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Pattern-recognition receptors in plant innate immunity

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Perception of pathogen-associated molecular patterns (PAMPs) constitutes the first layer of plant innate immunity and is referred to as PAMP-triggered immunity (PTI). For a long time, part of the plant community was sceptical about the importance of PAMP perception in plants. Genetic and biochemical studies have recently identified pattern-recognition receptors (PRRs) involved in the perception of bacteria, fungi and oomycetes. Interestingly, some of the structural domains present in PRRs are similar in plants and animals, suggesting convergent evolution. Lack of PAMP perception leads to enhanced disease susceptibility, demonstrating the importance of PAMP perception for immunity against pathogens *in vivo*. Recently, proteins with known roles in development have been shown to control immediate PRR-signalling, revealing unexpected complexity in plant signalling. Although many PAMPs recognised by plants have been described and more are likely to be discovered, the number of PRRs known currently is limited. The study of PTI is still in its infancy but constitutes a highly active and competitive field of research. New PRRs and regulators are likely to be soon identified.

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Introduction

Plants lack the adaptive immunity mechanisms of jawed vertebrates, so rely on innate immune responses for defense. As sessile organisms they are subject to changing environmental conditions including constant pathogen attack. However, would-be pathogens must first penetrate barriers such as wax layers or rigid cell walls. A pathogen that overcomes these obstacles is subject to molecular recognition by plant cells. Plants lack circulating cells specialised in microbe recognition such as macrophages. Instead, each cell is able to recognise and respond to pathogens autonomously. In addition, systemic signalling can be triggered in response to microbial stimuli that prepare naïve tissue for imminent attack. Overall, plant innate immunity is very efficient and most plants are resistant to most microbes. Part of this success is because of an amazing spectrum of recognition specificities encoded by all cells.

Plants initially sense microbes via perception of pathogen-associated molecular patterns (PAMPs) by pattern-recognition receptors (PRRs) located on the cell surface. PAMPs are conserved, indispensable molecules that are characteristic of a whole class of microbes and therefore are difficult to mutate or delete. They are also referred to as microbe-associated molecular patterns (MAMPs), as they are not restricted to pathogenic microbes. This first level of recognition is referred to as PAMP-triggered immunity (PTI). Intracellular responses associated with PTI include rapid ion fluxes across the plasma membrane, MAP kinase activation, production of reactive-oxygen species, rapid changes in gene expression and cell wall reinforcement. Successful pathogens have evolved strategies to infect host plants, either by evading recognition or by suppressing the subsequent signalling steps. In many cases, suppression of PTI involves secretion of virulence effectors by the pathogens. In a dynamic co-evolution between plants and pathogens, some plants have evolved resistance proteins (R proteins) to recognise these effectors directly or indirectly. This so-called effector-triggered immunity (ETI) is often accompanied by local cell death known as the hypersensitive response (HR). In turn, pathogens have evolved effectors capable of suppressing ETI, and so the arms-race between host and pathogens unfolds.

In this model, PTI is the first facet of active plant defense and can therefore be considered as the primary driving force of plant–microbe interactions. Given the complexity of plant innate immunity as a whole, I will focus here on recent developments in PAMP perception by plants. For aspects related to PTI signalling, PTI suppression by effectors and ETI, readers are directed to excellent recent reviews [1••,2••,3–7].

PAMP perception in mammals mostly depends on transmembrane proteins, such as Toll-like receptors (TLRs), 'Triggering Receptors Expressed on Myeloid cells' (TREMs), Siglec5 and C-type lectin receptors (CLRs) [8]. However, the important role of cytoplasmic Nod (nucleotide-binding oligomerisation domain)-like receptors (NLRs) as mammalian PRRs has also been recently demonstrated [9]. Although plant ETI mostly involves NLR-like R proteins, no cytoplasmic plant PRRs have yet been identified and known plant PRRs correspond so far only to transmembrane or secreted proteins. Plants do

not possess obvious orthologues of mammalian transmembrane PRRs. However, some of the domains potentially involved in PAMP recognition and signalling are conserved between plants and animals, suggesting that the different kingdoms have recruited similar mechanisms to perceive microbes [10,11].

Flagellin recognition: an ever-expanding model

The best-characterised PAMP in plants is the flagellin protein that constitutes the main building block of eubacterial flagella. Most plant species recognise a highly conserved 22-amino-acid epitope, flg22, present in the flagellin N-terminus [12]. The PRR responsible for flagellin recognition in the plant model *Arabidopsis thaliana* is the leucine-rich repeat receptor-like kinase (LRR-RLK) FLAGELLIN-SENSING 2 (FLS2) [13••]. LRR-RLKs are single-pass transmembrane proteins composed of an LRR ectodomain (eLRR), a transmembrane domain and a Ser/Thr protein kinase domain related to *Drosophila* Pelle [14]. Although the exact flg22-binding site is unknown, FLS2 directly binds to flg22 and contributes to recognition specificity [13••]. Functional FLS2 orthologues have been recently identified in the *Solanaceae* plants *Nicotiana benthamiana* and tomato [15•,16••]. Comparisons between orthologous FLS2 proteins will be useful to determine the molecular-binding determinants because Arabidopsis and tomato plants have different recognition specificities for flagellin [13••,15•].

Arabidopsis plants mutated in *FLS2* are more susceptible to infections with the pathogenic bacterium *Pseudomonas syringae* pv. *tomato* DC3000 (*Pto* DC3000) when surface-inoculated [17], but also allow more growth of the non-adapted bacterium *Pseudomonas syringae* pv. *phaseolicola* (*Pph*, a bean pathogen) [18•] or to a *Pseudomonas syringae* pv. *tabaci* (*Pta*, a tobacco pathogen) strain devoid of flagellin (*FliC*$^{-}$ mutant) [19]. Finally, *N. benthamiana* plants silenced for *NbFLS2* are more susceptible to a range of adapted and non-adapted bacteria [16••]. Multiple examples of successful pathogens that evade recognition because of mutations within flg22 epitope also exist [12,20,21], further demonstrating the importance of flagellin perception on plant–bacteria interactions.

Despite the importance of flg22/FLS2 perception system as a model to study PAMP recognition and associated signalling, flagellin seems to be recognised by the other means in certain plant species. For example, rice does not respond to the flg22 epitope, but flagellin induces cell death indicative of a defense response on this species [12,22,23]. Whether this recognition is FLS2 dependent is still unknown. Furthermore, the glycosylation status of flagellin proteins with otherwise identical flg22 domains is a key emerging determinant of recognition of adapted and non-adapted bacteria by *Solanaceae* plants, such as tobacco and tomato [24,25].

EF-Tu: an unexpected PAMP?

Elongation factor Tu (EF-Tu) is the most abundant bacterial protein and is recognised as a PAMP in Arabidopsis and other members of the family *Brassicaceae* [26]. A highly conserved *N*-acetylated 18 amino acid peptide, elf18, is sufficient to trigger those responses induced by full-length EF-Tu. Peptides derived from plant mitochondrial or plastid EF-Tu are inactive as PAMPs, revealing that this perception is specific to the infectious non-self.

The PRR for EF-Tu is the LRR-RLK EF-TU RECEPTOR (EFR) of the same subfamily (LRRXII) as FLS2 [27••]. Interestingly, expression of *AtEFR* in *N. benthamiana*, a plant normally blind to EF-Tu, results in elf18 binding and responsiveness. This result indicates that signalling components downstream of PRRs are conserved across plant families and open the possibility of trans-species transfer of PRRs to improve disease resistance. Arabidopsis *efr* mutants are more susceptible to *Agrobacterium tumefaciens* bacteria [27••] and to weak strains of *Pto* DC3000 (Zipfel, unpublished), demonstrating the *in vivo* importance of EF-Tu perception in defense against bacteria.

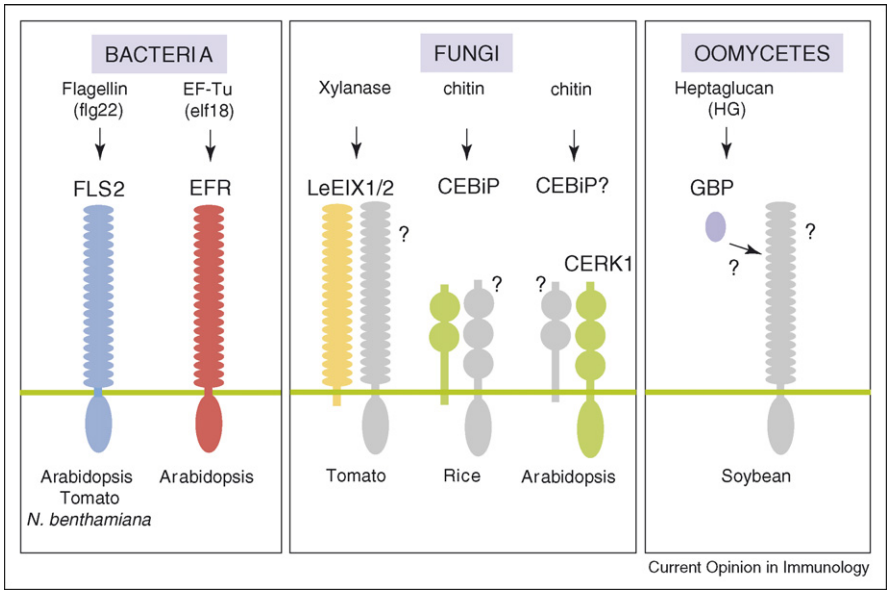
EF-Tu possesses all the characteristics of a typical PAMP: highly abundant, high sequence conservation over thousands of bacterial species and vital for microbial survival. Although EF-Tu is fundamentally involved in translation of bacterial mRNAs, it is also recognised externally by EFR at the host plasma membrane. This raises the recurring question of how EF-Tu becomes visible to the plant. Given the abundance of EF-Tu protein and the picomolar sensitivity of EF-Tu perception, lysis of dying bacteria during plant colonisation should release sufficient EF-Tu to stimulate the receptor. However, increasing evidence suggests that EF-Tu is also surface localised, though it lacks classical signal and transport sequences. EF-Tu from *Mycoplasma pneumonia* binds host fibronectin [28] and *Lactobacillus johnsonii* EF-Tu mediates attachment of the bacteria to human instestinal cells and mucins [29]. Recently, surface-localised EF-Tu from *Pseudomonas aeruginosa* was shown to bind to human complement regulator Factor H and plasminogen to evade complement activation [30,31].

How EF-Tu is secreted and whether mammals have also acquired the ability to recognise EF-Tu as a PAMP, are interesting questions for the future.

LRR-receptor kinases do not explain everything

FLS2 and EFR are so far the only known PRRs in Arabidopsis, but also the only known PRRs that recognise bacterial PAMPs in plants. Other examples of plant PRRs are very scarce (Figure 1).

Figure 1



Plant PRRs. Bacterial flagellin (flg22) and EF-Tu (elf18) are recognised by the LRR-RLKs FLS2 and EFR, respectively. Orthologues of FLS2 have been cloned and characterised in tomato and *N. benthamiana*. In tomato, xylanase is recognised by the RLPs LeEIX1 and LeEIX2. Although both LeEIX1 and LeEIX2 can bind to EIX, only LeEIX2 is able to trigger signalling. The chitin high-affinity-binding site in rice corresponds to CEBiP, a transmembrane protein with two extracellular LysM domains. In legumes, the soluble glucan-binding protein (GBP) directly binds oomycetal heptaglucan. As LeEIX, CEBiP and GBP lack obvious signalling domains, they are likely to interact with yet unknown transmembrane proteins. In Arabidopsis, the LRR-RLK CERK1 is required for chitin response. It is still unknown if CERK1 constitutes the Arabidopsis chitin-binding site, or if it interacts with CEBiP orthologues.

In legumes, a soluble β-glucan-binding protein (GBP) is the specific binding site for the 1,6-β-linked and 1,3-β-branched heptaglucoside (HG) present in the cell wall of the oomycete *Phytophtora sojae*. Interestingly, GBP also exhibits an intrinsic endo-1,3-β-glucanase activity [32]. Therefore, GBP can both potentially release and bind ligands during contact with *Phytophtora*. In contrast to the situation with *EFR*, expression of *GmGBP* in tomato, a plant normally blind to HG, did not result in signal transduction after HG treatment, though high-affinity binding could be detected [33]. This, and the fact that GBP orthologues exist in many plant species insensitive to GBP [32], suggests that signalling after HG perception requires as yet unknown additional components.

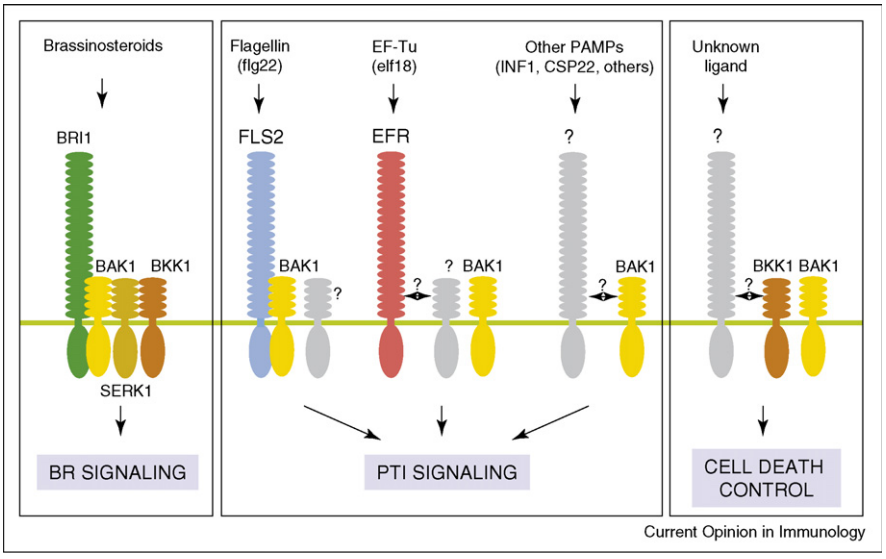
Two PRRs for fungal PAMPs have been recently identified. Perception of the ethylene-inducing xylanase (EIX) in tomato requires the receptor-like proteins (RLPs) LeEIX1 and LeEIX2 [34]. RLPs are transmembrane proteins with eLRRs and a short cytoplasmic tail [35]. Although both proteins are capable of binding EIX independently, only LeEIX2 confers signalling when expressed heterologously in tobacco.

Finally, a high-affinity-binding protein for chitin, a β-1,4-linked polymer of *N*-acetylglucosamine that is a major structural component of fungal cell walls, has been identified in rice [36••]. The chitin oligosaccharide elicitor-binding protein (CEBiP) is a transmembrane protein with two extracellular LysM domains and a short cytoplasmic tail. Silencing of *CEBiP* expression leads to specific reduction in binding and responses triggered by chitin in rice cell culture.

Arabidopsis can recognise both chitin octamers and EIX. Clear orthologues of CEBiP and LeEIX1/2 exist in Arabidopsis, but their roles in perception of these PAMPs are still unknown. Furthermore, GBP, LeEIX1/2 and CEBiP all lack obvious intracellular signalling domains. This suggests that other yet unknown signalling components are required. RLKs possessing extracellular LRRs or other extracellular domains are primary candidates to fulfil such functions. Indeed, an RLK with three extracellular LysM domains, named CERK1 is required for chitin responses in Arabidopsis [57]. Whether CERK1 constitutes the Arabidopsis chitin receptor, or acts together with CEBiP orthologues, remains to be determined.

Interestingly, RLKs with extracellular LysM domains are also involved in the perception of bacterial chitin-like molecules (Nod factors) during the nitrogen fixing legume–Rhizobium symbiosis [37,38].

Figure 2



Multiple roles of BAK1. BAK1/SERK3 was originally found as a BRI1 interactor and positive regulator of brassinosteroid (BR) signalling in Arabidopsis. The BRI1 complex also includes SERK1 and BKK1/SERK4. Interaction of BRI1 with its interactors is ligand-dependent. FLS2 and EFR signalling also require BAK1/SERK3. FLS2 and BAK1/SERK3 interact rapidly upon flg22 treatment. As EFR responses are less affected by the *bak1* mutation, EFR might interact preferentially with another SERK. Similarly, the FLS2 complex might also include another SERK. BAK1/SERK3 also regulates other PRRs, including unknown PRRs for necrotroph pathogens in Arabidopsis, bacterial cold-shock protein (CSP22) and the oomycetal INF1 in *N. benthamiana*. Together with BKK1, BAK1 is also involved in cell death control. This control might require a RLK recognising an unknown endogenous ligand.

PRRs do not signal alone

The best-studied LRR-RLK in plants is BRASSINOSTEROID INSENSITIVE 1 (BRI1), the receptor for the brassinosteroid hormones (BRs) which control many aspects of growth and development. Although BRI1 contains the BR-binding site, it requires another LRR-RLK named BRI1-ASSOCIATED KINASE 1 (BAK1) for proper signalling [39]. Unexpectedly, BAK1 was identified as a positive regulator of both FLS2 and EFR [40••,41••]. BAK1 is dispensable for flg22 binding, but interacts with FLS2 in a ligand-dependent manner shortly after elicitation [40••,41••]. Silencing of *BAK1* expression in *N. benthamiana* affects responses to diverse PAMPs in addition to flg22, including bacterial cold-shock protein (CSP22) and oomycete INF1, suggesting that BAK1 also regulates the function of their corresponding but unknown PRRs [41••]. Furthermore, *BAK1*-silenced plants are more susceptible to adapted and non-adapted *Pseudomonas* and to the oomycete *Hyaloperonospora parasitica* [41••]. Although Arabidopsis *bak1* mutants are not significantly more susceptible to bacterial pathogens, they show extreme susceptibility to necrotrophic fungi [42••]. In addition, Arabidopsis plants mutated in both *BAK1* and its closest paralog *BKK1* show spontaneous cell death occurring within two weeks following germination [43••]. BAK1 seems to be crucial for response to necrotrophic pathogens, while BKK1 plays a complementary role in restricting cell death. Interestingly, in all these examples, BAK1 function appears to be BR-independent [40••,41••,42••,43••]. BAK1 can therefore interact with several different RLKs to control PAMP responses, execution of cell death and different aspects of plant growth (Figure 2).

BAK1 belongs to the LRR type II subfamily, which contains 14 members, 5 of which were previously named SERK1-5 (SOMATIC EMBRYOGENESIS RECEPTOR KINASE 1–5). The fact that *bak1* mutants are not fully insensitive to flg22, or more importantly to elf18, suggests that other LRRII members might act redundantly with BAK1, as shown previously for other members of the SERK family [44–46].

Given their central role in PTI signalling, BAK1 and potentially other LRRII members are potential targets for pathogen effectors.

Another LRR-RLK, ERECTA was shown to interact genetically with its closest paralogs and other LRR-RLKs to control development [47]. In addition, ERECTA is also involved in resistance to the bacterium *Ralstonia solanacearum* and to the necrotrophic fungus *Plectosphaerella cucumeria* [48,49]. This suggests that ERECTA could also interact with LRR-RLKs involved in immunity, potentially PRRs.

BAK1 and ERECTA thus have dual roles in development and immunity, and in this sense are reminiscent of *Drosophila* TOLL, which plays roles in larval development and innate immunity in adult flies.

Conclusions and perspectives

We clearly need to identify new PAMPs and their corresponding PRRs to reveal the span of PAMP perception in a given plant species. Classical bacterial PAMPs recognised in animals, such as lipopolysaccharides [50•] and peptidoglycans [51•] are also recognised by plants, but their receptors are still unknown. Plants can also recognise microbial toxins to activate defense [52•]. Plants are also able to sense the infectious-self, that is, host molecules that are normally not available for recognition, but that are released following microbe detection, wounding or during the infection process. Examples include oligogalacturonides released from the plant cell wall [53], or endogenous peptides [54•]. Interestingly, the receptor for the Arabidopsis endogenous peptide AtPep1 has been identified recently as the LRR-RLK PEPR1. Release and recognition of these peptides by the plant are proposed to be part of a positive feedback loop to amplify the response triggered by PAMP perception [54•].

Plants possess numerous potential PRRs. The Arabidopsis genome for example encode >600 RLKs and >50 RLPs [14,35]. Other transmembrane or secreted proteins could also act as PRRs, as seen for GBP. It is also unknown whether some of the ~150 cytoplasmic NBS-LRR proteins present in Arabidopsis [55], for example, could also act as intracellular PRRs, as recently demonstrated in mammals [56]. Finally, the availability of new plant genome sequences and the development of new genomic resources should enable the discovery of new PRRs from non-model crop species.

The characterisation of further plant PRRs will enable us to address the following questions: Do PRRs cooperate during infection to create new specificities or to recognise multiple PAMPs? Do all PRRs share a common signalling cascade? Can PAMP perception tailor responses to different classes of pathogens? Are PRRs direct targets of pathogen virulence effectors?

The understanding of this important layer of plant innate immunity should provide better strategies for broad-spectrum, sustainable disease control.

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. Chisholm ST, Coaker G, Day B, Staskawicz BJ: **Host–microbe** •• **interactions: shaping the evolution of the plant immune response**. *Cell* 2006, **124**:803-814.

2. Jones JD, Dangl JL: **The plant immune system**. *Nature* 2006, •• **444**:323-329.
These reviews provide a comprehensive overview and define a new unified modern synthesis of plant innate immunity. A must read.

3. Abramovitch RB, Anderson JC, Martin GB: **Bacterial elicitation and evasion of plant innate immunity**. *Nat Rev Mol Cell Biol* 2006, **7**:601-611.

4. Bent AF, Mackey D: **Elicitors, effectors, and R genes: the new paradigm and a lifetime supply of questions**. *Annu Rev Phytopathol* 2007, **45**:399-436.

5. Altenbach D, Robatzek S: **Pattern recognition receptors: from the cell surface to intracellular dynamics**. *Mol Plant Microbe Interact* 2007, **20**:1031-1039.

6. Bittel P, Robatzek S: **Microbe-associated molecular patterns (MAMPs) probe plant immunity**. *Curr Opin Plant Biol* 2007, **10**:335-341.

7. Bray Speth E, Lee YN, He SY: **Pathogen virulence factors as molecular probes of basic plant cellular functions**. *Curr Opin Plant Biol* 2007, **10**:580-586.

8. Sansonetti PJ: **The innate signaling of dangers and the dangers of innate signaling**. *Nat Immunol* 2006, **7**:1237-1242.

9. Kufer TA, Sansonetti PJ: **Sensing of bacteria: NOD a lonely job**. *Curr Opin Microbiol* 2007, **10**:62-69.

10. Ausubel FM: **Are innate immune signaling pathways in plants and animals conserved?** *Nat Immunol* 2005, **6**:973-979.

11. Zipfel C, Felix G: **Plants and animals: a different taste for microbes?** *Curr Opin Plant Biol* 2005, **8**:353-360.

12. Felix G, Duran JD, Volko S, Boller T: **Plants have a sensitive perception system for the most conserved domain of bacterial flagellin**. *Plant J* 1999, **18**:265-276.

13. Chinchilla D, Bauer Z, Regenass M, Boller T, Felix G: **The** •• **Arabidopsis receptor kinase FLS2 binds flg22 and determines the specificity of flagellin perception**. *Plant Cell* 2006, **18**:465-476.
Although FLS2 was known to be required for flg22 perception, the authors demonstrated that FLS2 is indeed the flg22-binding site and provides specificity recognition between different flg22-derived peptides.

14. Shiu SH, Bleecker AB: **Receptor-like kinases from Arabidopsis form a monophyletic gene family related to animal receptor kinases**. *Proc Natl Acad Sci U S A* 2001, **98**:10763-10768.

15. Robatzek S, Bittel P, Chinchilla D, Kochner P, Felix G, Shiu SH, • Boller T: **Molecular identification and characterization of the tomato flagellin receptor LeFLS2, an orthologue of Arabidopsis FLS2 exhibiting characteristically different perception specificities**. *Plant Mol Biol* 2007, **64**:539-547.
This paper reports the cloning of FLS2 in tomato, a species which is extremely sensitive to flagellin and that has distinct recognition specificities compared to Arabidopsis.

16. Hann DR, Rathjen JP: **Early events in the pathogenicity of** •• ***Pseudomonas syringae* on Nicotiana benthamiana**. *Plant J* 2007, **49**:607-618.
The authors identified the *FLS2* orthologue in *N. benthamiana* and showed that silencing of *NbFLS2* expression leads to enhanced susceptibility to a range of adapted and non-adapted bacteria.

17. Zipfel C, Robatzek S, Navarro L, Oakeley EJ, Jones JD, Felix G, Boller T: **Bacterial disease resistance in Arabidopsis through flagellin perception**. *Nature* 2004, **428**:764-767.

18. de Torres M, Mansfield JW, Grabov N, Brown IR, Ammouneh H, • Tsiamis G, Forsyth A, Robatzek S, Grant M, Boch J: **Pseudomonas syringae effector AvrPtoB suppresses basal defence in Arabidopsis**. *Plant J* 2006, **47**:368-382.
In this paper, the authors showed that the expression of the effector avrPtoB allows more growth of non-adapted *Pseudomonas syringae* pv.

Phaseolicola, a bean pathogen. More importantly, they showed that this effect is enhanced in plants lacking FLS2, demonstrating the role of flagellin perception in the resistance against this bacterium.

19. Li X, Lin H, Zhang W, Zou Y, Zhang J, Tang X, Zhou JM: **Flagellin induces innate immunity in nonhost interactions that is suppressed by Pseudomonas syringae effectors**. *Proc Natl Acad Sci U S A* 2005, **102**:12990-12995.

20. Sun W, Dunning FM, Pfund C, Weingarten R, Bent AF: **Within-species flagellin polymorphism in *Xanthomonas campestris* pv. campestris and its impact on elicitation of Arabidopsis FLAGELLIN SENSING2-dependent defenses**. *Plant Cell* 2006, **18**:764-779.

21. Pfund C, Tans-Kersten J, Dunning FM, Alonso JM, Ecker JR, Allen C, Bent AF: **Flagellin is not a major defense elicitor in Ralstonia solanacearum cells or extracts applied to *Arabidopsis thaliana***. *Mol Plant Microbe Interact* 2004, **17**:696-706.

22. Takai R, Kaneda T, Isogai A, Takayama S, Che FS: **A new method of defense response analysis using a transient expression system in rice protoplasts**. *Biosci Biotechnol Biochem* 2007, **71**:590-593.

23. Fujiwara S, Tanaka N, Kaneda T, Takayama S, Isogai A, Che FS: **Rice cDNA microarray-based gene expression profiling of the response to flagellin perception in cultured rice cells**. *Mol Plant Microbe Interact* 2004, **17**:986-998.

24. Takeuchi K, Ono H, Yoshida M, Ishii T, Katoh E, Taguchi F, Miki R, Murata K, Kaku H, Ichinose Y: **Flagellin glycans from two pathovars of Pseudomonas syringae contain rhamnose in D and L configurations in different ratios and modified 4-amino-4,6-dideoxyglucose**. *J Bacteriol* 2007, **189**:6945-6956.

25. Taguchi F, Takeuchi K, Katoh E, Murata K, Suzuki T, Marutani M, Kawasaki T, Eguchi M, Katoh S, Kaku H *et al.*: **Identification of glycosylation genes and glycosylated amino acids of flagellin in *Pseudomonas syringae* pv. tabaci**. *Cell Microbiol* 2006, **8**:923-938.

26. Kunze G, Zipfel C, Robatzek S, Niehaus K, Boller T, Felix G: **The N terminus of bacterial elongation factor Tu elicits innate immunity in Arabidopsis plants**. *Plant Cell* 2004, **16**:3496-3507.

27. •• Zipfel C, Kunze G, Chinchilla D, Caniard A, Jones JD, Boller T, Felix G: **Perception of the bacterial PAMP EF-Tu by the receptor EFR restricts Agrobacterium-mediated transformation**. *Cell* 2006, **125**:749-760.

This paper reports the identification and the characterisation of the LRR-RLK EFR as the EF-Tu receptor. It also showed that transformation of plant cells by the bacterium *Agrobacterium tumefaciens* is normally restricted by plant defenses.

28. Dallo SF, Kannan TR, Blaylock MW, Baseman JB: **Elongation factor Tu and E1 beta subunit of pyruvate dehydrogenase complex act as fibronectin binding proteins in *Mycoplasma pneumoniae***. *Mol Microbiol* 2002, **46**:1041-1051.

29. Granato D, Bergonzelli GE, Pridmore RD, Marvin L, Rouvet M, Corthesy-Theulaz IE: **Cell surface-associated elongation factor Tu mediates the attachment of *Lactobacillus johnsonii* NCC533 (La1) to human intestinal cells and mucins**. *Infect Immun* 2004, **72**:2160-2169.

30. Kunert A, Losse J, Gruszin C, Huhn M, Kaendler K, Mikkat S, Volke D, Hoffmann R, Jokiranta TS, Seeberger H *et al.*: **Immune evasion of the human pathogen *Pseudomonas aeruginosa*: elongation factor Tuf is a factor H and plasminogen binding protein**. *J Immunol* 2007, **179**:2979-2988.

31. Xolalpa W, Vallecillo AJ, Lara M, Mendoza-Hernandez G, Comini M, Spallek R, Singh M, Espitia C: **Identification of novel bacterial plasminogen-binding proteins in the human pathogen *Mycobacterium tuberculosis***. *Proteomics* 2007, **7**:3332-3341.

32. Fliegmann J, Mithofer A, Wanner G, Ebel J: **An ancient enzyme domain hidden in the putative beta-glucan elicitor receptor of soybean may play an active part in the perception of pathogen-associated molecular patterns during broad host resistance**. *J Biol Chem* 2004, **279**:1132-1140.

33. Mithofer A, Fliegmann J, Neuhaus-Url G, Schwarz H, Ebel J: **The hepta-beta-glucoside elicitor-binding proteins from legumes represent a putative receptor family**. *Biol Chem* 2000, **381**:705-713.

34. Ron M, Avni A: **The receptor for the fungal elicitor ethylene-inducing xylanase is a member of a resistance-like gene family in tomato**. *Plant Cell* 2004, **16**:1604-1615.

35. Fritz-Laylin LK, Krishnamurthy N, Tor M, Sjolander KV, Jones JDG: **Phylogenomic analysis of the receptor-like proteins of rice and Arabidopsis**. *Plant Physiol* 2005, **138**:611-623.

36. •• Kaku H, Nishizawa Y, Ishii-Minami N, Akimoto-Tomiyama C, Dohmae N, Takio K, Minami E, Shibuya N: **Plant cells recognize chitin fragments for defense signaling through a plasma membrane receptor**. *Proc Natl Acad Sci U S A* 2006, **103**:11086-11091.

Although chitin was known for many years as a PAMP recognised by plants, its receptor was still unknown. Here, the specific high-affinity-binding site for chitin in rice was identified biochemically as the trans-membrane protein CEBiP carrying two extracellular LysM domains. Silencing of CEBiP expression strongly reduce chitin responses.

37. Radutoiu S, Madsen LH, Madsen EB, Jurkiewicz A, Fukai E, Quistgaard EM, Albrektsen AS, James EK, Thirup S, Stougaard J: **LysM domains mediate lipochitin-oligosaccharide recognition and Nfr genes extend the symbiotic host range**. *EMBO J* 2007, **26**:3923-3935.

38. Zhang XC, Wu X, Findley S, Wan J, Libault M, Nguyen HT, Cannon SB, Stacey G: **Molecular evolution of lysin motif-type receptor-like kinases in plants**. *Plant Physiol* 2007, **144**:623-636.

39. Li J, Jin H: **Regulation of brassinosteroid signaling**. *Trends Plant Sci* 2007, **12**:37-41.

40. •• Chinchilla D, Zipfel C, Robatzek S, Kemmerling B, Nurnberger T, Jones JD, Felix G, Boller T: **A flagellin-induced complex of the receptor FLS2 and BAK1 initiates plant defence**. *Nature* 2007, **448**:497-500.

In a reverse-genetic approach focusing on *LRR-RLK* genes rapidly induced by flg22, the authors found that plants mutated in *BAK1*, a gene known to be involved in brassinosteroid signalling, were strongly affected in flg22 and elf18 responses. Although BAK1 is dispensable for flg22 binding, BAK1 and FLS2 indeed rapidly interact in a ligand-dependent manner, showing that BAK1 acts downstream of FLS2 perception to regulate signalling.

41. •• Heese A, Hann DR, Gimenez-Ibanez S, Jones AM, He K, Li J, Schroeder JI, Peck SC, Rathjen JP: **The receptor-like kinase SERK3/BAK1 is a central regulator of innate immunity in plants**. *Proc Natl Acad Sci U S A* 2007, **104**:12217-12222.

Using a proteomic approach, the authors also identified BAK1 as a FLS2 interactor and positive regulator of flg22 signalling. Interestingly, silencing of *NbBAK1* in *Nicotiana benthamiana* results in decreased responsiveness to flg22, but also to the PAMPs CSP22 and INF1. NbBAK1-silenced plants are also more susceptible to a range of bacteria, but also to an oomycete.

42. •• Kemmerling B, Schwedt A, Rodriguez P, Mazzotta S, Frank M, Qamar SA, Mengiste T, Betsuyaku S, Parker JE, Mussig C *et al.*: **The BRI1-associated kinase 1, BAK1, has a brassinolide-independent role in plant cell-death control**. *Curr Biol* 2007, **17**:1116-1122.

In this study, focusing on LRR-RLK genes induced by infection, the authors found that *bak1* mutant plants are more susceptible to necrotrophic fungal pathogens, revealing a role for BAK1 in infection-induced cell death. Similarly to the above studies, the effects of BAK1 are brassinosteroid-independent, revealing that BAK1 controls signalling triggered by several different LRR-RLKs.

43. •• He K, Gou X, Yuan T, Lin H, Asami T, Yoshida S, Russell SD, Li J: **BAK1 and BKK1 regulate brassinosteroid-dependent growth and brassinosteroid-independent cell-death pathways**. *Curr Biol* 2007, **17**:1109-1115.

The closest BAK1 paralog, named BKK1, plays a redundant role in controlling brassinosteroid signalling. Furthermore, plants mutated for both *BAK1* and *BKK1* die rapidly revealing a role of BAK1 and BKK1 in controlling cell death.

44. Karlova R, Boeren S, Russinova E, Aker J, Vervoort J, de Vries S: **The Arabidopsis SOMATIC EMBRYOGENESIS RECEPTOR-LIKE KINASE1 protein complex includes BRASSINOSTEROID-INSENSITIVE1**. *Plant Cell* 2006, **18**:626-638.

45. Albrecht C, Russinova E, Hecht V, Baaijens E, de Vries S: **The *Arabidopsis thaliana* SOMATIC EMBRYOGENESIS**

RECEPTOR-LIKE KINASES1 and 2 control male sporogenesis. *Plant Cell* 2005, **17**:3337-3349.

46. Colcombet J, Boisson-Dernier A, Ros-Palau R, Vera CE, Schroeder JI: **Arabidopsis SOMATIC EMBRYOGENESIS RECEPTOR KINASES1 and 2 are essential for Tapetum development and microspore maturation**. *Plant Cell* 2005, **17**:3350-3361.

47. Ingram GC, Waites R: **Keeping it together: co-ordinating plant growth**. *Curr Opin Plant Biol* 2006, **9**:12-20.

48. Godiard L, Sauviac L, Torii KU, Grenon O, Mangin B, Grimsley NH, Marco Y: **ERECTA, an LRR receptor-like kinase protein controlling development pleiotropically affects resistance to bacterial wilt**. *Plant J* 2003, **36**:353-365.

49. Llorente F, Alonso-Blanco C, Sanchez-Rodriguez C, Jorda L, Molina A: **ERECTA receptor-like kinase and heterotrimeric G protein from Arabidopsis are required for resistance to the necrotrophic fungus Plectosphaerella cucumerina**. *Plant J* 2005, **43**:165-180.

50. • Newman M-A, Dow JM, Molinaro A, Parrilli M: **Invited review: priming, induction and modulation of plant defence responses by bacterial lipopolysaccharides**. *J Endotoxin Res* 2007, **13**:69-84.
A comprehensive review on LPS recognition and subsequent signalling in plants.

51. • Gust AA, Biswas R, Lenz HD, Rauhut T, Ranf S, Kemmerling B, Gotz F, Glawischnig E, Lee J, Felix G *et al.*: **Bacteria-derived peptidoglycans constitute pathogen-associated molecular patterns triggering innate immunity in Arabidopsis**. *J Biol Chem* 2007, **282**:32338-32348.
The first clear demonstration that plants recognise peptidoglycans (PGNs). The authors showed that purified PGNs from *Staphylococcus aureus* induce defense response in Arabidopsis. The eliciting active part of PGN corresponds to the glycan backbone.

52. • Qutob D, Kemmerling B, Brunner F, Kufner I, Engelhardt S, Gust AA, Luberacki B, Seitz HU, Stahl D, Rauhut T *et al.*: **Phytotoxicity and innate immune responses induced by Nep1-like proteins**. *Plant Cell* 2006, **18**:3721-3744.
The authors have extensively characterised the plant defense responses induced by conserved Nep1-like proteins present in oomycetes, fungi and bacteria. This provides clear evidence for toxin-triggered immunity in plants.

53. Ferrari S, Galletti R, Denoux C, De Lorenzo G, Ausubel FM, Dewdney J: **Resistance to Botrytis cinerea induced in Arabidopsis by elicitors is independent of salicylic acid, ethylene, or jasmonate signaling but requires PHYTOALEXIN DEFICIENT3**. *Plant Physiol* 2007, **144**:367-379.

54. • Ryan CA, Huffaker A, Yamaguchi Y: **New insights into innate immunity in Arabidopsis**. *Cell Microbiol* 2007, **9**:1902-1908.
This review summarises recent findings that recognition of the endogenous peptides AtPep1 and its paralogs by the LRR-RLK PEPR1 activates plant defense and could provide a positive feedback loop mechanism to amplify PAMP-induced responses.

55. McHale L, Tan X, Koehl P, Michelmore RW: **Plant NBS-LRR proteins: adaptable guards**. *Genome Biol* 2006, **7**:212.

56. Mariathasan S, Monack DM: **Inflammasome adaptors and sensors: intracellular regulators of infection and inflammation**. *Nat Rev Immunol* 2007, **7**:31-40.

57. Miya A, Albert P, Shinya T, Desaki Y, Ichimura K, Shirasu K, Narusaka Y, Kawakami N, Kaku H, Shibuya N: **CERK1, a LysM receptor kinase, is essential for chitin elicitor signaling in Arabidopsis**. *Proc Natl Acad Sci U S A* 2007, **104**:19613-19618.