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Mini review

Signaling through the CLAVATA1 receptor complex

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Abbreviations: CLV, CLAVATA; EPTM, extracellular peri-transmembrane; FHA, forkhead-associated; KAPP, kinase-associated protein phosphotase, KI, kinase-interacting; LRR, leucine-rich repeat; POL, POLTERGEIST; RLK, receptor-like kinase; RLP, receptor-like protein; TM, transmembrane; WUS, WUSCHEL

Introduction

Meristem regulation is a process that is critical to the development of plants. Because a plant continues to form organs throughout its life, the proper balance between cell differentiation and cell division in the meristem is crucial for continued organogenesis and normal plant development. Several genes and their corresponding proteins have been implicated in this process including the *CLAVATA* (*CLV*) loci. Mutations in *CLV1*, *CLV2*, or *CLV3* result in an accumulation of stem cells in the shoot and floral meristems (Clark *et al*., 1993, 1995; Kayes and Clark, 1998). Genetic analysis has determined that these genes act in a common pathway and examination of the proteins encoded by these genes has revealed that they are likely components of a signal transduction pathway (Clark *et al*., 1995, 1997; Kayes and Clark, 1998; Fletcher *et al*., 1999; Jeong *et al*., 1999).

The *Arabidopsis* receptor kinase, CLV1, serves as an excellent model with which to study signaling in plants. CLV1 has a clear developmental role, continual function throughout development, a variety of mutant alleles available, and a well-defined genetic pathway, all of which contribute useful tools to study CLV1 function. Information on CLV1 signaling will likely provide insight into the function of other plant receptors, and perhaps signaling in animals as well.

CLV1

The *CLV1* gene encodes a protein with an extracellular domain containing leucine-rich repeats (LRRs), a putative transmembrane (TM) domain, and a functional serine-threonine protein kinase domain (Clark *et al*., 1997; Williams *et al*., 1997; Stone *et al*., 1998). CLV1 is predicted to be a plasma membrane protein, but its actual subcellular localization has not yet been determined. The extracellular receptor domain of CLV1 contains 21 tandem LRRs with each repeat putatively containing a single β-strand. The LRRs are predicted to be arranged such that the β-strands from different repeats combine to form a β-barrel structure that may facilitate ligand binding. Similar extracellular domains in animal receptors recognize peptide ligands (Kobe and Deisenhofer, 1993; Anderson, 2000). The CLV1 kinase domain has been shown to auto-phosphorylate multiple serine residues when expressed in bacteria suggesting that it may act as a receptor-kinase involved in signal transduction (Williams *et al*., 1997; Stone *et al*., 1998).

CLV1 is associated with at least two multimeric protein complexes *in vivo*. One of these complexes is ca. 185 kDa and the other is ca. 450 kDa as determined by gel chromatography (Trotochaud *et al*., 1999). The addition of a reducing agent to protein extracts results in exclusively monomeric CLV1 (ca. 105 kDa) which indicates that disulfide bonds may be important for complex formation (Trotochaud *et al*., 1999). When fractions from total protein extracts are electrophoresed under non-reducing, denaturing con-

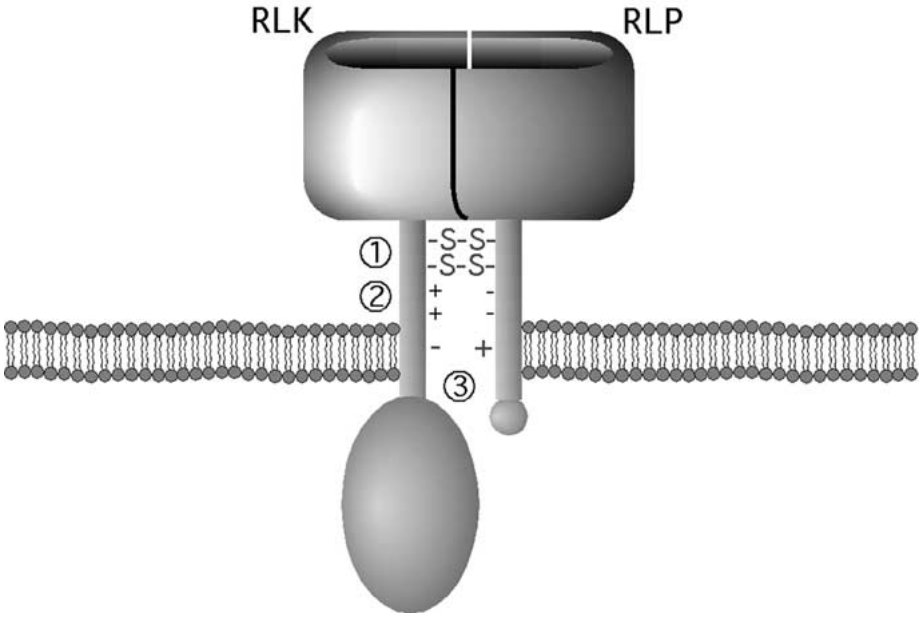

Figure 1. At least three factors may play a role in RLK-RLP dimerization. 1. The LRR domains of receptor-like kinases (RLKs) and receptor-like proteins (RLPs) are flanked by two pairs of cysteine residues that are possibly involved in inter-molecular disulfide linkages. 2. The extracellular peri-transmembrane (EPTM) domains of RLKs are basic while the EPTM domains of RLPs are acidic. This charge difference may also stabilize the interaction of RLKs and RLPs. 3. In addition to charged EPTM domains, some RLKs and RLPs contain charged residues in their transmembrane (TM) domains. These charged residues are usually acidic for RLKs and basic for RLPs, however RLKs with basic residues and RLPs with acidic residues also exist. The charge difference may provide specificity for RLK-RLP interaction.

ditions an anti-CLV1 antibody only recognizes a band at 185 kDa. This suggests that the 450 kDa complex contains the 185 kDa complex and that disulfide bonds are involved in intermolecular interactions stabilizing the 185 kDa complex. Consistent with this idea, CLV1 has two pairs of cysteine residues that flank the LRR domain of the protein (Clark *et al*., 1997). These cysteines are conserved among a large majority of plant receptor-like kinases (RLKs) containing predicted extracellular LRR domains and may be involved in stabilizing protein-protein interactions (Figure 1) (Jones and Jones, 1996; Jeong *et al*., 1999; Trotochaud *et al*., 1999). Because the monomeric size of CLV1 is ca. 105 kDa, the 185 kDa complex may be a disulfide-linked CLV1 homo- or hetero-multimer (see below).

clv1 mutant alleles vary greatly in phenotypic severity and contain lesions in several regions of the coding sequence (Figure 2) (Clark *et al*., 1997; Pogany *et al*., 1998). These *clv1* mutant alleles in combination with mutations in other meristem-regulating genes were utilized to further understand the function of CLV1 protein complexes. Alleles with missense mutations in the kinase domain show a correlation between the severity of phenotype, loss of *in vitro* kinase activity, and reduction in amount of CLV1 protein associated with the 450 kDa complex (Clark *et al*., 1997; Williams *et al*., 1997; Stone *et al*., 1998; Trotochaud *et al*., 1999). The *clv1-10* mutant protein, which has no detectable *in vitro* activity when the kinase domain is expressed in *Escherichia coli*, does not accumulate in the 450 kDa complex *in vivo* (Trotochaud *et al*., 1999). This demonstrates that the activity of the CLV1 kinase domain is required for formation of the 450 kDa complex suggesting that the 450 kDa complex contains the active form of CLV1. This also suggests that phosphorylation of CLV1 is essential for its activation, allowing it to associate with regulators and downstream signaling molecules. Association with other proteins would account for CLV1 in a larger-sized complex. This is consistent with animal receptor tyrosine kinases in which phosphorylated tyrosines in the kinase domain act as binding sites for downstream effector molecules. In many animal and yeast signal transduction models, dimerized receptor kinase proteins are trans-phosphorylated when ligand is bound and this leads to the binding of downstream signaling molecules, eventually altering gene expression in the nucleus. In plants, the 185 kDa CLV1 protein complex may bind the ligand signal, trans-phosphorylate, and

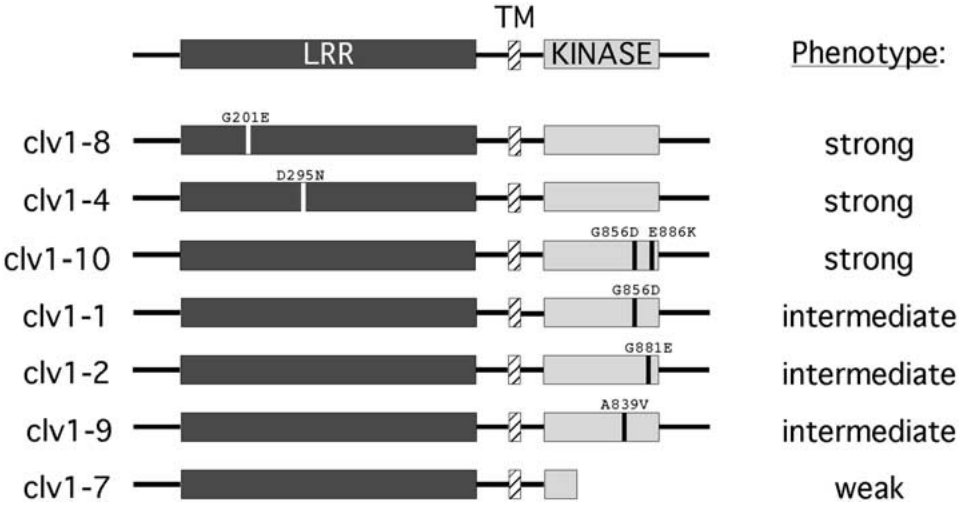

Figure 2. Predicted proteins encoded by the *clv1-8*, *clv1-4*, *clv1-10*, *clv1-1*, *clv1-2*, *clv1-9*, and *clv1-7* mutant alleles of the *CLV1* gene. As a reference, a wild-type CLV1 protein is depicted at the top with the leucine-rich repeat domain (LRR) indicated by a black bar, the putative transmembrane (TM) domain indicated by a hatched bar, and the kinase domain indicated by a gray bar. The relative severity of the mutant phenotype is listed in the last column. Missense mutations are indicated by a white bar in the LRR domain or a black bar in the kinase domain with the amino acid substitution shown above the bar. Nonsense mutations are indicated by the absence of the corresponding regions of the protein.

associate with regulators and downstream signaling molecules forming the 450 kDa complex.

clv1 mutants with lesions in the extracellular domain accumulate reduced levels of the 450 kDa complex and also accumulate monomeric mutant CLV1 protein (Trotochaud *et al*., 1999). This suggests that the LRR domain may be necessary for the formation of the disulfide linkage of the 185 kDa CLV1 homo- or hetero-multimer.

CLV3

CLV3 encodes a small protein (~9 kD) that is predicted to be secreted (Fletcher *et al.*, 1999). Genetic analysis of *clv1* and *clv3* double mutants has shown that these genes act in the same pathway, and exhibit dominant interactions (Clark *et al.*, 1995. While previous genetic evidence indicated that the *CLV* genes all function in the same pathway the similarity of the mutant phenotypes prevented any ordering of the genes within the pathway. Two lines of evidence have suggested that CLV3 is an upstream factor in the CLV pathway. The CLV1 protein in *clv3* null mutants is only present in the 185-kD complex indicating that CLV3 is required for CLV1 activation (Trotochaud *et al.*, 1999). Overexpression of CLV3 gives a *wuschel*-like phenotype (i.e., premature terminations of the shoot and flower meristems) however, overexpression of CLV3 in *clv1* or *clv2* mutant backgrounds has no effect (Brand *et al.*, 2000). Three roles for the CLV3 protein can be proposed from these findings (Figure 3). CLV3 may be involved in the production or release of the ligand. For example. *CLV3* could encode an enzyme that is involved in the processing of the ligand to a mature form, or encode a factor that is involved in the release of the ligand from a protein complex or the cell surface. Alternatively, CLV3 may facilitate the binding of the ligand to CLV1. If this were true, CLV3 would bind to the inactive CLV1 receptor complex, making it competent for ligand binding. Finally, CLV3 may be the ligand for CLV1. Biochemical analysis suggests that the scenario in which CLV3 is the ligand may be the most accurate (Trotochaud *et al.*, 2000).

How does CLV3 compare to other known proteinaceous ligands in plants? Previous known or suspected ligands in plants, such as systemin, enod40, or pathogen elicitors, are either very short peptides, or cysteine-knot proteins with putative disulfide-linkages (Franssen, 1998; van den Hooven *et al.*, 2001). CLV3 falls into neither category, having a relatively long predicted mature protein of 78 amino acids, but lacking any cysteine residues within the predicted mature protein. These features may make CLV3 less readily diffusible and less stable. CLV3 is not the only known or suspected protein within plants to contain these fea-

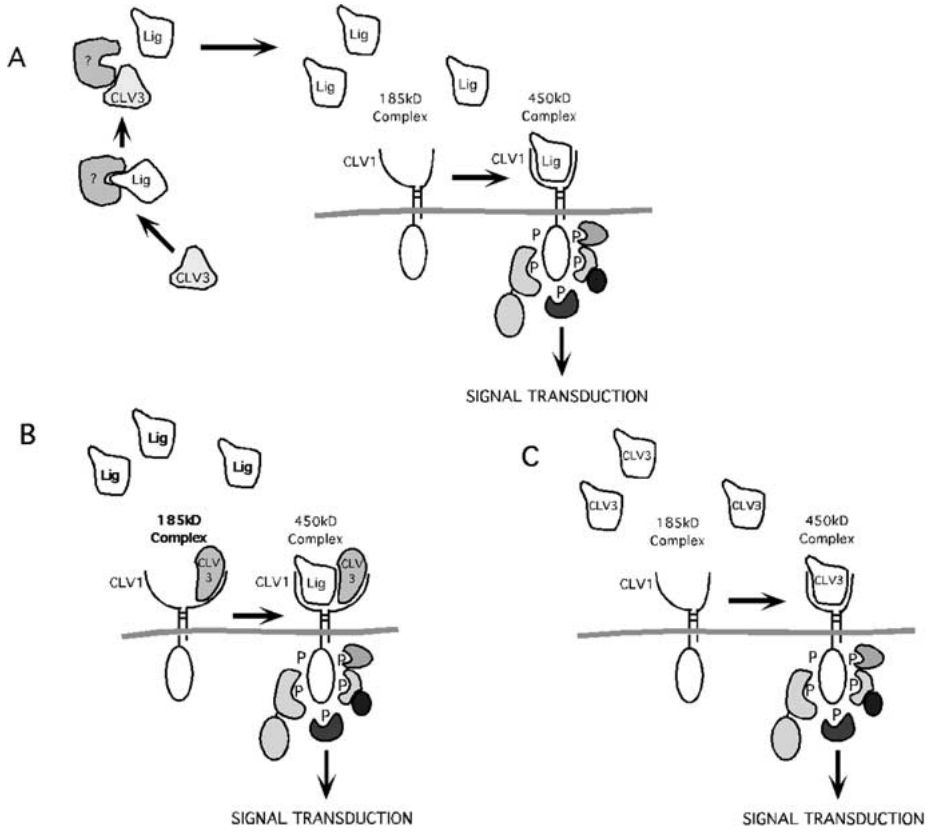

Figure 3. Three possible models for CLV3 action. A. CLV3 may be involved in production or release of the ligand allowing it to bind to CLV1. Here, CLV3 competes with the ligand for binding to an unknown ligand sequestering protein modulating the level of CLV3 that is available for binding to the CLV1 complex. B. CLV3 may facilitate ligand binding. Here, CLV3 is an adapter mediating the binding of the ligand to the receptor complex. C. CLV3 may be the ligand for the CLV1 receptor complex.

tures. There are at least 20 other reading frames in the Arabidopsis genome that encode proteins that are predicted to be secreted and contain a region of similarity to CLV3 at their carboxy terminus (Figure 4). While the function of these genes is unknown, the similarity of the encoded proteins to CLV3 raises that possibility that they act as ligands in other signaling systems. This conserved domain is also found outside of Arabidopsis in the proteins encoded by genes expressed in the maize endosperm surrounding region (Opsahl-Ferstad *et al.*, 1997). While the function of this conserved motif is also unknown, the *clv3-1* mutation is a G to A transition resulting in a substitution of glutamic acid for the conserved glycine in this domain. This suggests that the motif may play an important role in CLV3 function. Further investigation of the importance of this motif in CLV3 binding may provide information as to the function, if any, of these residues in ligand-receptor interaction.

CLV2

The *CLV2* gene acts in the same pathway as *CLV1* and *CLV3* based on genetic analysis (Kayes and Clark, 1998). The *CLV2* gene has been cloned and encodes a receptor-like protein (RLP) that is similar to CLV1, but lacks a kinase domain (Jeong *et al.*, 1999). Insight into a possible role for CLV2 was provided by analysis of CLV1 protein in *clv2* mutants. *clv2* mutants fail to accumulate CLV1 protein, despite the fact that *CLV1* is transcribed normally (Kayes and Clark, 1998; Jeong *et al.*, 1999). This prompted Jeong *et al.* (1999) to hypothesize that CLV2 may form a hetero-dimer pair with CLV1 in the 185 kDa complex. The CLV2 mature protein is predicted to be ca. 80 kDa which, in addition to CLV1, would account for the mass of the 185 kDa complex (Jeong *et al.*, 1999). CLV2 also has two pairs of cysteine residues, conserved among RLPs, flanking the LRR domain that may be involved in disulfide bond formation with CLV1 (Jeong *et al.*, 1999).

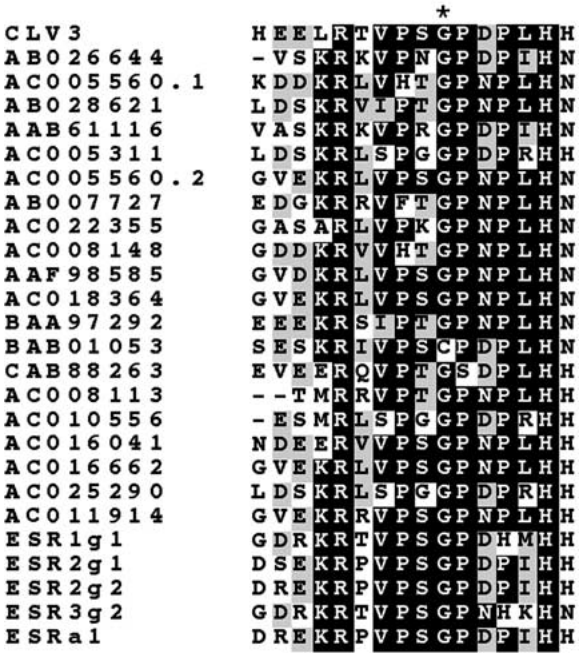

Figure 4. CLV3 contains a conserved domain of unknown function. Database searches revealed five maize and 21 *Arabidopsis* proteins (including CLV3) with a conserved motif. The function of this motif is unknown but it may encode a regulatory region or play a role in ligand multimerization or receptor binding. Sequences are labeled with their protein name, or the Genbank accession number if the proteins were not annotated. * Denotes the glycine that is substituted with a glutamic acid in the clv3-1 mutant protein.

Interestingly, CLV2 contains an acidic residue in its predicted TM domain (Jeong *et al*., 1999). Although few single pass transmembrane domains with charged residues have been described to date, this may be a common feature of plant RLKs and RLPs. Jeong *et al.* examined the TM and extracellular peritransmembrane (EPTM) domains of 43 RLKs and 12 RLPs from the *Arabidopsis* genome and found that five RLKs contained an acidic residue and six RLPs a basic residue in their predicted transmembrane domains. In addition, all of the RLKs examined contained basic EPTMs and all of the RLPs contained acidic EPTMs. The combination of charged TM and EPTM domains may stabilize specific interactions between RLP and RLK pairing partners (Figure 1). Similarly, charged residues in the transmembrane domains of T-cell receptor complex proteins have been shown to be necessary and sufficient for protein-protein interactions and the formation of the complex (Cosson and Bonifacino, 1992).

Another indirect but interesting result of this analysis was the finding that there are about four times as many RLKs as there are RLPs in the *Arabidopsis* genome. If this holds true upon the analysis of the entire genome, then the question of why there are more RLKs than RLPs arises. If RLKs require an RLP for protein stability then one RLP would interact with about four different RLKs on average. Perhaps a specific RLK/RLP combination would provide ligand specificity allowing for the recognition of a large number of ligands using a relatively small number of receptors. Plants may also express specific RLPs and RLKs in different tissues, at different developmental stages, or in response to different environmental conditions allowing specific cell types to respond uniquely to a single ligand or allowing the use of common signal transduction pathways for multiple ligands. The former is supported by the finding that CLV2 is involved in multiple developmental pathways independent of CLV1 and CLV3. In addition to defects in meristem regulation, mutations at the *CLV2* locus result in defects in gynoecium, pedicel, and stamen development (Kayes and Clark, 1998).

CLV1 interacting proteins

The evidence discussed thus far supports the hypothesis that CLV1 is a receptor kinase protein involved in signal transduction. Assuming that signal transduction in plants is similar to signal transduction in yeast and animals, one would expect CLV1 to associate with downstream signaling components or regulatory molecules. These proteins may include, but are not limited to phosphatases, kinases, guanine nucleotide binding proteins, nucleotide exchange factors, nucleotide binding protein activators, or adapter proteins (Sprague, 1998; Hardie, 1999; Kjoller and Hall, 1999). Since these types of proteins would be involved in active signal transduction, they would most likely be directly or indirectly associated with the active (450 kDa) CLV1 complex and not the inactive (185 kDa) CLV1 complex. Recently, both genetic and biochemical methods have been used to determine the existence of such proteins and to elucidate their role in CLV1 signaling.

Kinase-associated protein phosphatase (KAPP) contains a type I signal anchor, a type 2C protein phosphatase, and a forkhead-associated (FHA) homology domain that is required for binding phospho-serine residues (Stone *et al*., 1994; Li *et al*., 1999). The kinase interacting (KI) domain of KAPP, which contains the FHA domain, is capable of binding the

kinase domains of *Arabidopsis*, *Brassica,* and maize RLK proteins, such as TMK1, RLK4, RLK5 (HAE), SRK-A14, and KIK1, in a phosphorylation-dependent manner (Chang *et al*., 1992; Walker, 1993; Glavin *et al*., 1994; Horn and Walker, 1994; Stone *et al*., 1994; Braun *et al*., 1997). Spurred by this discovery, the possible role of KAPP in the regulation of CLV1 signaling was investigated. Because the phosphorylation state of the CLV1 kinase domain seems important for the association of CLV1 with CLV3 and other 450 kDa complex members, the presence of a protein phosphatase could potentially provide a negative regulatory mechanism for CLV1 signaling. This indeed seems to be the case for KAPP (Williams *et al*., 1997; Stone *et al*., 1998). Over-expression of the KAPP mRNA resulted in a clv-like phenotype, while sense suppression of KAPP expression reduced the severity of the phenotype of *clv1* mutant plants (Williams *et al*., 1997; Stone *et al*., 1998). Both results suggest that KAPP negatively regulates CLV1 signaling. KAPP was also shown to be capable of binding CLV1 in a phosphorylation-dependent manner *in vitro* and to bind to active CLV1 in vivo (Williams *et al*., 1997; Stone *et al*., 1998; Trotochaud *et al*., 1999).

In extracts from wild-type plants, KAPP elutes both at the expected monomeric form (ca. 65 kDa) and also in a broad range (ca. 300 to ca. 670 kDa) of larger-molecular-mass complexes (Trotochaud *et al*., 1999). The broad elution range of KAPP is presumably the result of its association with a number of RLK proteins (Stone *et al*., 1994; Braun *et al*., 1997). In fact, the elution pattern of KAPP is not changed in *clv3-2* mutant plants that lack the 450 kDa CLV1 complex (Trotochaud *et al*., 1999). This suggests that the association with the CLV1 complex is only one of the many roles of KAPP.

Ras is an important signaling intermediate in many well-characterized signal transduction pathways. Surprisingly, proteins with sequence similarity to Ras have not been found in plants, however a protein with similar structure has been identified (Frary *et al*., 2000). In addition, a family of Rho/Rac-like GTPases, termed Rop, exists in plants (Winge *et al*., 1997; Li *et al*., 1998). Multiple *Arabidopsis* Rop proteins cross-react with an antibody generated against the Rop1Ps protein from pea (Lin *et al*., 1996). At least one antigenically related protein is present in the CLV1 450 kDa complex as shown by co-immunoprecipitation (Trotochaud *et al*., 1999). This suggests that a Rop may function as a downstream component of CLV1 signaling. In animal and yeast systems, Ras is known to indirectly associate with phosphorylated receptor kinase domains and activate downstream signaling molecules (e.g. a MAPK cascade). Rho proteins, which have not been shown to associate with receptor kinases in animals, may interact directly with receptor kinases in plants. This new role for Rho proteins may be specific to plants.

An alternative hypothesis is that Rho may function to promote endocytosis of activated CLV1 receptor. Arf and Rab GTPases have been shown to be involved in intracellular trafficking and some Rho GTPases have also been implicated in endocytic traffic (Chavrier and Goud, 1999; Ellis and Mellor, 2000). Yet another possibility is that the CLV1-associated Rho may interact with the cytoskeleton to establish apical/basolateral polarity of cells within the meristem.

Evidence for redundant proteins

Several lines of evidence are inconsistent with the simple model of CLV1 function as described above. For example, *clv1-7* mutant codes for a protein lacking the kinase domain, yet most of a much less severe mutant phenotype than *clv1-1* mutants, whose protein contains partial kinase activity (Figure 2) (Trotochaud *et al*., 1999). Because the proper phosphorylation of the CLV1 kinase domain is necessary for the formation of the 450 kDa complex and CLV1 signal transduction, one might expect the phenotype of the *clv1-7* mutant plants to be the most severe. This observation prompts speculation as to why the deletion of most of the kinase domain does not cause a more severe mutant phenotype. Perhaps the most obvious explanation is that redundant receptors exist that are able to functionally replace CLV1 signaling activity.

Multi-gene receptor families have been identified in other signal transduction pathways in plants. Five receptors in the ethylene signaling pathway have been identified. They seem to form two subfamilies in *Arabidopsis* and to act in a functionally redundant manner (Chang *et al*., 1993; Hua *et al*., 1995, 1998; Sakai *et al*., 1998; Chang and Shockey, 1999). The genome sequencing project has identified more than one hundred genes that encode RLK proteins, the vast majority with unidentified functions. The possibility exists that among these RLKs are proteins that may be functionally redundant with CLV1.

Why would evolution favor the redundancy of CLV1 function? Plant development is influenced by

a number of extracellular signals and the coordination of cells in the meristem is most likely a complex regulatory function. Organ formation must be sensitive to growth and cell proliferation rates for proper development to occur. Perhaps proteins redundant with CLV1 differ in such biochemical properties as ligand binding affinity or kinase activity providing the cells with a more diverse system with which to perceive their environment in the meristem. For example, the existence of receptors with different ligand affinity would allow the meristem cells to fine tune their signal perception. This would be similar to the observation that multiple ethylene receptors may be necessary for plants to sense ethylene over four orders of magnitude (Chen and Bleecker, 1995). It is also possible that CLV1-redundant proteins could be expressed in different patterns or different stages of development. In cases where the CLV1 protein is not functional, these CLV1-like proteins may be expressed to recover normal signal transduction.

In addition, it has been noted that the mutant phenotype of *clv2* plants is suppressed when the plants are grown under short-day photoperiod conditions (Kayes and Clark, 1998). This suggests that an unknown protein expressed under short day conditions is able to functionally replace the activity of CLV2, allowing normal signaling through the CLV1 receptor. One explanation is the existence of an RLP that may be differentially expressed under specific environmental conditions. This redundant protein may allow for restored signaling with the same components of the CLV1 long-day signaling pathway. This hypothesis could be tested by examining the CLV1 complex formation under short-day conditions.

As discussed above, there are more than 12 isoforms of Rop in *Arabidopsis* and because their association with the CLV1 450 kDa complex was determined by an antibody that recognizes multiple *Arabidopsis* Rop proteins, it is unclear which of these proteins are associated with the CLV1 450 kDa complex. These Rop proteins may be redundant with one another, or they may function to pass the signal from the CLV1 active complex to multiple signal cascades within the cell.

In order to better understand the function of CLV1 and its signaling complex, the identity of the redundant proteins discussed above must be elucidated. Determining the existence and roles of proteins redundant with CLV1 may identify more downstream signaling molecules or regulators of CLV1 activity. Proteins that interact with CLV1 may play a common role in multiple RLK signaling complexes (e.g. CLV2 and KAPP) or they may have specific interactions with CLV1 (e.g. CLV3). These proteins may also provide a means for the interaction between multiple receptor complexes. Identification of CLV1-redundant proteins may also help in elucidating the role of CLV2 and CLV3 in these signaling complexes.

To identify components that act downstream of the receptor complex in the CLV1 signaling pathway it must be determined which of the Rop proteins actually associate with CLV1. If Rop is taking the place of Ras in plant signal transduction, then identification of the Rop protein(s) specifically associated with the 450 kDa CLV1 complex may help to identify the next step in the signaling cascade.

In addition, it is likely that other, yet unidentified proteins are associated with the CLV1 450 kDa complex. If equal stoichiometry is assumed, then the molecular weight of the proteins identified so far totals a meager 295 kDa. The other members of the CLV1 450 kDa signaling complex must be identified before the signal transduction mechanism can be completely understood.

Conclusions

If cells express CLV1 to determine their relative position in the meristem, one might expect CLV1 to exist mostly in an active, ligand-bound form in a subset of cells, while the remaining cells would primarily contain CLV1 in an inactive form. Consistent with this, CLV1 is found in at least two high-molecular-weight complexes in *Arabidopsis*. The larger 450 kDa complex contains CLV1, a CLV3-containing multimer, KAPP, and Rop and requires CLV2 and CLV3 for formation. Because *clv2* null mutants form neither the 185 kDa nor the 450 kDa complexes, it is believed that CLV2 is a component of both complexes. Genetic data, *CLV3* overexpression analysis, and biochemical studies all support the hypothesis that CLV3 is the ligand for the CLV1 receptor complex. Mutations at the *CLV1* locus that inactivate the CLV1 kinase domain accumulate little or none of the 450 kDa complex, suggesting that CLV1 phosphorylation is important for 450 kDa complex formation. Indeed KAPP and Rop bind to the phosphorylated CLV1 kinase domain. Taken together these points argue that the 450 kDa CLV1 complex is an active signaling complex containing a small CLV3 complex as ligand, CLV1 and CLV2 as receptors, KAPP as a negative regulator of

CLV1 kinase activity, and Rop as a means to transfer the signal to downstream components.

Although many components of the CLV1 receptor complexes have been identified, much of the signal transduction pathway remains unknown. In addition to the possibility for redundant proteins, as discussed above, the downstream targets of the complex have not been identified. A pathway by which the CLV1 signal is transmitted from the membrane to the nucleus remains to be characterized. Two genes, *POLTERGEIST* (*POL*) and *WUSCHEL* (*WUS*), are thought to be members of this signal transduction pathway. Genetic evidence suggests that *POL* and *WUS* function downstream but in the same pathway as *CLV1* (Mayer *et al*., 1998; Schoof *et al*., 2000; Yu *et al*., 2000). Consistent with this, *WUS* encodes a protein with similarity to homeodomain transcription factors and may be the key target of the CLV1 signaling pathway (Mayer *et al*., 1998; Schoof *et al*., 2000). The identity of *POL* has not yet been reported, but it appears to act downstream as a negative regulator of CLV1 signaling (Yu *et al*., 2000). The elucidation of signaling intermediates will be an exciting step in the characterization of the CLV1 signaling pathway. This, along with the discovery of redundant proteins and their functions and the characterization of the binding and signaling parameters of CLV1 interacting proteins, will reveal a potentially new mechanism for signal transduction not only in plants, but in all organisms.

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