The Meaning of an End: N-Terminal Acetyltransferase NAA50 Controls Plant Growth and Stress Responses

At least 80% of eukaryotic proteins are estimated to undergo N-terminal acetylation (NTA), making it likely that your favorite protein is also regulated by NTA (Linster and Wirtz, 2018). This transfer of an acetyl group to the N terminus can modulate a protein's interaction partners, i.e. folding, localization, aggregation, and degradation (Gibbs, 2015). NTA is catalyzed by several distinct N-terminal acetyltransferase (Nat) complexes (NatA, NatB, NatC, and NatE), which each modify different N-terminal amino acids and consist of catalytic and auxiliary subunits. For instance, the catalytic subunits of NatA (NAA10) and NatE (NAA50) in humans target a distinct set of substrates but share the same ribosome binding auxiliary subunit, facilitating cotranslational acetylation of target proteins. However, such characterization of individual Nat subunits in plants is lacking, and currently hinders our understanding of how NTA regulates biological processes.

In this issue of *Plant Physiology*, two back-to-back publications characterize the Arabidopsis (*Arabidopsis thaliana*) catalytic NatE subunit NAA50 (Armbruster et al., 2020; Neubauer and Innes, 2020). Together, the articles show that NAA50 localizes to the nucleus, the cytosol, and the endoplasmic reticulum (ER), and acetylates a broad range of N-terminal substrates in vitro. Moreover, they show that *naa50* mutants are strongly limited in plant growth, fertility, and development (Fig. 1). These findings are consistent with an additional recent report showing that NAA50 is essential for plant growth (Feng et al., 2020). To examine if the limited growth of *naa50* mutants is caused by a loss of functional NAA50, the authors complemented the mutants with several modified versions of NAA50. Expression of Arabidopsis NAA50 fully restored the growth and developmental deficiencies of the mutant. Furthermore, Armbruster et al. (2020) show that NAA50 function is conserved between humans and plants, as even the human homolog of NAA50 could complement *naa50*. They could also map this activity to a conserved NAA50 region that is only present in higher eukaryotes, as yeast NAA50 could not rescue the impaired growth phenotype. In yeast (*Saccharomyces cerevisiae*), NAA50 is essential to position the NatA complex at the exit tunnel of the ribosome (Knorr et al., 2019). However, in this study no abnormalities in the acetylation of known NatA substrates were identified in *naa50* (Armbruster et al., 2020). Collectively, these findings strongly suggest that Arabidopsis NAA50 is an enzymatically active NatE, but does not contribute to NatA activity.

To uncover how loss of NAA50 represses growth, Neubauer and Innes (2020) quantified the transcriptome

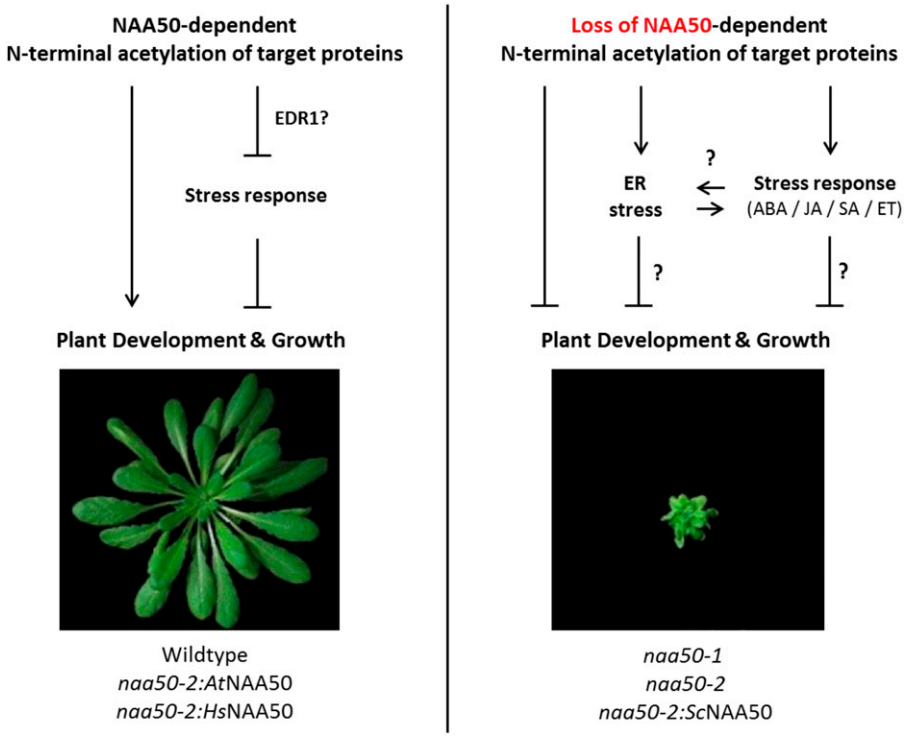

Figure 1. Left, Functionally active Arabidopsis (*At*) or human (*Hs*) NAA50 is required for normal development, growth, and the repression of stress responses in Arabidopsis. NAA50 was shown to interact with the negative defense regulator ENHANCED DISEASE RESISTANCE1 [EDR1]. Right, Loss of functional NAA50 (*naa50* mutants ± complementation with yeast *Sc*NAA50) leads to strongly impaired plant growth and development. Reduced *NAA50* levels also result in ER stress, constitutive stress responses, and hormone signaling (abscisic acid [ABA], jasmonic acid [JA], SA, and ethylene [ET]) at both the transcriptional (Neubauer and Innes, 2020) and proteome levels (Armbruster et al., 2020). These altered processes may directly or indirectly contribute to the impaired growth and development of *naa50* mutants. Images were adapted from figure 4C of Armbruster et al. (2020).

of a hormone-inducible *NAA50* artificial microRNA line and Armbruster et al. (2020) examined the proteome in an *naa50* mutant. Both approaches revealed that loss of NAA50 leads to constitutive ER stress and (a)biotic stress responses. The enhanced defense response also corresponded with increased signaling of the stress-associated hormones salicylic acid (SA), jasmonic acid, abscisic acid, and ethylene (Fig. 1). In addition, Neubauer and Innes (2020) show that NAA50 interacts with the negative-stress regulator ENHANCED DISEASE RESISTANCE1, providing a potential mechanism for how NAA50 dampens defense responses. The authors suggest that the observed ER stress could be the result of accumulating unfolded and aggregated proteins in the *naa50* mutant. Interestingly, previous research has shown that crosstalk between ER stress and the defense response can regulate the tradeoff between plant growth and stress responses (Meng et al., 2017). Indeed, SA can divert energy from fueling plant growth to the amelioration of ER stress, while ER stress, in turn, switches on defense responses (Meng et al., 2017; Srivastava et al., 2018). Together, these observations suggest that the reduced growth of *naa50* mutants depends on a shifting growth–defense balance that may depend on crosstalk between ER stress and defense responses (Fig. 1). To unravel if the *naa50*-impaired growth is indeed the result of constitutively induced defense hormone signaling, future experiments could attempt to rescue the growth phenotype by crossing *naa50* with the corresponding hormone biosynthesis and signaling mutants.

This work convincingly adds another piece to the complex NTA puzzle and allows us to examine which proteins directly undergo cotranslational NTA by NAA50, and identify how NAA50 dynamics modulate specific stress responses. Other recent studies also highlight the importance of post-translational NTA at the plasma membrane and in plastids (Bienvenut et al., 2020; Linster et al., 2020). Collectively, these reports demonstrate that NTA and Nat complexes deserve our full attention when we aim to understand the regulation of plant growth, development, and stress responses (Feng et al., 2020; Huber et al., 2020).

Sjon Hartman[1,2]
ORCID ID: 0000-0002-6709-6436
Plant Ecophysiology,
Institute of Environmental Biology,
Utrecht University, 3584 CH, Utrecht,
The Netherlands

LITERATURE CITED

Armbruster L, Linster E, Boyer J-B, Brünje A, Eirich J, Stephan I, Bienvenut WV, Weidenhausen J, Meinnel T, Hell R, et al (2020) NAA50 is an enzymatically active N^{α}-acetyltransferase that is crucial for development and regulation of stress responses. Plant Physiol **183:** 1502–1516

Bienvenut WV, Brünje A, Boyer JB, Mühlenbeck JS, Bernal G, Lassowskat I, Dian C, Linster E, Dinh TV, Koskela MM, et al (2020). Dual lysine and N-terminal acetyltransferases reveal the complexity underpinning protein acetylation. Mol Syst Biol **16:** e9464

Feng J, Hu J, Li Y, Li R, Yu H, Ma L (2020) The N-terminal acetyltransferase NAA50 regulates Arabidopsis growth and osmotic stress response. Plant Cell Physiol pcaa081, doi:10.1093/pcp/pcaa081

Gibbs DJ (2015) Emerging functions for N-terminal protein acetylation in plants. Trends Plant Sci **20:** 599–601

Huber M, Bienvenut WV, Linster E, Stephan I, Armbruster L, Sticht C, Layer D, Lapouge K, Meinnel T, Sinning I, et al (2020) NatB-mediated N-terminal acetylation affects growth and biotic stress responses. Plant Physiol **182:** 792–806

Knorr AG, Schmidt C, Tesina P, Berninghausen O, Becker T, Beatrix B, Beckmann R (2019) Ribosome-NatA architecture reveals that rRNA expansion segments coordinate N-terminal acetylation. Nat Struct Mol Biol **26:** 35–39

Linster E, Layer D, Bienvenut WV, Dinh TV, Weyer FA, Leemhuis W, Brünje A, Hoffrichter M, Miklankova P, Kopp J, et al (2020) The Arabidopsis N^{α}-acetyltransferase NAA60 locates to the plasma membrane and is vital for the high salt stress response. New Phytol doi: 10.1111/nph.16747

Linster E, Wirtz M (2018) N-terminal acetylation: An essential protein modification emerges as an important regulator of stress responses. J Exp Bot **69:** 4555–4568

Meng Z, Ruberti C, Gong Z, Brandizzi F (2017) CPR5 modulates salicylic acid and the unfolded protein response to manage tradeoffs between plant growth and stress responses. Plant J **89:** 486–501

Neubauer M, Innes RW (2020) Loss of the acetyltransferase NAA50 induces ER stress and immune responses and suppresses growth. Plant Physiol **183:** 1838–1854

Srivastava R, Li Z, Russo G, Tang J, Bi R, Muppirala U, Chudalayandi S, Severin A, He M, Vaitkevicius SI, et al (2018) Response to persistent ER stress in plants: A multiphasic process that transitions cells from prosurvival activities to cell death. Plant Cell **30:** 1220–1242

[1]Author for contact: j.g.w.hartman@uu.nl.
[2]Senior author.
www.plantphysiol.org/cgi/doi/10.1104/pp.20.00794