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Cell biology

Enzyme shatters cell skeleton

The process by which stress-activated enzymes destabilize a cell's molecular scaffold could one day be directed against cancer

Plant and animal cells are supported by a framework of tubular proteins, called microtubules, that are crucial in many cellular processes. In plants, environmental stress can cause this framework to break down, but the molecular mechanisms underlying this disintegration have remained elusive. NAIST researchers have now discovered that a protein known as PHS1 plays a key role in dismantling the microtubule scaffold[1].

Takashi Hashimoto and colleagues at NAIST's Plant Cell Function Laboratory studied the function of the protein by using mutants of *Arabidopsis* — small flowering plants related to cabbage — that were deficient in PHS1. They found that PHS1 contains two parts: a kinase and a phosphatase (see figure).

The kinase causes the transfer of a phosphate group to microtubule proteins, which destabilizes the entire microtubule skeleton.

The kinase is usually inactive, but Hashimoto's team showed that it is permanently active in mutants with defective phosphatase domains. This suggests that the phosphatase acts as a switch controlling the kinase. Furthermore, when the researchers applied stress such as a high salt concentration, they found that the phosphatase 'switched on' the kinase. This, they report, "provides an efficient strategy for reversibly and rapidly regulating microtubule stability in response to biotic and abiotic signals."

Although proteins with multiple functions are fairly common, 'autoregulated' proteins such as PHS1, with two opposing domains are rare, according to Hashimoto. "I do not recall any kinase having a juxtaposed phosphatase domain," he notes.

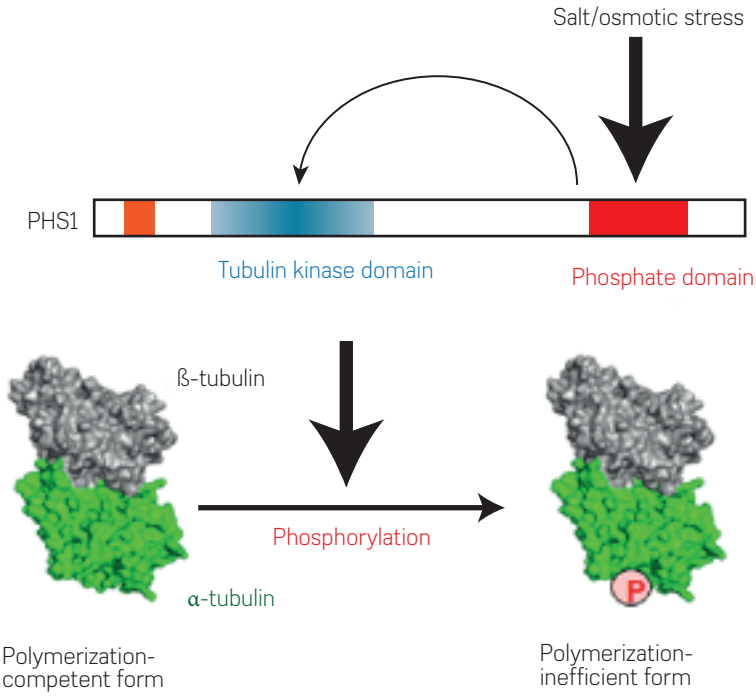
> **"Our current preferred idea is that PHS1 acts to halt plant growth temporarily under water stress, allowing the plant to adapt to changing water resources. This is one of the most important questions we want to address."**

The functional significance of PHS1 in nature remains unclear and is something the team is actively investigating. "Our current preferred idea is that PHS1 acts to halt plant growth temporarily under water stress, allowing the plant to adapt to changing water resources. This is one of the most important questions we want to address," says Hashimoto.

PHS1 is thought to be unique to, but universal in, the plant kingdom. "All sequenced plant genomes have PHS1 genes," says Hashimoto, who has recently shown that mosses use the same system.

The protein also provides a useful tool for studying microtubule-based cellular processes and, because microtubules are central to all cell division, it could potentially be used to stop cancer cells proliferating. Tests on cultured monkey cells have shown that PHS1 can also destabilize mammalian microtubule arrays.

Hashimoto reasons that, since PHS1 also acts on animal microtubules, "it could be targeted to cancer cells to dysfunction their microtubules, thereby stopping proliferation." In the shorter term, his research provides useful experimental tools for studying cellular processes.



PHS1 comprises two domains: a kinase and its suppressor, a phosphatase. Environmental stress causes phosphatase to release the kinase, which then transfers a phosphate group to a tubulin molecule. This phosphorylation of tubulin results in the breakdown of cellular microtubule arrays.

Reference

1. Fujita, S., Pytela, J., Hotta, T., Kato, T., Hamada, T. *et al.* An atypical tubulin kinase mediates stress-induced microtubule depolymerization in *Arabidopsis*. *Current Biology* **23**, 1969–1978 (2013).

More information about the group's research can be found at the Plant Cell Function Laboratory webpage:
http://bsw3.naist.jp/eng/courses/courses103.html