

Shinozaki K, Yamaguchi-Shinozaki K. Molecular responses to dehydration and low temperature: differences and cross-talk between two stress signaling pathways. Curr Opin Plant Biol 2000;3:217–23.

Shinozaki K, Yamaguchi-Shinozaki K. Gene networks involved in drought stress response and tolerance. J Exp Bot 2007;58:221–7.

Shou H, Bordallo P, Fan J-B, Yeakley JM, Bibikova M, Sheen J, et al. Expression of an active tobacco mitogen-activated protein kinase kinase kinase enhances freezing tolerance in transgenic maize. Proc Natl Acad Sci U S A 2004a;101:3298–303.

Shou H, Bordallo P, Wang K. Expression of the Nicotiana protein kinase (NPK1) enhanced drought tolerance in transgenic maize. J Exp Bot 2004b;55:1013–9.

Sirichandra C, Gu D, Hu HC, Davanture M, Lee S, Djaoui M, et al. Phosphorylation of the Arabidopsis AtrbohF NADPH oxidase by OST1 protein kinase. FEBS Lett 2009;583:2982–6.

Song F, Goodman RM. OsBIMK1, a rice MAP kinase gene involved in disease resistance responses. Planta 2002;215:997–1005.

Soon F-F, Ng L-M, Zhou XE, West GM, Kovach A, Tan MHE, et al. Molecular mimicry regulates ABA signaling by SnRK2 kinases and PP2C phosphatases. Science 2012;335:85–8.

Strand A, Asami T, Alonso J, Ecker JR, Chory J. Chloroplast to nucleus communication triggered by accumulation of Mg-protoporphyrinIX. Nature 2003;421:79–83.

Su SH, Bush SM, Zaman N, Stecker K, Sussman MR, Krysan P. Deletion of a tandem gene family in Arabidopsis: increased MEKK2 abundance triggers autoimmunity when the MEKK1-MKK1/2-MPK4 signaling cascade is disrupted. Plant Cell 2013;25:1895–910.

Suarez-Rodriguez MC, Adams-Phillips L, Liu Y, Wang H, Su S-H, Jester PJ, et al. MEKK1 Is required for flg22-Induced MPK4 activation in Arabidopsis plants. Plant Physiol 2007;143:661–9.

Surpin M, Larkin RM, Chory J. Signal transduction between the chloroplast and the nucleus. Plant Cell 2002;14(Suppl.):S327–38.

Taj G, Agarwal P, Grant M, Kumar A. MAPK machinery in plants: recognition and response to different stresses through multiple signal transduction pathways. Plant Signal Behav 2010;5:1370–8.

Takahashi F, Yoshida R, Ichimura K, Mizoguchi T, Seo S, Yonezawa M, et al. The mitogen-activated protein kinase cascade MKK3–MPK6 is an important part of the jasmonate signal transduction pathway in Arabidopsis. Plant Cell 2007;19:805–18.

Takahashi Y, Soyano T, Kosetsu K, Sasabe M, Machida Y. HINKEL kinesin, ANP MAPKKKs and MKK6/ANQ MAPKK, which phosphorylates and activates MPK4 MAPK, constitute a pathway that is required for cytokinesis in Arabidopsis thaliana. Plant Cell Physiol 2010;51:1766–76.

Takahashi F, Mizoguchi T, Yoshida R, Ichimura K, Shinozaki K. Calmodulin-dependent activation of MAP kinase for ROS homeostasis in Arabidopsis. Mol Cell 2011;41:649–60.

Tan BC, Schwartz SH, Zeevaart JAD, McCarty DR. Genetic control of abscisic acid biosynthesis in maize. Proc Natl Acad Sci U S A 1997;94:12235–40.

Teige M, Scheikl E, Eulgem T, Doczi R, Ichimura K, Shinozaki K, et al. The MKK2 pathway mediates cold and salt stress signaling in Arabidopsis. Mol Cell 2004;15:141–52.

Tena G, Asai T, Chiu WL, Sheen J. Plant mitogen-activated protein kinase signaling cascades. Curr Opin Plant Biol 2001;4:392.

Tuteja N. Abscisic Acid and abiotic stress signaling. Plant Signal Behav 2007;2:135–8.

Umezawa T, Sugiyama N, Mizoguchi M, Hayashi S, Myouga F, Yamaguchi-Shinozaki K, et al. Type 2C protein phosphatases directly regulate abscisic acid-activated protein kinases in Arabidopsis. Proc Natl Acad Sci U S A 2009;106:17588–93.

Umezawa T, Nakashima K, Miyakawa T, Kuromori T, Tanokura M, Shinozaki K, et al. Molecular basis of the core regulatory network in ABA responses: sensing, signaling and transport. Plant Cell Physiol 2010;51:1821–39.

Umezawa T, Sugiyama N, Takahashi F, Anderson JC, Ishihama Y, Peck SC, et al. Genetics and phosphoproteomics reveal a protein phosphorylation network in the abscisic acid signaling pathway in *Arabidopsis thaliana*. Sci Signal 2013;6:rs8.

Uno Y, Furihata T, Abe H, Yoshida R, Shinozaki K, Yamaguchi-Shinozaki K. Arabidopsis basic leucine zipper transcription factors involved in an abscisic acid-dependent signal transduction pathway under drought and high-salinity conditions. Proc Natl Acad Sci U S A 2000;97:11632–7.

Vahisalu T, Kollist H, Wang YF, Nishimura N, Chan WY, Valerio G, et al. SLAC1 is required for plant guard cell S-type anion channel function in stomatal signalling. Nature 2008;452:487–91.

Verslues PE, Agarwal M, Katiyar-Agarwal S, Zhu J, Zhu JK. Methods and concepts in quantifying resistance to drought, salt and freezing, abiotic stresses that affect plant water status. Plant J 2006;45:523–39.

Vlad F, Rubio S, Rodrigues A, Sirichandra C, Belin C, Robert N, et al. Protein phosphatases 2C regulate the activation of the Snf1-related kinase OST1 by abscisic acid in Arabidopsis. The Plant Cell Online 2009;21:3170–84.

Walker CJ, Willows RD. Mechanism and regulation of Mg-chelatase. Biochem J 1997;327(Pt 2):321–33.

Wang WX, Vinocur B, Shoseyov O, Altman A. Biotechnology of plant osmotic stress tolerance: physiological and molecular considerations. Acta Horticult 2001;560:285–92.

Wang W, Vinocur B, Altman A. Plant responses to drought, salinity and extreme temperatures: towards genetic engineering for stress tolerance. Planta 2003;218:1–14.

Wang H, Ngwenyama N, Liu Y, Walker JC, Zhang S. Stomatal development and patterning are regulated by environmentally responsive mitogen-activated protein kinases in Arabidopsis. Plant Cell 2007;19:63–73.

Wang H, Liu Y, Bruffett K, Lee J, Hause G, Walker JC, et al. Haplo-insufficiency of MPK3 in MPK6 mutant background uncovers a novel function of these two MAPKs in Arabidopsis ovule development. Plant Cell Online 2008;20:602–13.

Wang J, Ding H, Zhang A, Ma F, Cao J, Jiang M. A novel mitogen-activated protein kinase gene in maize (Zea mays), ZmMPK3, is involved in response to diverse environmental cues. J Integr Plant Biol 2010a;52:442–52.

Wang XJ, Zhu SY, Lu YF, Zhao R, Xin Q, Wang XF, et al. Two coupled components of the mitogen-activated protein kinase cascade MdMPK1 and MdMKK1 from apple function in ABA signal transduction. Plant Cell Physiol 2010b;51:754–66.

Wang RS, Pandey S, Li S, Gookin TE, Zhao Z, Albert R, et al. Common and unique elements of the ABA-regulated transcriptome of Arabidopsis guard cells. BMC Genomics 2011;12:216.

Wasilewska A, Vlad F, Sirichandra C, Redko Y, Jammes F, Valon C, et al. An update on abscisic acid signaling in plants and more. Mol Plant 2008;1:198–217.

Wen JQ, Oono K, Imai R. Two novel mitogen-activated protein signaling components, OsMEK1 and OsMAP1, are involved in a moderate low-temperature signaling pathway in rice. Plant Physiol 2002;129:1880–91.

Wu FQ, Xin Q, Cao Z, Liu ZQ, Du SY, Mei C, et al. The magnesium-chelatase H subunit binds abscisic acid and functions in abscisic acid signaling: new evidence in Arabidopsis. Plant Physiol 2009;150:1940–54.

Xie X, Wang Y, Williamson L, Holroyd GH, Tagliavia C, Murchie E, et al. The identification of genes involved in the stomatal response to reduced atmospheric relative humidity. Curr Biol 2006;16:882–7.

Xing Y, Jia W, Zhang J. AtMKK1 mediates ABA-induced CAT1 expression and H_2O_2 production via AtMPK6-coupled signaling in Arabidopsis. Plant J 2008;54:440–51.

Xiong L, Yang Y. Disease resistance and abiotic stress tolerance in rice are inversely modulated by an abscisic acid–inducible mitogen-activated protein kinase. Plant Cell Online 2003;15:745–59.

Xiong L, Wang RG, Mao G, Koczan JM. Identification of drought tolerance determinants by genetic analysis of root response to drought stress and abscisic Acid. Plant Physiol 2006;142:1065–74.

Xu ZJ, Nakajima M, Suzuki Y, Yamaguchi I. Cloning and characterization of the abscisic acid-specific glucosyltransferase gene from adzuki bean seedlings. Plant Physiol 2002;129:1285–95.

Xu H, Wang X, Sun X, Shi Q, Yang F, Du D. Molecular cloning and characterization of a cucumber MAP kinase gene in response to excess NO_3^- and other abiotic stresses. Sci Hortic 2008;117:1–8.

Xu ZY, Lee KH, Dong T, Jeong JC, Jin JB, Kanno Y, et al. A vacuolar beta-glucosidase homolog that possesses glucose-conjugated abscisic acid hydrolyzing activity plays an important role in osmotic stress responses in Arabidopsis. Plant Cell 2012;24:2184–99.

Yamaguchi-Shinozaki K, Shinozaki K. Transcriptional regulatory networks in cellular responses and tolerance to dehydration and cold stresses. Annu Rev Plant Biol 2006;57:781–803.

Yin P, Fan H, Hao Q, Yuan X, Wu D, Pang Y, et al. Structural insights into the mechanism of abscisic acid signaling by PYL proteins. Nat Struct Mol Biol 2009;16:1230–6.

Yin H, Zhao X, Bai X, Du Y. Molecular cloning and characterization of a *Brassica napus* L. MAP kinase involved in oligochitosan-induced defense signaling. Plant Mol Biol Report 2010;28:292–301.

Yoo SD, Cho YH, Tena G, Xiong Y, Sheen J. Dual control of nuclear EIN3 by bifurcate MAPK cascades in C2H4 signalling. Nature 2008;451:789–95.

Yoshida R, Hobo T, Ichimura K, Mizoguchi T, Takahashi F, Aronso J, et al. ABA-activated SnRK2 protein kinase is required for dehydration stress signaling in Arabidopsis. Plant Cell Physiol 2002;43:1473–83.

Yoshida R, Umezawa T, Mizoguchi T, Takahashi S, Takahashi F, Shinozaki K. The regulatory domain of SRK2E/OST1/SnRK2.6 interacts with ABI1 and integrates abscisic acid (ABA) and osmotic stress signals controlling stomatal closure in Arabidopsis. J Biol Chem 2006a;281:5310–8.

Yoshida T, Nishimura N, Kitahata N, Kuromori T, Ito T, Asami T, et al. ABA-Hypersensitive Germination3 encodes a Protein Phosphatase 2C (AtPP2CA) that strongly regulates abscisic acid signaling during germination among Arabidopsis Protein Phosphatase 2Cs. Plant Physiol 2006b;140:115–26.

Yoshida T, Fujita Y, Sayama H, Kidokoro S, Maruyama K, Mizoi J, et al. AREB1, AREB2, and ABF3 are master transcription factors that cooperatively regulate ABRE-dependent ABA signaling involved in drought stress tolerance and require ABA for full activation. Plant J 2010;61:672–85.

You MK, Oh SI, Ok SH, Cho SK, Shin HY, Jeung JU, et al. Identification of putative MAPK kinases in *Oryza minuta* and *O. sativa* responsive to biotic stresses. Mol Cells 2007;23:108–14.

Zeevaart JAD, Creelman RA. Metabolism and physiology of abscisic acid. Annu Rev Plant Physiol Plant Mol Biol 1988;39:439–73.

Zeng Q, Chen JG, Ellis BE. AtMPK4 is required for male-specific meiotic cytokinesis in Arabidopsis. Plant J 2011;67:895–906.

Zhang S, Klessig DF. MAPK cascades in plant defense signaling. Trends Plant Sci 2001;6:520.

Zhang X, Miao YC, An GY, Zhou Y, Shangguan ZP, Gao JF, et al. K^+ channels inhibited by hydrogen peroxide mediate abscisic acid signaling in Vicia guard cells. Cell Res 2001;11:195–202.

Zhang D-P, Wu Z-Y, Li X-Y, Zhao Z-X. Purification and identification of a 42-kilodalton abscisic acid-specific-binding protein from epidermis of broad bean leaves. Plant Physiol 2002;128:714–25.

Please cite this article as: Danquah A, et al, The role of ABA and MAPK signaling pathways in plant abiotic stress responses, Biotechnol Adv (2013), http://dx.doi.org/10.1016/j.biotechadv.2013.09.006

ARTICLE IN PRESS

Zhang W, Ruan J, Ho TH, You Y, Yu T, Quatrano RS. Cis-regulatory element based targeted gene finding: genome-wide identification of abscisic acid- and abiotic stress-responsive genes in *Arabidopsis thaliana*. Bioinformatics 2005;21:3074–81.

Zhang T, Liu Y, Xue L, Xu S, Chen T, Yang T, et al. Molecular cloning and characterization of a novel MAP kinase gene in *Chorispora bungeana*. Plant Physiol Biochem 2006a;44:78–84.

Zhang A, Jiang M, Zhang J, Tan M, Hu X. Mitogen-activated protein kinase is involved in abscisic acid-induced antioxidant defense and acts downstream of reactive oxygen species production in leaves of maize plants. Plant Physiol 2006b;141:475–87.

Zhang X, Dai Y, Xiong Y, DeFraia C, Li J, Dong X, et al. Overexpression of Arabidopsis MAP kinase kinase 7 leads to activation of plant basal and systemic acquired resistance. Plant J 2007a;52:1066–79.

Zhang A, Jiang M, Zhang J, Ding H, Xu S, Hu X, et al. Nitric oxide induced by hydrogen peroxide mediates abscisic acid-induced activation of the mitogen-activated protein kinase cascade involved in antioxidant defense in maize leaves. New Phytol 2007b;175:36–50.

Zhang A, Zhang J, Ye N, Cao J, Tan M, Zhang J, et al. ZmMPK5 is required for the NADPH oxidase-mediated self-propagation of apoplastic H_2O_2 in brassinosteroid-induced antioxidant defence in leaves of maize. J Exp Bot 2010;61:4399–411.

Zhang M, Pan J, Kong X, Zhou Y, Liu Y, Sun L, et al. ZmMKK3, a novel maize group B mitogen-activated protein kinase kinase gene, mediates osmotic stress and ABA signal responses. J Plant Physiol 2012;169:1501–10.

Zhou R, Cutler AJ, Ambrose SJ, Galka MM, Nelson KM, Squires TM, et al. A new abscisic acid catabolic pathway. Plant Physiol 2004;134:361–9.

Zong XJ, Li DP, Gu LK, Li DQ, Liu LX, Hu XL. Abscisic acid and hydrogen peroxide induce a novel maize group C MAP kinase gene, ZmMPK7, which is responsible for the removal of reactive oxygen species. Planta 2009;229:485–95.

Zou J, Abrams G, Barton D, Taylor D, Pomeroy M, Abrams S. Induction of lipid and oleosin biosynthesis by (+)-abscisic acid and its metabolites in microspore-derived embryos of *Brassica napus* L. cv Reston (biological responses in the presence of 8′-hydroxyabscisic acid). Plant Physiol 1995;108:563–71.

Please cite this article as: Danquah A, et al, The role of ABA and MAPK signaling pathways in plant abiotic stress responses, Biotechnol Adv (2013), http://dx.doi.org/10.1016/j.biotechadv.2013.09.006