

The multifaceted function of BAK1/SERK3

Plant immunity to pathogens and responses to insect herbivores

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Abbreviations: BR, brassinosteroid; BRI1, brassinosteroid insensitive 1; BAK1, BRI1-associated receptor kinase 1; FLS2, flagellin-sensing 2; JA, jasmonic acid; JA-Ile, jasmonic acid-isoleucine; MAPK, mitogen-activated protein kinase; OS, oral secretions; SERK, somatic embryogenesis receptor kinase

Almost a decade ago BRI1-associated kinase 1 (BAK1) was identified as a co-receptor of brassinosteroid (BR) insensitive 1 (BRI1), the receptor for BRs, which plays an essential role in transducing BR signaling to regulate plant development. BAK1 is also critical in resistance to various pathogens. BAK1 rapidly binds to certain receptors for pathogen/microbe-associated molecular patterns (PAMPs/MAMPs) after the perception of pathogen elicitors and is required for the full elicitation of pathogen-induced defense responses, such as the activation of the mitogen-activated protein kinase 6 (MPK6) and production of reactive oxygen species. Thus, BAK1 functions in both BR signaling and PAMP-triggered immunity (PTI). Recently BAK1 was also found to play an important role in mediating defense responses against an insect herbivore (*Manduca sexta*) of *Nicotiana attenuata*. In this interaction, BAK1 positively modulates wound- or herbivore feeding-induced accumulation of jasmonic acid (JA) and JA-isoleucine (JA-Ile). This mini-review summarizes recent advances in our understanding of the functions of BAK1 in resistance to pathogens and herbivores.

Introduction

Leucine-rich repeat receptor-like kinases (LRR-RLKs) comprise a large gene family in plants (216 genes in Arabidopsis genome).¹ Among these, the cell membrane-located brassinosteroid-insensitive 1 (BRI1) is the receptor for steroid phytohormone brassinosteroids (BRs).^{2,3} Binding of BRs to an extracellular domain of BRI1 triggers BR-dependent plant growth and development.⁴ Another LRR-RLK, BRI1-associated kinase 1 (BAK1)/SERK3, belongs to a small somatic embryogenesis receptor kinase (SERK) family that consists of five members in Arabidopsis.^{5,6} Genetic and biochemical approaches revealed that BAK1 is a co-receptor

of BRI1, which is required for full activation of BR signaling by physically interacting with BRI1.^{5,6}

In addition to its function in BR-regulated plant development, BAK1 also plays an essential role in plant immunity to pathogens.⁷⁻⁹ *Nicotiana benthamiana* plants silenced in *BAK1* are compromised in their resistance to bacterial and oomycete pathogens.^{8,10} Recently, it was also found that in a wild tobacco plant, *Nicotiana attenuata*, BAK1 regulates insect feeding- and mechanical wound-induced accumulation of jasmonic acid (JA) and JA-isoleucine (JA-Ile), two important phytohormones that control plant defense levels.¹¹ Therefore, BAK1 appears to be an important hub that functions in various signaling pathways.

Many excellent reviews have covered the function of BAK1 in BR signaling and plant development.^{12,13} Here we briefly summarize our current understanding of the roles of BAK1 plays in resistance to pathogens and herbivores.

BAK1 in Immunity to Pathogens

Plants rely on their innate immunity for pathogen resistance. Two forms of resistance are recognized that differ in their modes of action. Plants can perceive pathogen/microbe-associated molecular patterns (PAMPs/MAMPs) by pattern-recognition receptors (PRRs) and activate PAMP-triggered immunity (PTI).^{14,15} In addition, certain plant species or populations of a species detect pathogen-derived effectors by R (resistance) proteins and activate effector-triggered immunity (ETI),¹⁵ which usually leads to strong defense reactions, such as the hypersensitive response (a form of programmed cell death).¹⁶

Among the identified PRRs, flagellin-sensing 2 (FLS2) is a well-characterized receptor for bacterial flagellin.^{17,18} FLS2 binds to a specific part of bacterial flagellin (named flg22) and initiates defense responses, including the activation of mitogen-activated protein kinase (MAPK) cascades.¹⁹ Recently, it was found that after flg22 application, BAK1 rapidly forms a complex with FLS2 in a ligand (flg22) binding-dependent manner^{7,8,20} and flg22 also rapidly (within 15 s) induces phosphorylation of BAK1 and FLS2.²⁰ The levels of both ROS (reactive oxygen species) and MPK6 (mitogen-activated protein kinase 6) activity are rapidly

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elevated after flg22 perception and these pathogen resistance-related reactions are compromised in Arabidopsis *bak1* mutants and in *BAK1*-silenced *N. benthamiana*.⁸ In addition, *N. benthamiana* lacking BAK1 function also has attenuated levels of defense-related transcript.⁸ Heese et al. also demonstrated that two other pathogen-derived elicitors, the CSP22 peptide (part of bacterial cold-shock protein) and the INF1 (an oomycete elicitor), elicit decreased levels of ROS in *BAK1*-silenced *N. benthamiana* and that the INF1-induced cell death phenotype is also diminished in these plants. Arabidopsis perceives the bacterial elongation factor Tu (EF-Tu) by the EFR receptor, which is another LRR-RLK, and activates ROS production and MAPKs. Similarly, Chinchila et al.⁷ found that *bak1* mutants have decreased ROS levels and MAPK activity after being challenged with elf18 (a part of bacterial EF-Tu). Therefore, it was proposed that BAK1 serves as a common signaling partner for many pattern recognition receptors and thus it is important for many PAMP-elicited resistance responses.²¹ The biological significance of BAK1 in pathogen defense was demonstrated in Arabidopsis and *N. benthamiana*: bacterial, fungal and oomycete pathogens proliferate better in Arabidopsis and *N. benthamiana* whose BAK1 is abolished than in plants with normal BAK1 function.⁸

The exact mechanism by which BAK1 confers innate immunity remains unclear. Exogenously applying BR to *bak1* mutants rescues the retarded growth of *bak1* but does not affect flg22-induced root growth inhibition.⁷ Furthermore, BAK1 mediates resistance to necrotic fungi in a BR signaling-independent manner.⁹ Therefore, the function of BAK1 in pathogen resistance is most likely not correlated with its function in BR signaling. It's likely that the kinase activity of BAK1 is somehow important for its function in innate immunity.²⁰ Furthermore, a receptor-like cytoplasmic kinase BIK1 physically associates with FLS2 and BAK1.²² BIK1 is likely first phosphorylated upon flagellin perception and subsequently transphosphorylates FLS2 and BAK1.²² Therefore, BIK1 might be a component in the BAK1-mediated signaling pathway that mediates resistance against pathogens.

BAK1 in Defense against Herbivores

In comparison to plant-pathogen interactions, little is known about how plants recognize herbivore attack and which signaling networks are involved in plant-herbivore interactions. Plants may recognize damage-associated molecular patterns (DAMPs),²³ or herbivory-associated molecular patterns (HAMPs),²⁴ to activate defense responses. Some HAMPs have been identified in a few herbivore species.^{25,26} Among these, fatty acid-amino acid conjugates (FACs) constitute the best studied family of HAMPs. Application of volicitin (a hydroxylated FAC) to *Zea mays* results in emission of volatiles²⁷ and FACs activate biosynthesis of JA and ethylene in *N. attenuata*,²⁸ two important hormones that activate defense-related reactions.

JA and its derivatives, collectively named as jasmonates, are involved in plant development and play critical roles in defense against attack from herbivores.²⁹⁻³¹ Plants impaired in JA biosynthesis or perception have greatly increased susceptibility to herbivores, since JA signaling is the major regulator of the accumulation

of defense-related secondary metabolites.^{32,33} After mechanical wounding or herbivore attack, JA is rapidly produced. Given the rapid nature of JA biosynthesis, which usually happens before the transcriptional changes of JA biosynthetic genes, and the abundance of JA biosynthetic enzymes, it is generally believed that the JA burst elicited by wounding and herbivore feeding is controlled post-transcriptionally.²⁹ Although almost all the JA biosynthetic enzymes have been identified, how JA biosynthesis is regulated remains still poorly understood.

One of the best studied model plants for understanding plant-herbivore interactions is *N. attenuata* (2n = 24), an annual wild tobacco plant, that germinates and grows after sensing smoke-derived cues from fires in its desert habitats (the Great Basin Desert of North America). Among the herbivores that attack *N. attenuata*, the larvae of leaf-chewing insect *Manduca sexta* (Lepidoptera, Sphingidae) are one of the most damaging defoliators.

Feeding of *M. sexta* larvae elicits numerous defense responses in *N. attenuata*, including kinase activation, jasmonate accumulation, and the production of anti-herbivore secondary metabolites. One of the earliest cellular events in *M. sexta*-attacked *N. attenuata* is the activation of MAPKs. *N. attenuata* perceives FACs in the oral secretions (OS) of *M. sexta* which are introduced into wounds during feeding and rapidly activates salicylic acid-induced protein kinase (SIPK) and wound-induced protein kinase (WIPK), two mitogen-activated protein kinases (MAPKs). Using a reverse genetic approach, Wu et al.³⁴ demonstrated that both SIPK and WIPK are required for wounding- and herbivore feeding-induced accumulation of JA, JA-Ile and ethylene, the important phytohormones mediating responses to herbivores. It is well known that MAPK cascades are usually activated by receptors and sensors. Application of *M. sexta* OS or FACs to wounded *N. attenuata* leaves activates higher and longer-lasting SIPK and WIPK activity than does mechanical wounding alone;³⁴ furthermore, volicitin (a hydroxylated FAC) binds to the cell membranes of *Zea mays*.³⁵ These are all consistent with the notion that certain plant species have herbivore elicitor-specific receptors. It is very likely that the FAC components in *M. sexta* oral secretions bind to FAC receptors and elicit downstream defense responses in *N. attenuata*, including MAPK activation and JA and ethylene biosynthesis.

The function of BAK1 in plant-herbivore interactions was investigated in *N. attenuata*.¹¹ Silencing *BAK1* leads to attenuated JA and JA-Ile levels in wounding- and herbivory-treated plants without compromising salicylic acid and ethylene levels. How BAK1 modulates wounding- and herbivore feeding-induced JA accumulation is unclear. Transcriptional analysis indicated that BAK1 does not influence the transcript levels of JA biosynthetic enzymes. Thus, it is possible that BAK1 somehow influences the activity of certain JA biosynthetic enzymes on a post-transcriptional level. In plant-pathogen interactions, BAK1 is associated with receptors that perceive PAMPs, which dictate the downstream defense responses including activation of MAPK cascades.^{14,21,36} However, in plant-herbivore interactions, BAK1 does not seem to participate in the perception of wounding or herbivore feeding, given that neither wounding- nor OS-induced SIPK and WIPK activity was impaired in BAK1-deficient plants, which are most likely located immediately

downstream of these receptors/sensors.¹¹ It would be interesting to explore whether the BAK1-mediated JA biosynthesis is BR signaling-dependent and this could be examined in *BR1*-silenced or BR biosynthesis-impaired plants. Whether BAK1 is also involved in plant-herbivore interactions in other plant species, such as *Arabidopsis*, needs to be examined.

In *Arabidopsis*, Pep1, which belongs to a small Pep family consists of 7 members (Pep1 to Pep7), was identified as an endogenous peptide elicitor derived from *Arabidopsis* itself to activate two innate immune responses, the transcription of defensin gene (*PDF1.2*) and production of H₂O₂.^{37,38P} Precursor gene of *Pep1* is induced by wounding and the cell surface LRR receptor kinase, PEPR1, binds to Pep1 and functions as the receptor of Pep1 in *Arabidopsis*.³⁹ Thus, Peps are thought to be DAMPs.³⁶ Recently it was found that BAK1 interacts with PEPR1 shortly after application of Pep1, indicating that BAK1 is involved in Pep1-mediated responses.²⁰ Whether BAK1 interacts with PEPR1 in *Arabidopsis* and thus regulates wound- and herbivory-induced responses remains to be explored.

Very little is known about other forms of DAMPs and HAMPs in plant-herbivore interactions.^{25,26,36} Furthermore, it seems that

different species have evolved the ability to recognize distinct DAMPs and HAMPs that are specific to their natural herbivore guilds.³⁶ Much research needs to be done to further understand how different plants perceive herbivore attacks (DAMPs and HAMPs) and it would be important to examine whether BAK1 is involved in these DAMP- or HAMP-induced signaling pathways.

Conclusion and Perspectives

BAK1 not only regulates BR-dependent developmental responses but also modulates pathways involved in resistance to pathogen infection and herbivore attack, although BAK1 seems to function in these two forms of biotic stresses with very different mechanisms. More studies are needed to examine whether BAK1 is involved other plant-pathogen and plant-herbivore interactions and to further unravel the exact mode of action of BAK1 in these stress responses.

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