PLANT CELL BIOLOGY

Shedding light on auxin action

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The unusual mechanism by which auxin activates SCF^{TIR1} might have significance beyond plant biology...

Auxin is a crucial plant hormone that controls many aspects of plant growth and development. Although auxin has been studied for over a century, its cellular receptor has only recently been discovered. Auxin binds to the F-box protein transport inhibitor response-1 (TIR1), which is part of the ubiquitin ligase SCF^{TIR1} complex, to regulate gene transcription through the ubiquitin-dependent degradation of the Aux/IAA family of transcriptional repressors. Zheng and colleagues have determined structures of TIR1 in complex with the SCF^{TIR1} adaptor protein ASK1 to reveal how auxin activates TIR1.

The structure of the TIR1–ASK1 complex is mushroom shaped, with much of TIR1 contributing to the mushroom cap. The auxin-binding pocket is formed by a Leu-rich repeat

(LRR) domain of TIR1 in the cap surface. Most strikingly, structures of the TIR–ASK1 complex, both with and without auxin bound, indicate that auxin does not induce large conformational changes in the structure of TIR–ASK1 upon binding. Therefore, auxin is not an allosteric regulator of SCF^{TIR1}.

At the base of the auxin-binding pocket lies an inositol hexakisphosphate (InsP₆) molecule. This could be a structural cofactor that is required for the detection of auxin by TIR1. And considering that InsP₆ could not be removed under various conditions, it might be constitutively present. Auxin, and a number of other auxin-mimetic molecules, bind above InsP₆.

The structures of TIR1–ASK in complex with different auxin compounds revealed that the binding site

is composed of several highly selective TIR1–auxin interactions and a region that allows for more flexible binding. This partially promiscuous binding pocket allows for various auxin-like structures to be accommodated. Structures of TIR1–ASK1 with both auxin and an Aux/IAA-derived peptide bound show that the Aux/IAA gene repressor binds on top of auxin, through extensive hydrophobic interactions with TIR1. This orients the repressor towards the predicted position of the SCF^{TIR1} subunit that has ubiquitin-conjugating activity.

Instead of an allosteric switch, the authors propose that auxin — sandwiched between TIR1 and the repressor — functions as ‘molecular glue’ that fills a cavity in the binding pocket and increases the surface area that is available for protein–protein interactions. The unusual mechanism by which auxin activates SCF^{TIR1} might have significance beyond plant biology: the principle that small molecules can influence protein–protein interactions is an approach that might lead to new drugs for various diseases.

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ORIGINAL RESEARCH PAPER Tan, X. et al. Mechanism of auxin perception by the TIR1 ubiquitin ligase. *Nature* **446**, 640–645 (2007)

FURTHER READING Teale, W. D. et al. Auxin in action: signalling, transport and the control of plant growth and development. *Nature Rev. Mol. Cell Biol.* **7**, 847–859 (2006)

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