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Review

Diverse signals converge at MAPK cascades in plant

T. Zhang[a,b], Y. Liu[c], T. Yang[a], L. Zhang[a], S. Xu[a], L. Xue[a], L. An[a,c,*]

[a] Key Laboratory of Arid and Grassland Ecology of Ministry of Education, Lanzhou University, Lanzhou 730000, PR China
[b] Life Science College, Northwest Normal University, Lanzhou 730000, PR China
[c] Cold and Arid Regions Environmental and Engineering Research Institute, Chinese Academy of Sciences, Lanzhou 730000, PR China

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Abstract

Mitogen-activated protein kinases (MAPKs) are important signal transducing enzymes that connects diverse receptors/sensors to a wide range of cellular responses in mammals, yeasts and plants. In recent years, a large number of different components of plant MAPK cascades were isolated. Molecular and biochemical studies have revealed that plant MAPKs play important role in the response to a broad variety of biotic and abiotic stresses, including wounding, pathogen infection, temperature, drought, salinity, but also in the signaling of plant hormones and the cell division. This review briefly summaries the recent research results about the cross-talk and complexity of MAP kinase cascades in plant obtained from functional analyses.

Keywords: MAP kinase cascades; Environmental stress; Hormone; Cell division; Signal transduction

1. Introduction

Plants possess integrated signaling networks that mediate the responses to environmental stresses. Protein phosphorylation is one of the major mechanisms for controlling cellular functions in response to external signals. The mitogen-activated protein kinase (MAPK) cascades are important signaling modules in eukaryotic cells that convert signals generated from the receptors/sensors to cellular responses. MAPK cascades are composed of three protein kinase modules: MAPKK kinases (MAPKKKs), MAPK kinases (MAPKKs), and MAPKs, which are linked in various ways to upstream receptors and downstream targets [1]. MAPKs are activated when both tyrosine and threonine residues in the TXY motif are phosphorylated by dual-specificity kinases MAPKKs. MAPKKs are activated when serine and serine/threonine residues in the S/T-X_{3-5}-S/T motif are phosphorylated by serine/threonine kinases MAPKKKs [1]. MAPK cascades are evolutionarily conserved signaling modules in eukaryotes, including animals, yeasts and plants [2]. In plants, a number of studies have demonstrated that MAPKs are activated by abiotic stresses, wounding, hormones, during plant–pathogen interactions and cell division. The initial study of MAPKs cascades in plant were focused on new cDNA cloning, used the MAPK in-gel assay, Northern blot analyses, and kinase inhibitors to connect signals to MAPKs cascades [2]. However, in recent years, the loss-of-function mutant, the gain-of-function mutant and other additional tools were used to research the plant MAPK cascades. The functions of the individual MAPK cascade gene in particular signal transduction pathway were described. Expressly, the first plant MAPK substrate was identified in vivo [3]. In this review, we highlight recent progress in understanding the plant MAPK, MAPKK, MAPKKK genes in specific signal transduction pathways, and in revealing the complex gene networks and cross-talk of plant MAPK cascades in diverse signal pathways.

2. Components of plant MAPK cascades

In plant, a variety of genes encoding MAPKs have been identified. There are 20 MPK genes in the *Arabidopsis* genome, which suggests that the MAPK cascades in plants may be quite complex [4]. Compared with mammalian MAPKs, all plant MAPKs have highest homology to the extracellular signal-regulated kinase (ERK) subfamily. The predicted

* Corresponding author. Tel.: +86 931 496 7181; fax: +86 931 496 7181.
E-mail address: lizhean@lzu.edu.cn (L. An).

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amino acid sequences of these plant MAPKs show high conservation over the entire lengths with highest similarity in the eleven domains that are necessary for the catalytic function of serine/threonine protein kinase. The N- and C-terminal extensions outside the eleven subdomains are more divergent than the catalytic core, but these sequences have important biological function. Comparisons of deduced amino acid sequences indicate that plant MAPKs can be grouped into at least four distinct families [5]. MAPKs within one branch serve similar function in different species, the MAPKs in family I, including *Arabidopsis* MPK3, MPK4, alfalfa SIMK, tobacco WIPK, are mostly involved in environmental and hormonal response. Some of the MAPKs of family II are involved in cell cycle regulation and some involved in environmental stress responses, the functions of MAPKs in family III are little known at present, family IV MAPKs, have the TDY motif instead of TEY in their T-loop and also have the extended C-terminal region.

Analysis of the *Arabidopsis* genome for MAPKKs reveals four different groups with a total of 10 MKKs [5]. The number of MKKs in *Arabidopsis* genome is only half of MPKs, so MKKs are likely to activate multiple MPKs, and that cross-talk between various signal-transduction pathways might be concentrated at this level in plant MAPK cascades [5]. Plant MKKs have the S/T-X_5-S/T motif as the phosphorylation site, and a putative MAPK-docking domain K/R-K/R-K/R-$X_{1\text{-}6}$-L-X-L/V/I. Several MAPKKs have been identified from different plants, including *Arabidopsis* MKK1 (renamed from MEK1) and MKK2-5, alfalfa SIMKK and PRKK, tomato LeMEK1, tobacco NtMEK1-2 and SIPKK, and maize ZmMEK1. *Arabidopsis* MKK1 was activated by wounding and abiotic stress [6]. PRKK activate SIMK, MMK3 and SAMK in response to the fungal elicitor [7]. SIMKK conducts both salt and elicitor-induced signals with different substrate specificities [7,8]. Dexamethasone-induced transient overproduction of a constitutively active form of tobacco NtMEK2 in tobacco leaves caused not only activation of SIPK and WIPK but also hypersensitive cell death [9].

There are 60 putative MAPKKKs in *Arabidopsis*. Plant MAPKKKs can be divided into two subfamilies, Typified by their mammalian homologs: MEKK-like protein kinases, and Raf-like protein kinases [5]. Homologs of MAPKKKs have been identified in plant species. Including the MEKK-like protein kinases, OMTK1 (oxidative stress-activated MAP triple-kinase 1) from alfalfa [10], ANP1, ANP2, ANP3 [11], YDA [12] from *Arabidopsis*, NPK1 (nicotiana protein kinase 1) from tobacco [13]; Raf-like protein kinases, EDR1 (enhanced disease resistance 1), and CTR1 (constitutive triple response 1) from *Arabidopsis* [14,15].

3. MAPKs cascades in abiotic stress signaling and pathogen defense

The ability to sense extreme changes of abiotic environmental conditions has been shown to be essential for a plant to launch the processes underlying acclimation [16]. Abiotic stresses include high and low temperature, drought, ozone, UV light, salinity and osmotic stress. To survive these conditions, plants have developed specific mechanisms to withstand abiotic stress, such as the synthesis of stress hormones like abscisic acid (ABA) that triggers second responses and the expression of specific sets of genes that result in changes in the composition of the major cell components [17]. While plants may sense the threatened of a wide variety of pathogens through wounding, pathogens are also recognized by cell wall components and microbial elicitors. To withstand pathogen attack, sensing of elicitors is followed by intracellular signal transduction resulting in defense reactions such as programmed cell death, the reinforcement of cell walls, the rapid production of reactive oxygen species, the synthesis of pathogen-related proteins and phytoalexins, and transcriptional activation of defense genes. Several MAPK cascades component are activated by more than one type of abiotic and biotic stress, which suggests that MAPK cascades act as points of convergence in stress signaling. In tomato, a 50 kDa MAP kinase is activated by heat stress in cell suspension cultures. When temperature increase from 26 to 38 °C, the 50 kDa MAP kinase is transiently activated 1 min after the treatment. Using *in solution* kinase assays, recombinant heat stress factor HsfA3 is incubated in the presence of the heat-activated MAP kinase, heat stress factor HsfA3 is phosphorylated strongly. So HsfA3 is a possible physiological substrate of MAP kinases in plant [18]. Expression of *MPK3* in *Arabidopsis thaliana*, increased markedly in response to cold, touch, and salinity stress. MPK4 and MPK6 are activated by low temperature, low humidity, osmotic stress, touch and wounding, But MPK4 and MPK6 are involved in distinct signal transduction pathways responding to these environmental stresses [19]. The role of a MAPK kinase, MKK1, in abiotic stress signaling was confirmed by Matsuoka et al. [6]. Analysis of MKK1 using a specific antibody revealed that multiple abiotic stresses such as wounding, cold, drought and high salt stress activated MKK1, which activates its downstream target MPK4 [6] (Fig. 1). The *Arabidopsis mpk4* mutants have elevated SA levels and exhibits constitutive systemic acquired resistance (SAR), and then constitutive express of pathogenesis-related genes. These results suggest that MPK4 was also act as negative regulator of SA-mediated defenses [20]. H_2O_2 can activate a specific MAPKK kinase, ANP1, in *Arabidopsis*, which initiates a MAPK cascade involving MPK3 and MPK6 and its positive regulator, nucleoside diphosphate kinase2 (Fig. 1). This H_2O_2-induced MAPK pathway blocks auxin-responsive genes, indicating that there is cross-talk between the oxidative-stress and auxin pathways [11,21]. Two *Arabidopsis* MAPKKs, MKK4 and MKK5 (renamed from MEK4 and MEK5), are functionally interchangeable with tobacco NtMEK2 in activating the downstream MAPKs. The appearance of cell death in active mutants $MKK4^{DD}$ (T224D/S230D) and $MKK5^{DD}$ (T215D/S221D) transgenic plants under induced condition is preceded by the generation of hydrogen peroxide, suggesting that MAPK-induced HR-like cell death might be mediated by the H_2O_2 generation [22] (Fig. 1). Extensive cross-talks between different pathways at