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Cytokinins are key regulators of a large number of processes in plant development, which is highly plastic and adaptive, and remarkably resilient and self-perpetuating. Cytokinin signaling involves a multistep two-component system, also called a phosphorelay signaling system. Genes encoding the central components to build the cytokinin phosphorelay system are found in diverse plant species, resulting in the establishment of a canonical model of cytokinin signaling that is likely representative and conserved in plants. The cytokinin signaling pathway can be modulated by nutrients, stress, and other hormones, and is integrated into a signaling network in both shoots and roots.

Description

This record contains general information about the Cytokinin Signaling Pathway collected across species.

Cytokinins are essential plant hormones that control cell division, shoot meristem initiation, leaf and root differentiation, chloroplast biogenesis, stress tolerance, and senescence (*1*–*8*). Together with another plant hormone, auxin, cytokinins can reprogram terminally differentiated leaf cells to stem cells and can support shoot regeneration indefinitely in plant tissue culture. Thus, cytokinins are important regulators of plant growth and development, processes that are highly plastic and adaptive, as well as remarkably resilient and self-perpetuating. There are four major steps of the cytokinin phosphorelay: (i) ligand sensation and signal initiation by a histidine kinase (HK), (ii) histidine phosphotransfer protein (HPT) nuclear translocation, (iii) transcriptional activation of response regulator (RR), and (iv) a negative-feedback loop through cytokinin-inducible RR gene products (*2*, *3*, *5*–*7*).

The first plant hormone belonging to the class now called cytokinins was discovered more than 50 years ago, based on its ability to strongly stimulate growth and cell division in cultured tobacco cells (*9*, *10*). Since then, many additional roles have been attributed to cytokinins. These include control of the stem cell pool in the shoot apical meristem, leaf and root differentiation, vasculature patterning, chloroplast biogenesis, photomorphogenesis, fertility, seed development, senescence, and stress tolerance (*1*–*7*). Thus, cytokinins control key aspects of plant growth and development.

Cytokinin signaling is mediated by a multistep two-component circuitry through histidine (His) and aspartate (Asp) phosphorelay (Fig. 1). Two-component systems are prevalent in bacteria. Typically, they are composed of two proteins: The HK and the RR. Simple HKs contain two functional domains, a variable ligand sensor and a conserved His-containing catalytic protein kinase. The RRs harbor a conserved Asp-containing receiver domain and a variable output domain. Upon signal reception, phosphoryl groups are transferred from His to Asp. In a more complex multistep system like the cytokinin pathway, they are transferred from His to Asp to His to Asp. The multistep phosphorelay results from the addition of (i) a receiver domain to the HK to form a hybrid HK, and (ii) a phosphotransfer protein basically consisting of a conserved His-containing domain. These multistep systems facilitate signaling links in the different cellular compartments that have evolved in eukaryotes and provide more points of regulation and integration to other signaling networks (*11*).

Cytokinins are a class of ligands that bind to a CHASE (cyclase- and HK-associated sensing extracellular) domain of transmembrane receptors with a hybrid HK. Cytokinins include a large array of natural adenine derivatives that are produced by plants and some bacteria through specific enzymatic pathways and nucleic acid degradation, as well as some that are artificially generated by chemical synthesis, such as phenylurea derivatives (*1*, *8*, *12*). Ligand binding triggers phosphorylation at the conserved His residue within the receptors. In cytokinin signaling, the phosphoryl group is first transferred from His to a conserved Asp residue in the receptor's receiver domain. It is further transferred to a His phosphotransfer protein (HPT) that translocates to the nucleus, where the phosphoryl group gets passed over to a conserved Asp residue in the receiver domain of a RR protein. There are two types of cytokinin RRs: A- and B-type. Both have a conserved receiver domain at the N-terminus. B-type RRs contain extra C-terminal domains for DNA binding and transcription activation. In contrast, A-type RRs have a short and poorly defined C-terminal domain, and they inhibit cytokinin signaling. Because A-type RRs also represent immediate-early transcriptional targets, they establish a negative-feedback loop in the pathway (*2*, *3*, *5*–*7*). Interestingly, some response regulators are structurally and functionally similar to the A-type, but the genes are not transcriptionally induced by cytokinin (*13, 14*). Genes encoding the key components to build a phosphorelay system can be found in a variety of plants, including *Arabidopsis thaliana*, maize, rice, wheat, and poplar, suggesting a conservation of the cytokinin signaling mechanism in plants (*2*, *3*–*7*, *15*, *16*).

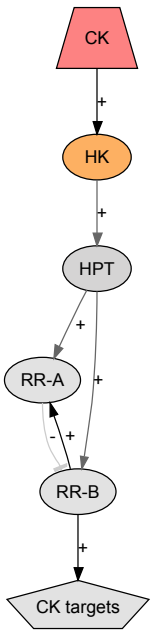

Fig. 1. Pathway image captured from the dynamic graphical display of the information in the Connections Maps available 13 September 2007. For a key to the colors and symbols and to access the underlying data, please visit the pathway (http://stke.sciencemag.org/cgi/cm/stkecm;CMP_9724).

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Specific pathway	URL	Species
Arabidopsis cytokinin signaling pathway	http://stke.sciencemag.org/cgi/cm/stkecm;CMP_10021	Plants: *Arabidopsis*

Table 1. Specific examples of the cytokinin signaling pathway in the Database of Cell Signaling. These specific pathways are based on the canonical Cytokinin Signaling Pathway.

Pathway Details

URL: http://stke.sciencemag.org/cgi/cm/stkecm;CMP_9724
Scope: Canonical

References

1. D. W. Mok, M. C. Mok, Cytokinin metabolism and action. *Annu. Rev. Plant Physiol. Plant Mol. Biol.* **52**, 89–118 (2001).
2. I. Hwang, H. C. Chen, J. Sheen, Two-component signal transduction pathways in Arabidopsis. *Plant Physiol.* **129**, 500–515 (2002).
3. A. Heyl, T. Schmülling, Cytokinin signal perception and transduction. *Curr. Opin. Plant Biol.* **6**, 480–488 (2003).
4. S. H. Howell, S. Lall, P. Che, Cytokinins and shoot development. *Trends Plant Sci.* **8**, 453–459 (2003).
5. T. Kakimoto, Perception and signal transduction of cytokinins. *Annu. Rev. Plant Biol.* **54**, 605–627 (2003).
6. T. Mizuno, Plant response regulators implicated in signal transduction and circadian rhythm. *Curr. Opin. Plant Biol.* **7**, 499–505 (2004).
7. F. J. Ferreira, J. J. Kieber, Cytokinin signaling. *Curr. Opin. Plant Biol.* **8**, 518–525 (2005).
8. H. Sakakibara, Cytokinins: Activity, biosynthesis, and translocation. *Annu. Rev. Plant Biol.* **57**, 431–449 (2006).
9. C. Miller, F. Skoog, M. Von Saltza, F. Strong, Kinetin, a cell division factor from deoxyribonucleic acid. *J. Am. Chem. Soc.* **77**, 1392 (1955).
10. R. Amasino, 1955: Kinetin arrives: The 50th anniversary of a new plant hormone. *Plant Physiol.* **138**, 1177–1184 (2005).
11. A. H. West, A. M. Stock, Histidine kinases and response regulator proteins in two-component signaling systems. *Trends Biochem. Sci.* **26**, 369–376 (2001).
12. K. Miyawaki, P. Tarkowski, M. Matsumoto-Kitano, T. Kato, S. Sato, D. Tarkowska, S. Tabata, G. Sandberg, T. Kakimoto, Roles of *Arabidopsis* ATP/ADP isopentenyltransferases and tRNA isopentenyltransferases in cytokinin biosynthesis. *Proc. Natl. Acad. Sci. U.S.A.* **103**, 16598–16603 (2006).
13. T. Kiba, K. Aoki, H. Sakakibara, T. Mizuno, Arabidopsis response regulator, ARR22, ectopic expression of which results in phenotypes similar to the WOL cytokinin-receptor mutant. *Plant Cell Physiol.* **45**, 1063–1077 (2004).
14. S. Gattolin, M. Alandete-Saez, K. Elliott, Z. Gonzalez-Carranza, E. Naomab, C. Powell, J. A. Roberts, Spatial and temporal expression of the response regulators ARR22 and ARR24 in *Arabidopsis thaliana*. *J. Exp. Bot.* **57**, 4225–4233 (2006).
15. Y. Ito, N. Kurata, Identification and characterization of cytokinin-signalling gene families in rice. *Gene* **382**, 57–65 (2006).
16. G. A. Tuskan, S. DiFazio, S. Jansson, J. Bohlmann, I. Grigoriev, U. Hellsten, N. Putnam, S. Ralph, S. Rombauts, A. Salamov, J. Schein, L. Sterck, A. Aerts, R. R. Bhalerao, R. P. Bhalerao, D. Blaudez, W. Boerjan, A. Brun, A. Brunner, V. Busov, M. Campbell, J. Carlson, M. Chalot, J. Chapman, G.-L. Chen, D. Cooper, P. M. Coutinho, J. Couturier, S. Covert, Q. Cronk, R. Cunningham, J. Davis, S. Degroeve, A. Déjardin, C. dePamphilis, J. Detter, B. Dirks, I. Dubchak, S. Duplessis, J. Ehlting, B. Ellis, K. Gendler, D. Goodstein, M. Gribskov, J. Grimwood, A. Groover, L. Gunter, B. Hamberger, B. Heinze, Y. Helariutta, B. Henrissat, D. Holligan, R. Holt, W. Huang, N. Islam-Faridi, S. Jones, M. Jones-Rhoades, R. Jorgensen, C. Joshi, J. Kangasjärvi, J. Karlsson, C. Kelleher, R. Kirkpatrick, M. Kirst, A. Kohler, U. Kalluri, F. Larimer, J. Leebens-Mack, J.-C. Leplé, P. Locascio, Y. Lou, S. Lucas, F. Martin, B. Montanini, C. Napoli, D. R. Nelson, C. Nelson, K. Nieminen, O. Nilsson, V. Pereda, G. Peter, R. Philippe, G. Pilate, A. Poliakov, J. Razumovskaya, P. Richardson, C. Rinaldi, K. Ritland, P. Rouzé, D. Ryaboy, J. Schmutz, J. Schrader, B. Segerman, H. Shin, A. Siddiqui, F. Sterky, A. Terry, C.-J. Tsai, E. Uberbacher, P. Unneberg, J. Vahala, K. Wall, S. Wessler, G. Yang, T. Yin, C. Douglas, M. Marra, G. Sandberg, Y. Van de Peer, D. Rokhsar, The genome of black cottonwood, *Populus trichocarpa* (Torr. & Gray). *Science* **313**, 1596–1604 (2006).

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