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Cell wall integrity maintenance in plants
Lessons to be learned from yeast?

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The plant cell wall is involved in different biological processes like cell morphogenesis and response to biotic/abiotic stress. Functional integrity of the wall is apparently being maintained during these processes by changing structure/composition and coordinating cell wall with cellular metabolism. In *S. cerevisiae* a well-characterized mechanism exists that is maintaining functional integrity of the yeast cell wall during similar processes. During recent years it has become obvious that plants have evolved a mechanism to monitor and maintain functional integrity of their cell walls. However, our understanding of the mechanism is rather limited. The available evidence suggests that similar signaling cascades may be involved and particular protein activities may be conserved between plants and yeast. Here we review the available evidence briefly and highlight similarities between yeast and plants that could help us to understand the mode of action of the signaling cascades maintaining plant cell wall integrity.

The plant cell wall is involved in different biological processes such as cell morphogenesis and biotic/abiotic stress responses.[1,2] Maintaining functional integrity of the cell wall during these different processes is essential. In *S. cerevisiae* a dedicated mechanism monitoring and maintaining functional integrity of the cell wall has been described.[3,4] Although this specialized mechanism exists, the available data shows that both osmo- and mechano-perception mechanisms are also involved in cell wall integrity (CWI) maintenance in yeast.[3,4] Recently, evidence has accumulated suggesting that a similar CWI maintenance mechanism exists in plants, and several excellent reviews have covered this area to some extent.[5,6] However, it has become increasingly obvious that plant CWI maintenance may additionally involve osmo- and damage associated molecular pattern (DAMP)-perception.[2,7] DAMPs are low-molecular weight molecules like oligogalacturonides (OGs) derived from plant cell walls named in analogy to pathogen associated molecular patterns (PAMP).[8] They are thought to arise during exposure of cell walls to abiotic/biotic stress and possibly during cell morphogenesis. These observations suggest that the plant CWI maintenance mechanism could actually be just one component of a matrix of signaling cascades coordinating and tailoring cellular responses to maintain plant cell wall integrity during interaction with the environment and development.[9] Combining knowledge derived from yeast and plant research, this review aims to highlight how different plant signaling cascades could interact to maintain functional plant CWI.

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The Yeast Cell Wall Integrity Matrix

Three different sensor systems can monitor the functional integrity of the yeast cell wall and modulate responses to maintain CWI upon cell wall damage (CWD): The MID1 CCH1 based mechano-perception pathway; the high-osmolarity glycerol (HOG) pathway and the CWI maintenance mechanism.[3] The signal generated by the CCH1 MID1 complex upon membrane stretch is relayed via calcineurin and CRZ1 to activate response genes like the glucan synthase FKS2.[10] FKS2 activity is additionally regulated by the CWI pathway. Two different sensors (SHO1; SLN1/YPD1/SSK1) perceive hyperosmotic stress and generate signals relayed to the MAPKinase HOG1.[11,12] These signals lead to activation of the transcriptional response via SKN7.[3,13] SKN7 also mediates responses induced by the plasma membrane localized CWI sensor MID2 through interaction with CRZ1.[3,14] Sequence similarity between the different yeast CWI sensor proteins WSC1, 2, 3, MTL1 and MID2 is limited and they appear to be required during distinct biological processes.[15] Their extracellular regions, formed by cysteine rich domains (CRD) and highly O-mannosylated serine/threonine rich (STR) domains, project antenna-like into the yeast cell wall.[16] The CRD domain is considered capable of interacting with glucans thus linking the extracellular domain of the sensor closely to the cell wall.[17] Biophysical evidence suggests that the STR domain has properties of a nanospring thus enabling it to translate any conformational change of the extracellular domain when triggered by strain on the cell wall or the membrane, to the cytoplasmic part of the sensor.[18] The cytoplasmic region of the sensors interact with the GDP/GTP exchange factor ROM2 generating a signal that is translated via protein kinase C and a MAPkinase module that includes SLT2.[19] Interestingly, the hyperosmotic stress activated HOG pathway interacts with the CWI pathway when induced by hypo-osmotic shock, thus modulating the response of the yeast cells to low pH, heat shock and zymolyase treatment.[4] During the response to zymolase (an enzyme mix consisting mostly of β-1,3glucanase activity) treatment the molecular mechanism

coordinating both signaling cascades involves the MAPKinases SLT2, HOG1 and the PTP2 phosphatase.[20-22] In a *SLT2* deficient strain *PTP2* expression is not induced by zymolase treatment, the phosphorylation level of the HOG1 MAPKinase is increased and expression of several stress response genes is induced.[20] To summarize; in yeast, three different signaling mechanisms monitor events(membrane stretch, CWD and osmo-stress) indicative of possible CWI impairment and mediate the responses to maintain CWI. In certain situations exemplified here by zymolyase treatment different signaling mechanisms interact to modulate the response to a particular type of stress indicating a CWI signaling matrix exists in yeast.

The Plant Cell Wall Integrity Maintenance Mechanism

Evidence for the existence of a plant CWI maintenance mechanism has accumulated recently. A wide range of responses to different types of CWD has been described. Examples include enhanced pathogen resistance, ectopic lignin deposition, increased production of jasmonic acid, deposition of neutral cell wall sugars and changes in carbohydrate metabolism[7,23-28] (Wormit A, et al. unpublished). Previously, three qualitatively different classes of signaling cascades have been described that could be involved in CWI monitoring and maintenance either directly or indirectly. For the sake of brevity we will focus on selected examples to represent the different signaling mechanisms capable of detecting a variety of stimuli. More detailed overviews can be found in the following reviews in references 5 and 6.

The first group consists of receptor-like kinases (RLKs), capable of detecting cell wall fragments (DAMPs) or changes in cell wall composition/structure. More than 600 RLKs have been identified in the Arabidopsis genome.[29] They consist of an extracellular ligand-binding domain, a single trans-membrane segment and a cytosolic kinase domain. Cell wall fragments can be generated by cell wall degrading enzymes secreted by pathogens during infection. A classic example are the Endo-polygalacturonases (PGs), enzymes which cleave linkages between α-1,4 D-galacturonic acid residues in non-methylated homogalacturonan, the major component of pectin.[30] During the hydrolysis of homogalacturonan, PGs apparently release OGs from the pectin matrix, (embedded in the cellulose-hemicellulose network). *WALL-ASSOCIATED KINASE1* (WAK1) from Arabidopsis has been shown to reside in the plasma membrane, bind tightly to cell walls and respond to OGs derived from pectic polysaccharides.[31,32] WAKs have been shown to bind covalently to pectic homogalacturonan in plants and non-covalently to Ca^{2+}crosslinked OGs in culture.[33,34] *WAK2* has been implicated in turgor pressure-sensitive processes linking pectin perception with activation of an invertase that can modulate soluble sugar levels in planta, which in turn affects turgor pressure.[35,36] These observations suggest that plant WAKs might be the functional analogs of the yeast CWI sensors monitoring the functional integrity of the plant cell wall through interaction with pectic polysaccharides. Downstream elements of the signaling cascade might be MAPKinases 3 and 6, but the signal transduction between these elements of cascade remains to be determined.[36] *THESEUS (THE)*, *HERCULES1 (HERK1)* and *FERONIA* (*FER*) belong to the *Cataranthus roseus*-like RLK (CrRLK1L) family and have been implicated in CWI maintenance during development.[37-39] HERK1 and FER affect cell elongation, but no CWD response phenotypes have been described to date.[38] The seedlings exhibit defects in cell morphogenesis and CBI-induced lignin deposition suggesting that the same CWI maintenance mechanism may be active during both processes.[37] While all these kinases have been implicated in CWI maintenance their specific functions and ligands remain to be characterized. To summarize, WAKs could represent the plant analogs of yeast CWI sensors. In the case of WAK2 the signals generated activate an invertase that can change soluble sugar levels, which in turn could affect turgor pressure.

Representative examples for the second group of sensors are *MID1-COMPLEMENTING ACTIVITY1* and *2* (*MCA1* and *2*).[40,41] These putatively stretch-activated, plasma membrane localized Ca^{2+}-channels can partially complement the mutant phenotype of a MID1 deficient yeast strain. *mca1* Arabidopsis seedling roots exhibit root growth defects, calcium influx in root cells upon mechano-stimulation is reduced and less ectopic lignin is deposited upon cellulose biosynthesis inhibition (CBI).[9,40,41] CBI is a well-established method to cause highly specific cell wall damage by weakening the cellulose microfibril based exoskeleton, providing most of the structural support to a plant cell.[42,43] These observations implicate *MCA1* and Ca^{2+}-based signaling processes in the response to CWD. Furthermore, calcium signaling inhibitors prevent CBI-induced lignin and reactive oxygen species (ROS) and JA production in a concentration dependent manner.[9] CBI-induced ROS is generated by the NADPHoxidase RBOHD, which is synergistically activated by Ca^{2+} and phosphorylation.[9,44] In *rbohD* seedlings, the CBI-induced ROS production is reduced and JA production enhanced.[9] These observations suggest that THE is required for ROS biosynthesis and is not the only CWD sensor in Arabidopsis. In addition, it indicates that JA/ROS may form a negative feedback loop inhibiting each other's production.[9] The extent of CWD-induced lignin deposition seems to be modulated by JA/ROS signaling due to lignin being reduced in ROS signaling/production (*OXI1*, *rbohDF*) mutants while being enhanced in JA signaling and biosynthesis mutants.[9] To summarize JA, ROS and Ca^{2+}-based signaling mechanisms mediate the response to CWD in plants. Interestingly, Arabidopsis MCA1 is able to rescue the MID1 yeast mutant while also being required for CWD-induced lignin deposition in Arabidopsis.

The third group of sensors is exemplified by the *ARABIDOPSIS HISTIDINE KINASES* (*AHK1–3, AHK4/CRE1*). They form part of a two-component system consisting of a histidine kinase acting as environmental sensor and a phosphor-relay system to translate the signal generated.[45] The available literature has implicated these genes in cytokinin and osmo-perception as well as ABA-dependent abiotic plant stress responses.[46,47] Expression of CRE1 in a SLN1 deficient yeast strain rescues the mutant phenotype if cytokinin is present.[48] Previous work has shown that provision of osmotic support prevents ectopic lignification and

necrosis induced by cellulose inhibition.[7] CBI also induces starch increases in Arabidopsis seedlings, which can be suppressed by osmotic support (Wormit et al. under review). These results implicate osmosensing in CWI maintenance, but do not clarify the specific function of turgor pressure in this context. Turgor pressure could function as an indicator of plant CWI or similarly, as in yeast, complement the activity of the CWI maintenance pathway. In *ahk1*, *ahk4*/*cre1* and *mca1* seedlings the CBI-induced starch increase is detectable. However, the osmotic suppression is not detectable in *ahk4*/*cre1* and *mca1* seedlings (Wormit et al. under review). These observations suggest that CRE1 and MCA1 but not AHK1 are mediating the observed osmotic support effect. Since the CBI-induced starch increases are detectable in both *cre1* and *mca1* seedlings CWD perception itself is either occurring in parallel to turgor perception, or is redundantly specified. More importantly, the responses to CWD can be modulated by turgor pressure changes and CRE1 and MCA1 are required for this mechanism, as shown by the observed effects on starch levels in the mutant seedlings.

Conclusions

The available data suggest both design similarities and functional conservation between the yeast and plant cell wall integrity monitoring and maintenance systems. These are illustrated by the color-coding in **Figure 1A and B** of signaling cascades in yeast (oval) and plant cells (rectangular). Despite the CWI sensor proteins being well characterized in yeast, our understanding of the corresponding plant proteins is limited. The strongest candidates in plants to perform this function are DAMP receptors and WAKs. DAMP receptors are plant specific and nothing similar has been observed in yeast. They could represent an additional level of detection enabling plants to deal with biotic stresses that yeast cells do not experience. Based on this knowledge, it is likely that WAKs represent the group of plant proteins most similar to CWI sensors in yeast based on their mode of action and apparent biological activities. Data from WAK2 implicates turgor pressure perception in the modulation of the CWD response in plants. Previous work in yeast has shown that the CWI and the HOG signaling/osmosensing pathway regulate the response to zymolase treatment jointly. The effects of zymolase and CBI on yeast and plant cell walls are similar (breakdown of the load-bearing cell wall elements). The Arabidopsis protein CRE1 can functionally replace one of the two osmo sensors (SLN1) of the HOG pathway. Accordingly, it is intriguing that osmotic support can neutralize the effects of CBI on starch levels in Arabidopsis wild type seedlings but not in *cre1* seedlings. Recent work has shown that the Arabidopsis MCA1 protein can complement a MID1 deficient yeast strain, and *mca1* seedlings are impaired in CBI induced lignin deposition. These observations suggest that in yeast and Arabidopsis, a similar matrix of signaling cascades may mediate the response to impairment of CWI, and that protein activities are conserved to a certain degree between both species. From the current perspective this research area represents a novel, original approach to understand the mode of action of plant pathogen response mechanisms and environmental stress by placing the plant cell wall at the heart of initial perception, signaling and response to environmental and developmental stimuli.

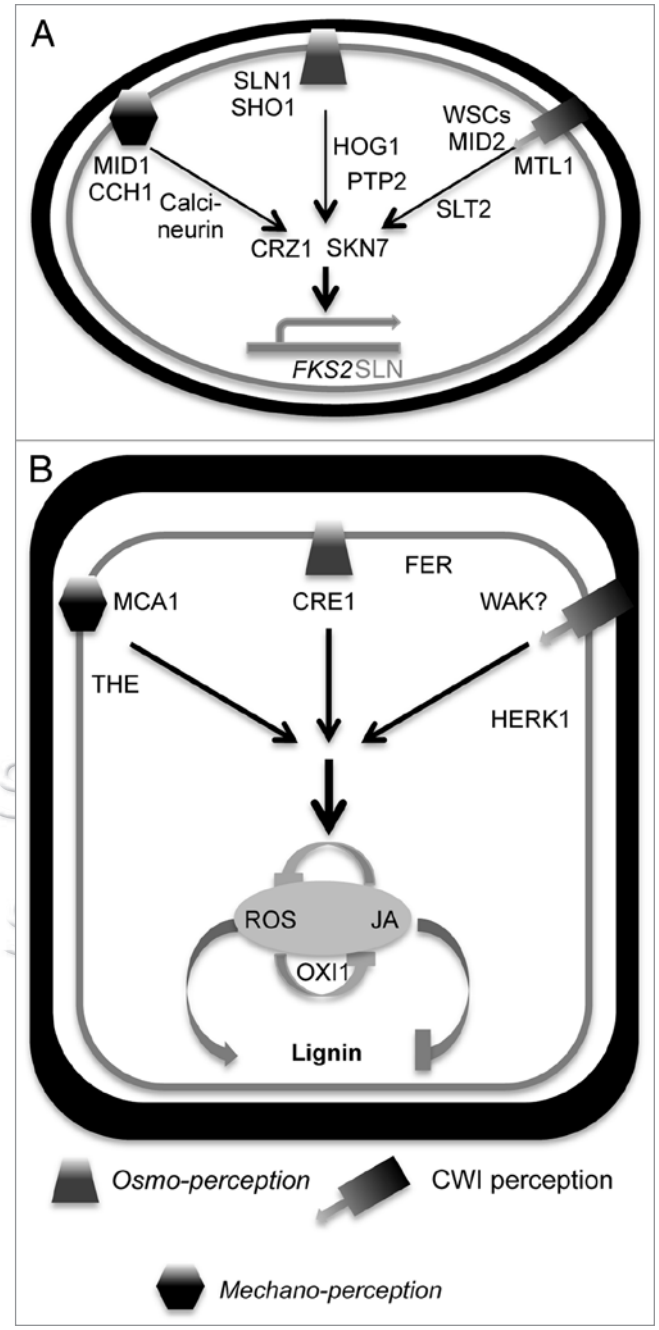

Figure 1. Schematic overview of signaling cascades implicated in CWI maintenance in a yeast (A, oval) and a plant (B, rectangular) cell. The cell wall is marked in black, the plasma membrane in light-gray and gene expression in dark gray.

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References

1. Szymanski DB, Cosgrove DJ. Dynamic coordination of cytoskeletal and cell wall systems during plant cell morphogenesis. Curr Biol 2009; 19:800-11; PMID:19906582; DOI:10.1016/j.cub.2009.07.056.
2. Hématy K, Cherk C, Somerville S. Host-pathogen warfare at the plant cell wall. Curr Opin Plant Biol 2009; 12:406-13; PMID:19616468; DOI:10.1016/j.pbi.2009.06.007.
3. Levin DE. Cell wall integrity signaling in *Saccharomyces cerevisiae*. Microbiol Mol Biol Rev 2005; 69:262-91; PMID:15944456; DOI:10.1128/MMBR.69.2.262-91.2005.
4. Rodríguez-Peña JM, Garcia R, Nombela C, Arroyo J. The high-osmolarity glycerol (HOG) and cell wall integrity (CWI) signalling pathways interplay: a yeast dialogue between MAPK routes. Yeast 2010; 27:495-502; PMID:20641030; DOI:10.1002/yea.1792.
5. Ringli C. Monitoring the outside: cell wall-sensing mechanisms. Plant Physiol 2010; 153:1445-52; PMID:20508141; DOI:10.1104/pp.110.154518.
6. Seifert GJ, Blaukopf C. Irritable walls: the plant extracellular matrix and signaling. Plant Physiol 2010; 153:467-78; PMID:20154095; DOI:10.1104/pp.110.153940.
7. Hamann T, Bennett M, Mansfield J, Somerville C. Identification of cell-wall stress as a hexose-dependent and osmosensitive regulator of plant responses. Plant J 2009; 57:1015-26; PMID:19036034; DOI:10.1111/j.1365-313X.2008.03744.x.
8. Zipfel C. Early molecular events in PAMP-triggered immunity. Curr Opin Plant Biol 2009; 12:414-20; PMID:19608450; DOI:10.1016/j.pbi.2009.06.003.
9. Denness L, McKenna JF, Segonzac C, Wormit A, Madhou P, Bennett M, et al. Cell wall damage-induced lignin biosynthesis is regulated by a ROS- and jasmonic acid dependent process in *Arabidopsis thaliana*. Plant Physiol 2011; 156:1364-74 PMID:21546454; DOI:10.1104/pp.111.175737.
10. Zhao C, Jung US, Garrett-Engele P, Roe T, Cyert MS, Levin DE. Temperature-induced expression of yeast FKS2 is under the dual control of protein kinase C and calcineurin. Mol Cell Biol 1998; 18:1013-22; PMID:9447998.
11. Posas F, Saito H. Activation of the yeast SSK2 MAP kinase kinase kinase by the SSK1 two-component response regulator. EMBO J 1998; 17:1385-94; PMID:9482735; DOI:10.1093/emboj/17.5.1385.
12. Hohmann S. Control of high osmolarity signalling in the yeast *Saccharomyces cerevisiae*. FEBS Lett 2009; 583:4025-9; PMID:19878680; DOI:10.1016/j.febslet.2009.10.069.
13. Lesage G, Sdicu AM, Menard P, Shapiro J, Hussein S, Bussey H. Analysis of beta-1,3-glucan assembly in *Saccharomyces cerevisiae* using a synthetic interaction network and altered sensitivity to caspofungin. Genetics 2004; 167:35-49; PMID:15166135; DOI:10.1534/genetics.167.1.35.
14. Williams KE, Cyert MS. The eukaryotic response regulator Skn7p regulates calcineurin signaling through stabilization of Crz1p. EMBO J 2001; 20:3473-83; PMID:11432834; DOI:10.1093/emboj/20.13.3473.
15. Rodicio R, Heinisch JJ. Together we are strong-cell wall integrity sensors in yeasts. Yeast 2010; 27:531-40; PMID:20641024; DOI:10.1002/yea.1785.
16. Lommel M, Bagnat M, Strahl S. Aberrant processing of the WSC family and Mid2p cell surface sensors results in cell death of *Saccharomyces cerevisiae* O-mannosylation mutants. Mol Cell Biol 2004; 24:46-57; PMID:14673142; DOI:10.1128/MCB.24.1.46-57.2004.
17. Ponting CP, Hofmann K, Bork P. A latrophilin/CL-1-like GPS domain in polycystin-1. Curr Biol 1999; 9:585-8; PMID:10469603; DOI:10.1016/S0960-9822(99)80379-0.
18. Heinisch JJ, Dupres V, Alsteens D, Dufrene YF. Measurement of the mechanical behavior of yeast membrane sensors using single-molecule atomic force microscopy. Nat Protoc 2010; 5:670-7; PMID:20360762; DOI:10.1038/nprot.2010.19.
19. Vay HA, Philip B, Levin DE. Mutational analysis of the cytoplasmic domain of the Wsc1 cell wall stress sensor. Microbiology 2004; 150:3281-8; PMID:15470108; DOI:10.1099/mic.0.27264-0.
20. García R, Rodriguez-Pena JM, Bermejo C, Nombela C, Arroyo J. The high osmotic response and cell wall integrity pathways cooperate to regulate transcriptional responses to zymolyase-induced cell wall stress in *Saccharomyces cerevisiae*. J Biol Chem 2009; 284:10901-11; PMID:19234305; DOI:10.1074/jbc.M808693200.
21. Jacoby T, Flanagan H, Faykin A, Seto AG, Mattison C, Ota I. Two protein-tyrosine phosphatases inactivate the osmotic stress response pathway in yeast by targeting the mitogen-activated protein kinase, Hog1. J Biol Chem 1997; 272:17749-55; PMID:9211927; DOI:10.1074/jbc.272.28.17749.
22. Martín H, Flandez M, Nombela C, Molina M. Protein phosphatases in MAPK signalling: we keep learning from yeast. Mol Microbiol 2005; 58:6-16; PMID:16164545; DOI:10.1111/j.1365-2958.2005.04822.x.
23. Caño-Delgado A, Penfield S, Smith C, Catley M, Bevan M. Reduced cellulose synthesis invokes lignification and defense responses in *Arabidopsis thaliana*. Plant J 2003; 34:351-62; PMID:12713541; DOI:10.1046/j.1365-313X.2003.01729.x.
24. Ellis C, Karafyllidis I, Wasternack C, Turner JG. The Arabidopsis mutant *cev1* links cell wall signaling to jasmonate and ethylene responses. Plant Cell 2002; 14:1557-66; PMID:12119374; DOI:10.1105/tpc.002022.
25. Hernández-Blanco C, Feng DX, Hu J, Sanchez-Vallet A, Deslandes L, Llorente F, et al. Impairment of cellulose synthases required for Arabidopsis secondary cell wall formation enhances disease resistance. Plant Cell 2007; 19:890-903; PMID:17351116; DOI:10.1105/tpc.106.048058.
26. Vogel JP, Raab TK, Somerville CR, Somerville SC. Mutations in PMR5 result in powdery mildew resistance and altered cell wall composition. Plant J 2004; 40:968-78; PMID:15584961; DOI:10.1111/j.1365-313X.2004.02264.x.
27. Vogel JP, Raab TK, Schiff C, Somerville SC. PMR6, a pectate lyase-like gene required for powdery mildew susceptibility in Arabidopsis. Plant Cell 2002; 14:2095-106; PMID:12215508; DOI:10.1105/tpc.003509.
28. Nishimura MT, Stein M, Hou BH, Vogel JP, Edwards H, Somerville SC. Loss of a callose synthase results in salicylic acid-dependent disease resistance. Science 2003; 301:969-72; PMID:12920300; DOI:10.1126/science.1086716.
29. Sanabria N, Goring D, Nurnberger T, Dubery I. Self/nonself perception and recognition mechanisms in plants: a comparison of self-incompatibility and innate immunity. New Phytol 2008; 178:503-14; PMID:18346103; DOI:10.1111/j.1469-8137.2008.02403.x.
30. De Lorenzo G, D'Ovidio R, Cervone F. The role of polygalacturonase-inhibiting proteins (PGIPs) in defense against pathogenic fungi. Annu Rev Phytopathol 2001; 39:313-35; PMID:11701868; DOI:10.1146/annurev.phyto.39.1.313.
31. He ZH, Fujiki M, Kohorn BD. A cell wall-associated, receptor-like protein kinase. J Biol Chem 1996; 271:19789-93; PMID:8702686; DOI:10.1074/jbc.271.33.19789.
32. Brutus A, Sicilia F, Macone A, Cervone F, De Lorenzo G. A domain swap approach reveals a role of the plant wall-associated kinase 1 (WAK1) as a receptor of oligogalacturonides. Proc Natl Acad Sci USA 2010; 107:9452-7; PMID:20439716; DOI:10.1073/pnas.1000675107.
33. Wagner TA, Kohorn BD. Wall-associated kinases are expressed throughout plant development and are required for cell expansion. Plant Cell 2001; 13:303-18; PMID:11226187.
34. Decreux A, Messiaen J. Wall-associated kinase WAK1 interacts with cell wall pectins in a calcium-induced conformation. Plant Cell Physiol 2005; 46:268-78; PMID:15769808; DOI:10.1093/pcp/pci026.
35. Kohorn BD, Kobayashi M, Johansen S, Riese J, Huang LF, Koch K, et al. An Arabidopsis cell wall-associated kinase required for invertase activity and cell growth. Plant J 2006; 46:307-16; PMID:16623892; DOI:10.1111/j.1365-313X.2006.02695.x.
36. Kohorn BD, Johansen S, Shishido A, Todorova T, Martinez R, Defeo E, et al. Pectin activation of MAP kinase and gene expression is WAK2 dependent. Plant J 2009; 60:974-82; PMID:19737363; DOI:10.1111/j.1365-313X.2009.04016.x.
37. Hématy K, Sado PE, Van Tuinen A, Rochange S, Desnos T, Balzergue S, et al. A receptor-like kinase mediates the response of Arabidopsis cells to the inhibition of cellulose synthesis. Curr Biol 2007; 17:922-31; PMID:17540573; DOI:10.1016/j.cub.2007.05.018.
38. Guo H, Li L, Ye H, Yu X, Algreen A, Yin Y. Three related receptor-like kinases are required for optimal cell elongation in *Arabidopsis thaliana*. Proc Natl Acad Sci USA 2009; 106:7648-53; PMID:19383785; DOI:10.1073/pnas.0812346106.
39. Escobar-Restrepo JM, Huck N, Kessler S, Gagliardini V, Gheyselinck J, Yang WC, et al. The FERONIA receptor-like kinase mediates male-female interactions during pollen tube reception. Science 2007; 317:656-60; PMID:17673660; DOI:10.1126/science.1143562.
40. Yamanaka T, Nakagawa Y, Mori K, Nakano M, Imamura T, Kataoka H, et al. MCA1 and MCA2 that mediate Ca^{2+} uptake have distinct and overlapping roles in Arabidopsis. Plant Physiol 2010; 152:1284-96; PMID:20097794; DOI:10.1104/pp.109.147371.
41. Nakagawa Y, Katagiri T, Shinozaki K, Qi Z, Tatsumi H, Furuichi T, et al. Arabidopsis plasma membrane protein crucial for Ca^{2+} influx and touch sensing in roots. Proc Natl Acad Sci USA 2007; 104:3639-44; PMID:17360695; DOI:10.1073/pnas.0607703104.
42. Desprez T, Vernhettes S, Fagard M, Refregier G, Desnos T, Aletti E, et al. Resistance against herbicide isoxaben and cellulose deficiency caused by distinct mutations in same cellulose synthase isoform CESA6. Plant Physiol 2002; 128:482-90; PMID:11842152; DOI:10.1104/pp.010822.
43. Scheible WR, Eshed R, Richmond T, Delmer D, Somerville C. Modifications of cellulose synthase confer resistance to isoxaben and thiazolidinone herbicides in Arabidopsis Ixr1 mutants. Proc Natl Acad Sci USA 2001; 98:10079-84; PMID:11517344; DOI:10.1073/pnas.191361598.
44. Ogasawara Y, Kaya H, Hiraoka G, Yumoto F, Kimura S, Kadota Y, et al. Synergistic activation of the Arabidopsis NADPH oxidase AtrbohD by Ca^{2+} and phosphorylation. J Biol Chem 2008; 283:8885-92; PMID:18218618; DOI:10.1074/jbc.M708106200.
45. Romir J, Harter K, Stehle T. Two-component systems in *Arabidopsis thaliana*—A structural view. Eur J Cell Biol 2010; 89:270-2; PMID:19944478; DOI:10.1016/j.ejcb.2009.11.007.
46. Riefler M, Novak O, Strnad M, Schmulling T. Arabidopsis cytokinin receptor mutants reveal functions in shoot growth, leaf senescence, seed size, germination, root development and cytokinin metabolism. Plant Cell 2006; 18:40-54; PMID:16361392; DOI:10.1105/tpc.105.037796.
47. Tran LS, Urao T, Qin F, Maruyama K, Kakimoto T, Shinozaki K, et al. Functional analysis of AHK1/ATHK1 and cytokinin receptor histidine kinases in response to abscisic acid, drought and salt stress in Arabidopsis. Proc Natl Acad Sci USA 2007; 104:20623-8; PMID:18077346; DOI:10.1073/pnas.0706547105.
48. Inoue T, Higuchi M, Hashimoto Y, Seki M, Kobayashi M, Kato T, et al. Identification of CRE1 as a cytokinin receptor from Arabidopsis. Nature 2001; 409:1060-3; PMID:11234017; DOI:10.1038/35059117.