

MS02 Infection and Disease/hot structures

MS2-05

Using crystallographic 'failures' to identify artificial and endogenous inhibitors for plant growth and defence pathways

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Abstract

Plants cannot move to obtain nutrients or avoid predation. To cope with this constraint, plants have developed an arsenal of regulatory mechanisms that are markedly more sophisticated and influential than those used by animals. Understanding and controlling the molecular basis for plants' decision-making on growth and defence strategies may help improve food security.

We present two converging tales of how "failed" X-ray crystallography experiments provided not only a novel lead compound for specific enzyme inhibition but also helped reveal regulation feedback mechanisms that determine plant growth and pathogen resistance. Based on more than a dozen different crystal structures, biophysical and in planta data we show how members of two enzyme families (the HTL/D14/KAI2 hydrolases and NATA1/2 acetyltransferases) integrate endogenous and external stimuli to allow plants to make informed decisions [1,2 and unpublished]. Collectively, our findings expand the range of molecular regulatory mechanisms used in plants to balance growth and defence, and reveal unexpected lead compounds to control them.

References

[1] Shahul Hameed U, Haider I, Jamil M, Guo X, Zarban RA, Kim D, Al-Babili S, Arold ST.; EMBO Rep 2018; doi: 10.15252/embr.201745619

[2] Zarban Zarban RA, Hameed UFS, Jamil M, Ota T, Wang JY, Arold ST, Asami T, Al-Babili S; Plant Physiol. 2022; doi: 10.1093/plphys/kiab547

Striga hermonthica HTL7 and NATA1 with ligands



TOP Left: The parasitic plant *Striga hermonthica* (pink flowers) causes billions of USD of losses every year by draining nutrients from crops. **Middle:** The crystallographic structure of ShHTL7, the key sensor used by *Striga* to identify the host plant. **Right:** Serendipitously identified specific inhibitor in its 2fofc electron density map [1]. **BOTTOM Left:** Dimeric NATA1 with cofactors and inhibitor [unpublished]. **Right:** Serendipitous inhibitor in 2fofc map.