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The Green MAPKs

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Abstract: This review analyses the similarities in the MAPK pathways of plants and elucidates the involvement of MAPKs in the regulation of processes within the plant system which includes biotic and abiotic stress regulation.

Key words: Mitogen activated protein kinases, plant defense, abiotic stresses, biotic stresses, molecular diversity

INTRODUCTION

Plants have an integrated complex signaling network which mediates the perception of and responses to hormones, nutrients, environmental cues and stresses that govern both plant growth and development (Craig *et al.*, 2008; Tena *et al.*, 2001; Widmann *et al.*, 1999). The current knowledge on plant signal transduction pathways was obtained through the identification of sensors and receptors of signal perception, transcription factors and target genes that were shown experimentally to coordinate plants response to their internal and external cues (Seo *et al.*, 1995). Though these factors have been isolated through studies conducted worldwide, the challenge still lies in understanding how kinases work and its involvement in various cellular processes in plants. All this information is necessary towards obtaining a bird's eyes view of the mitogen-activated protein kinase (MAPK) signal transduction in plants (Wilson *et al.*, 1995; Asai *et al.*, 2002). In this review we present an overview of the involvement of MAPK pathway in modulating various developmental, growth and stress responses in plants (Craig *et al.*, 2008; Mishra *et al.*, 2006; Schwacke and Voit, 2007).

THE CONSERVATION AND DIVERSITY OF MAPK

The myriad of cellular processes in eukaryotes require the concerted and coordinated activity of signal transduction proteins of which the protein kinase super-family is a prominent member. Within this super-family, the mitogen-activated protein kinases (MAPKs) form a distinctive and highly conserved protein kinase subfamily (Hamel *et al.*, 2006). The hierarchical organization of three classes of functionally-related kinases: the MAPKs themselves, the MAPK kinases (MAPKKs) and the MAPKK kinases (MAPKKK) allows these proteins to operate as a signal transmission cascade capable of efficiently amplifying, integrating and channeling information between the cellular environment and the metabolic and transcriptional response centres (Schwacke and Voit, 2007). Biochemical and genetic studies have shown that kinases are able to regulate a complex signaling network by responding to more than one upstream effector and transmitting the information to more than one target (Marshall, 1994; Ruis and Schuller, 1995). In addition, the availability of multiple related kinases and the interaction with modifying proteins (Duerr *et al.*, 1993; Jonak *et al.*, 1993) and protein phosphatases (Jonak *et al.*, 1995, 1996; Mishra *et al.*, 2006) have contributed towards creating a remarkably versatile signaling matrix.

The MAPK cascade operates as part of the core signal transduction networks in eukaryotes. The kinase component has been highly conserved through evolution (Asai *et al.*, 2002; Mizoguchi *et al.*, 1993; Reyna and Yang, 2006). The amino acid sequences of various MAPKs from various organisms such as *Arabidopsis*, yeast, worm, fly and humans indicate that the three classes of kinases involved in the MAPK cascades (MAPKKKs, MAPKKs and MAPKs) always occur as gene families. Functional analysis on these gene families showed that these genes have a distinct role and that there exists a certain level of functional redundancy amongst these families (Mizoguchi *et al.*, 1994; Huttly and Phillips, 1995). The MAPK signaling has been extensively studied in the plant kingdom over the past decade. Due to the conservation in gene architecture and a high level of

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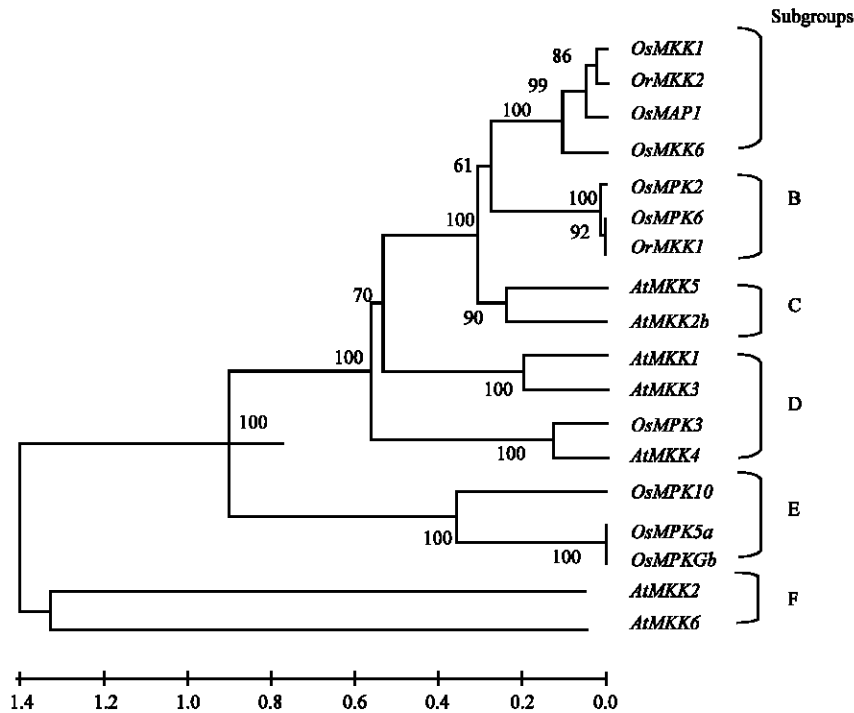Tel: 603-89213465 Fax: 60389252698

Fig. 1: The phylogenetic tree was created using the Mega4 UPGMA programme with the Poisson correlation. The *OrMKK2* sequences was analyzed with previously reported plant MAP kinases as follows: *OrMKK1, OsMKK1, OsMAP1, OsMAPK2, OsMAPK6, OsMPK3, OsMPK5a, OsMPK5b* and *OsMKK10* from rice (*O. sativa*), *AtMKK2b, AtMEK1, AtMKK2, AtMKK3, AtMKK4, AtMKK5* and *AtMKK6* from *Arabidopsis*. Numbers on the left show the bootstrap value generated with 1000 replications (Nadarajah *et al.*, 2009a)

sequence identity observed between MAPKs in various organisms, we are able to use this information to study in a broader sense signaling modalities between plants and other eukaryotic organisms.

Initial phylogenetic analysis of the MAPKs in the *Arabidopsis* genome suggested that these genes have been amplified, relative to yeast or model metazoan lineages (Ligterink *et al.*, 1997). The *Arabidopsis* genome contains twenty MAPK, ten MAPKK, sixty MAPKKK and ten MAP4K genes, but the functions of the corresponding proteins are still poorly characterized. The yeast model has so far shown only six MAPKs (Rudolf *et al.*, 2008) and six MAPKKs while sixteen MAPKs and twelve MAPKKs have been identified in human covering a wide range of activities from cardiac function, cell differentiation and so on (Manning *et al.*, 2002). It was not known whether the expansion of these families observed in *Arabidopsis* was generally representative of higher plants or if it represents a lineage-specific pattern. The recent completion of two additional higher plant genome-sequencing efforts (*Populus* and *Oryza*) has now made it possible to address this question directly. Information on transcriptional regulation of

individual *Arabidopsis* MAPK components has also been limited to reports of differences in transcription of a few specific MAPK genes in different organs, tissue and/or cell-types, or expression changes induced by extracellular stimuli (Colcombet and Hirt, 2008; Decroocq-Ferrant *et al.*, 1995). A phylogenetic tree (Fig. 1) that has been constructed using the sequences of MAPK of *Oryza sativa indica, Oryza sativa japonica, Oryza rufipogon* and *Arabidopsis thaliana* emphasizes the degree of structural and functional conservation in this signal transduction gene family in higher plants (Nadarajah *et al.*, 2009b).

The activation of MAPKs occurs through the process of phosphorylation at the conserved threonine and tyrosine residues that are located close to kinase domain VIII in all MAPKs (Ichimura *et al.*, 2002) (Fig. 2). A given dual-specificity MAPKK can only activate a specific MAPK and cannot functionally substitute other MAPKKs. MAPKKs are themselves activated by phosphorylation by upstream kinases that belong to the class of MAPKK kinases (MAPKKKs), *raf* and *mos* proteins (Reyna and Yang, 2006). A specific set of three functionally interlinked protein kinases i.e., MAPKKK-
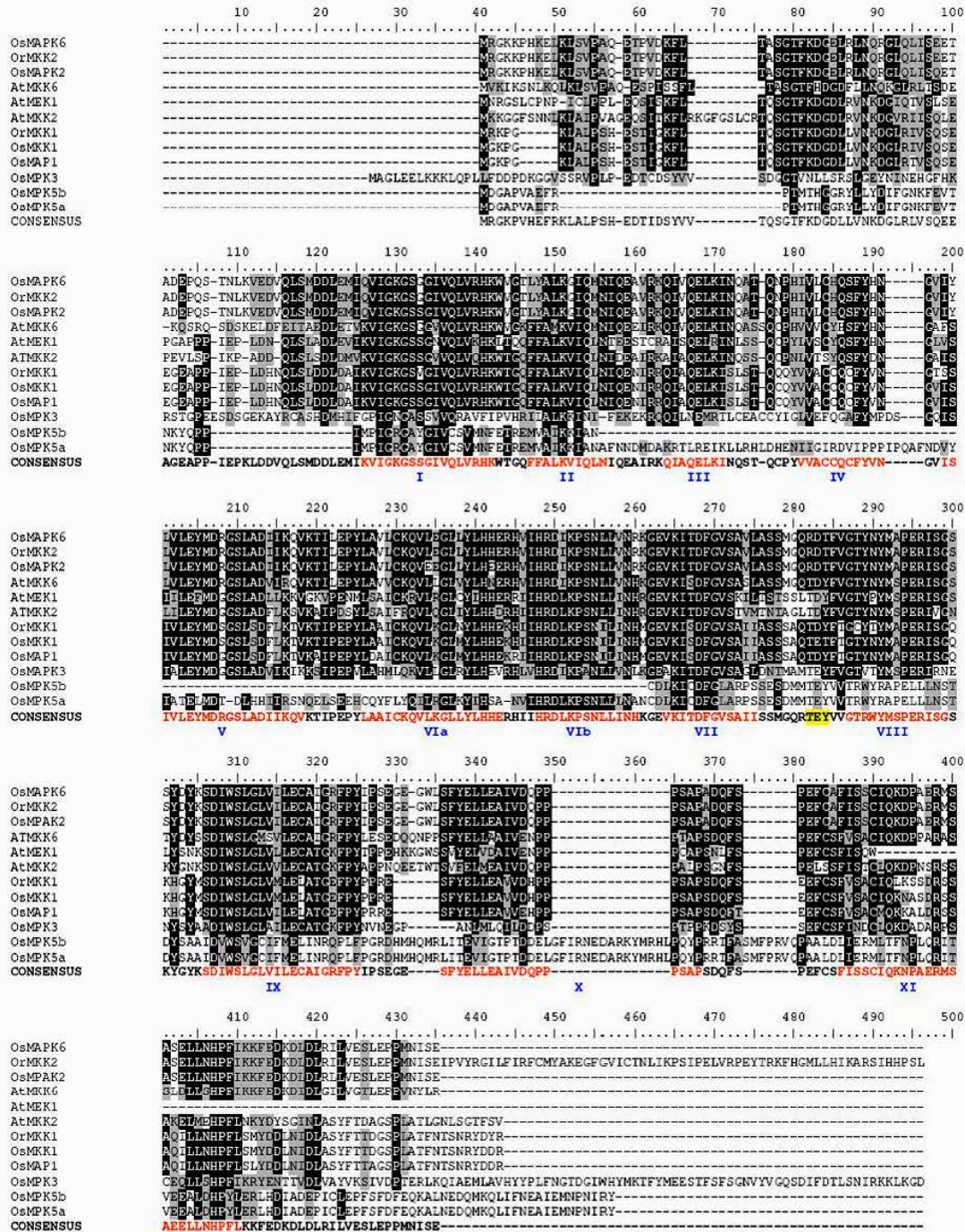
Fig. 2: Comparison of *OrMKK2* and Representative MAPKs from Rice and *Arabidopsis*. Conserved amino acid residues are shown in the consensus sequence. *OrMKK1, ORMKK2, OsMKK1, OsMAP1, OsMAPK2, OsMAPK6, OsMPK3, OsMPK5a* and *OsMPK5b* from rice (*O. sativa*), *AtMEK1* and *AtMKK2* from *Arabidopsis*. The 11 subdomains of the protein kinases are indicated below in the consensus sequences with Roman numerals. Thr (T) and Tyr (Y), two residues normally phosphorylated for the activation of MAPKs, are highlighted (location of TEY/TDY) in yellow (Nadarajah *et al.*, 2009a)

MAPKK-MAPK forms the basic module of a MAPK pathway. MAPK pathways may integrate a variety of upstream signals through interaction with other kinases or G proteins, such as ras or heterotrimeric complexes. The latter factors often function as coupling agents between a plasma membrane-located receptor protein that senses an extracellular stimulus and a MAPK module (Hamel *et al.*, 2006).

The downstream activation of the cytoplasmic MAPK module often induces the translocation of the MAPK into the nucleus, where amongst other genes the kinase are also activated through the phosphorylation of specific transcription factors. There are cases where a given MAPK may translocate to other sites in the cytoplasm to phosphorylate specific enzymes (protein kinases, phosphatases, lipases etc.) or cytoskeletal components (Ren *et al.*, 2008). The various MAPK pathways that are in cells can mediate signaling of a multitude of extracellular signals and result in a variety of responses that are tightly regulated by signaling components and substrates in cells, tissues or organs.

MAPKs ARE INVOLVED IN SIGNAL TRANSDUCTION IN EUKARYOTES

The best studied eukaryotic MAPK system is in yeast and this organism is viewed as a model on MAPK regulation in multicellular organism. The MAPK genes in yeast have been isolated, fully sequenced and characterized (Widmann *et al.*, 1999). There are MAPKs that have been shown to be involved in response to pheromone, production of pseudohyphal growth in response to nitrogen starvation and adaptation to a hypoosmolar environment. In mammals, MAPKs or ERKs (extracellular signal-regulated kinases) were originally identified as transducers of mitogens. Later, MAPKs were also shown to be involved in signaling mediated by hormones, neurotransmitters and signals for differentiation (Nakagami *et al.*, 2005).

Two new groups of protein kinases have been added to the family of mammalian MAPKs (Hamel *et al.*, 2006). The Stress-Activated Protein Kinases (SAPKs) or Jun kinases (JNKs) were identified by their ability to specifically phosphorylate the transcription factor *c-jun* which facilitates responses to ultraviolet radiation, proinflammatory cytokines and environmental stress (Mizuno *et al.*, 2008). The second family, the p38 kinases, are activated in response to bacterial endotoxin, interleukin-1 and hyperosmolarity stress. A p38 kinase is also induced by heat shock activating yet another protein kinase that phosphorylates small heat shock proteins. The JNK and p38 MAPKs share functional similarities in terms of stress signaling.

In a variety of mammalian host cells, microbial infection has been demonstrated to influence MAPK activity. For example, infection by Borna Disease Virus (BDV) in neurons (Hans *et al.*, 2004) and Respiratory Syncytial Virus (RSV) in bronchial epithelial cells affects ERK MAP kinase activation. In addition, activity of JNK MAP kinase is reported to be affected by Yersinia (Tatoo and Hunter, 2002) *T. gondii* (Luder *et al.*, 2009) and Theleria (Luder *et al.*, 2009) infections. In *Plasmodium* infections, the use of a MAPK inhibitor has been shown to inhibit invasion of host by the parasite (Dluzewski and Garcia, 1996).

In higher plants, a variety of genes encoding MAPKs have been identified in alfalfa (Duerr *et al.*, 1993), *Arabidopsis* (Mizuguchi *et al.*, 1993, 1994), *Avena* (Huttly and Phillips, 1995), parsley (Ligterink *et al.*, 1997), pea (Stafstrom *et al.*, 1993), petunia (Decroocq *et al.*, 1995) and tobacco (Wilson *et al.*, 1993; Seo *et al.*, 1995; Wilson *et al.*, 1995; Zhang and Klessig, 1997). Each of these groups of MAPKs when compared with one another show high level of sequence similarity in the eleven domains necessary for the catalytic function of serine: threonine protein kinases indicating that these sequences have important biological functions possibly in relation to substrate specificity or to interactions with other proteins (Fig. 2). The sequences outside these domains may show little homology within different MAPKs. The phosphorylation of the threonine and tyrosine residues is necessary for activation of MAPKs found in all plant MAPKs between subdomains VII and VIII of the catalytic core (highlighted in Fig. 2). Plant MAPKs may be grouped into at least four distinct families. The significance of the branching into different families is not fully understood, but so far this suggests that MAPKs within one branch serve similar functions in different species. According to the available information, MAPKs of families I and II are mostly involved in signaling pathogens and abiotic stress, whereas at least some of the MAPKs of family III are involved in cell cycle regulation. Therefore, the sequence divergence most likely reflects different substrate specificities and functions (Nadarajah *et al.*, 2009a, b).

MAPKs MEDIATE MECHANICAL STRESS REGULATION

Plants as immobile organisms are exposed to a variety of environmental stresses, including changes in temperature, water conditions, radiation and wind. Wind is a mechanical stress and can lead to major changes in the growth pattern of plants, diverting energy into strengthening plant stature, which is exemplified in the

short stature of wind-exposed trees in the mountains or in coastal areas. Experiments showing that mechanical manipulation of *Arabidopsis* leaves, induces transcription of particular MAPK and MAPKK genes (Mizoguchi *et al.*, 1996) links the MAPK pathway to mechanical stimuli-induced signaling.

MAPKs PLAY A ROLE IN ABIOTIC STRESS SIGNALING

Drought, salinity and extreme temperatures are limiting factors for the development and growth of all plants (Craig *et al.*, 2008). Plants grown in different soil conditions and weather conditions from different climatic zones have developed specific mechanisms to withstand these stresses. Plants adaptive strategies to biotic stresses include the expression of specific genes that are related to stress modulation that result in the composition of the major cell components. Recent reports have shown that MAPKs are involved in the signal transduction of drought and cold (Fig. 3) (Jonak *et al.*, 1996; Nadarajah *et al.*, 2009a). The MAPK genes were transcriptionally activated in response to the above stress. The levels of MAPKs were differentially expressed in tissues and organs. In the example of drought stress, roots of the plants showed higher levels of MAPK expression compared to leaves. The levels in roots remained high until the stress is removed (Nadarajah *et al.*, 2009a; Xiong and Yang, 2003). The activation of the MAPK is not a general stress response,

because heat or hypo- and hyperosmolar stress were unable to induce the kinase. Another interesting MAPK is the *Ntf4*, a tobacco MAPK, that was activated in pollen (Wilson *et al.*, 1997). Both the expression and the activity of *Ntf4* are developmentally controlled during pollen maturation; hydration of the mature dry pollen can stimulate the activity of *Ntf4* much further. Unhydrated pollens will not initiate the fertilization process.

The idea that a MAPK is involved in osmotic stress adaptation may find support in the report where the pea PsD5 MAPK was shown to complement HOG1- deficient yeast for their ability to grow on a hyperosmolarity medium (Popping *et al.*, 1996). However, it is still unclear if hyperosmolar stress may activate PsD5 or any MAPK in plants. Precaution must be taken in extending functional complementation data from yeast to other organisms. For example, even though alfalfa MMK2 has been shown to complement the MPK1 pathway necessary for hypoosmolar signaling in yeast suggesting the involvement of MMK2 in hypoosmolar stress signaling in plants, no evidence for such a role was found (Jonak *et al.*, 1995). Assuming induction of MAPK gene expression by a particular stimulus as evidence for a role in signal transduction, it is likely that MAPK pathways also play a role in response to other physical stresses, because transcript amounts of specific *Arabidopsis* MAPK and MAPKK genes are increased upon exposure to water stress, cold, touch and high salt (Mizoguchi *et al.*, 1996).
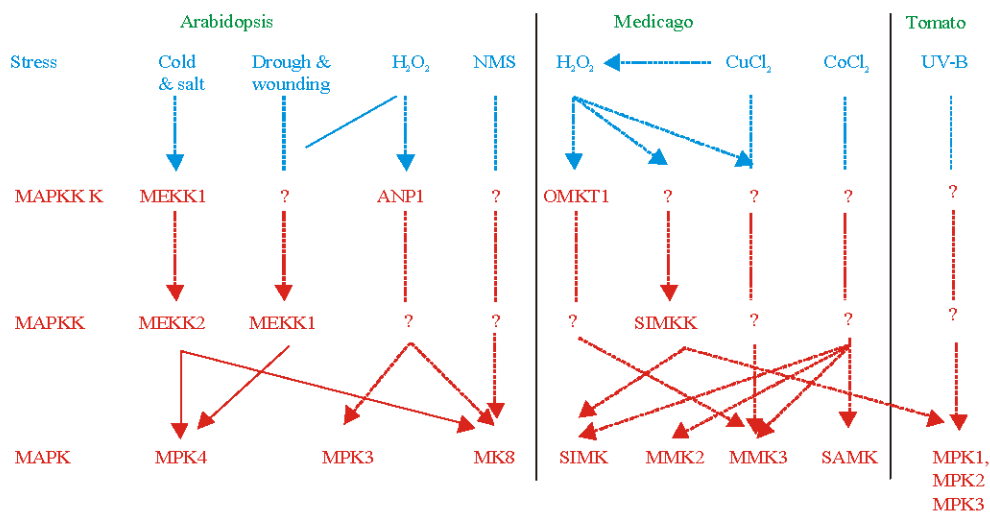

Fig. 3: Model describing the role of *Arabidopsis, Medicago* and tomato MAPK pathways in abiotic stress responses. Broken arrows indicate hypothetical pathways; question marks indicate unknown cascade components. Abbreviation: MMS, methyl methanesulfonate (Tena *et al.*, 2001)

MAPKs AS MEDIATORS OF WOUND SIGNALING

One of the most severe environmental stresses to which plants can be subjected to is wounding. This can be caused by either mechanical injury, pathogen or herbivore attack. Plants have developed a defense systems that is mostly based on the activation of particular sets of genes encoding a variety of enzymes, such as Pathogen Related (PR) proteins or proteinase inhibitors (PIs) (Lee *et al.*, 2004). Some of these genes are induced locally at the site of attack, while others are systemically induced throughout the plant to protect it against attack at distant sites. Several of the genes involved in defense response have been identified and studied, but relatively little is known about how a plant senses wounding and transmits the signal to the nucleus before induction of the respective defense-related genes. Several reports have implicated a MAPK in the process of wound perception in both monocots and dicots (Deng *et al.*, 2006). Activation of this MAPK occurs within less than 1 min of wound infliction, placing this process in the very first line of responses to a wound signal. In a separate study, it was shown that wounding tobacco leaves also lead to the rapid accumulation of a wound-induced protein kinase, WIPK gene (a MAPK gene) transcript (Seo *et al.*, 1995). Overexpression of the *WIPK* gene in transgenic tobacco led to inactivation of the endogenous copies and as a consequence to suppression of the wound response. In studying the MAPK (*OrMKK1*) in rice, Nadarajah *et al.* (2009a, b) showed that MAPK was induced in response to mechanical wounding as well as wounding caused by pathogen infections caused by *Magnaporthe grisea* (Reyna and Yang, 2006). Both injuries elevated the levels of MAPK expression at the site of injury rapidly i.e., in 30 min post injury.

MAPKs ARE ACTIVATED BY MICROBIAL ELICITORS

Plants perceive the presence of pathogens through the process of wounding and the presence of microbial elicitor proteins on plant surfaces. Plant cells respond to elicitors by rapid changes in the phosphorylation status of proteins (Dietrich *et al.*, 1990; Felix *et al.*, 1991; Reyna and Yang, 2006) and it was demonstrated that treating tobacco cells with fungal elicitors, derived from *Phytophthora infestans* cell walls, activated a protein kinase which has properties of a MAPK (Suzuki and Shinshi, 1995; Nadarajah and Xie, 2004; Park *et al.*, 2008; Ren *et al.*, 2008) (Fig. 4).

In addition, elicitors from *Phythophthora parasitica* differentially activated three kinases (Lee *et al.*, 2004) in parsley. One of these three kinases was identified as SIPK, a MAPK that was previously identified to be
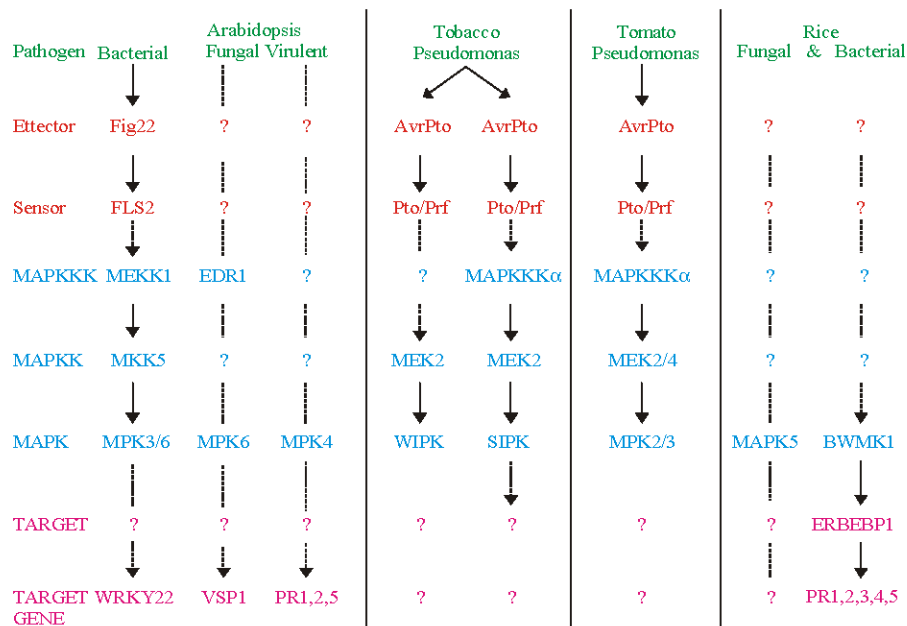

Fig. 4: Model describing the role of *Arabidopsis*, tobacco, tomato, parsley and rice MAPK pathways in biotic stresses. Broken arrows indicate hypothetical pathways; question marks indicate unknown factors (Tena *et al.*, 2001)

activated by salicylic acid (Zhang and Klessig, 1997). Collectively the work conducted in deciphering the plant-pathogen interaction has proposed a model where the peptide elicitor of the pathogen binds to a plasma membrane-located receptor and in so doing sequentially activates various ion channels, a nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (resulting in an oxidative burst) and induction of PR (pathogen related) genes and phytoalexin synthesis (Jabs *et al.*, 1997). The studies by Ligterink *et al.* (1997) showed that within this model the three components of the MAPK were activated by microbial elicitors in various different plant tissues studied.

In parsley cells, elicitor caused a rapid translocation of ERMK from the cytoplasm into the nucleus, suggesting a direct role of ERMK in the regulation of elicitor-induced gene transcription (Ligterink *et al.*, 1997). Similarly, harpin proteins from *Erwinia amylovora*, caused necrosis to occur in tobacco plants within 24 h. Necrosis is a defense response in plants towards microbial infections. This in turn activates the defense systems in the plants which involves the MAPK cascade. These results indicate that not only fungal but bacterial elicitors are able to activate MAPK pathways in plants (Ren *et al.*, 2008; Xiong and Yang, 2003; Song and Goodman, 2002).

ROLE OF MAPKs IN INTRACELLULAR SIGNALING OF PLANT HORMONES

Despite intense efforts to understand how plant hormone signals are perceived and transmitted, many of the molecular mechanisms involved still remains unclear. Increasing evidence suggests that MAPK pathways are involved in mediating abscisic acid (ABA), auxin (AU) and ethylene (ET) responses in plants. ABA has been shown to be involved in many plant physiology processes such as embryo development and seed germination and also in abiotic stress responses including adaptation to drought and salt stresses (Craig *et al.*, 2008). Certain MAPKs are however, not activated by ABA e.g., *OrMKKI* an abiotic stress-induced gene from *Oryza rufipogon*. Expression profiles of this gene in rice showed basal level activity, indicating that this gene did not respond to extracellular application of ABA (Nadarajah and Kassim, 2009).

Genetic analysis of the ethylene pathway in *Arabidopsis* indicates the possible involvement of a MAP kinase module. A number of mutants (*ctr-1, cpm-1*) have been isolated that show a Constitutive Triple Response (CTR) in the absence of ethylene. The *ctr*1 mutant was isolated and the affected gene cloned and analyzed (Kieber *et al.*, 1993) and the encoded CTR1 protein was found to be similar to mammalian *Raf* kinase, an upstream activator of MAPKKs (Yue *et al.*, 2006). Upstream components in the CTR1 pathway appear to be the plasma membrane-located ethylene receptors ETR1 and ERS (Chang, 1996). The *etr*1 gene was isolated in a mutant screen for ethylene insensitivity and encodes a protein with homology to two-component sensor regulator proteins that are well-known bacterial signaling transducers. In a study using transgenic OrMKK1 lines carrying a MAPK gene from wild rice, ethylene positively regulated the expression of the MAPK gene. *OrMKK1* expression remained high until 12 h post-treatment (Nadarajah and Kassim, 2009).

Most plant cell cultures require auxins for proliferation, which suggests that auxin may act as a mitogen under certain conditions. Whereas auxin starvation arrests cell division in a tobacco cell suspension culture, readdition starts the cell cycle. During this process, a MAPKK and a protein kinase that has the properties of a MAPK are activated, suggesting that a MAPK pathway is involved in auxin signal transduction (Dai *et al.*, 2006; Mizoguchi *et al.*, 1994).

ROLE OF SIGNAL MOLECULES IN THE ACTIVATION OF MAPKs

Several lines of evidence have suggested that MAPK genes can be induced by more than one signaling molecule such as Jasmonic Acid (JA) and Salicylic Acid (SA). Typical examples are *SIPK* (Zhang *et al.*, 1998; Lee *et al.*, 2001) (induced by SA and nitrous oxide (NO)), *OsEDR1* (Song and Goodman, 2002) (induced by JA, SA, ABA, hydrogen peroxide (H_2O_2) and ET), *OsBIMK1* (Song and Goodman, 2002) (induced by BTH (analog of SA) and blast fungus) and *OsMAPK5* (Xiong and Yang, 2003) (induced by blast fungus, ABA, JA and SA) (Nadarajah and Xie, 2004; Nadarajah and Turner, 2003; Nadarajah, 2001).

Nadarajah and Kassim (2009) showed that *OrMKK1* is transiently but strongly induced by JA, SA, ET and BTH. The response was however weak towards ABA. Unlike other reported rice MAP kinases, such as *OsMAPK5* (Xiong and Yang, 2003), *OrMKK1* is not induced by abiotic stresses (Nadarajah *et al.*, 2009b) but by JA, SA and BTH. Since both JA and SA are endogenous-signaling molecules involved in plant defense responses the results in this study suggest that *OrMKK1* may be a component of a novel MAPK-signaling cascade that is associated with JA, SA and ET defense signaling in rice. Further function analysis of *OrMKK1*, however, is required to claim the discrete role of this gene in JA- and SA-mediated signal transduction

pathways and their involvement in the defense signaling and defense responses in rice.

CONCLUSIONS

Over the past few years, we have seen a surge of results indicating the involvement of MAPKs in a variety of plant signaling processes. In many cases, however, only indirect proof was provided and the responsible protein kinase gene was not identified. Without these results, we should keep in mind that other types of protein kinases share many of the properties of MAP kinases (similar substrate specificities, similar sizes etc.). Therefore, it will be essential to obtain the proper tools to identify the specific MAP kinases and isolate the respective genes encoding the enzymes. Biochemical and genetic approaches will be essential and should equally contribute to study the function of MAPK pathways in the different processes. Assuming that the present evidence will hold, how is it that so many signals can be transmitted by MAPK pathways? From a theoretical standpoint, there are distinctly different MAPK genes in the plant genomes that may be assigned a specific role in the MAPK pathways. However, experience from a growing number of investigations of mammalian indicates that the MAPK cascade a complicated and involves cross talking and interlinking between various pathways. This is exhibited by the multiple pathways that are activated by extracellular signals and the possibility of a single pathway being activated by a number of unrelated signals. The same signal may activate different pathways in different cells. Last but not least, the activation of a pathway is not an all-or-none process, but can be a transient or a constitutive event and may differ in amplitude. Changing only one of the above parameters has been shown to dramatically affect the outcome of the cellular response. Contemplating along these lines, signal transduction is likely to be a question of pathway combinatorics and the responses at the chromatin level may depend on which of the many protein kinase pathways are active and to what extent at a given moment.

REFERENCES

Asai, T., G. Tena, J. Plotnikova, M.R. Willmann and W.L. Chiu *et al.*, 2002. MAP kinase signaling cascade in *Arabidopsis* innate immunity. Nature, 415: 977-983.

Chang, C., 1996. The ethylene signal transduction pathway in *Arabidopsis*: An emerging paradigm? Trends Biochem. Sci., 21: 129-133.

Colcombet, J. and H. Hirt, 2008. Arabidopsis MAPKs: A complex signaling network involved in multiple biological processes. Biochem. J., 413: 217-226.

Craig, E.A., M.V. Stevens, R.R. Vaillancourt and T.D. Camenisch, 2008. MAP3Ks as central regulators of cell fate during development. Dev. Dyn., 237: 3102-3114.

Dai, Y., H. Wang, B. Li, J. Huang and X. Liu *et al.*, 2006. Increased expression of MAP kinase kinase 7 causes deficiency in polar auxin transport and leads to plant architectural abnormality in *Arabidopsis*. Plant Cell, 18: 308-320.

Decroocq-Ferrant, V., S. Decroocq, J. van Went, E. Schmidt and M. Kreis, 1995. A homolog of the MAP: ERK family of protein kinase genes is expressed in vegetative and in female reproductive organs of *Petunia hybrida*. Plant Mol. Biol., 27: 339-350.

Deng, M., W.L. Chen, A. Takatori, M. Peng and L. Zhang *et al.*, 2006. A role for the mitogen-activated protein kinase kinase kinase 1 in epithelial wound healing. Mol. Biol. Cell, 17: 3446-3455.

Dietrich, A., J.E. Mayer and K. Hahlbrock, 1990. Fungal elicitor triggers rapid, transient and specific protein phosphorylation in parsley cell suspension cultures. J. Biol. Chem., 265: 6360-6368.

Dluzewski, A.R. and C.R. Garcia, 1996. Inhibition of invasion and intraerythrocytic development of *Plasmodium falciparum* by kinase inhibitors. Experientia, 52: 621-623.

Duerr, B., M. Gawienowski, T. Ropp and T. Jacobs, 1993. MsERK1: A mitogen-activated protein kinase from a flowering plant. Plant Cell, 5: 87-96.

Felix, G., D.G. Grosskopf, M. Regenass and T. Boller, 1991. Rapid changes of protein phosphorylation are involved in transduction of the elicitor signal in plant cells. Proc. Natl. Acad. Sci. USA., 88: 8831-8834.

Hamel, L.P., M.C. Nicole S. Sritubtim M.J. Morency and M. Ellis *et al.*, 2006. Ancient signals: Comparative genomics of plant MAPK and MAPKK gene families. Trends Plant Sci., 11: 192-198.

Hans, A., J.J. Bajramovic, S. Syan, E. Perret, I. Dunia, M. Brahic and D. Gonzalez-Dunia, 2004. Persistent, noncytolytic infection of neurons by Borna disease virus interferes with ERK 1/2 signaling and abrogates BDNF-induced synaptogenesis. FASEB J., 18: 863-865.

Huttly, A. and A.L. Phillips, 1995. Giberellin-regulated expression in oat aleurone cells of two kinases that show homology to MAP kinase and a ribosomal protein kinase. Plant Mol. Biol., 27: 1043-1052.

Ichimura, K., K. Shinozaki, G. Tena, J. Sheen and Y. Henry *et al.*, 2002. Mitogen-activated protein kinase cascades in plants: A new nomenclature. Trends Plant Sci., 7: 301-308.

Jabs, T., M. Tschope, C. Colling, K. Hahlbrock and D. Scheel, 1997. Elicitor-stimulated ion fluxes and O$_2$-from the oxidative burst are essential components in triggering defense gene activation and phytoalexin synthesis in parsley. Proc. Natl. Acad. Sci. USA., 94: 4800-4805.

Jonak, C., A. Pay, L. Bogre, H. Hirt and E. Heberle-Bors, 1993. The plant homolog of MAP kinase is expressed in a cell cycle-dependent and organ specific manner. Plant J., 3: 611-617.

Jonak, C., S. Kiegerl, C. Lloyd, J. Chan and H. Hirt, 1995. MMK2, a novel alfalfa MAP kinase, specifically complements the yeast MPK1 function. Mol. Gen. Genet., 248: 686-694.

Jonak, C., S. Kiegerl, W. Ligterink, P.J. Barker, N.S. Huskisson and H. Hirt, 1996. Stress signaling in plants: A mitogen-activated protein kinase pathway is activated by cold and drought. Proc. Natl. Acad. Sci. USA., 93: 11274-11279.

Kieber, J.J., M. Rothenberg, G. Roman, K.A. Feldmann and J.R. Ecker, 1993. CTR1, a negative regulator of the ethylene response pathway in *Arabidopsis*, encodes a member of the Raf family of protein kinases. Cell, 72: 427-441.

Lee, M.W., M. Qi and Y. Yang, 2001. A novel jasmonic acid-inducible rice *myb* gene associates with fungal infection and host cell death. Mol. Plant Microbe Interact., 14: 527-535.

Lee, J., J.J. Rudd, V.K. Macioszek and D. Scheel, 2004. Dynamic changes in the localization of MAPK cascade components controlling pathogenesis-related (PR) gene expression during innate immunity in parsley. J. Biol. Chem., 279: 22440-22448.

Ligterink, W., T. Kroj, U. zur Nieden, H. Hirt and D. Scheel, 1997. Receptor-mediated activation of a MAP kinase in pathogen defense of plants. Science, 276: 2054-2057.

Luder, C.G.K., R.R. Stanway, M. Chaussepied, G. Langsley and V.T. Heussler, 2009. Intracellular survival of apicomplexan parasites and host cell modification. Int. J. Parasitol., 39: 163-173.

Manning, G., D.B. Whyte, R. Martinez, T. Hunter and S. Sudarsanam, 2002. The protein kinase complement of the human genome. Science, 298: 1912-1934.

Marshall, C., 1994. MAP kinase kinase kinase, MAP kinase kinase and MAP kinase. Curr. Opin. Gen. Dev., 4: 82-89.

Mishra, N.S., R. Tuteja and N. Tuteja, 2006. Signaling through MAP kinase networks in plants. Arch. Biochem. Biophys., 452: 55-68.

Mizoguchi, T., N. Hayashida, K. Yamaguchi-Shinozaki, H. Kamada and K. Shinozaki, 1993. ATMPKs: A gene family of plant MAP kinases in *Arabidopsis thaliana*. FEBS Lett., 336: 440-444.

Mizoguchi, T., Y. Gotoh, E. Nishida, K. Yamaguchi-Shinozaki, N. Hayashida and T. Iwasaki, 1994. Characterization of two cDNAs that encode MAP kinase homologues in *Arabidopsis thaliana* and analysis of the possible role of auxin in activating such kinase activities in cultured cells. Plant J., 5: 111-122.

Mizoguchi, T., K. Irie, T. Hirayama, N. Hayashida and K. Yamaguchi-Shinozaki *et al.*, 1996. 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. USA., 93: 765-769.

Mizuno, T., K. Fujiki, A. Sasakawa, N. Hisamoto and K. Matsumoto, 2008. Role of the *Caenorhabditis elegans* Shc adaptor protein in the c-Jun N-terminal kinase signaling pathway. Mol. Cell Biol., 28: 7041-7049.

Nadarajah, K., 2001. The signaling pathway involved in plant-pathogen interaction in *Arabidopsis thaliana*. Pak. J. Biol. Sci., 4: 508-510.

Nadarajah, K. and J.G. Turner, 2003. The role of jasmonate in plant-pathogen interactions in *Arabidopsis thaliana*. J. Teknologi, 39: 9-16.

Nadarajah, K. and D.X. Xie, 2004. Isolation and characterisation of clones corresponding to genes involved in jasmonate regulation of *Arabidopsis thaliana*. Malaysian J. Biochem. Mol. Biol., 10: 39-46.

Nakagami, H., A. Pitzschke and H. Hirt, 2005. Emerging MAP kinase pathways in plant stress signaling. Trends Plant Sci., 10: 339-346.

Nadarajah, K., N.M. Kasim and V.V. Fui, 2009a. Function of mitogen-activated protein kinase gene in biotic stress. Asian J. Plant Sci., 85: 191-198

Nadarajah, K., N.M. Kasim and V.V. Fui, 2009b. The modulation of abiotic stresses by mitogen-activated protein kinase in rice. J. Biol. Sci., 9: 402-412.

Nadarajah, K. and N.M. Kassim, 2009. Effect of signal molecules and hormones on the expression of protein kinase gene *OrMKK1* in rice. J. Plant Sci., 416: 32-42.

Park, G., S. Pan and K.A. Borkovich, 2008. Mitogen-activated protein kinase cascade required for regulation of development and secondary metabolism in *Neurospora crassa*. Eukaryot Cell., 7: 2113-2122.

Popping, B., T. Gibbons and M.D. Watson, 1996. The *Pisum sativum* MAP kinase homologue (PsMAPK) rescues the *Saccharomyces cerevisiae* hog1 deletion mutant under conditions of high osmotic stress. Plant Mol. Biol., 31: 355-363.

Ren, D., Y. Liu, K.Y. Yang, L. Hanm and G. Mao *et al.*, 2008. A fungal-responsive MAPK cascade regulates phytoalexin biosynthesis in *Arabidopsis*. Proc. Natl. Acad. Sci. USA., 105: 5638-5643.

Reyna, N.S. and Y. Yang, 2006. Molecular analysis of the rice MAP kinase gene family in relation to *Magnaporthe grisea* infection. Mol. Plant Microbe Interact., 19: 530-540.

Rudolf, F., S. Pelet and M. Peter, 2008. Regulation of MAPK signaling in yeast. Topics Curr. Genet., 20: 187-204.

Ruis, H. and C. Schuller, 1995. Stress signaling in yeast. Bioessays, 17: 959-965.

Schwacke, J.H. and E.O. Voit, 2007. Concentration-dependent effects on the rapid and efficient activation of the MAP kinase signaling cascade. Proteomics, 7: 890-899.

Seo, S., M. Okamoto, H. Seto, K. Ishizuka, H. Sano and Y. Ohashi, 1995. Tobacco MAP kinase: A possible mediator in wound signal transduction pathways. Science, 270: 1988-1992.

Song, F. and R.M. Goodman, 2002. OsBIMK1: A rice MAP kinase gene involved in disease resistance response. Planta, 215: 997-1005.

Stafstrom, J.P., M. Altschuler and D.H. Anderson, 1993. Molecular cloning and expression of a MAP kinase homologue from pea. Plant Mol. Biol., 22: 83-90.

Suzuki, K. and H. Shinshi, 1995. Transient activation and tyrosine phosphorylation of a protein kinase in tobacco cells treated with a fungal elicitor. Plant Cell, 7: 639-647.

Tatoo, C.M. and C.A. Hunter, 2002. Host-pathogen interactions: Subversion and Utilization of the NF-B pathway during infection. Infect. Immun., 7: 3311-3317.

Tena, G., T. Asai, W.L. Chiu and J. Sheen, 2001. Plant mitogen activated protein kinase signaling cascades. Curr. Opin. Plant Biol., 4: 392-400.

Widmann, C., S. Gibson, M.B. Jarpe and G.L. Johnson, 1999. Mitogen-activated protein kinase: Conservation of a three-kinase module from yeast to human. Physiol. Rev., 79: 143-180.

Wilson, C., N. Eller, A. Gartner, O. Vicente and E. Heberle-Bors, 1993. Isolation and characterisation of a tobacco cDNA clone encoding a putative MAP kinase. Plant Mol. Biol., 23: 543-551.

Wilson, C., R. Anglmayer, O. Vicente and E. Heberle-Bors, 1995. Molecular cloning, functional expression in *Escherichia coli* and characterisation of multiple mitogen-activated protein kinases from tobacco. Eur. J. Biochem., 233: 249-257.

Wilson, C., V. Voronin, A. Touraev, O. Vicente and E. Heberle-Bors, 1997. A developmentally regulated MAP kinase activated by hydration in tobacco pollen. Plant Cell, 9: 2093-2100.

Xiong, L. and Y. Yang, 2003. Disease resistance and abiotic stress tolerance in rice are inversely modulated by an abscisic acid-inducible mitogen-activated protein kinase. Plant Cell, 15: 745-759.

Yue, J., W. Xiong and J.E. Ferrell, 2006. B-Raf and C-Raf are required for Ras-stimulated p42 MAP kinase activation in Xenopus egg extracts. Oncogene, 25: 3307-3315.

Zhang, S. and D.F. Klessig, 1997. Salicylic acid activates a 48 kDa MAP kinase in tobacco, Plant Cell, 9: 809-824.

Zhang, S., H. Du and D.F. Klessig, 1998. Activation of the tobacco SIP kinase by both a cell wall-derived carbohydrate elicitor and purified proteinaceous elicitins from *Phythophthora* spp. Plant Cell, 10: 435-449.