丝裂原活化蛋白激酶激酶(MAPKK)对植物发育及抗逆功能的调控研究进展

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摘要: 植物的三种蛋白激酶MAPKKK、MAPKK和MAPK组成了丝裂原活化蛋白激酶(MAPK)级联信号系统, 可快速放大胞外刺激并将其转化为胞内响应。在此过程中, 丝裂原活化蛋白激酶激酶(MAPKK)是MAPK通路的中间环节, 在信号放大和传递过程中至关重要。大量研究表明, MAPKK在植物生长发育及胁迫响应等过程中发挥重要作用。本文从植物MAPKK的结构特征、细胞定位、生长发育调控、生物及非生物胁迫响应等方面进行了综述, 并展望了未来的研究方向, 期望对相关研究提供借鉴。

关键词: 植物; MAPKK; 生长发育; 非生物胁迫; 生物胁迫

丝裂原活化蛋白激酶(mitogen-activated protein kinase, MAPK或MPK)级联通路是广泛存在于酵母、植物、动物等真核生物中且高度保守的信号系统(Tena等2001)。该通路在植物的激素传导(Knetsch等1996)、胞质分裂(Soyano等2003)、花粉发育(Voronin等2004)等生理过程及氧化应激(Samuel等2000)、生物和非生物胁迫(Jonak等2004)过程中发挥着至关重要的作用。MAPK级联信号途径通常由MAPK激酶激酶(mitogen-activated protein kinase kinase kinase, MAPKKK或MEKK或MAP3K)、MAPK激酶(mitogen-activated protein kinase kinase, MAPKK或MKK或MEK或MAP2K)及MAPK三种蛋白激酶逐级磷酸化传递信号(Schaeffer和Weber 1999)。当细胞表面的模式识别受体(pattern recognition receptor, PRRs)感受到胞外刺激, 随即发生同源或异源二聚化, 进而磷酸化细胞质中的受体类胞质激酶(receptor-like cytoplasmic kinases, RLCKs), 被活化的RLCKs磷酸化激活MAPKKK, 从而将胞外信号传递给MAPK级联信号通路(Cui等2018; Liang和Zhou 2018)。例如, 拟南芥细胞表面的PRR——几丁质激发子受体激酶1 (chitin elicitor receptor kinase1, CERK1)和赖氨酸基序受体激酶5 (lysine motif receptor kinase 5, LYK5)形成的四聚体与胞外几丁质结合, 形成几丁质诱导复合物, 进而磷酸化RLCK VII, 并由其激活MAPKKK3/5–MKK4/5–MPK3/6级联通路(Bi等2018)。

MAPK级联通路首先被激活的是MAPKKK, 它能够识别MAPKK中保守的丝氨酸/苏氨酸基序S/T-$X_{3\sim5}$-S/T (S: 丝氨酸; T: 苏氨酸; X: 任意氨基酸; 3~5: 氨基酸数目)并使其磷酸化, 导致MAPKK的激活; MAPKK属于双特异性蛋白激酶, 既能磷酸化酪氨酸残基也能磷酸化丝/苏氨酸残基。它识别MAPK中的T-X-Y基序, 并磷酸化苏氨酸和酪氨酸残基, 激活MAPK (Chang和Karin 2001); MAPK同属于丝氨酸和苏氨酸蛋白激酶, 是级联信号通路的最后一环, 被激活后在细胞的不同位置发挥作用: 进入细胞核激活特定的转录因子, 引起基因表达变化; 也可停留在细胞质中激活其他蛋白激酶或细胞骨架, 从而行使不同的功能(Nakagami等2005)。

在同一种植物中, MAPKK的数量显著少于MAPKKK和MAPK, 如拟南芥(*Arabidopsis thaliana*)有60个MAPKKKs, 20个MAPKs, 10个MAPKKs (Ichimura等2002); 水稻(*Oryza sativa*)有74个MAPKKKs, 17个MAPKs, 8个MAPKKs (Kumar等2008; Rao等2010); 番茄(*Lycopersicon esculentum*, 异名*Solanum lycopersicum*)有89个MAPKKKs, 16个MAPKs, 5个MAPKKs (Kong等2012; Wu等2014); 玉米(*Zea mays*)有74个MAPKKKs, 19个

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MAPKs, 9个MAPKKs (Kong等2013a, b); 二倍体棉花雷蒙德氏棉(*Gossypium raimondii*)有78个MAPKKKs, 28个MAPKs, 11个MAPKKs (Yin等2013; Zhang等2014, 2016)。由此暗示, MAPK级联系统中的串扰可能发生在MAPKK水平, 一个MAPKK可能参与多个MAPKs级联信号通路, 执行不同的生物学功能, 即一种MAPKK可以被多种上游MAPKKKs激活, 同时能够磷酸化多个下游的MAPKs (Andreasson和Ellis 2010)。因此, MAPKK作为MAPK级联反应汇聚点, 在信号级联放大、信息整合以及胞外刺激和胞内响应之间的信息传递中发挥着重要的作用。基于此, 本文拟从植物MAPKK的结构分类、细胞定位、参与生长发育过程及响应生物和非生物胁迫等方面进行综合论述, 期望为MAPKK的功能及调控机制研究提供参考依据。

1 植物MAPKK的结构、分类及细胞定位

1.1 MAPKK的结构与分类

MAPKK处于级联反应的中间, 可以磷酸化下游的MAPK, 也能被MAPKKK磷酸化; 同时一个MAPKK可能有多个MAPKKKs靶点, 也可能激活多个MAPKs (Rodriguez等2010)。这意味着MAPKK需要复杂多样的结构域来行使不同的功能。

MAPKK家族一般具有11个保守的亚结构域(I~XI), 其中S/T-$X_{3\sim5}$-S/T基序是其磷酸化激活位点; N-末端具有高度保守的MAPK的结合位点(docking domain, D-domain) (Ichimura等2002)。然而, 在拟南芥AtMKK3、AtMKK8和玉米ZmMAPKK1中则缺少典型的基序(Kumar等2008)。在植物中, D-domain由[K/R][K/R][K/R]$X_{2\sim7}$[L/I/V]X[L/I/V]X[L/I/V]组成(K: 赖氨酸; R: 精氨酸; X: 任意氨基酸; 2~7: 氨基酸数目; L: 亮氨酸; I: 异亮氨酸; V: 缬氨酸), 即由至少2个碱性氨基酸残基开始, 随后2~7个任意氨基酸隔开, 紧接着是疏水-X-疏水结构(Kumar等2008)。MAPK上的共同结合位点(common docking site, CD-domain)可以帮助D-domain与其调节的MAPK结合(Tanoue等2000)。

在植物中, 根据蛋白质一级序列和系统发育分析, MAPKK通常被分为A、B、C和D四组(Ichimura等2002; Hamel等2006), 表1对部分植物的MAPKK的分类进行了总结。目前关于拟南芥MAPKK的研究较为充分, 数据显示, A组可能在参与防御反应, 介导植物激素、信号传导, 提高对非生物胁迫的耐受性等方面, 具有多种生物学功能(Hamel等2006)。B组特有核转移因子(nuclear transfer factor 2, NTF2)结构域(Ichimura等2002; Hamel等2006), NTF2是一种小蛋白, 介导Ran-GDP的核输入, 并与Ran-GDP和含有FxFG重复序列的核孔蛋白结合(Quimby等2000), 如B组的拟南芥AtMKK3 (Ichimura等2002)、水稻OsMKK3 (Kumar等2008)、毛果杨PtMKK3 (Hamel等2006)中均具有NTF2结构域。C和D组MAPKK基因没有内含子, 这一现象在拟南芥(Ichimura等2002)、毛果杨(Nicole等2006)、水稻(Kumar等2008)、雷蒙德氏棉(Zhang等2016)、番茄(Wu等2014)、香蕉(Wang等2017b)等植物中得到了验证。除D组外, 其余3组在VII和VIII亚结构域之间均含有一段保守的S/T-$X_{3\sim5}$-S/T基序, 该基序中的丝氨酸/苏氨酸残基的磷酸化是激活MAPKK所必需的(Ichimura等2002)。目前D组如何发生磷酸化尚不清楚。

1.2 MAPKK的亚细胞定位及功能

蛋白质的亚细胞定位与其发挥功能密切相关。很多蛋白质的分布是一个动态过程, 其定位受多种因素的影响。MAPKK作为重要的信号传递组分, 位于MAPK级联信号通路的中间, 通过磷酸化与MAPKKK及MAPK相互作用, 因此, MAPKK的细胞定位及可能的变化对探索MAPK级联通路在信号转导中的作用极为重要。

基于目前已有的报道, MAPKK在细胞的各亚细胞区域都有分布, 频率较高的是定位于细胞核。除了B组因特有NTF2结构域而定位于细胞核中, 许多含有核定位信号肽(序列为PKKKRKV)的其他组的MAPKK也定位于细胞核中(Sánchez-Mir等2012), 如C组的玉米非生物胁迫应答蛋白ZmMKK4在细胞核中通过激活转录因子发挥功能(Kong等2011); D组中的拟南芥AtMKK9 (与发育及非生物胁迫相关)也定位于细胞核中, 并通过激活AtMAPK3/6促进转录因子EIN3 (ethylene-insensitive 3)传递乙烯信号(Yoo等2008)。即使缺乏核

表1 部分植物MAPKK的分类

Table 1 Classification of MAPKK in some plant species

物种名	类别	成员	蛋白数	总蛋白数	参考文献
拟南芥(*Arabidopsis thaliana*)	A	MKK1/2/6	3	10	Ichimura等2002
	B	MKK3	1		
	C	MKK4/5	2		
	D	MKK7/8/9/10	4		
水稻(*Oryza sativa*)	A	MKK1/6	2	8	Kumar等2008
	B	MKK3	1		
	C	MKK4/5	2		
	D	MKK10.1/10.2/10.3	3		
玉米(*Zea mays*)	A	MKK1/6	2	9	Kong等2013a
	B	MKK3-1/3-2/3-3	3		
	C	MKK4/5	2		
	D	MKK10-1/10-2	2		
雷蒙德氏棉(*Gossypium raimondii*)	A	MKK1/2-1/2-2/6	4	11	Zhang等2016
	B	MKK3	1		
	C	MKK4/5	2		
	D	MKK7/9/10-1/10-2	4		
毛果杨(*Populus trichocarpa*)	A	MKK2-1/2-2/6	3	11	Nicole等2006
	B	MKK3	1		
	C	MKK4/5	2		
	D	MKK7/9/10/11-1/11-2	5		
二穗短柄草(*Brachypodium distachyon*)	A	MKK1/6	2	12	Chen等2012
	B	MKK3-1/3-2/3-3	3		
	C	MKK4/5	2		
	D	MKK10-1/10-2/10-3/10-4/10-5	5		
大豆(*Glycine max*)	A	MKK1/2-1/2-2/6-1/6-2	5	11	Neupane等2013
	B	MKK3-1/3-2	2		
	C	MKK4/5	2		
	D	MKK8/10	2		
番茄(*Solanum lycopersicum*)	A	MKK1/3	2	5	Wu等2014
	B	MKK5	1		
	C	MKK2	1		
	D	MKK4	1		
葡萄(*Vitis vinifera*)	A	MKK2/3	2	5	Çakir和Kılıçkaya 2015
	B	MKK5	1		
	C	MKK4	1		
	D	MKK1	1		
黄瓜(*Cucumis sativus*)	A	MKK2-1/2-2/6	3	6	Wang等2015
	B	MKK3	1		
	C	MKK4	1		
	D	MKK9	1		
杜仲(*Eucommia ulmoides*)	A	MKK2/6	2	5	Jing等2017
	B	MKK3	1		
	C	MKK5	1		
	D	MKK9	1		
野草莓(*Fragaria vesca*)	A	MKK3	1	7	Zhou等2017
	B	MKK5	1		
	C	MKK2	1		
	D	MKK1/4/6/7	4		
香蕉(*Musa nana*)	A	MKK6	1	10	Wang等2017b
	B	MKK4/8/9	3		
	C	MKK3/5/10	3		
	D	MKK1/2/7	3		

定位信号, MAPKK也可能定位于细胞核中, 如本氏烟草(*Nicotiana benthamiana*)中D组的NbMKK1 (Takahashi等2007)、陆地棉(*Gossypium hirsutum*)中A组的GhMKK1 (Lu等2013)和C组的GhMKK5 (Zhang等2012a)等。

定位于细胞质的MAPKK同样发挥着重要的功能。拟南芥AtMKK4在细胞质中可能激活AtMPK6发挥不同的功能(Rodriguez等2010), AtMKK6定位于细胞质中的赤道板上, 控制细胞板的合成(Yoo等2008; Takahashi等2010)。玉米ZmMKK3 (Zhang等2012b)、油菜(*Brassica napus*) BnMKK2/3/4 (Liang等2013)同时存在于细胞质和细胞核中, 在胞质中可能作为信号转导组分, 而在核内可能激活转录因子发挥作用。

研究显示, MAPKK在某些条件下会发生转位现象。目前MAPKK的转移过程主要在动物细胞中被发现(Jaaro等1997)。在植物中, 欧芹(*Petroselinum crispum*) PcMKK5始终位于细胞质, 而下游的MAPKs则在细胞质和细胞核中穿梭(Lee等2004)。玉米ZmMKK1主要定位于细胞质, 将激活环的丝氨酸(S)-217和苏氨酸(T)-223残基的双磷酸化位点突变为天冬氨酸(D)而获得的组成型激活的ZmMKK1$^{\mathrm{DD}}$, 则既可定位于细胞质又可在细胞核中与相关底物发生相互作用(Cai等2014b)。拟南芥AtMKK7/9在细胞核、细胞质和细胞膜上均有分布, 而当磷脂酸或NaCl处理后则转位到细胞膜上(Shen等2019)。目前的研究表明, MAPKK亚细胞定位具有多变性, 由此显示其复杂多样的功能特征。

2 植物MAPKK对生长发育的调控

MAPKK可参与植物生长发育的各方面, 包括胞质分裂、胚胎发育、气孔发育、花结构发育、侧根形成、叶片衰老等过程(表2)。

2.1 胞质分裂

拟南芥AtMKK6和烟草(*Nicotiana tabacum*) NtMEK1能通过调控细胞板的形成控制胞质分裂。拟南芥驱动蛋白HIK调控ANP1/3 (MAPKKK)激活AtMKK6, 进而导致AtMPK4磷酸化, 最终完成对胞质分裂的调控(Takahashi等2010)。在烟草中, 驱动蛋白NACK1/2通过NPK1 (MAPKKK)激活NtMEK1, 随后磷酸化NRK1 (MAPK), 进而调控胞质分裂(Soyano等2003)。

2.2 胚胎发育

拟南芥AtMKK4/5–MPK6级联通路调控胚胎在母体中的发育(Zhang等2017)。水稻OsMKK4影响籽粒大小, 且可能与油菜素内酯途径存在关联(Duan等2013); 进一步研究表明, OsMKKK10–MKK4–MAPK6级联通路通过促进小穗颖壳中的细胞增殖, 从而正向调控水稻的籽粒大小和重量(Xu等2018)。组织表达谱分析显示, 玉米*ZmMKK3*和*ZmMKK6*在胚胎中表达量较高, 说明它们可能与胚胎发育有关; 而ZmMKK10可能对种子发育具有负调控作用(Kong等2013a)。

表2 MAPKK在植物生长发育过程中的作用

Table 2 The role of MAPKK in plant growth and development

物种名	MAPKK类型	功能	参考文献
拟南芥(*A. thaliana*)	AtMKK4/5	花序结构、气孔发育、花器官脱落、花粉发育、胚胎发育、侧根形成	Wang等2007; Cho等2008; Meng等2012; Lampard等2014; Zhang等2017; Zheng等2018; Huang等2019; Zhu等2019
	AtMKK6	胞质分裂	Takahashi等2010
	AtMKK7	气孔发育、负调控生长素极性运输、侧根形成	Dai等2006; Lampard等2014; Jia等2016
	AtMKK9	气孔发育、叶片衰老	Zhou等2009; Lampard等2014
烟草(*N. tabacum*)	NtMEK1	胞质分裂	Soyano等2003
	NtMEK2	花粉发育	Voronin等2004
油菜(*B. napus*)	BnMKK1	植株矮小	Yu等2014
水稻(*O. sativa*)	OsMKK4	籽粒大小	Duan等2013; Xu等2018
玉米(*Z. mays*)	ZmMEK1	叶片衰老	Hardin和Wolniak 1998, 2001; Li等2016

2.3 气孔发育

拟南芥YODA (又称YDA, 属于MAPKKK)–MKK4/5–MPK3/6级联信号通路与气孔发育相关(Wang等2007)。在*yoda*单突变体、*mkk4*/*mkk5*双突变体或*mpk3*/*mpk6*双突变体中, 细胞呈异常的不对称分裂, 原来的表皮细胞发育成气孔, 导致气孔聚集在一起; 而*mkk4*或*mkk5*单突变体和*mpk3*或*mpk6*单突变体中, 没有显著的气孔聚集现象, 暗示MKK4/5和MPK3/6存在冗余功能。相反, 在*MKK4*/*5*过量表达植株中, 气孔发育受到抑制, 表皮仅由互相嵌合的表皮细胞组成(Wang等2007)。另外, AtMKK7/9也有干扰气孔发育的功能, 但与AtMKK4/5的功能有所不同(Lampard等2014)。

2.4 花结构发育

拟南芥中, 植物受体样蛋白激酶(plant receptor-like protein kinases, RLKs) ER (ERECTA)组分下游的YODA–MKK4/5–MPK3/6级联通路在调节局部细胞增殖、控制花序结构中发挥关键作用(Meng等2012)。抑制*AtMKK4*和*AtMKK5*的表达导致拟南芥的花瓣不能脱落; 而在*mpk3*突变背景下, 干扰*AtMPK6*的表达也会抑制花瓣脱落(Cho等2008)。烟草NtMEK2通过激活p45Ntf4和SIPK (MAPKs)促进花粉发育, *NtMEK2*突变则导致花粉发育异常(Voronin等2004)。转基因烟草中过量表达油菜*BnMKK1*会导致开花时间明显延迟(Yu等2014)。花粉发育过程中, 淀粉粒和脂质体的积累是花粉萌发、花粉管发育和受精成功的关键。AtMKK4/5–MPK3/6–WRKY2/34级联通路通过调控*GPT1* (*GLUCOSE-6-PHOSPHATE/PHOSPHATE TRANSLOCATOR 1*)的表达, 在花粉成熟过程中控制脂质体的生物合成(Zheng等2018)。

2.5 侧根形成

拟南芥MKK7–MPK6级联途径通过磷酸化生长素输出载体PIN1上的Ser337来控制侧根的形成(Jia等2016)。生长素还通过跨膜蛋白激酶TMK1/4 (transmembrane kinases 1/4)激活AtMKK4/5–MPK3/6级联通路, 调节侧根形成(Huang等2019)。此外, 质膜受体HAE (HAESA)和HSL2 (HAESA-LIKE2)感应配体IDA (inflorescence deficient in abscission)信号后, 激活MAPKKK–MKK4/5–MPK3/6级联通路, 从而增强*CWR* (*CELL WALL REMODELLING*)基因的表达, 导致果胶降解, 最终促进侧根的形成(Zhu等2019)。

2.6 叶片衰老

拟南芥AtMKK9–AtMPK6级联途径在叶片衰老过程中起重要作用, 过量表达*AtMKK9*、*AtMPK6*的拟南芥出现早衰表型; 而敲除该基因则导致叶片衰老延迟(Zhou等2009)。基于MKK9激活MPK3/6可诱导乙烯合成的事实, MKK9–MPK6级联通路调控叶片衰老可能与其在诱导乙烯合成中的功能有关(Xu等2008)。通过表达丰度和磷酸化水平的检测, 玉米*ZmMEK1*可能通过水杨酸的积累诱导叶片衰老(Hardin和Wolniak 1998, 2001; Li等2016)。

2.7 对其他发育过程的调控

拟南芥AtMKK7可以调控生长素的极性运输, 过量表达导致植株出现浓密矮化的表型(Dai等2006); 油菜*BnMKK1*的转基因烟草株型矮小(Yu等2014)。AtMKK7–MPK6级联通路可调控枝条分枝、下胚轴向地性及花丝伸长; 而AtMKK7–MPK3级联通路则主要调控叶片形态(Jia等2016)。

3 植物MAPKK参与非生物胁迫响应

植物遭遇逆境时会通过一系列的形态、生理及分子生物学改变以免受胁迫伤害从而适应环境变化(Tuteja 2007)。MAPK级联系统是植物响应生物及非生物胁迫最常见的信号通路之一(Colcombet和Hirt 2008), MAPKK作为其重要组成部分, 广泛参与盐、旱、极端温度、损伤等非生物胁迫响应(表3)。

3.1 盐胁迫

拟南芥的AtMEKK1–MKK2–MPK4/6级联通路能够被盐激活, 从而提高盐胁迫耐受性, 过量表达*AtMKK2*会引起152个细胞防御和应激基因的表达变化(Teige等2004)。研究表明, 过量表达*AtMKK9*导致拟南芥对盐胁迫高度敏感, 而通过插入T-DNA使*AtMKK9*失活的拟南芥产生了盐不敏感表型, 并诱导了胁迫相关的*RD22*和*RD29*基因表达, 表明*AtMKK9*负调控盐胁迫响应(Alzwiy和Morris 2007; Xu等2008)。另一个级联系统AtMEKK1–

表3 MAPKK在植物非生物胁迫响应中的作用

Table 3 The role of MAPKK in plant abiotic stress responses

物种名	MAPKK类型	胁迫响应类型	参考文献
拟南芥(*A. thaliana*)	AtMKK1	干旱、UV-B	Matsuoka等2002; Menges等2008; Xing等2008
	AtMKK2	盐、低温、UV-B	Teige等2004; Menges等2008
	AtMKK3	干旱	Li等2017
	AtMKK4	盐、损伤、UV-B、高温、铁	Menges等2008; Kim等2011; Ye等2015; Li等2018; Samakovli等2020
	AtMKK5	损伤、臭氧、高温、铁	Miles等2009; Ye等2015; Li等2018; Samakovli等2020
	AtMKK9	盐、UV-B、磷、氮	Alzwiy和Morris 2007; Menges等2008; Xu等2008; Lei等2014; Luo等2017
水稻(*O. sativa*)	OsMKK1	盐、干旱、中低温	Wen等2002; Kumar等2008
	OsMKK4	盐、低温、砷离子	Kumar等2008; Rao等2011
	OsMKK6	盐、低温	Kumar等2008; Xie等2012
	OsMKK10.2	干旱、低温	Kumar等2008; Ma等2017
玉米(*Z. mays*)	ZmMKK1	盐、干旱、低温	Cai等2014a, b
	ZmMKK4	盐、低温	Kong等2011
陆地棉(*G. hirsutum*)	GhMKK1/5	盐、干旱	Zhang等2012a; Lu等2013
	GhMKK3	干旱	Wang等2016
番茄(*S. lycopersicum*)	SlMKK1/3/4	干旱、高温	Wu等2014
	SlMKK2/5	盐、干旱、高温	
紫花苜蓿(*M. sativa*)	SIMKK	盐、铜离子	Kiegerl等2000; Jonak等2004
油菜(*B. napus*)	BnMKK1	干旱	Yu等2014
枸杞(*L. chinense*)	LcMKK	盐、干旱	Wu等2015
藜(*C. album*)	CaMKK1	盐、干旱	Wang等2017a
臂状盐角藻(*S. brachiata*)	SbMKK	盐、低温	Agarwal等2010
二穗短柄草(*B. distachyon*)	BdMKK6.2	干旱、低温、高温	Sun等2016
野草莓(*F. vesca*)	FvMKK1/3	盐、高温	Zhou等2017
	FvMKK5	盐	
	FvMKK6/7	高温	

MKK4–MPK3也参与拟南芥盐胁迫响应, 拟南芥过量表达*AtMKK4*后胁迫相关基因*NCED3*和*RD29A*表达上调, 而突变株系两个基因则下调(Kim等2011)。通过拟南芥转基因研究发现, 玉米ZmMKK1通过ABA依赖的方式促进气孔关闭, 诱导ABA依赖的胁迫响应基因*RAB18*和*RD29A*表达, 有效清除过量的活性氧(reactive oxygen species, ROS), 增加盐胁迫的耐受性(Cai等2014a); ZmMKK4通过清除ROS来调节渗透胁迫, 增强对盐胁迫的耐受性(Kong等2011)。在烟草中过表达藜(*Chenopodium album*) *CaMKK1*可有效清除ROS并上调胁迫响应基因(*NtDREB2*、*NtDREB3*、*NtDREB4*)的表达, 增强植株对盐胁迫的耐受性(Wang等2017a)。水稻(Kumar等2008)、陆地棉(Lu等2013)、紫花苜蓿(*Medicago sativa*, Kiegerl等2000)、番茄(Wu等2014)、野草莓(Zhou等2017)、枸杞(*Lycium chinense*, Wu等2015)、臂状盐角藻(*Salicornia brachiata*, Agarwal等2010)等物种不同类型的*MKK*基因均能介导植株对盐胁迫的积极响应(Kiegerl等2000)。然而也有相反的报道, 如在烟草中过表达陆地棉*GhMKK5*基因可以诱发ROS相关基因和细胞死亡标记基因(如*NtRbohA*和*NtCDM*)表达增加, 并导致H_2O_2的积累以及类过敏性反应(hypersensitive response, HR)的细胞死亡, 降低了烟草对盐胁迫的耐受性(Zhang等2012a)。

3.2 干旱胁迫

拟南芥ABA依赖的AtMKK1–MPK6级联系统通过调节过氧化氢酶CAT1活性以降低ROS水平,

从而提高抗旱性; *AtMKK1*突变导致植株对干旱胁迫的敏感性增加(Xing等2008)。同样是ABA依赖的AtMAPKK3被AtMAPKKK18磷酸化激活后能够增强拟南芥的抗旱性(Li等2017)。OsMPKK10.2通过磷酸化激活MPK3介导的ABA信号通路, 可提高水稻对干旱胁迫的耐受性(Ma等2017)。陆地棉中过量表达*GhMKK3*以调节气孔大小及根毛生长的方式增加抗旱性(Wang等2016)。玉米*ZmMKK1* (Cai等2014a)、陆地棉*GhMKK1* (Lu等2013)、枸杞*LcMKK* (Wu等2015)、藜*CaMKK1* (Wang等2017a)、水稻*OsMKK1* (Kumar等2008) 、番茄*SlMAPKK1*、*2*、*3*、*4*、*5* (Wu等2014)均能积极响应干旱胁迫。但过量表达油菜*BnMKK1* (Yu等2014)、陆地棉*GhMKK5* (Zhang等2012a)和二穗短柄草*BdMKK6.2* (Sun等2016)则导致植株迅速失水, 增加了对干旱胁迫的敏感性。

3.3 极端温度胁迫

AtMEKK1–MKK2–MPK4/6级联通路不仅能被盐激活, 也能积极响应冷胁迫。过量表达*AtMKK2*的拟南芥抗寒性明显增强, 而*AtMKK2*突变体的抗寒性降低(Teige等2004)。过量表达玉米*ZmMKK4*可以通过上调低温胁迫相关基因*AtCBF1*、*AtCBF2*、*AtCBF3*的表达, 增强转基因拟南芥对低温的耐受性(Kong等2011)。玉米*ZmMKK1*通过增加脯氨酸和可溶性糖含量、增强ROS的清除能力以及上调胁迫响应基因的表达, 从而提高转基因烟草对低温胁迫的耐受性(Cai等2014b)。水稻中ROS诱导的OsMKK6–MPK3/6级联通路增强了水稻的耐冷性(Xie等2012); OsMEK1 (Wen等2002)、OsMKK4、OsMKK6和OsMKK10.2参与了水稻的冷胁迫(Kumar等2008)。低温胁迫可诱导臂状盐角藻*SbMAPKK* (Agarwal等2010)和二穗短柄草*BdMKK6.2* (Sun等2016)的上调表达。

高温处理后, 番茄*SlMAPKK1*、*2*、*3*、*4*、*5* (Wu等2014)、二穗短柄草*BdMKK6.2* (Sun等2016)和野草莓*FvMAPKK1*、*3*、*6*、*7* (Zhou等2017)的转录水平显著提高。拟南芥受到热胁迫时, HSP90 (heat shock protein 90)与YODA相互作用, 激活下游AtMKK4/5–MPK3/6级联通路, 通过控制气孔发育从而适应热环境(Samakovli等2020)。

3.4 其他非生物胁迫

MAPKK也参与损伤、重金属、紫外线(UV)、营养等胁迫响应。损伤可能由非生物因素(例如风、大雨、冰雹和雪)或生物因素(尤其是草食性生物, 如昆虫)所引起, 能够严重破坏植物组织并促进病原体的进入(Savatin等2014)。拟南芥AtMKK1被损伤刺激激活后, 可能通过激活MAPK上的TEY基序, 并磷酸化苏氨酸和酪氨酸残基来调节AtMPK4的活性(Matsuoka等2002)。AtMKK4/5–MPK3/6级联通路响应损伤刺激后, *ACS* (*ACC SYNTHASE*)基因表达增强, 从而促进了乙烯的生物合成(Li等2018)。

金属离子是植物新陈代谢和生长发育所必需, 但过多将导致细胞损伤(Schützendübel和Polle 2002)。在高浓度铜离子胁迫下, 紫花苜蓿SIMKK特异性激活下游*SIMK*和*SAMK*的表达, 共同响应离子伤害(Jonak等2004)。砷离子胁迫诱导水稻*OsMKK4*在叶和根中的表达(Rao等2011)。

当拟南芥受到UV-B胁迫时, 早、中、晚期分别检测到*AtMKK9*、*AtMKK4*、*AtMKK1*和*AtMKK2*依次上调表达(Menges等2008)。降低*AtMKK5*表达会阻碍臭氧诱导的信号传递至MPK3/6, 导致拟南芥中H_2O_2的积累及对臭氧的敏感性增强(Miles等2009)。

尽管土壤中含有丰富的磷, 但作为植物可利用的磷酸盐却很少。AtMKK9–MPK3/6级联通路通过调节WRKY75, 激活磷酸盐吸收相关基因的表达, 通过抑制花青素的积累, 促进植株对磷酸盐的吸收(Lei等2014)。低氮诱导AtMKK9的表达, 组成型激活的MKK9^{DD}增强氮素吸收相关基因的表达, 促进了氮素的摄入(Luo等2017)。缺铁时, AtMKK4/5–MPK3/6级联通路被激活, 促进乙烯合成基因*ACS2/6*的转录, 从而增强乙烯的生物合成, 而乙烯是缺铁响应基因*FRO2* (*FERRIC-CHELATE REDUCTASE OXIDASE 2*)和*IRT1* (*Fe*$^{2+}$ *TRANSPORTER 1*)转录调控所必需的(Ye等2015)。

4 植物MAPKK参与生物胁迫响应

除响应非生物胁迫, 植物MAPK级联通路也在应对细菌、真菌、病毒、植食性昆虫等生物胁迫中发挥重要作用(表4)。

4.1 细菌与真菌侵害

目前, 在拟南芥富含亮氨酸重复序列(leucine-rich-repeat, LRR)受体激酶FLS2的下游, 发现了一个完整的植物MAPK级联反应途径MEKK1–MKK4/5–MPK3/6–WRKY22/29, 能够通过促进抗病基因的表达赋予植物对细菌和真菌的抗性(Asai等2002); AtMKK1被激发因子flg22 (鞭毛蛋白flagellin N端保守的22个氨基酸多肽)激活后使AtMPK4磷酸化, 从而诱导激发因子应答基因的表达, 在丁香假单胞菌番茄致病变种(*Pseudomonas syringae* pv. *tomato* DC3000, *Pst* DC3000)的防御中发挥重要作用(Mészáros等2006)。过表达*AtMKK3*基因可促进多个病程相关(*pathogenesis-related*, *PR*)基因的表达, 并增强拟南芥对*Pst* DC3000的抗性(Dóczi等2007)。*AtMKK7*在局部叶片中的异位表达可诱导*PR*基因表达, 以增强植株对紫丁香假单胞菌(*Pseudomonas syringae* pv. *maculicola* ES4326, *Psm* ES4326)的抗性(Zhang等2007)。

本氏烟草NbMKK1是植物免疫相关的细胞死亡关键因子, 过表达该基因导致蛋白质向细胞核聚集, 细胞迅速死亡, 已证实NbMKK1在细胞死亡调控中有积极作用; 而沉默*NbMKK1*则会减弱对非寄主病原体西科里假单胞菌(*Pseudomonas cichorii*)的抗性(Takahashi等2007)。水稻OsMPKK10.2通过磷酸化激活MPK6介导的SA信号传导, 从而提高细菌性条斑病[病原为稻生黄单胞菌条斑致病变种(*Xanthomonase oryzae* pv. *oryzicola*, *Xoc*)]的抗性(Ma等2017)。沉默番茄*SlMKK2*和*SlMKK4*后, 减弱了番茄中防御基因的表达, 从而降低了对灰霉菌(*Botrytis cinerea*)的抗性(Li等2014); 抑制*SlMKK2*表达导致番茄叶片中辣椒疮痂病[病原为野油菜黄单胞辣椒斑点病致病型(*Xanthomonas campestris* pv. *vesicatoria*)]的细菌数量显著增加(Melech-Bonfil和Sessa 2011); 丁香假单胞菌(*Pseudomonas sy-*

表4 MAPKK在植物生物胁迫响应中的作用

Table 4 The role of MAPKK in plant biotic stress responses

胁迫类型	MAPKK类型	病害类型	参考文献
细菌	AtMKK1	丁香假单胞菌番茄致病变种	Mészáros等2006
	AtMKK2	丁香假单胞菌番茄致病变种、胡萝卜软腐病	Brader等2007
	AtMKK3	丁香假单胞菌番茄致病变种	Dóczi等2007
	AtMKK4/5	丁香假单胞菌	Asai等2002
	AtMKK7	紫丁香假单胞菌	Zhang等2007
	NbMKK1	西科里假单胞菌	Takahashi等2007
	GhMKK1	青枯病(敏感)	Lu等2013
	GhMKK5	青枯病	Zhang等2012a
	OsMKK10.2	条斑病	Ma等2017
	SlMKK2	辣椒疮痂病	Melech-Bonfil和Sessa 2011
	SlMKK4	丁香假单胞菌	Wu等2014
	ZmMKK1	青枯病	Cai等2014b
真菌	AtMKK2	芸薹生链格孢菌(敏感)	Brader等2007
	AtMKK4/5	灰霉菌	Asai等2002
	GhMKK2	大丽轮枝菌	Gao等2011
	GhMKK5	黑胫病(敏感)	Zhang等2012a
	SlMKK2/4	灰霉菌	Li等2014
	ZmMKK1	灰霉菌(敏感)	Cai等2014b
病毒	NtMEK1/2	烟草花叶病毒	Jin等2003; Liu等2004
	NbMEK1、NbMKK	马铃薯X病毒与Y病毒(PVX-PVY)	Aguilar等2017
	NbMEK2	烟草花叶病毒(TMV)	Deng等2016
植食性昆虫	AtMKK3	海灰翅夜蛾	Sözen等2020
	NaMEK1、NaMEK2、NaMKK1、NaSIPKK、NaNPK2	烟草天蛾	Heinrich等2011, 2012

ringae)处理后, *SlMKK4*的表达水平显著上调(Wu等2014)。陆地棉中不同类型的MAPKK具有相反的作用, 如转基因烟草中过量表达陆地棉*GhMKK1*使*PR*基因的表达降低, 植株对青枯病[病原为茄科雷尔氏菌(*Ralstonia solanacearum*)]的侵染更加敏感(Lu等2013); 而沉默陆地棉*GhMKK2*后植株对大丽轮枝菌(*Verticillium dahliae*)抗性显著降低并呈现更严重的枯萎表型(Gao等2011)。

MAPKK对不同致病菌具有不同的效应。*AtMKK2*提高了拟南芥对*Pst* DC3000和胡萝卜软腐病[病原为马铃薯软腐病菌(*Erwinia carotovora* subsp. *carotovora*)]的抗性, 但增加了对真菌芸薹生链格孢菌(*Alternaria brassicicola*)的敏感性(Brader等2007)。陆地棉*GhMKK5*在烟草中过量表达通过诱导*PR1a*、*PR2*、*PR4*、*PR5*和*NPR1*等抗病基因的表达, 从而提高植株对青枯病的抗性, 但却增加了烟草对黑胫病[病原为黑胫病菌(*Phytophthora parasitica* var. *nicotianae*)]的敏感性(Zhang等2012a)。同样, 过量表达玉米*ZmMKK1*通过诱导病害相关基因的表达, 提高了植株对青枯病的耐受性, 但增加了对灰霉病菌的敏感性(Cai等2014b)。

4.2 病毒侵害

当受到烟草花叶病毒(*Tobacco mosaic virus*, TMV)侵染后, 烟草NPK1 (MAPKKK)激活NtMEK1和NQK1 (MAPKKs), 随后激活的下游NTF6和NRK1 (MAPKs)进一步诱导相关基因的表达; 另一途径中NtMEK2激活WIPK (wounding-induced protein kinase)和SIPK (salicylic acid-induced protein kinase), 促使相关基因表达从而抵御TMV的侵害(Jin等2003; Liu等2004)。NtMEK2–SIPK/WIPK级联途径可能是通过调节植物抗毒素*HMGR* (*3-HYDROXY-3-METHYLGLUTARYL COA REDUCTASE*)和水杨酸生物合成关键酶*PAL* (*L-PHENYLALANINE AMMONIA LYASE*)两个防御基因的表达来抵御病毒侵害的(Yang等2001)。烟草NbMEK2–SIPK级联通路调控油菜素内酯诱导的RBOHB (respiratory burst oxidase homolog B)依赖的氧化爆发, 从而增强植物对TMV的抗性(Deng等2016)。NbMEK1和NbMKK1对马铃薯X病毒(*Potato virus X*, PVX)与Y病毒(PVY)协同作用引起的植物类过敏性细胞死亡具有正调节作用, 从而抵抗病毒感染(Aguilar等2017)。

4.3 植食性昆虫侵害

基于目前的研究, 拟南芥中有两条独立的MAPK级联通路响应植食性昆虫的侵害。一条是不依赖于茉莉酸(jasmonic acid, JA)的AtMKK4/5–MPK3/6级联通路调节乙烯的产生(Li等2018); 另一条是依赖于JA的AtMAP3K14–MKK3–MPK1/2/7/14级联通路, 植食性昆虫引起创伤后可迅速触发植物激素JA的积累, JA及其受体COI1 (CORONATINE INSENSITIVE 1)激活该通路, 可抑制海灰翅夜蛾(*Spodoptera littoralis*)的生长(Sözen等2020)。

渐狭叶烟草(*Nicotiana attenuata*) NaMEK1、NaMEK2、NaMKK1、NaSIPKK和NaNPK2 (MAPKKs)在防御烟草天蛾(*Manduca sexta*)中起作用, 这5个MAPKKs都能调节胰蛋白酶抑制剂的水平, 从而抑制昆虫胰蛋白酶活性。其中NaMEK2激活SIPK和WIPK, 积累JA并促进乙烯的生物合成, 在防御植食性昆虫中起重要作用; NaSIPKK和NaMEK1能促进JA的积累; NaMKK1和NaNPK2可能通过一种独立于SIPK和WIPK (MAPKs)以及JA信号的机制来抵御植食性昆虫对植物的侵害(Heinrich等2011, 2012)。

5 展望

同一植物中, 一个MAPKK可能被多个MAPKKKs激活, 也可能激活多个MAPKs, 从而发挥不同的功能(Rodriguez等2010), 但目前关于同一个MAPKK如何调控多种途径的机制尚不清楚。目前在MAPKK的四个亚组A、B、C、D (Ichimura等2002)中, D组并没有发现必需的磷酸化位点的保守基序S/T-$X_{3\sim5}$-S/T, 因此, 关于D组如何磷酸化激活的机制尚无定论。研究发现, 同一个MAPKK在不同的生物和非生物胁迫中可能发挥不同的功能; 而不同类型的MAPKK有正向调节也可能有负向调节作用, 这种现象产生的原因和不同调控之间的关系仍需深入研究。MAPKK的亚细胞定位与功能密切相关, MAPKK可能受到不同条件刺激发生细胞定位的改变, 关于植物MAPKK定位变化机制尚待解析。尽管目前对植物MAPKK已有较

多前期研究基础, 但是也存在不少亟待解决的问题, 因此仍需对MAPKK的作用机制开展更深入的研究, 从而完善植物MAPK级联信号途径。

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Progress in regulation of mitogen-activated protein kinase kinase (MAPKK) in plant development and stress tolerance

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Abstract: The plant mitogen-activated protein kinase (MAPK) cascades are composed of three protein kinases (MAPKKK, MAPKK and MAPK), which can quickly magnify the extracellular stimulation and convert it as intracellular response. In this relationship, mitogen-activated protein kinase kinase (MAPKK) is the intermediate link of MAPK cascades, which is vital in signal amplification and transmission. A large number of reports have shown that MAPKK plays a crucial role in plant growth and development, as well as response to the biotic and abiotic stresses. In this paper, the plant MAPKK is reviewed and discussed in the structural characteristics, cell localization, regulation of growth and development, response to biotic and abiotic stresses, and the ideas for the further study is prospected, which is expected to provide reference for related research.

Key words: plant; MAPKK; growth and development; abiotic stress; biotic stress

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