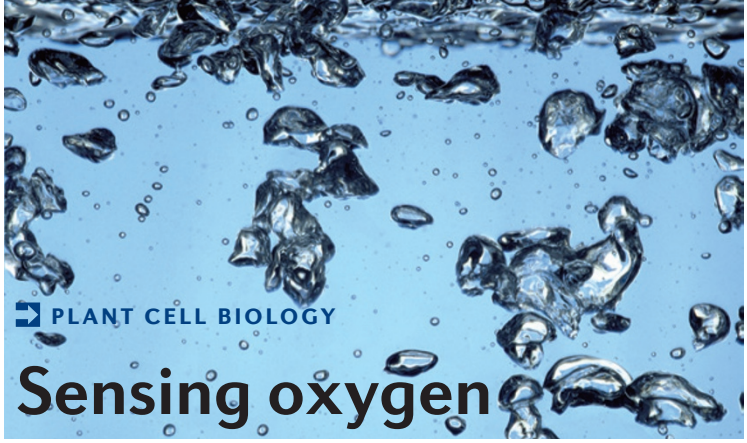

PLANT CELL BIOLOGY

Sensing oxygen

To minimize damage caused by low levels of oxygen (hypoxia), cells rely on oxygen-sensing mechanisms, which drive downstream adaptive responses. Two studies now show that the N-end rule degradation pathway is part of the oxygen-sensing mechanism in *Arabidopsis thaliana*.

Proteins carrying particular amino-terminal sequences (known as N degrons) can be targeted for proteasomal degradation via the N-end rule pathway, following Arg conjugation by the Arg transferase ATE and subsequent ubiquitylation by the ligase PROTEOLYSIS 6 (PRT6). Gibbs *et al.* found that *ate* and *prt6* mutant seedlings constitutively expressed genes important for anaerobic metabolism and hypoxia at high levels, and were more resistant to long-term oxygen deprivation. Licausi *et al.* also showed that *ate* and *prt6* mutants had altered hypoxia responses, which demonstrates a link between the N-end rule pathway and the response to hypoxia.

In *A. thaliana*, tolerance to hypoxia is in part mediated by members of subgroup VII of the ETHYLENE RESPONSE FACTOR (ERF) transcription factor family, which are potential substrates of the N-end rule pathway. To confirm whether subgroup VII ERFs are N-end rule substrates, both groups examined the importance of the N-terminal sequence in protein stability and function. Gibbs *et al.* showed that the stability of HRE1 and HRE2, which are subgroup VII ERFs, was dependent on their N terminus. Furthermore, Licausi *et al.* observed that constitutive overexpression of RAP2-12 resulted in higher expression of hypoxia-responsive genes in hypoxic conditions; by contrast, overexpression of RAP2-12 with a modified or truncated N terminus led to constant induction of hypoxia genes even after re-oxygenation, ultimately impairing plant growth. Licausi *et al.* also found that RAP2-12 lacking the N-end rule N degron remained active in the nucleus after re-oxygenation. Thus, the N-terminal residues of subgroup VII ERFs are important for their stability and function during hypoxia.

Further findings from both groups show that group VII ERFs are regulated by the N-end rule pathway. Licausi *et al.* found that the hypoxia responses of *ate* and *prt6* mutants were impaired in a manner similar to that of plants expressing RAP2-12 proteins modified at their N terminus. Furthermore, they revealed that RAP2-12 is sequestered to the plasma membrane and is released to the nucleus only upon hypoxia, activating the subsequent expression of hypoxia-related genes. Consistently, Gibbs *et al.* observed that the stability of all group VII ERFs was enhanced following mutation of Cys2 — which is part of the N degron — or inhibition of the N-end rule pathway *in vitro*. Furthermore, HRE2 stability was increased in *ptr6* mutants.

These studies show that group VII ERFs are substrates of the N-end rule pathway and sense oxygen levels, probably through oxidation of their Cys2 residue. Both groups demonstrated that degradation of these proteins by the N-end rule pathway was oxygen-dependent, and that they were stabilized under hypoxia in plants. Whether oxidation is directly related to molecular oxygen or other cellular changes remains to be determined.

Kim Baumann

> “group VII ERFs are substrates of the N-end rule pathway and sense oxygen levels”

ORIGINAL RESEARCH PAPERS Gibbs, D. J. *et al.* Homeostatic response to hypoxia is regulated by the N-end rule pathway in plants. *Nature* 23 Oct 2011 (doi:10.1038/nature10534) | Licausi, F. *et al.* Oxygen sensing in plants is mediated by an N-end rule pathway for protein destabilization. *Nature* 23 Oct 2011 (doi:10.1038/nature10536)

FURTHER READING Sriram, S. M., Kim, B. Y. & Kwon, Y. T. The N-end rule pathway: emerging functions and molecular principles of substrate recognition. *Nature Rev. Mol. Cell Biol.* **12**, 735–747 (2011)