REVIEW / SYNTHÈSE

Receptor kinase signalling in plants

Yosr Z. Haffani, Nancy F. Silva, and Daphne R. Goring

Abstract: Recent plant genome analyses have revealed a large family of plant receptor kinases with very divergent extracellular domains. While a large proportion of this family remains uncharacterized, emerging functions for several plant receptor kinases reveal roles in a variety of biological processes including growth, development, hormone perception, and plant–microbe interactions. Significant progress has also been made in the understanding of four plant receptor kinase systems including their respective ligands and signalling pathways. Interestingly, a wide range of signalling proteins have been identified as functioning with these receptor kinases. In this review, an overview of plant receptor kinases, their biological functions, and their signalling pathways is presented.

Key words: plants, *Arabidopsis*, receptor kinase, signal transduction.

Résumé : Des analyses récentes de génomes végétaux ont mis à jour une grande famille de kinases réceptrices végétales montrant des domaines extracellulaires très divergents. Bien qu'une forte proportion de cette famille ne soit pas encore caractérisée, des fonctions émergentes pour plusieurs kinases réceptrices végétales révèlent des rôles dans une variété de processus biologiques incluant la croissance, le développement, la perception hormonale et les interactions plantes – microorganismes. Des progrès significatifs ont été réalisés dans la compréhension de quatre systèmes de kinases réceptrices, incluant leurs ligands respectifs et leurs sentiers de signalisation. Une large gamme de protéines de signalisation ont été identifiées comme fonctionnant avec ces kinases réceptrices. Les auteurs présentent une revue des kinases réceptrices végétales, de leurs fonctions biologiques et de leurs sentiers de signalisation.

Mots clés : végétaux, *Arabidopsis*, kinases réceptrices, transduction de signaux.

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Introduction

Receptor protein kinases play fundamental signalling roles in a variety of processes regulating growth and development in plants and animals. In both the *Arabidopsis* and rice genome sequences, there are large numbers of predicted receptor kinase genes. For example, the *Arabidopsis* genome contains 417 predicted proteins with the typical structure of a receptor kinase with an extracellular domain followed by the transmembrane domain and the kinase domain (Shiu and Bleecker 2001*a*). In contrast, analysis of predicted kinases in the human genome has only uncovered 12 predicted receptor serine/threonine kinases belonging to the transforming growth factor-β/activin family and 58 predicted receptor tyrosine kinases (Manning et al. 2002). Thus, there has been a much greater expansion of receptor kinases in plants and may reflect the fact that plants perceive internal cues as well as environmental stimuli to regulate growth and development. However, very little functional information is known for most of these receptor kinases.

Members of the plant receptor kinase family all share highly conserved catalytic kinase domains that have been predicted or shown to phosphorylate serine and threonine residues, although some receptor kinases have been found to also phosphorylate tyrosine residues (Chang et al. 1992; Goring and Rothstein 1992; Mu et al. 1994; Shiu and Bleecker 2001*a*). The extracellular domains of the predicted plant receptor kinases are quite divergent and have been grouped into 15 subfamilies based on the properties of the extracellular domains (Shiu and Bleecker 2001*a*, 2001*b*, 2003). This divergence would likely allow these proteins to respond to a wide range of external signals. Phylogenetic analysis of the predicted *Arabidopsis* receptor kinases based on kinase domains revealed that clustered kinases also tended to have similar extracellular domains, indicating that expansion of the subfamilies occurred after the initial fusion of the kinase domains to different extracellular domains (Shiu and Bleecker 2001*a*).

The 15 extracellular domain classifications given to plant receptor kinases are the C-type lectin, CRINKLY4-like, CrRLK1-like, DUF26, extensin, legume lectin (L-lectin), LRK10-like, leucine-rich repeat, LysM, URK1, PERK-like, RKF3-like, S-domain, thaumatin, and WAK-like (for more details, see Shiu and Bleecker 2001*a*, 2001*b*, 2003). These

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predicted extracellular domains are very different from those identified in animal receptor kinases as well as in receptor proteins in general. The exception is the leucine-rich repeat extracellular domains, which are also found in the Toll family of animal receptors and make up the most prevalent extracellular domain in plant receptor kinases (Shiu and Bleecker 2001*a*; Dunne and O'Neill 2003). Within the predicted extracellular domains of plant receptor kinases, a number of different protein motifs have been identified (Shiu and Bleecker 2001*b*). Many of these motifs are found in proteins present in microorganisms, plants, and animals (e.g., epidermal growth factor (EGF), leucine-rich repeat, PAN, LysM, tumour necrosis factor receptor (TNFR)) whereas other motifs appear to be more specific to plant proteins (e.g., domain of unknown function 26 (DUF26), L-lectin). Some of these motifs are known to mediate protein–protein interactions (leucine-rich repeat, PAN) and may be present in the extracellular domains of plant receptor kinases to mediate interactions with protein ligands.

Several carbohydrate-binding motifs represent the second most prevalent class of extracellular motifs detected in plant receptor kinases (e.g., LysM, L-lectins, C-type lectins, PAN) (Hervé et al. 1999; Shiu and Bleecker 2001*a*, 2001*b*). These receptor kinases may have a role in binding cell wall components and glycoproteins, perhaps in the regulation of plant cell walls or in plant defense responses (Shiu and Bleecker 2001*b*). The LysM domain is a widespread protein module first identified in enzymes involved in bacterial cell wall degradation and is known to bind polymers that contain *N*-acetylglucosamine (Birkeland 1994; Bateman and Bycroft 2000). Very recent and exciting research has revealed that LysM receptor kinases are involved in nodulation and rhizobial symbiosis in legumes (Limpens et al. 2003; Madsen et al. 2003; Radutoiu et al. 2003). Interestingly, these LysM receptor kinases act at a very early stage in the potential recognition of rhizobial Nod factors, which contain *N*-acetylglucosamine molecules (Limpens et al. 2003; Madsen et al. 2003; Radutoiu et al. 2003). L-lectins are thought to act as defense proteins involved in the recognition of foreign plant pathogen glycans, and therefore the L-lectin receptor kinases may participate in pathogen detection (Bateman and Bycroft 2000). Other extracellular domain motifs with potential antimicrobial activity include the *Arabidopsis* PR5K receptor kinase with a thaumatin domain that is related to the group of acidic PR5 proteins shown to possess antifungal activity (Wang et al. 1996; Pan et al. 1999). The chitinase-related domain identified in the *Nicotiana tabacum* CHRK1 receptor kinase is also implicated in binding components of fungal cell walls (Kim et al. 2000).

In recent years, many different biological roles have emerged for plant receptor kinases (Table 1). These include disease resistance to microbial pathogens, regulation of nodulation in rhizobial symbioses, and the regulation of many different aspects of plant growth and development. Of the 15 different extracellular domain classes for plant receptor kinases, biological functions are only known for less than half the classes (Table 1). The following sections describe plant receptor kinases that have been studied in more detail and include examples of known ligands and signalling pathways.

Leucine-rich repeat receptor kinases

The leucine-rich repeat receptor kinases represent the largest group of receptor kinases comprising approximately half of the predicted receptor kinases in *Arabidopsis* (Shiu and Bleecker 2001*a*). Leucine-rich repeats are common motifs in signal transduction proteins and are thought to mediate protein–protein interactions (Kobe and Deisenhofer 1994; Shiu and Bleecker 2001*a*, 2001*b*). There exist at least eight different leucine-rich repeat domain organizations in the *Arabidopsis* family of receptor kinases with variations in the numbers and arrangements of the leucine-rich repeats as well as other sequences interspersed between the leucine-rich repeats motifs (Shiu and Bleecker 2001*a*, 2001*b*). For example, the extracellular domain of the brassinosteroid-insensitive-1 (BRI1) receptor kinase includes 25 tandem leucine-rich repeats flanked by two cysteine pairs, a distinct 70 amino acid region between leucine-rich repeats 21 and 22, and a leucine zipper motif (Li and Chory 1997). Leucine-rich repeat receptor kinases are involved in a wide range of biological functions including hormone perception, growth and development, and plant–microbe interactions (Table 1). Some of the more well-studied leucine-rich repeat receptor kinases are described below, and signalling pathways for BRI1, clavata-1 (CLV1), and flagellin-sensing-2 (FLS2) are included at the end of this review.

HAESA, formerly named RLK5, encodes an *Arabidopsis* leucine-rich repeat receptor kinase known to function in the control of floral organ abscission (Walker 1993; Jinn et al. 2000). Histochemical analyses of transgenic *Arabidopsis* plants harbouring a HAESA::GUS reporter gene fusion and in situ RNA hybridization experiments revealed a restricted pattern of HAESA expression in abscission zones at the base of flowers as well as at the base of petioles where leaves attach to the stem (Jinn et al. 2000). Furthermore, HAESA expression appeared to be developmentally regulated coinciding with the stages when flowers acquire the competence to self-pollinate (Jinn et al. 2000). A role in abscission was demonstrated in *Arabidopsis* transgenic plants expressing a constitutive antisense HAESA construct and analyzed for defects in floral organ abscission. The severity of the phenotype in these transgenic plants was directly correlated with the levels of HAESA protein, in that lines expressing the least amount of HAESA protein exhibited the strongest phenotype where floral organs failed to abscise (Jinn et al. 2000).

HAESA was the first plant receptor kinase used in a screen for proteins that interacted with the kinase domain of a plant receptor kinase (Stone et al. 1994). The type 2C protein phosphatase called the kinase-associated protein phosphatase (KAPP) was isolated from this screen and found to only bind phosphorylated HAESA (Stone et al. 1994). This interaction occurred via a region of KAPP called the kinase interaction domain, which was subsequently found to interact with a number of other plant receptor kinases (Braun et al. 1997; Gòmez-Gòmez et al. 2001; Li et al. 1999; Van der Knaap et al. 1999; Park et al. 2001; Shah et al. 2002). The centre of this kinase interaction region contains a 52 amino acid forkhead-associated domain that is essential for the interactions with the plant receptor kinases (Braun et al. 1997;

Table 1. Biological functions for plant receptor kinases.

Gene name	Biological function	Reference(s)
CRINKLY4-like receptor kinases		
CRINKLY4	Cell differentiation	Becraft et al. 1996
Leucine-rich repeat receptor kinases		
CLV1	Apical meristem maintenance	Clark et al. 1993 1997
ERECTA	Organ initiation and elongation	Torii et al. 1996
EXS	Anther and embryo development	Canales et al. 2002
EMS1	Microsporogenesis and tapetal cell development	Zhao et al. 2002
HAESA	Floral organ abscission	Jinn et al. 2000
PRK1	Pollen development	Mu et al. 1994
VH1	Vascular development	Clay and Nelson 2002
BAK1	Brassinosteroid signalling	Li et al. 2002; Nam and Li 2002
BRI1	Brassinosteroid signalling	Li and Chory 1997
PSK	Phytosulfokine signalling	Matsubayashi et al. 2002
Xa21	Race-specific resistance to bacterial blight in rice	Song et al. 1995
FLS2	Flagellin perception in the innate immunity response	Gómez-Gómez and Boller 2000
HAR1/NARK	Rhizobial symbiosis and control of nodule proliferation in legumes	Krusell et al. 2002; Nishimura et al. 2002; Searle et al. 2003
SYMRK/NORK	Rhizobial symbiosis and nodule initiation in legumes	Endre et al. 2002; Stracke et al. 2002
LRK10-like receptor kinases		
LRK10	Resistance to wheat rust fungi	Feuillet et al. 1997
LysM receptor kinases		
NFR1/LYK3, NFR5	Rhizobial symbiosis and nodule initiation in legumes	Limpens et al. 2003; Madsen et al. 2003; Radutoiu et al. 2003
S-domain receptor kinases		
SRK	Female determinant of *Brassica* self-incompatibility	Takasaki et al. 2000; Silva et al. 2001
WAK-like receptor kinases		
WAKs	Cell expansion	Lally et al. 2001; Anderson et al. 2001

Li et al. 1999). Thus, KAPP is thought to function downstream of a number of plant receptor kinases and appears to act as a negative regulator of some receptor kinase signalling systems (Williams et al. 1997; Stone et al. 1998; Shah et al. 2002).

The somatic embryogenesis receptor kinase (SERK) was first identified in cultured *Daucus carota* suspension cells as a marker for single somatic cells capable of forming embryos (Schmidt et al. 1997). *Arabidopsis* SERK1 was shown to be expressed in developing ovules, early embryos, and during somatic embryogenesis. Overexpression of SERK1 resulted in increased embryogenic potential of *Arabidopsis* cultures, indicating that SERK1 functions to promote embryogenic competence (Hecht et al. 2001). SERK1 was found to be plasma membrane localized and able to form dimers (Shah et al. 2001). Transient expression studies, however, revealed that only a small portion of SERK1 existed as oligomers, suggesting that SERK1 may undergo ligand-dependent dimerization (Shah et al. 2001). Finally, SERK1 was found to interact in vitro with KAPP in a phosphorylation-dependent manner (Shah et al. 2002). In addition, transient expression studies showed that the coexpression of SERK1 with KAPP resulted in SERK1 sequestration into intracellular vesicles (Shah et al. 2002). This suggested that KAPP may function in receptor inactivation, coupled to endocytosis of the activated SERK1 receptor (Shah et al. 2002). In animal systems, receptor internalization has been shown to play an important role in signalling where, for example, the activated EGF receptor kinase is internalized into endosomes for degradation and recycling (Stahl and Barbieri 2002).

The *Petunia inflata* leucine-rich repeat receptor kinase, pollen-receptor-like kinase 1 (PRK1), was the first pollen-expressed receptor kinase to be identified (Mu et al. 1994). PRK1 transcripts were detected in anthers when microspores underwent pollen mitosis to produce bicellular microspores, with the highest levels of expression detected in mature pollen and growing pollen tubes (Mu et al. 1994). Antisense PRK1 transgenic plants expressing reduced levels of endogenous PRK1 produced equal numbers of normal and aborted pollen grains. Microscopic examination of microspores at various stages of anther development revealed that the aborted pollen grains arrested at the unicellular stage of microspore development whereas normal microspores would have completed mitosis to become bicellular (Lee et al. 1996). Furthermore, transgenic plants showing the aborted pollen phenotype also exhibited abnormal embryo sac development, strongly implicating the requirement of PRK1 for the proper postmeiotic development of both the male and female gametophytes (Lee et al. 1996). The kinase interacting protein-1 (KIP1) was recently identified in a yeast two-hybrid screen as an interacting protein of PRK1 (Skirpan et

al. 2001). Analysis of KIP1 expression was predominantly restricted to the pollen, with a similar temporal pattern of expression as that of PRK1. The predicted KIP1 contains an EF-hand Ca^{2+}-binding motif, nine coiled-coil motifs implicated in protein interactions, and a motif found in the microtubule-associated protein, Tau (Skirpan et al. 2001). Yeast two-hybrid screens and in vitro interaction studies also revealed an interaction between PRK1 and a putative *N. tabacum* β subunit of the translation initiation factor 2B (Kim et al. 2001). However, the cellular functions of KIP1 and the β subunit of the translation initiation factor 2B in PRK1 signalling have not yet been established.

In tomato, LePRK1, LePRK2, and LePRK3 are three pollen-specific receptor kinases that are detected in the pollen grain as well as in the growing pollen tube with overlapping patterns of localization in the pollen tube (Muschietti et al. 1998; Kim et al. 2002). Recently, the extracellular domain of LePRK2 was found to interact with LAT52, implicating this protein as a potential ligand for LePRK2 (Tang et al. 2002). LAT52 was previously isolated as a pollen-specific gene that encoded a small cysteine-rich protein required for pollen germination and hydration (Muschietti et al. 1994). LAT52 was found to only interact with the extracellular domain of LePRK2 and not with that of LePRK1 and LePRK3. In addition, while LAT52–LePRK2 could be detected in mature pollen extracts, it was not detected in germinated pollen extracts (Tang et al. 2002). The in vivo implications of this interaction are not known but may be related to the role of LAT52 in pollen germination and hydration. The subsequent dissociation of LAT52 from LePRK2 upon germination perhaps allows LePRK2 to then bind other proteins and initiate its signalling cascade (Tang et al. 2002).

Leucine-rich repeat receptor kinases and LysM receptor kinases in root nodule symbioses

Recently, a number of reports have been published implicating two leucine-rich repeat receptor kinases (Endre et al. 2002; Krusell et al. 2002; Nishimura et al. 2002; Stracke et al. 2002; Searle et al. 2003) and two LysM receptor kinases (Limpens et al. 2003; Madsen et al. 2003; Radutoiu et al. 2003) in root nodule symbioses. In response to nodulation (Nod) factors secreted by symbiotic *Rhizobium* and *Frankia* bacteria, leguminous plants initiate root nodule formation. Mutant screens were conducted in several different legumes to identify plant genes that were required for nodule formation and maintenance (for a review, see Gresshoff 2003). *Lotus japonicus*, *Medicago sativa*, *Medicago truncatula*, and *Pisum sativum* mutants were identified that failed to form root nodules and contained a mutation in the SYMRK/NORK leucine-rich repeat receptor kinase gene (Endre et al. 2002; Stracke et al. 2002). Other nonnodulating *M. sativa* and *L. japonicus* mutants were recently found to have mutations in the NFR1/LYK3 and NFR5 LysM receptor kinase genes (Limpens et al. 2003; Madsen et al. 2003; Radutoiu et al. 2003). Based on root hair responses to Nod factors, the NFR1 and NFR5 LysM receptor kinases were proposed to function just upstream of the SYMRK/NORK leucine-rich repeat receptor kinase in nodule formation (Radutoiu et al. 2003). Interestingly, rhizobial Nod factors contain an *N*-acetylglucosamine backbone, which is known to be bound by LysM domain containing proteins, further supporting the role of the NFR1/LYK3 and NFR5 LysM receptor kinases in the initial perception of Nod factors (Parniske and Downie 2003).

Mutant screens in *L. japonicus*, *P. sativum*, and *Glycine max* also identified another class of mutants displaying enhanced nodulation with a dramatic increase in the number of root nodules (Krusell et al. 2002; Nishimura et al. 2002; Searle et al. 2003). Because excessive nodulation is detrimental to the host plant, there is a feedback regulatory mechanism controlling nodule proliferation that ensures that developed nodules suppress the emergence of nodules in younger tissues, thereby restricting the nodulation zone in the root. In these hypernodulation mutants, the HAR1/NARK leucine-rich repeat receptor kinase was found to be mutated (Krusell et al. 2002; Nishimura et al. 2002; Searle et al. 2003). Interestingly, these mutants also had aberrant root phenotypes in the absence of nodules. Grafting experiments with wild-type and *har1* mutant *L. japonicus* plants revealed that the mutant shoots grafted onto wild-type roots induced hypernodulation of the wild-type roots. However, the reciprocal graft resulted in normal nodule formation (Krusell et al. 2002; Nishimura et al. 2002).

S-domain and cysteine-rich repeat receptor kinases

The S-domain receptor kinases comprise a smaller group with 40 predicted members in *Arabidopsis*. The first plant receptor kinase to be isolated, the *Zea maize* receptor kinase ZmPK1, is a member of this group (Walker and Zhang 1990). This motif is also present in the *Brassica S* receptor kinase (SRK) and is based on homology to the *S* locus glycoprotein (SLG) (Stein et al. 1991; Goring and Rothstein 1992). Both SLG and SRK are involved in *Brassica* self-incompatibility response, described later in this review. The S-domain is cysteine rich and typically contains an EGF repeat, an agglutinin motif, and a PAN motif (Shiu and Bleecker 2001*a*). Based on its homology to lectins, the agglutinin motif may bind α-mannose, and the PAN motif has been implicated in mediating protein–protein interactions and protein–carbohydrate interactions (Tordai et al. 1999; Loris 2002).

Other S-domain receptor kinases include the *Arabidopsis* ARK1, ARK2, and ARK3 and *Brassica* SFR1, SFR2, and SFR3 genes, which are expressed in both vegetative and floral tissues with overlapping but distinct patterns of expression (Dwyer et al. 1994; Tobias and Nasrallah 1996; Pastuglia et al. 1997, 2002). The *Arabidopsis* ARK1 and ARK3 and *Brassica* SFR2 and SFR3 transcript levels were also found to increase following wounding or bacterial infections, suggesting potential roles in plant defense (Pastuglia et al. 1997, 2002). Overexpression of ARK1 in *Arabidopsis* resulted in plants exhibiting a stunted growth phenotype with reduced root systems and decreased cell expansion, suggesting a role for ARK1 in regulating plant growth (Tobias and Nasrallah 1996).

A class related to the S-domain receptor kinase class with 38 members is the DUF26 class, also known as the cysteine-rich repeat class (Chen 2001; Shiu and Bleecker 2001*a*,

2001*b*; Takahashi et al. 1998). The limited homology among the extracellular domains of these proteins is restricted to a 60 amino acid residue region that contains four highly conserved cysteine residues (Du and Chen 2000; Shiu and Bleecker 2001*a*). These conserved cysteine residues may act to maintain a three-dimensional structure or form zinc finger motifs to mediate protein–protein interactions and may be involved in sensing redox changes in the extracellular space during plant defense responses (Chen 2001; Hardie 1999). Given that several *Arabidopsis* DUF26 receptor kinase genes are inducible upon pathogen infection or treatment with reactive oxygen species and salicylic acid, members of this class may be involved in and therefore participate in plant perception and response to biotic and (or) abiotic stress signals (Czernic 1999; Du and Chen 2000; Ohtake et al. 2000; Chen 2001).

WAK-like receptor kinases

The *Arabidopsis* wall-associated receptor kinases (WAK) with 23 members comprise a second class with EGF repeats in the extracellular domains, although the organization is very different from that found in the S-domain receptor kinases class (Kohorn et al. 1992; He et al. 1999; Shiu and Bleecker 2001*a*). Initially, five members were isolated (WAK1–WAK5) and found to be arranged in a tandem cluster within 30 kb (He et al. 1999). They are expressed in a variety of tissues and developmental stages, with WAK1 and WAK2 transcripts being the most abundant (He et al. 1999; Lally et al. 2001; Wagner and Kohorn 2001). WAKs are plasma membrane associated proteins and tightly bound in the cell wall, given that only pectinase treatment was found to effectively release WAK from the cell wall (Anderson et al. 2001). The extracellular domain of WAK1 was also found to bind the *Arabidopsis* glycine-rich protein-3 (GRP-3) (Park et al. 2001). In vitro binding studies indicated that GRP-3 was the only isoform among the six GRPs tested to specifically interacted with WAKs. As well, in vivo binding of GRP-3 to WAK1 was required for a 500-kDa multimeric complex formed in association with KAPP (Park et al. 2001).

In *Arabidopsis*, members of the WAK family have been implicated in pathogen defense responses (He et al. 1999; Anderson et al. 2001). WAK1 mRNA expression levels are induced following wound stimulus and treatment with the bacterial pathogen *Pseudomonas syringae*. In addition, treatment with defense-inducing compounds, salicylic acid and dichloroisonicotinic acid, results in increased levels of WAK1, WAK2, WAK3, and WAK5 transcripts (He et al. 1998, 1999). Furthermore, the induction of WAK1 expression appears to be required for plants to survive stimulation with dichloroisonicotinic acid, thereby suggesting that the expression of WAK1 may protect plants from the detrimental effects ensued by a pathogen attack (He et al. 1998).

WAKs are also predicted to function in plant development and are required for cell expansion (Lally et al. 2001; Wagner and Kohorn 2001; Anderson et al. 2001). Transgenic plants carrying the WAK2 antisense construct under the control of the dexamethasone-inducible promoter had small rosette leaves, a characteristic phenotype determined to be the result of a defect in cell expansion and not cell division (Wagner and Kohorn 2001). In addition, transgenic plants with dexamethasone-induced WAK4 antisense expression were found to be defective in cell elongation (Lally et al. 2001). These dexamethasone-treated antisense plants had small rosette leaves, condensed inflorescence stems, short siliques, unopened miniature flowers, and short primary roots. Scanning electron micrographs of antisense plants showed a reduction in leaf epidermal size and elongation (Lally et al. 2001). Therefore, WAKs may facilitate cell expansion through their physical link and interactions with cell wall components (Wagner and Kohorn 2001).

PERK and CRINKLY4 receptor kinases

Other smaller *Arabidopsis* receptor kinase families include the proline-rich extensin-like receptor kinases (PERK) and the CRINKLY4 receptor kinases (Becraft et al. 1996; Shiu and Bleecker 2001*a*; Silva and Goring 2002). The PERKs have a predicted extracellular domain that is proline rich and shares sequence similarity with extensins (Silva and Goring 2002). This raises the possibility that PERKs, similarly to extensins, are associated with the cell wall. In contrast with the other receptor kinases, the PERK family members have only a single membrane-spanning region with no predicted signal peptide at the N terminus (Silva and Goring 2002). Despite the lack of a signal peptide, PERK1 has been shown to be plasma membrane localized (Silva and Goring 2002).

In *Brassica*, PERK1 is ubiquitously expressed, and mRNA levels rapidly increase in response to various wounding stimuli and infection with the fungal pathogen *Sclerotinia sclerotiorum* (Silva and Goring 2002). RNA expression analysis of 14 *Arabidopsis* PERK members has revealed that some members are ubiquitously expressed, while others show a restricted pattern of expression to the buds, bolt, or roots (A. Nakhamchik, Z. Zhao, R. Cameron, and D.R. Goring, data not shown). In addition, overexpression of PERK1 in *Arabidopsis* causes increased height, number of lateral branches, root growth, and seed production. In contrast, PERK1 antisense suppression (likely leading to the suppression of several PERK genes) results in stunted plants with altered root growth (T.Z. Haffani, N.F. Silva, and D.R. Goring, data not shown). Therefore, the PERK receptor kinases appear to have a role in regulating plant growth, and the wound-inducible expression may be related to some type of tissue repair mechanism.

The CRINKLY4-like receptor kinase group has an extracellular domain with an RCC1-like propeller structure implicated in protein–protein interactions and a cysteine-rich region similar to the ligand-binding domain of the mammalian TNFR (Becraft et al. 1996; McCarty and Chory 2000). The CRINKLY4 gene in *Z. maize* controls a variety of cell differentiation responses, particularly in the leaf epidermis and in the aleurone of the endosperm (Becraft et al. 1996; Jin et al. 2000). In mutant *crinkly4* kernels, sporadic patches of the aleurone fail to differentiate and appear as starchy endosperm, suggesting a possible function for CRINKLY4 in aleurone cell fate differentiation (Becraft and Asuncion-Crabb 2000). CRINKLY4 is also required for the proper differentiation of the leaf epidermis, given that mutant epidermal cells showed irregularities in both cell shape and size

(Becraft et al. 1996). Phenotypic analyses of additional mutant alleles showed that while CRINKLY4 functions preferentially in the leaf epidermis, it is also required for the control of cellular development throughout the shoot (Jin et al. 2000).

Plant receptor kinase signalling pathways

While many diverse biological roles are rapidly emerging for plant receptor kinases, less is known about their ligands and signalling pathways. There are four plant receptor kinases, SRK, BRI1, CLV1, and FLS2, for which significant progress has been made. This includes the identification of potential ligand molecules and downstream signalling components as well as biochemical studies on receptor complex formation. In these systems, there appears to be differences at the molecular and cellular level in the way they function; however, as more information becomes available, more common themes may emerge on plant receptor kinase signalling.

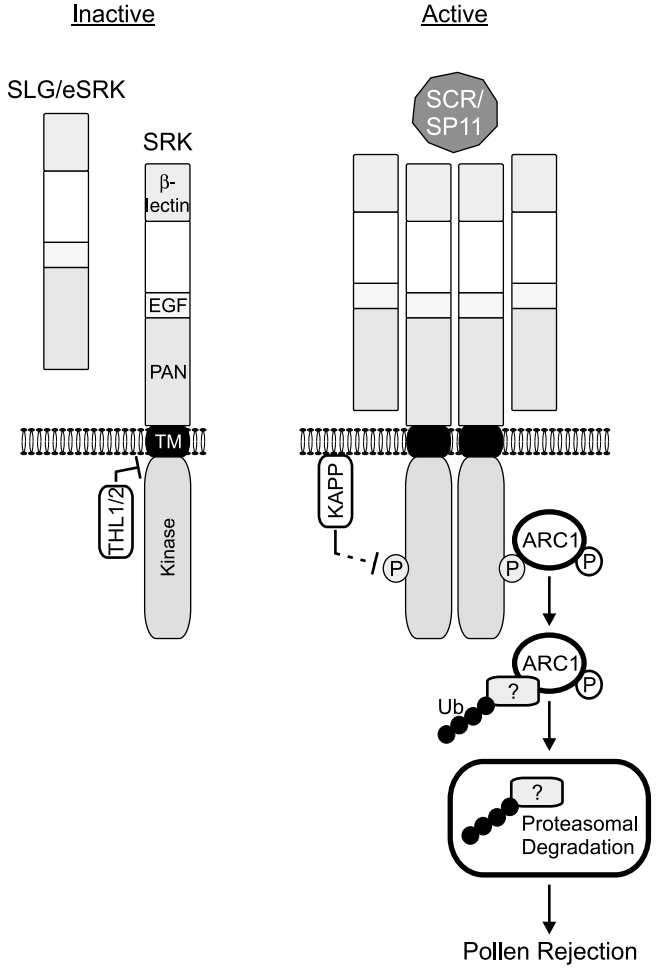
SRK and *Brassica* self-incompatibility

The self-incompatibility response in *Brassica* involves a pollen–pistil interaction at the stigmatic surface leading to the rejection of self-pollen. When the pollen-derived parent and the pistil share common *S* alleles, pollen hydration, pollen germination, and pollen tube growth are inhibited, thus preventing self-fertilization. Three genes have been linked to the *S* locus region, and these genes exhibit the polymorphic nature expected for this multiallelic system (for a more extensive review, see Takayama and Isogai 2003). Given the involvement of more than one multiallelic locus, the term *S* haplotype has been used. The first gene identified was the SLG gene that encodes a secreted glycoprotein that accumulates in the stigmatic papilla cell wall (Nasrallah et al. 1987; Kandasamy et al. 1989). SLG is not essential for this response but may enhance the self-incompatibility response for some *S* haplotypes (Takasaki et al. 2000; Suzuki et al. 2000; Silva et al. 2001).

The second component in the self-incompatibility response is the SRK gene. SRK showed pistil-specific expression and was predicted to encode a receptor kinase with an extracellular domain that shares extensive homology with SLG (S-domain) followed by a single membrane-spanning domain and a cytoplasmic domain (Stein et al. 1991; Goring and Rothstein 1992) (Fig. 1). The cytoplasmic domain was shown to have serine/threonine kinase activity when expressed in *Escherichia coli* (Goring and Rothstein 1992; Stein and Nasrallah 1993). In the pistil, SRK was found to be plasma membrane localized as predicted (Delorme et al. 1995; Stein et al. 1996; Giranton et al. 2000). In some *S* haplotypes, SRK was shown to encode in addition to the integral membrane SRK protein, a soluble truncated form corresponding to the S-domain of SRK, known as the eSRK protein, which may be functionally similar to SLG (Giranton et al. 1995). SRK is essential for self-incompatibility and is the primary determinant of self-incompatibility in the pistil (Takasaki et al. 2000; Silva et al. 2001).

The third component is a small cysteine-rich protein called *S* locus protein 11 (SP11) (Suzuki et al. 1999) or *S* locus cysteine-rich protein (SCR) (Schopfer et al. 1999).

Fig. 1. SRK signalling in the *Brassica* self-incompatibility response. In the absence of incompatible pollen, SRK is proposed to be inhibited by the thioredoxin *h* proteins THL1 and THL2, and this inhibition is released upon the addition of the haplotype-specific SP11/SCR pollen ligand. In an incompatible pollination, the SP11/SCR ligand binds to and activates SRK. Whether SLG participates in the SRK complex is unclear, since the haplotype-specific SLG is not always required. Activated SRK is proposed to autophosphorylate serine and threonines, and some of these phosphorylation sites represent docking sites for downstream signalling proteins such as ARC1. ARC1 is an E3 ubiquitin ligase that interacts with the activated SRK kinase domain through its arm repeat domain, resulting in its phosphorylation. Phosphorylated ARC1 relocalizes from the cytosol to the proteasome/CSN present on the cytosolic face of endoplasmic reticulum membranes and promotes the ubiquitination and proteasomal degradation of unknown substrate proteins, thereby leading to pollen rejection.



SP11/SCR is localized in the pollen coat and is the male determinant of self-incompatibility (Schopfer et al. 1999; Takayama et al. 2000; Shiba et al. 2001). Thus, in this self-incompatibility system, SRK determines the *S* allele specificity of the pistil, and SP11/SCR determines the *S* allele specificity of pollen. Interestingly, *Arabidopsis lyrata*, a close relative of *Brassica* and *Arabidopsis thaliana*, was also found to have an SCR/SRK system regulating self-

incompatibility (Kusaba et al. 2001; Schierup et al. 2001). The *A. lyrata* SRK locus showed allelic polymorphisms with even higher sequence diversity than in *Brassica* (Schierup et al. 2001). This *A. lyrata S* locus region does not appear to encode an SLG ortholog (Kusaba et al. 2001). While *A. thaliana* is a self-compatible species, transformation of the *A. lyrata* SCR and SRK genes into *A. thaliana* briefly confers pollen rejection on freshly opened flowers, but the transformed plants remain compatible (Nasrallah et al. 2002)

Following a self-incompatible pollination, the SP11/SCR protein is proposed to function as a ligand and bind to the extracellular domain of SRK. SLG and eSRK may not be part of this complex depending on the *S* haplotypes involved (Fig. 1). SP11/SCR and pollen coat proteins containing SP11/SCR were shown to induce SRK phosphophorylation in an *S* haplotype specific manner (Cabrillac et al. 2001; Takayama et al. 2001). SP11/SCR from the S_8 haplotype was also shown to bind specifically to microsomal membranes from homozygous S_8 stigmatic cells and to bind to proteins of the expected size for SRK and SLG/eSRK (Takayama et al. 2001). Kachroo et al. (2001) demonstrated the binding of SP11/SCR to SRK using recombinantly expressed proteins. Thus, the haplotype-specific binding of SP11/SCR to SRK leads to SRK phosphorylation, which is subsequently proposed to activate a signalling pathway in the stigmatic papilla leading to pollen rejection (Fig. 1).

For several years, we have been studying the signalling pathway functioning downstream of SRK to determine the cellular events leading to pollen rejection. Through yeast two-hybrid screens with the kinase domain from SRK_{910}, three interacting proteins were isolated: thioredoxin-H-like-1 and thioredoxin-H-like-2 (THL1 and THL2) and arm-repeat-containing-1 (ARC1) (Bower et al. 1996; Gu et al. 1998). THL1 and THL2 are thioredoxin *h* proteins that were found to interact with receptor kinase domains possessing a cysteine residue at the end of the transmembrane domain. Interestingly, this cysteine was conserved in different SRK alleles but not in other related receptor kinases (Mazzurco et al. 2001). These results suggest that the redox activity of the thioredoxins is required for SRK regulation. Cabrillac et al. (2001) demonstrated that in the absence of pollen, there was a stigmatic factor that inhibited SRK phosphorylation in vitro, and this factor was thioredoxin. The addition of pollen coat proteins was able to overcome the inhibitory effects of thioredoxin and induce SRK autophosphorylation (Cabrillac et al. 2001). Therefore, THL1 and THL2 may act to maintain SRK in a reduced form in the absence of pollen, thereby reducing any basal phosphorylation activity. Following self-incompatible pollinations, SP11/SCR binds to SRK and is able to overcome this inhibitory activity and activate SRK phosphorylation (Fig. 1).

More recently, we have studied the function of THL1/THL2 in vivo through the analysis of transgenic *Brassica napus* cv. Westar carrying an antisense THL1 or THL2 vector under the control of the SLR1 promoter that directs expression to the stigmatic papillae (Y.Z. Haffani, T. Gaude, J.M. Cock, and D.R. Goring, data not shown). The transgenic 'Westar' lines showed suppression of both the THL1 and THL2 transcripts. 'Westar' is normally a self-compatible line; however, in the antisense THL1/THL2 'Westar' lines, we detected a constitutive partial rejection of pollen. One possible explanation for these results is that 'Westar' carries a functional SRK that normally does not cause pollen rejection. However, the removal of the THL1/THL2 inhibitors led to some basal phosphorylation and partial activation of this SRK leading to partial pollen rejection. Further investigations revealed that 'Westar' expresses a functional SRK_{15} protein that may be responsible for the constitutive rejection response in the antisense THL1/THL2 'Westar' plants (Y.Z. Haffani, T. Gaude, J.M. Cock, and D.R. Goring, data not shown).

ARC1 is a protein that we have shown to act positively in the SRK signalling pathway. ARC1 only binds to phosphorylated SRK, suggesting that SRK kinase activation is required for ARC1 binding (Gu et al. 1998). In addition, antisense ARC1 transgenic lines in the *B. napus* cv. W1 background ('W1' is normally self-incompatible) showed a partial breakdown in the self-incompatibility response, which indicates that ARC1 is required to promote this response (Stone et al. 1999). More recently, we have shown that ARC1 is an E3 ubiquitin ligase that promotes ubiquitination of proteins following self-incompatible pollination (Stone et al. 2003). Proteasomal inhibitors were also found to cause a breakdown in the pollen rejection response, suggesting that ARC1 promotes the ubiquitination and degradation of stigmatic proteins (Fig. 1). ARC1 has a number of different motifs that were analyzed by transient expression and immunolocalization studies in *N. tabacum* BY2 cells. ARC1 contains a functional nuclear localization signal and two nuclear export signals, and it appears to shuttle in and out of the nucleus ending up predominantly in the cytosol. However, in the presence of SRK, ARC1 localizes to proteasomes associated with the endoplasmic reticulum. This suggests that SRK may phosphorylate ARC1, which leads to the proteasomal localization of ARC1 along with its putative substrates. These substrates may normally be required for pollen acceptance and, when degraded, leads to pollen rejection (Stone et al. 2003).

KAPP has also been found to bind SRK in vitro (Braun et al. 1997; Vanoosthuyse et al. 2003) (Fig. 1). If KAPP regulation of SRK is similar to that proposed for CLV1 and SERK, KAPP may be a negative regulator functioning after SRK activation to inactivate SRK. Recently, two other SRK kinase-interacting proteins, calmodulin and a sorting nexin, have been identified (Vanoosthuyse et al. 2003). Both of these interactors were found to interact with more than one receptor kinase and did not necessarily require the activated kinase for binding. For example, calmodulin was found have a calcium-dependent interaction with both the active and inactive forms of SRK and SFR1 and interacted with the RLK4 and CLV1 receptor kinases but not with the BRI1 receptor kinase. The sorting nexin was found to interacted with both the active and inactive forms of SRK, the active form of SFR1, and the inactive form of CLV1 (Vanoosthuyse et al. 2003). These in vitro results suggest that these proteins may have a more general role as regulators of receptor kinases, although not necessarily as downstream signalling components. The isolation of a sorting nexin is particularly interesting; sorting nexins have been implicated in receptor endocytosis in animal systems (Vanoosthuyse et al. 2003).

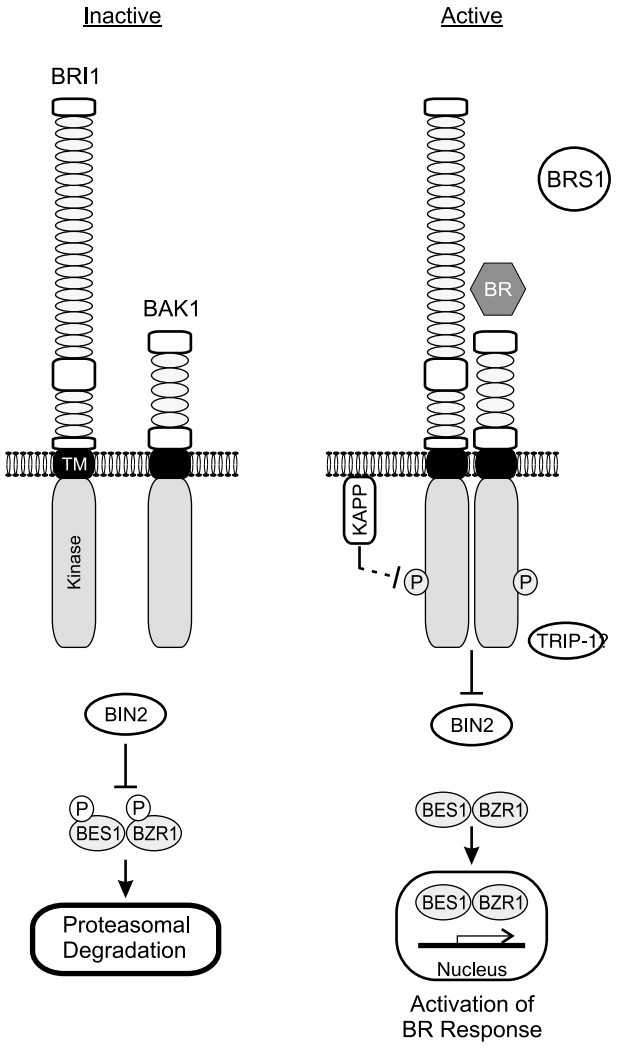
BRI1 and brassinosteroid signalling

Genetic screening for the brassinosteroid (BR) signalling mutants in *Arabidopsis* resulted in the identification of the BRI1 gene encoding a leucine-rich repeat receptor kinase (Clouse et al. 1996; Li and Chory 1997; for a more extensive review, see Clouse 2002). These BR-insensitive mutants exhibited morphological phenotypes nearly identical to the severe BR biosynthetic mutants, but in contrast with the biosynthetic mutants, *bri1* mutants could not be rescued by exogenous BR application, consistent with a role in BR signalling (Clouse et al. 1996; Li and Chory 1997). In addition to the original mutant analyses, other lines of evidence have supported that BRI1 is at least one component of the BR receptor complex. Chimeric receptors with the BRI1 extracellular, transmembrane, and juxtamembrane domains fused to the Xa21 kinase domain were able to elicit a downstream activation of disease resistance responses when treated with brassinolide (He et al. 2000). This indicated that the extracellular domain of BRI1 is involved in BR perception, which led to the activation of the Xa21 kinase domain resulting in an oxidative burst, defense gene expression, and cell death in rice suspension cultures (He et al. 2000). Overexpression of a BRI1::GFP fusion in *Arabidopsis* led to increased binding activity of brassinolide in membrane fractions (Wang et al. 2001). In the presence of brassinolide, the BRI1::GFP protein showed a shift in size owing to autophosphorylation of BRI1 (Wang et al. 2001).

More recently, the *Arabidopsis* BRI1-associated receptor kinase 1 (BAK1) was identified through a yeast two-hybrid screen for BRI1 interacting proteins (Nam and Li 2002) and as a dominant suppressor in an activation tagging screen in the *bri1-5* background (Li et al. 2002). BAK1 is a member of a subfamily of *Arabidopsis* leucine-rich repeat receptor kinases characterized by the presence of five leucine-rich repeats in their extracellular domains and sharing 80% sequence identity with the SERK1 receptor kinase (Li et al. 2002; Nam and Li 2002). Both BRI1 and BAK1 showed ubiquitous expression in *Arabidopsis* and are localized to the plasma membrane (Friedrichsen et al. 2000; Nam and Li 2002). The in vivo BRI1–BAK1 interaction was confirmed by co-immunoprecipitation experiments using transgenic *Arabidopsis* plants expressing tagged BRI1 and BAK1 proteins in which BAK1 was detected in BRI1-immunoprecipitated complexes (Li et al. 2002; Nam and Li 2002).

A number of other components involved in BR signalling have also been identified and incorporated into the BR pathway (Fig. 2). BRI1-suppressor-dominant-1 (BRS1) was identified as a suppressor of *bri1-5* in the same type of activation tagging screen that yielded BAK1 and encodes a secreted serine carboxypeptidase-like protein (Li et al. 2001*a*). Again, the suppression of the *bri1-5* phenotype was due to overexpression of BRS1. Interestingly, overexpression of BRS1 mutants predicted to abolish the protease activity failed to suppress the *bri1-5* mutant phenotype, and BRS1 was proposed to be involved in the processing of a protein involved in the perception and binding of BR (Li et al. 2001*a*). The brassinosteroid-insensitive-2 (BIN2) gene was identified as a semidominant mutant and found to encode a member of the GSK-3/SHAGGY kinase family (Li et al. 2001*b*; Nam and Li 2002; Choe et al. 2002). Overexpression of BIN2 in a weak *bri1* mutant background resulted in plants displaying a more pronounced dwarf phenotype, indicating that BIN2 was a negative regulator of this pathway (Nam and Li 2002). Thus, BIN2 was proposed to act as a negative regulator in the absence of BR by phosphorylating and inactivating downstream regulator proteins. However, activation of the BRI1/BAK1 receptor complex in response to BR was proposed to inhibit BIN2 and to relieve the inhibitory action of BIN2 (Nam and Li 2002; Choe et al. 2002) (Fig. 2).

Fig. 2. BRs and BRI1/BAK1 signalling. BRI1 and BAK1 are two leucine-rich repeat receptor kinases that may heterodimerize on the cell surface to initiate BR signalling. In the absence of BR, the BIN2 kinase is active and phosphorylates BES1/BZR1, targeting them for proteasomal degradation and suppressing BR responses in the nucleus. When BR is present, it may either bind directly to BRI1 or form complexes with an unidentified steroid-binding protein that may require processing by BRS1. BR binding activates the BRI1/ BAK1 receptor complex, leading to the inhibition of the BIN2 kinase. This allows for the accumulation of the BES1 and BZR1 proteins in the nucleus. BES1 activates BR-induced gene expression and induces growth responses. BZR1 mediates BR-regulated gene expression to confer growth response and feedback regulation of BR biosynthesis.



Potential substrates for the BIN2 kinase were identified by genetic and yeast two-hybrid screens and resulted in the isolation of BRI1-EMS-suppressor-1 (BES1) and brassinazole-resistant-1 (BZR1) (Wang et al. 2003; Yin et al. 2002; J. Zhao et al. 2002). BES1 and BZR1 are closely related proteins containing nuclear localization signals and multiple consensus sites for phosphorylation by GSK-3 kinases (Wang et al. 2003; Yin et al. 2002; J. Zhao et al. 2002). The BIN2 kinase was found to interact and phosphorylate BES1 and BZR1 (He et al. 2002; Yin et al. 2002; J. Zhao et al. 2002). In addition, the BIN2 kinase negatively regulated BES1 and BZR1 protein accumulation in vivo, and both BES1 and BZR1 appeared to be subjected to proteasomal degradation (He et al. 2002; Yin et al. 2002). Upon hormone treatment, the BR signalling pathway inhibits BIN2 activity, resulting in the dephosphorylation and increased nuclear localization of both BES1 and BZR1 whereby they promote BR-regulated gene expression (He et al. 2002; Yin et al. 2002) (Fig. 2).

Another potential downstream substrate of the BRI1/BAK1 receptor kinase complex is a plant homologue of TRIP-1, a WD-repeat protein that functions as a modulator of TGF-β signalling (Jiang and Clouse 2001). The expression of the plant TRIP-1 gene is regulated by BR in *Arabidopsis*, *N. tabacum*, and *Phaseolus vulgaris* under a variety of conditions. Furthermore, transgenic plants expressing antisense-TRIP1 RNA exhibit some of the characteristic phenotypes of BR-insensitive and -deficient mutants, suggesting that TRIP-1 may be involved in both BR signalling and other pathways important for normal plant development (Jiang and Clouse 2001). One last interesting finding is the recent isolation of the tomato BRI1 receptor kinase that revealed tBRI1 as being identical to the previously purified systemin receptor, SR160, involved in systemic wound responses (Montoya et al. 2002; Scheer and Ryan 2002). This raises the intriguing possibility that both BR and systemin may signal through the same cell surface receptor in tomato (Montoya et al. 2002).

CLV1 and meristem development

The shoot apical meristem is the basis of all aerial parts in the plant. To function as a site of permanent organ formation, the shoot meristem must preserve a population of undifferentiated cells from which offspring cells are directed toward differentiation and organ formation. The *Arabidopsis* CLV1, CLV2, and CLV3 genes are known to play critical roles in the process of shoot apical meristem maintenance by restricting the amount of stem cell accumulation in both shoot and floral meristems (Clark et al. 1993; Fletcher et al. 1999; Jeong et al. 1999; for a more extensive review, see Clark 2001). Plants with mutations in any of the CLV genes form greatly enlarged shoot and floral meristems, resulting in stem overgrowth and the production of additional flowers and floral organs (Clark et al. 1993; Fletcher et al. 1999; Jeong et al. 1999). Genetic analyses and biochemical approaches have revealed that these genes act in a common pathway, and the proteins encoded by this gene family are members of a signal transduction pathway involved in the regulation of meristem development.

CLV1 is a leucine-rich repeat receptor kinase with 21 tandem leucine-rich repeats in the extracellular domain (Clark et al. 1997). CVL2 is a receptor-like protein similar to CLV1, comprising a leucine-rich repeat extracellular domain followed by a transmembrane domain but lacks a cytoplasmic kinase domain (Jeong et al. 1999). CLV3 is a small 96 amino acid secreted protein that is predicted to be cleaved to form a 78 amino acid ligand for the CLV1 and CLV2 complex (Fletcher et al. 1999). Recent genetic evidence suggests that there may also be other receptor kinases involved in this process. This was based on the observations that null *clv1* alleles have very weak phenotypes and that the stronger *clv1* mutant alleles are likely the result of a dominant negative effect (Dievart et al. 2003). Therefore, there is some functional redundancy between the CVL1 receptor kinase other receptor kinases resulting in a weak phenotype for the null *clv1* alleles (Dievart et al. 2003). CLV1 is found in a large 450-kDa complex comprising CLV1, CLV2, KAPP, and a Rop GTPase related protein (Trotochaud et al. 1999). The function of a Rop GTPase in the 450-kDa complex is unknown but raises the possibility of some type of Ras-mediated signalling typically found in animal systems (Trotochaud et al. 1999).

A potential downstream signalling component in the CLV pathway is poltergeist (POL) for which mutations are known to partially suppress meristem defects in strong *clv1*, *clv2*, and *clv3* mutant backgrounds, and genetic evidence has placed POL functioning downstream of CLV1 (Yu et al. 2000). The POL gene was recently cloned and found to encode a functional protein phosphatase 2C (PP2C) with a predicted nuclear localization signal (Yu et al. 2003). The end result of the CLV signalling pathway is to repress the expression of the homeodomain transcription factor Wuschel (WUS), which is involved in specifying stem cell fate. As a result, WUS expression is restricted to a region of the meristem below the CLV3–CLV1 signalling domain, and a balance in the meristem size is maintained (Brand et al. 2000). In the *clv* mutants, the domain of WUS expression is expanded and associated with an enlarged meristem (Brand et al. 2000). Genetic evidence suggests that POL is a positive regulator of WUS as well as some other unknown factor in meristem maintenance. CLV signalling would then inhibit WUS expression through the inactivation of POL (Yu et al. 2003).

The presence of KAPP in the 450-kDa CLV complex is thought to serve as a negative regulator of the CLV1-mediated signal transduction pathway, possibly following CLV1 receptor activation. The kinase interaction domain of KAPP was shown to interact with the active and phosphorylated CLV1 kinase domain (Williams et al. 1997; Stone et al. 1998). In addition, the cosuppression of endogenous KAPP transcript in *Arabidopsis* plants carrying the intermediate *clv1-1* and *clv1-6* alleles resulted in the suppression of the *clv1* mutant phenotype in these plants (Williams et al. 1997; Stone et al. 1998). More recently, the Shepherd (*shd*) mutant, which has expanded shoot meristems similar to those of *clv* mutants, was shown to encode a heat shock protein 90 (HSP90)-like chaperone and to be required for CLV functions (Ishiguro et al. 2002). SHD protein is suggested to be required for the correct folding of CLV or for the formation of CLV–protein complexes.

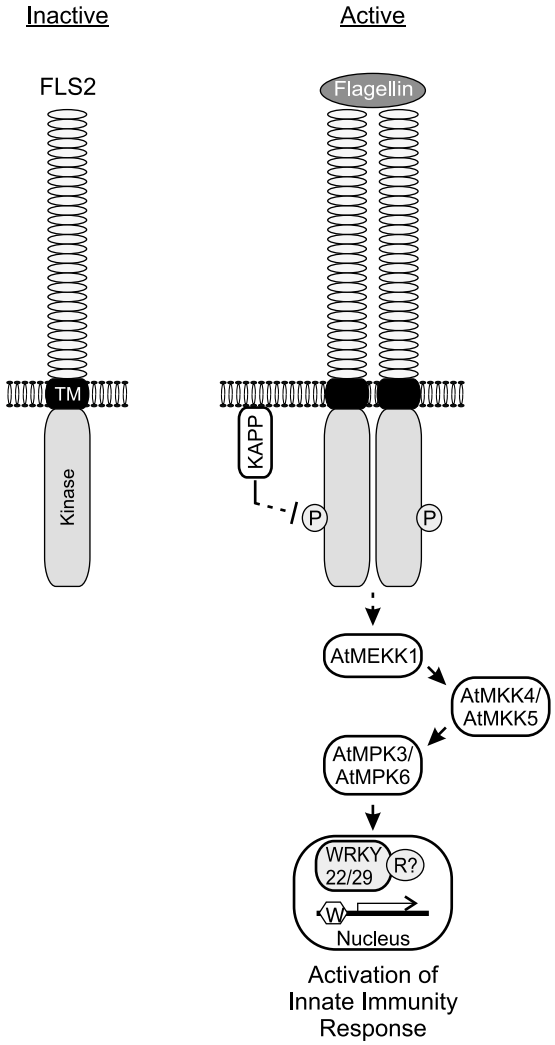
FLS2 and innate immunity

Recently, FLS2 was identified as a gene controlling an

innate immunity response in *Arabidopsis* when challenged with bacterial flagella (Gómez-Gómez and Boller 2000; for a more extensive review, see Gómez-Gómez and Boller 2002). FLS2 encodes a receptor kinase with 28 leucine-rich repeats in the extracellular domain. This extracellular domain resembles the Cf gene family of resistance genes that confer resistance to various strains of *Cladosporium fulvum* (Gómez-Gómez and Boller 2000) (Fig. 3). In response to flagellin, FLS2 induces responses reminiscent of pathogen-mediated defense responses, as expected for an innate immunity response (Gómez-Gómez and Boller 2000; Gómez-Gómez et al. 2001). A short peptide covering the conserved region of flagellin (flg22) is able to trigger this response (Gómez-Gómez et al. 2001).

Bauer et al. (2001) demonstrated that specific and saturable binding sites for flg22 are present in both intact cells and *Arabidopsis* membrane preparations. Complete absence of flg22 binding was observed for *fls2-24*, a mutant harbouring a single amino acid change in one of the leucine-rich repeat motifs within the extracellular domain of FLS2. Complementation of this mutant with FLS2 restored responses to flagellin as well as binding activity (Gómez-Gómez and Boller 2000; Gómez-Gómez et al. 2001). The flg22–FLS2 signalling pathway has been found to involve a complete plant MAPK cascade and WRKY transcription factors in *Arabidopsis* protoplasts (Asai et al. 2002) (Fig. 3). In addition, the ankyrin-containing protein *At*Phos43 shows a transient increase in phosphorylation following flg22 treatment (Peck et al. 2001). Finally, KAPP was found to interact with the kinase domain of FLS2 in a yeast two-hybrid screen, and the ectopic overexpression of KAPP renders *Arabidopsis* plants insensitive to flagellin treatment (Gómez-Gómez et al. 2001) (Fig. 3).

Fig. 3. FLS2 signalling and innate immunity. Bacteria on the surface of the plant enter through the root system, leaves, or other organs, and once inside the extracellular medium, the intact or degraded flagellin resembling the flg22 peptide interacts with the plasma membrane localized FLS2 receptor. This interaction induces the activation of the FLS2 kinase domain, which may be dependent on the dimerization and autophosphorylation of the receptor complex. FLS2 kinase activity is directly or indirectly responsible for the activation of a MAPK signalling cascade, which consists of the activation of the MAPKKK, *At*MEKK1, which in turn phosphorylates the MAPKKs, *At*MKK4/5. This subsequently activates the MAPKS, *At*MPK3/6, and culminates in the release of WRKY transcription factors from a repressor protein that induces the expression of defense genes including WRKY factors, thereby activating defense responses.



Conclusions

While our understanding of the mechanisms by which plants perceive and respond to signals is rapidly growing, there is still much to be discovered. There are increasing indications that many different signalling pathways share common components. For example, KAPP interacts with several receptor kinases in vitro and was found to be a negative regulator of at least two pathways. Plant receptor kinases also appear to function in large complexes with coreceptors and accessory factors such as in the case of BRI1/BAK1, CLV1/CLV2, and SRK/SLG complexes. Recent work with CLV1 and ERECTA also revealed that there are other receptors that function in similar regulatory pathways and are partially redundant in their functions with CLV1 and ERECTA (Dievart et al. 2003; Shpak et al. 2003). Biological functions are rapidly emerging for many receptor kinases, but there are still many more for which there is no known defined function or signalling pathway. Combined with expression studies, the T-DNA knockout mutants in *Arabidopsis* will help significantly to elucidate the function of these receptor kinases.

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