

· 专题论坛 ·

植物CBL-CIPK信号系统响应非生物胁迫的调控机制

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摘要 钙调磷酸酶B蛋白(CBLs)及其互作蛋白激酶(CIPKs)组成的信号系统是非生物逆境响应的重要调控网络。CBL-CIPK系统通过磷酸化感应并解码 Ca^{2+} 信号, 参与植物对非生物胁迫的应答调控。该文综述了CBLs和CIPKs结构、CBLs-CIPKs对不同底物磷酸化及其响应非生物胁迫调控机制的研究进展, 并展望了未来的研究方向, 以为作物抗逆性遗传改良提供思路。

关键词 非生物胁迫, 钙信号, CBL-CIPK, 离子通道, 磷酸化

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植物在生长过程中经常遇到干旱、盐碱、极端温度、缺 K^+ 以及病虫害等多种逆境胁迫(Peck and Mittler, 2020)。植物无法逃避逆境, 只能被动应对。因此, 植物在长期进化过程中演化出复杂的信号转导机制, 感知并传递外界变化的信号, 使其对逆境及时做出应激反应(Manik et al., 2015)。在植物体内, 许多信号转导途径和调控网络相互作用, 响应特定的生物或非生物胁迫。植物对逆境的响应与激酶、磷酸酶、激素、 Ca^{2+} 、ROS (reactive oxygen species)以及其它调节蛋白、化合物和小分子相互作用交织在一起, 形成复杂的调控网络(Steinhorst and Kudla, 2013; Sierla et al., 2016; Kudla et al., 2018; Zhang et al., 2018a)。

在细胞内, Ca^{2+} 被认为是无处不在、无时不有的功能性调节者, 对许多生理生化反应和发育过程具有重要调控作用(Yin et al., 2017; Köster et al., 2019)。 Ca^{2+} 信号通过 Ca^{2+} 感应蛋白解码并传递, 进而引起细胞内各种信号系统对环境变化的响应(张和臣等, 2007; Kudla et al., 2018)。在植物中, CBLs (Calcineurin B-like proteins)也称SCaBPs (SOS3-like calcium binding proteins), 是一类独特的 Ca^{2+} 感应蛋白, 其通过激活CIPKs

(CBL-interacting protein kinases)/PKS (protein kinase S) 解码 Ca^{2+} 信号(Sánchez-Barrena et al., 2005; 沈金秋等, 2014; Tang et al., 2020)。CBLs和CIPKs互作构成一个复杂的信号网络, 在植物对干旱、低温和盐碱等逆境的应答调控中起核心作用(张和臣等, 2007; Sun et al., 2015; Ma et al., 2017; Xi et al., 2017)。CBL家族一个成员可以与CIPK家族一个或多个成员相互作用, 建立不同信号级联, 从而形成精准的CBL-CIPK调控网络(Ma et al., 2020)。自CBL-CIPK信号系统被发现以来, 学术界对不同途径的CBL-CIPK复合物的功能、结构、基因表达和调控进行了广泛研究(Weinl and Kudla, 2009; Aslam et al., 2019)。本文综述了CBLs和CIPKs的结构、分类及其响应各种非生物胁迫的调控机制, 并展望了未来的研究方向, 以为作物抗逆性遗传改良提供思路。

1 植物CBL和CIPK结构

CBL和CIPK结构特征为其相互作用提供了基础。CBL4与CIPK24的C端调节域的复合物晶体结构首先被解析出来(Sánchez-Barrena et al., 2005), 进而揭

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示了CBL4-CIPK24复合物如何解码由细胞外刺激触发的细胞内 Ca^{2+} 信号转导(Sánchez-Barrena et al., 2013)。阐明CBLs和CIPKs结构特征有助于理解信号系统的调控机制。

1.1 CBL分子结构与分类

植物CBLs是与酵母(*Saccharomyces cerevisiae*)和动物中的CNB (calcineurin B subunit)最相似的一个 Ca^{2+} 传感器蛋白家族(Cui et al., 2018)。CBL感知应激信号中的 Ca^{2+} 信号,使植物适应环境变化(Bender et al., 2018; Tang et al., 2020)。CBL含有1个典型的 Ca^{2+} 结合基序,即4个手性延伸因子(elongation factor hands, EF-hands),每个EF-hands包含1个能与 Ca^{2+} 结合的保守 α -螺旋-环- α -螺旋结构(Lu et al., 2017)。EF-hands排列在固定的空间中,从EF-hand1到EF-hand4依次有22、25和32个氨基酸的距离(Sánchez-Barrena et al., 2005)。环区的特征是具有12个残基DKDGDGKIDFEE的保守序列(Kolukisaoglu et al., 2004)。位置1(X)、3(Y)、5(Z)、7(-X)、9(-Y)和12(-Z)中的氨基酸高度保守,并负责与 Ca^{2+} 配位(Sanyal et al., 2015)。值得注意的是,EF-hand1在X位置和Y位置之间包含2个插入氨基酸残基的位置(Sánchez-Barrena et al., 2013)。这个位置氨基酸的变化导致与 Ca^{2+} 结合的亲和力发生变化(Kolukisaoglu et al., 2004)。除了具有 Ca^{2+} 感应的EF-hands, CBL还具有N端定位基序和C端磷酸化基序(Beckmann et al., 2016)。研究表明,拟南芥(*Arabidopsis thaliana*) CBL家族4个成员(AtCBL1、-4、-5和-9)具有N-豆蔻酰化基序(Wang et al., 2019)。在SOS (salt overly sensitive)信号系统中, CBL4/SOS3的N-豆蔻酰化基序是植物耐盐性的必备条件(Kleist et al., 2014; Saito et al., 2018), 这为 Ca^{2+} 信号的传递提供了结构基础。

系统发育分析表明,拟南芥AtCBLs可分为3类。AtCBL10是第1类中唯一的成员,并且在CBL家族中具有最长的N端(Sánchez-Barrena et al., 2013)。共聚焦荧光显微分析表明, AtCBL10定位于质膜和液泡膜(Kim et al., 2007; Batistič et al., 2010)。第2类有5个成员(AtCBL1、-4、-5、-8和-9),它们具有N端很短的结构特点(Sánchez-Barrena et al., 2013); 其中大多数包含用于脂双层修饰的保守MGCXXS/T基序,

可帮助CBLs固定在膜上(Tang et al., 2015; Saito et al., 2018)。第3类成员具有相对较长的N端(Sánchez-Barrena et al., 2013), 它们均具有液泡膜靶向序列(tonoplast targeting sequence, TTS) MSQCXDGXK HXCXSSXXCF (除AtCBL7外) (Tang et al., 2012; Kleist et al., 2014)。TTS则有助于AtCBL2、-3和-6定位于液泡膜(Batistič et al., 2010; Tang et al., 2012)。CBL7和CBL3是串联复制,但它们的N端结构域明显不同(Kleist et al., 2014; Sanyal et al., 2016)。CBL7作为 Ca^{2+} 感应蛋白,能够解码细胞核和细胞质的 Ca^{2+} 信号(Batistič et al., 2010)。

1.2 CIPK分子结构与分类

植物CIPK在功能上类似于酵母SNF1 (sucrose non-fermenting 1)和哺乳动物AMPK (AMP-dependent kinase) (Mo et al., 2018; Niu et al., 2018)。CIPK由2个结构域组成,一个含有磷酸化位点激活环的保守N端激酶催化结构域,另一个具有NAF/FISL基序和PPI (protein phosphatase interaction)基序高度不同的C端调节域(Sánchez-Barrena et al., 2013; Sanyal et al., 2015)。NAF基序以其高度保守的氨基酸Asn (N)、Ala (A)、Phe (F)、Ile (I)、Ser (S)和Leu (L)而得名,是结合CBL的必需位点,其对于维持AtCIPK24和AtCBL4互作是必需的,并且能够连接AtCIPK24的C端调节结构域以覆盖其激活环,从而使激酶保持在自动抑制状态(Chaves-Sanjuan et al., 2014)。CIPK是具有激酶和调节结构域的Ser/Thr蛋白激酶(Tang et al., 2020)。显然,磷酸化是该系统发挥相应功能的主要作用方式。因此,磷酸化是CIPK调节靶标蛋白以及与CBL互作的优选方式(Sanyal et al., 2020)。

根据内含子丰富度,可将拟南芥AtCIPK家族分为富有内含子和稀有内含子2个进化分支(Mao et al., 2016)。在稀有内含子的进化分支中有17个成员(AtCIPK2、-4、-5、-6、-7、-10、-11、-12、-13、-14、-15、-16、-18、-19、-20、-22和-25),其它9个成员(CIPK1、-3、-8、-9、-17、-21、-23、-24和-26)在富有内含子的进化分支中。分段和串联重复的发现促进了这2个进化分支的扩展(Guo et al., 2001)。CIPK在细胞中通常定位于细胞质和细胞核,且可通过与CBLs互作靶向下游蛋白(Batistič et al., 2010)。此外,系统发育分析结果表明, AtCIPKs家族分为5个亚组:

A、B、C、D和E。有意思的是, 含有多个内含子的AtCIPK成员都聚集在A亚组中, 而其它4个亚组中的基因均为少有或无内含子的成员(Kolukisaoglu et al., 2004)。

CBL和CIPK的生理学功能首次在SOS途径中被发现(Zhu et al., 1998)。拟南芥突变体*atsos1*、*atsos2*和*atsos3*在高盐胁迫下产生相同的盐敏感表型。AtSOS3和AtSOS2也分别被称为AtCBL4和AtCIPK24, 而AtSOS3和AtSOS2已被证明协同正向调节质膜Na⁺/H⁺转运蛋白AtSOS1的活性, 在高盐胁迫下介导Na⁺外排(Zhu et al., 1998; Sanyal et al., 2015)。随后, 在拟南芥中鉴定出10个CBLs和26个CIPKs (Kolukisaoglu et al., 2004; Yu et al., 2007)。随着植物基因组测序的完成, 在不同物种中相继鉴定出数量不等的CBLs和CIPKs家族成员(表1)。

2 植物CBL-CIPK系统与磷酸化

CBL-CIPK复合物对下游靶标蛋白的调节主要通过磷酸化方式进行(Sanyal et al., 2020)。靶标蛋白主要有通道蛋白、转运蛋白和转录因子等(Sanyal et al., 2015)。已有研究表明, 可被CBL-CIPK复合物磷酸化的阳离子(H⁺、Na⁺、K⁺、Mg²⁺、Fe²⁺和NH₄⁺)相关蛋白如AHA2、SOS1、AMT1、ATL31、AKT1、HAK5、TPK1、ARF、ERF、SnRK2D和FIT, 而一些阴离子(OH⁻和NO₃⁻)转运蛋白如CHL1 (NRT1.1)、RBOH-F

和RBOH-C也可被CBL-CIPK磷酸化(Ragel et al., 2019; Lara et al., 2020; Sanyal et al., 2020; Dong et al., 2021)。

大量研究表明, CBL与CIPK互作并将其磷酸化是一种普遍的机制, 而且磷酸化能够增强CBL-CIPK复合物的相互作用, 进而提高CIPK的活性(Hashimoto et al., 2012; Sanyal et al., 2020)。在植物中, CIPK对CBL的磷酸化最初在豌豆(*Pisum sativum*)中被报道, PsCIPK可对PsCBL的Thr残基进行磷酸化(Mahajan et al., 2006), 随后在多个物种中相继发现了这种现象(Sanyal et al., 2016)。CBL的C端含有1个由23个氨基酸残基组成的基序, 其中有绝对保守的氨基酸残基P、M、L、F、P和F, 因此称作“PFPF基序”(FPSF结构域) (Sanyal et al., 2020)。CIPK能够将FPSF结构域中保守的Ser残基磷酸化(Sanyal et al., 2020)。海藻(*Sargassum* sp.)的部分CBL缺少该结构, 以Asp和Glu残基代替(Hashimoto et al., 2012)。CIPK介导CBL磷酸化是部分CBL-CIPK信号系统发挥具体功能的必要步骤。例如, AtCIPK24对AtCBL10的磷酸化可激活Na⁺转运蛋白NHX7 (Almeida et al., 2017), 而CIPK23对CBL1的磷酸化也可激活K⁺通道AKT1(Hashimoto et al., 2012; Sánchez-Barrena et al., 2020)。因此, CBL的磷酸化一方面可增强其与CIPK互作; 另一方面又促进CIPK对下游靶标蛋白的转磷酸作用(Lin et al., 2014; Sanyal et al., 2016)。

表1 不同物种的CBL和CIPK家族

Table 1 The CBL and CIPK families in different species

物种	CBLs数量	CIPKs数量	参考文献
拟南芥(<i>Arabidopsis thaliana</i>)	10	26	Kolukisaoglu et al., 2004
油菜(<i>Brassica napus</i>)	7	23	Zhang et al., 2014a
杨树(<i>Populus trichocarpa</i>)	10	25	Weinl and Kudla, 2009
辣椒(<i>Capsicum annuum</i>)	9	26	Ma et al., 2019
水稻(<i>Oryza sativa</i>)	10	31	Weinl and Kudla, 2009; Piao et al., 2010
茶(<i>Camellia sinensis</i>)	7	18	Liu et al., 2019
小麦(<i>Triticum aestivum</i>)	24	79	Sun et al., 2015; Liu et al., 2018
芜菁(<i>B. rapa</i> var. <i>rapa</i>)	19	51	Yin et al., 2017
木薯(<i>Manihot esculenta</i>)	8	26	Hu et al., 2015; Mo et al., 2018
茄子(<i>Solanum melongena</i>)	5	15	Li et al., 2016
菠萝(<i>Ananas comosus</i>)	8	21	Aslam et al., 2019
葡萄(<i>Vitis vinifera</i>)	8	20	Xi et al., 2017
玉米(<i>Zea mays</i>)	8	43	Chen et al., 2011
甜菜(<i>Beta vulgaris</i>)	7	20	未发表数据

3 植物CBL-CIPK信号系统在非生物胁迫响应中的调控机制

3.1 CBL-CIPK复合物对离子通道或转运蛋白的调控

植物通过根系从土壤中吸收必需的离子并分配在整个植物组织中(Köster et al., 2019; Srivastava et al., 2020)。大量研究表明, 无机离子在维持植物生长中扮演多种重要角色。 K^+ 、 NO_3^- 和 Cl^- 可维持细胞渗透压, 从而控制细胞膨压, 这对于细胞扩增、气孔运动和花粉管生长至关重要(Saito and Uozumi, 2019)。 NO_3^- 、 NH_4^+ 、 SO_4^{2-} 和 PO_4^{3-} 等被细胞代谢从而产生各种蛋白质和有机化合物(López-Arredondo et al., 2013, 2014)。

在这些必需的离子中, Ca^{2+} 浓度通常相对较低, 在细胞质中保持在 $0.1\text{ mmol}\cdot\text{L}^{-1}$ 左右(Hepler, 2005)。然而, 当植物遭遇干旱、盐碱、病原体侵害或营养缺乏等逆境时, Ca^{2+} 通过质膜离子通道流入细胞中或从细胞器中释放, 使胞质 Ca^{2+} 浓度迅速升高(Zhu, 2016; Manishankar et al., 2018; Toyota et al., 2018)。这导致 Ca^{2+} 结合的感应蛋白构象发生变化, 随之与下游效应蛋白以 Ca^{2+} 依赖方式相互作用并调控其功能(Tang et al., 2020)。胞内 Ca^{2+} 与CBL在其EF-hands处结合, 而CIPK的C端NAF/FISH结构域与CBL互作(Guo et al., 2001; Kolukisaoglu et al., 2004; Su et al., 2020)。CBL与CIPK结合使得CIPK的C端自抑制结构域释放N端激酶结构域, 从而增强CIPK活性(Zhou et al., 2016; Yin et al., 2020)。

在拟南芥中, CBL-CIPK信号系统调控许多离子转运蛋白(图1, 图2), 包括介导 K^+ (KAT1、KAT2、GORK、AKT1、AKT2、HAK5和SPIK)、 Na^+ (SOS1)、 NH_4^+ (AMT1;1和AMT1;2)、 NO_3^- (NRT1.1、NRT2.4和NRT2.5)、 Cl^- (SLAC1、SLAH2和SLAH3)和 H^+ (AHA2和V-ATPase)的通道或转运蛋白(Ho et al., 2009; Lérán et al., 2015; Liu et al., 2016; Straub et al., 2017; Ragel et al., 2019; Saito and Uozumi, 2019)。CBL-CIPK在响应C/N养分及Mg和Fe的摄取中也发挥重要作用(Sanyal et al., 2020)。这种 Ca^{2+} 依赖性磷酸化调节系统的功能可确保植物的生长, 并使其能耐受各种环境胁迫(Sanyal et al., 2020)。由此可见, CBL-CIPK复合物的磷酸化调控对象主要是各种

离子通道和转运蛋白。

低浓度 Na^+ 对植物生长有一定的刺激作用, 但高浓度 Na^+ 则会引起细胞渗透和离子毒害(Zhu, 2016)。拟南芥SOS信号途径是调节植物根耐盐性的重要机制(Zhu et al., 1998; Yin et al., 2020)。在盐胁迫下, AtCBL10与AtCIPK24 (SOS2)互作(图1; 表2), 将 Na^+ 区域化到液泡, 以保护植物地上部免受盐胁迫伤害(Hu et al., 2015; Plasencia et al., 2021)。这与SOS通路的耐盐机制不同(Yang et al., 2019)。被激活的SOS1利用 H^+ -ATPase (AHA2)产生的质子梯度能量将 Na^+ 转运出细胞(图1) (Yin et al., 2020)。CBL10与CIPK8形成的复合物介导SOS1的激活, 表明CIPK8在调节拟南芥地上部响应盐胁迫中起重要作用(Yin et al., 2020), 但其复合物下游靶标蛋白还有待深入鉴定。细胞内较高的 K^+/Na^+ 比是植物耐盐性的核心指标(Zhang et al., 2020)。研究表明, HKT1 (high affinity potassium transporters 1)能够维持细胞内高浓度的 K^+ 和低浓度 Na^+ (Almeida et al., 2017)。水稻 (*Oryza sativa*) OsHKT1;1主要在维管组织中表达, 高盐条件下可增强细胞的 Na^+ 外排能力(Campbell et al., 2017)。此外, 过表达OsHKT1;4的转基因植株木质部中 Na^+ 含量降低, 而根中的 Na^+ 含量增加, 从而提高对盐胁迫的敏感性(Oda et al., 2018)。CBL2/CBL3-CIPK21也参与植物的耐盐性, 该复合物主要在液泡中发挥作用, 但其下游靶点仍有待确定(Sanyal et al., 2016)。

K^+ 是植物细胞中最丰富的离子, 在调节细胞渗透压、膜电位和细胞内pH值方面发挥至关重要的作用(伍国强等, 2017; Almeida et al., 2017; Ragel et al., 2019)。 K^+ 亏缺会导致拟南芥根中 Ca^{2+} 迅速增加(Behera et al., 2017)。维持根系 K^+ 吸收的主要系统有 K^+ 通道AKT1和高亲和性 K^+ 转运蛋白HAK5 (图1; 表2) (Alemán et al., 2011)。CBL1/9与CIPK23结合并在质膜上聚集, CIPK23激活后将AKT1和HAK5磷酸化并激活, 以促进 K^+ 的吸收和转运(图1; 表2) (Lara et al., 2020)。此外, CBL4-CIPK6复合物作用于AKT2, 可应答 K^+ 的外排(图1) (Saito and Uozumi, 2020)。液泡膜CBL2/3-CIPK3/9/23/26复合物激活TPKs (two-pore K^+ channels), 以维持细胞内 K^+ 稳态(Tang et al., 2020; Dong et al., 2021)。

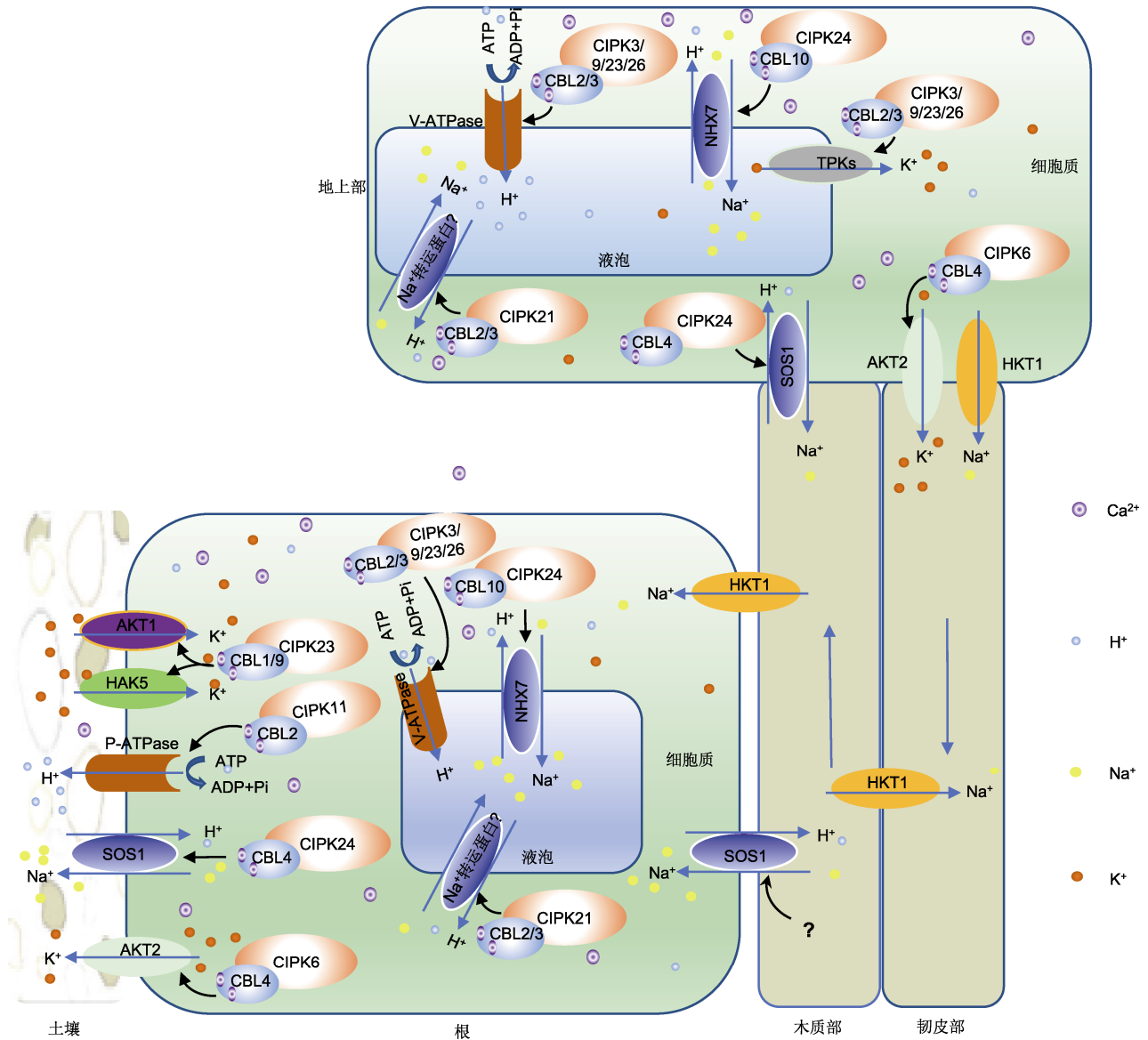


图1 调节拟南芥根部和地上部Na⁺和K⁺稳态的CBL-CIPK系统
蓝色箭头指示离子的流入/流出; 黑色箭头表示激活。

Figure 1 CBL-CIPKs in regulating Na⁺ and K⁺ homeostasis in *Arabidopsis thaliana* roots and shoots
Blue arrows indicate influx/efflux of ion; black arrows indicate activation.

NO₃⁻和NH₄⁺是植物根系从土壤中吸收的2种N素来源(Tang et al., 2020)。Ca²⁺调控多种NRT/NPF和SLAH转运蛋白进行NO₃⁻摄取和转运(Sanyal et al., 2020)。NPF6.3通过二聚体作用使NO₃⁻从低亲和性模式转换为高亲和性模式, 此过程通过CBL1/9-CIPK23对Thr101的磷酸化作用进行控制(Ho et al., 2009; Parker and Newstead, 2014; Sun et al., 2014; Chu et al., 2021)。NH₄⁺吸收由AMTs (ammonium

transporters)介导(Sanyal et al., 2020)。高浓度NH₄⁺会替代K⁺而产生毒害作用, 因此必须控制其在细胞的非毒性水平(Zheng et al., 2015)。AMT的2个成员(AMT1;1和AMT1;2)也可被CBL1-CIPK23复合物抑制(表2; 图2) (Straub et al., 2017)。因此, CBL1-CIPK23可能在维持根细胞K⁺稳态和免受NH₄⁺毒害中起关键作用(Zheng et al., 2015)。Weng等(2020)研究表明, 高浓度K⁺降低水稻根系对NH₄⁺的

吸收速率, 增强对H⁺的外排速率, 从而减轻NH₄⁺对水稻的毒害。此外, CBL1/9-CIPK23与SLAH2和SLAH3互作通过吸收或分泌NO₃⁻参与硝酸盐的转运(表2)(Ho et al., 2009; L  ran et al., 2015)。

CBL1/9-CIPK23与SLAC1或SLAC3相互作用(表2; 图2), 参与ABA (abscisic acid)对气孔大小的调节, 从而导致气孔关闭(Maierhofer et al., 2014a, 2014b)。研究表明, H⁺-ATPase也与相对应的CBL-CIPK互作而发挥作用(图1; 表2)。质膜H⁺-ATPase受CBL2-CIPK11调控(Saito and Uozumi, 2020), 而液泡膜H⁺-ATPase则受CBL2/3-CIPK3/9/23/26调控(Tang et al., 2012, 2015)。

3.2 CBL-CIPK复合物对转录因子的调控

已有研究表明, 在ABA信号通路中起作用的转录因子也会被CIPK磷酸化(Sanyal et al., 2016; Zhao et al., 2019)。最早的报道是ERF7 (ethylene respon-

sive factor 7)被CIPK15磷酸化(Song et al., 2005)。磷酸化后的ERF7可能通过2种机制发挥作用: 一是它们结合含有GCC盒的基因并抑制其转录; 二是ERF7可以将AtSin3和HDA19之间的阻遏复合物靶向移至相关基因的启动子, 以进一步抑制基因转录(Song et al., 2005)。与之相反, CIPK26介导的ABI5磷酸化是正向调节因子, 可稳定ABI5并启动ABA的下游反应(Lyzenga et al., 2017)。KEG (keep on going)使ABI5和CIPK26受到26S蛋白酶的降解, 从而抵消ABA的作用(Lyzenga et al., 2017)。此外, PKS5/CIPK11使ABI5在Ser42处磷酸化并激活, 从而调节基因表达(Zhou et al., 2015)。因此, CIPK26和PKS5/CIPK11可能在同一途径中发挥相似作用(Zhou et al., 2015)。CIPK3与ABR1 (ABA-repressor 1)相互作用并使其磷酸化, 从而调节种子萌发过程中的ABA应答反应(Sanyal et al., 2017; Wang et al., 2018)。

表2 拟南芥CBL-CIPK信号网络调控非生物胁迫
Table 2 *Arabidopsis thaliana* CBL-CIPK signal network regulates abiotic stresses

CBL	CIPK	靶标蛋白	定位	功能	参考文献
CBL4/SOS3	CIPK24/SOS2	SOS1	质膜	增强耐盐性	Zhu et al., 1998; Yin et al., 2020
CBL10	CIPK24	NHX7	质膜/液泡膜	增强耐盐性	Hu et al., 2015; Plasencia et al., 2021
CBL10	CIPK8	SOS1	质膜	增强耐盐性	Yin et al., 2020
CBL2/3	CIPK21	–	液泡膜	增强耐盐性	Sanyal et al., 2016
CBL2/7	CIPK11	H ⁺ -ATPase	质膜	维持pH平衡	Saito and Uozumi, 2020
CBL2/3	CIPK3/9/23/26	V-ATPase	液泡膜	维持pH平衡	Tang et al., 2012, 2015
CBL1	CIPK23	AMT1;1/AMT1;2	质膜	维持NH ₄ ⁺ 平衡	Straub et al., 2017
–	CIPK8	NRT2.1	–	维持NO ₃ ⁻ 稳态	Hu et al., 2009
CBL1/9	CIPK23	CHL1/NPF6.3	质膜	维持NO ₃ ⁻ 稳态	Ho et al., 2009; Chu et al., 2021
		SLAH2/SLAH3	质膜	维持NO ₃ ⁻ 稳态	L��ran et al., 2015
CBL7	–	NRT2.4/NRT2.5	–	维持NO ₃ ⁻ 稳态	Ma et al., 2015
CBL1/9	CIPK23	AKT1/HAK5	质膜	维持K ⁺ 稳态	Lara et al., 2020
CBL4	CIPK6	AKT2	质膜	维持K ⁺ 稳态	Saito and Uozumi, 2020
CBL2/3	CIPK3/9/23/26	TPK	液泡膜	维持K ⁺ 稳态	Tang et al., 2020; Dong et al., 2021
CBL1/9	CIPK26	RBOHF	质膜	响应ROS信号	Zhang et al., 2014b
CBL1/9	CIPK23	SLAC1/SLAC3	质膜	响应ABA信号	Maierhofer et al., 2014a, 2014b
CBL5	CIPK11	SLAC1	质膜	响应ABA信号	Saito et al., 2018
CBL1	CIPK15	ABI1/ABI2	–	响应ABA信号	Guo et al., 2002
CBL9	CIPK3	ABR1	–	响应ABA信号	Sanyal et al., 2017; Wang et al., 2018
CBL2/3	CIPK9/17	PAT10	液泡膜	响应ABA信号	Song et al., 2018
–	CIPK26/11	ABI5	–	响应ABA信号	Zhou et al., 2015; Lyzenga et al., 2017
CBL2/3	CIPK3/9/23/26	Mg ²⁺ 转运蛋白	液泡膜	维持Mg ²⁺ 平衡	Tang et al., 2015

– 表示无数据可用 – indicate no data available

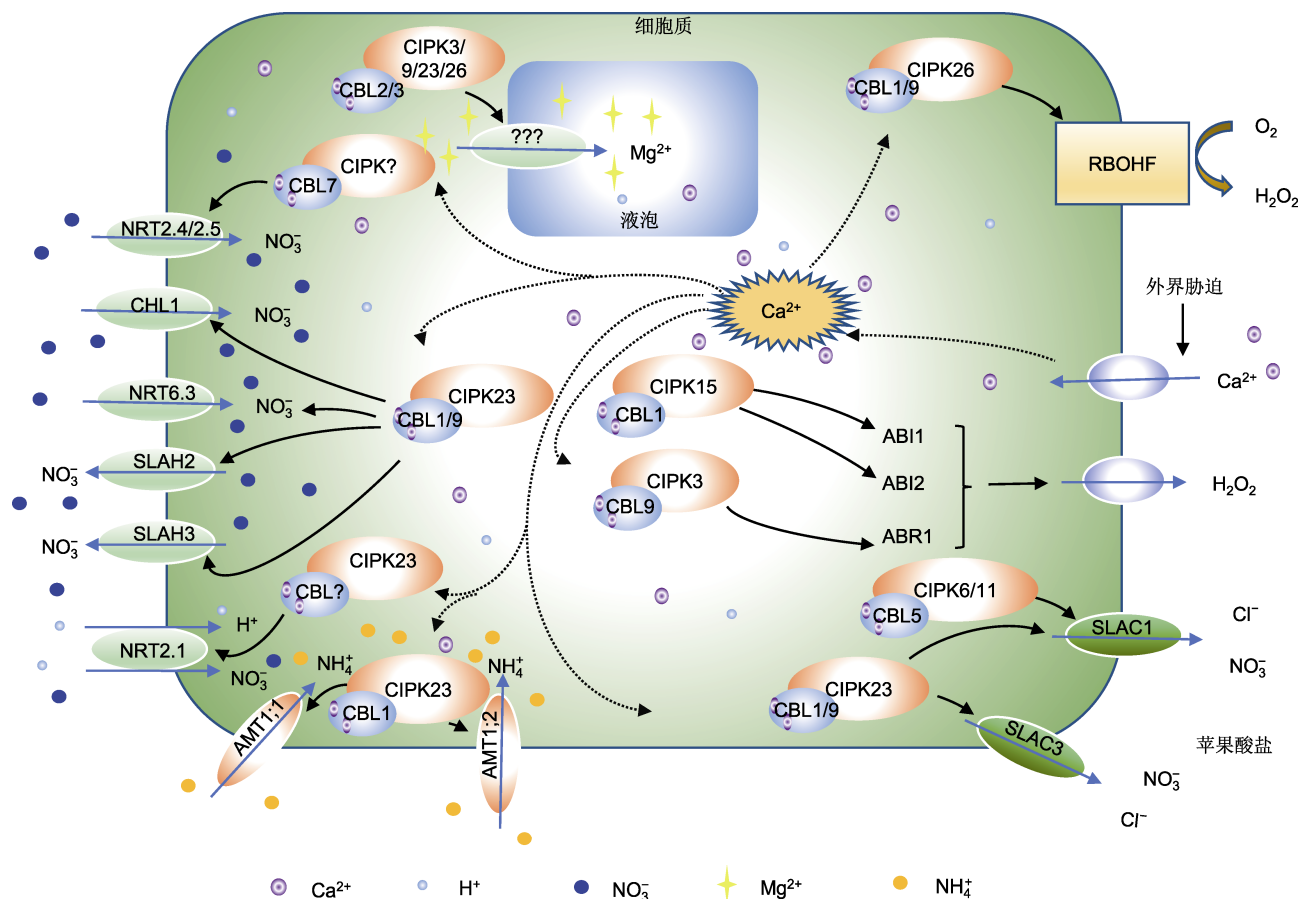


图2 拟南芥CBL-CIPK系统对硝酸盐转运、细胞氨毒性、ROS信号和ABA信号的响应

蓝色箭头表示离子和化合物的流入/流出；黑色箭头表示激活；虚线表示 Ca^{2+} 信号。RBOHF：呼吸爆发氧化酶同源因子

Figure 2 Responses of CBL-CIPK system to nitrate transport, cellular ammonia toxicity, ROS signaling, and ABA signaling in *Arabidopsis thaliana*

Blue arrows indicate influx/efflux of ion and compound; black arrows indicate activation; dashed lines indicate Ca^{2+} signaling. RBOHF: Respiratory burst oxidase homolog factor

3.3 CBL-CIPK复合物对酶的调控

与ROS有关的氧化酶RBOHF (respiratory burst oxidase homolog factor)受到CBL1/9-CIPK26的调控(表2; 图2) (Zhang et al., 2014b)。CIPK26可影响定位在质膜上的RBOHF活性(Kimura et al., 2013)。然而, 该结果是在异源表达系统中试验得到的, 因此CIPK26对RBOHF活性的调节作用尚缺乏足够的证据。但可以肯定的是, CBL1/CBL9介导CIPK26到质膜的定位导致RBOHF磷酸化(Zhang et al., 2018b; Han et al., 2019)。

3.4 CBL-CIPK复合物对植物激素的调控

目前, CBL-CIPK复合物对植物激素调控的研究主要

集中在ABA信号通路。研究发现, CBL9-CIPK3在ABA信号通路中起负向调控作用(Pandey et al., 2008)。拟南芥CBL9-CIPK3复合物通过将转录因子ABI1磷酸化, 形成CBL9-CIPK3-ABR1途径(表2), 从而介导种子萌发和ABA依赖的生理生化反应过程(Sanyal et al., 2017)。在小麦(*Triticum aestivum*)中, TaCBL1-TaCIPK23介导ABA信号途径, 并在干旱胁迫应答中起重要作用(Cui et al., 2018)。此外, 拟南芥CBL2和CBL3与CIPK9和CIPK27也参与ABA信号通路的负向调控(Song et al., 2018)。OsCBL2可正向调控赤霉素的合成(Hwang et al., 2005), 而AtCIPK6参与调控生长素的运输(Tripathi et al., 2009)。上述结果表明, CBL-CIPK复合物广泛参与多种植物激素的调控。

3.5 CBL-CIPK复合物对信号终止的调控

CIPK的C端存在1个PPI结构域(Guo et al., 2001)。在结构分析中, CBL相互作用域和PPI结构域可能有重叠, CBL和PP2C (protein phosphatase 2C)与CIPK的相互作用可能相反(Sanyal et al., 2020)。此结构特征可以提供一种有利的适应机制, 以防止CIPK被CBL激活和被CIPK磷酸酶失活同时进行, 从而为调控下游底物提供一个激酶-磷酸酶的分子开关(Tang et al., 2020)。

4 研究展望

目前, 对CBL-CIPK系统的分子结构已经解析得较清楚。在模式植物拟南芥CBL-CIPK研究基础上, 水稻、玉米(*Zea mays*)和小麦等物种CBL-CIPK相继被系统分析。可以肯定的是, 未来会有更多物种的CBL-CIPK系统被继续探究。磷酸化作为CBL-CIPK信号系统中发挥作用的主要方式备受关注。尤其是CBL与CIPK之间的磷酸化研究, 使植物 Ca^{2+} 信号转导途径的基本理论更加清晰。这些成果增进了人们对植物响应各种非生物胁迫机制的认识。然而, CBL-CIPK对植物非生物胁迫下的调控并非单一作用, 而是各个系统协同作用。由于植物CBL-CIPK系统相对复杂, 这方面的研究依然十分有限。此外, 已有研究表明, 在非生物胁迫下, CBL-CIPK系统与其它信号通路存在广泛的交叉, 但相应的报道依然不足。

近年来, 各种组学技术已经在通路研究中发挥重要作用, 而且生物信息学预测方法日趋成熟。因此, 通过生物信息预测和组学技术, 以及传统的分子生物学验证方法相结合, 相信在不久的将来对于CBL-CIPK系统调控植物响应非生物胁迫机理方面的认识会更加深入。

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Regulatory Mechanisms of the Plant CBL-CIPK Signaling System in Response to Abiotic Stress

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Abstract Calcineurin B-like proteins (CBLs) and their CBL-interacting protein kinases (CIPKs) are important regulatory network in response to abiotic stresses. The CBL-CIPK system senses and decodes Ca^{2+} -signals through phosphorylation to regulate plant response to abiotic stresses. In this review, the basic structures of CBLs and CIPKs, and their phosphorylation on different substrates, as well as regulatory mechanisms of plants in response to abiotic stresses were summarized. We also put forward a perspective on the future research directions of CBLs and CIPKs, as well as their potential applications in genetic improvement of crops for stress tolerance.

Key words abiotic stresses, calcium signaling, CBL-CIPK, ion channels, phosphorylation

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