Crosstalk between Gibberellin Signaling and Iron Uptake in Plants: An Achilles' Heel for Modern Cereal Varieties?

Nicolaus von Wirén[1,*] and Malcolm J. Bennett[2,*]
[1]Molecular Plant Nutrition, Leibniz Institute of Plant Genetics and Crop Plant Research, Corrensstr. 3, 06466 Gatersleben, Germany
[2]Centre for Plant Integrative Biology, School of Biosciences, University of Nottingham, Sutton Bonington Campus, Loughborough, LE12 5RD, UK
*Correspondence: vonwiren@ipk-gatersleben.de (N.v.W.), malcolm.bennett@nottingham.ac.uk (M.J.B.)
http://dx.doi.org/10.1016/j.devcel.2016.04.003

Plants utilize sophisticated morphological and physiological mechanisms to acquire iron from soil. In this issue of *Developmental Cell*, Wild et al. (2016) find that the hormone signal gibberellic acid is key in integrating these responses, raising questions about the impact of altering GA responses in modern cereal varieties on iron acquisition.

Iron is an essential microelement in all organisms where it functions as a cofactor for enzymes and directly mediates electron transport processes (White and Broadley, 2009). Due to the low solubility of iron in oxygenated and high pH environments, organisms have evolved a variety of mobilization strategies that mainly rely on iron chelation and ferric iron reduction. The mechanisms underlying iron adaptation differ not only among animal, microbial, or plant species, but also, as reported in this issue of *Developmental Cell* by Wild et al., even between different zones of the same plant root (Figure 1).

In roots of the model plant *Arabidopsis*, iron acquisition is facilitated by the release of protons and coumarin-type chelators to release ferric iron (Fe^{3+}) from precipitates and deliver it to the root surface for subsequent reduction by the plasma membrane-bound reductase FRO2 (Robinson et al., 1999) and import by a ferrous iron (Fe^{2+}) transporter IRT1 (Vert et al., 2002). Expression of these components of the iron acquisition machinery is coordinated by the basic-helix-loop-helix (bHLH) transcription factor FIT when hetero-dimerized with bHLH38 and 39 (Yuan et al., 2008). *FIT* itself is strongly upregulated under iron deficiency in roots and confined to outer root cells, i.e., the epidermis and cortex (Wild et al., 2016; Figure 1).

These physiological adaptations to low iron operate in parallel with morphological changes to the root system, such as formation of root hairs and inhibition of root elongation (Ivanov et al., 2012). However, until now it has been unclear whether these morphological alterations are directly coupled with physiological responses. To date, only the plant hormone ethylene has been shown to directly participate in the upregulation of iron acquisition machinery by stabilizing FIT under iron deficiency (Lingam et al., 2011), whereas its involvement in adapting root morphological traits to low iron has remained indirect. Wild et al. report that the plant hormone gibberellic acid (GA) and its signaling repressor DELLA exert such a dual function by combining morphological and physiological responses to low iron through cell-type-specific adjustment of DELLA abundance in different root zones (Figure 1).

Wild et al. (2016) initially described how low iron causes a reduction in *Arabidopsis* primary root length through the stabilization of DELLA growth repressor proteins (like RGA) in dividing cells in the root meristem. The authors demonstrate that DELLA stabilization is linked with decreased synthesis of the plant hormone GA, speculating that this reduction is facilitated by the requirement of an iron co-factor by the family of 2-oxoglutarate-dependent dioxygenases that catalyze GA synthesis (Figure 1).

In parallel, Wild et al. (2016) report that GA also regulates the FIT-dependent iron-deficiency response in *Arabidopsis* root epidermal cells (Figure 1). Surprisingly, DELLA functions to block FIT DNA binding activity. Hence, if low iron caused DELLA proteins to become stabilized in root epidermal cells (as they did in root meristem cells), rather paradoxically it would serve to block the induction of iron uptake genes like *FRO2* and *IRT1*. However, a RGA-GFP reporter fusion revealed that under low iron conditions, the DELLA protein is destabilized in epidermal cells in the root differentiation zone (Figure 1). How this is controlled is not yet clear. Nevertheless, the authors elegantly validated the functional importance of DELLA destabilization in this zone by demonstrating that targeted expression of a non-GA degradable DELLA mutant form in differentiating root epidermal cells disrupted induction of *FRO2* and *IRT1* under low-iron conditions. Hence, iron availability appears to control DELLA abundance in root tissues in a zone-specific manner (Figure 1).

It is not yet clear why *Arabidopsis* roots need to match an upregulation of the iron acquisition machinery in the root elongation zone with the repression of root elongation in the apical meristem through the same DELLA-dependent signaling pathway. One advantage from this combined but spatially distinct regulation of the GA-DELLA pathway is that assimilates required for cell division in the root apex can now be employed in the root elongation zone to fuel the synthesis and release of iron chelators and also to energize proton extrusion and iron reduction. Hence, the GA response pathway would coordinate and favor iron acquisition over root elongation under low-iron conditions (Figure 1).

In cereal crops such as wheat and rice, the genetic manipulation of GA response

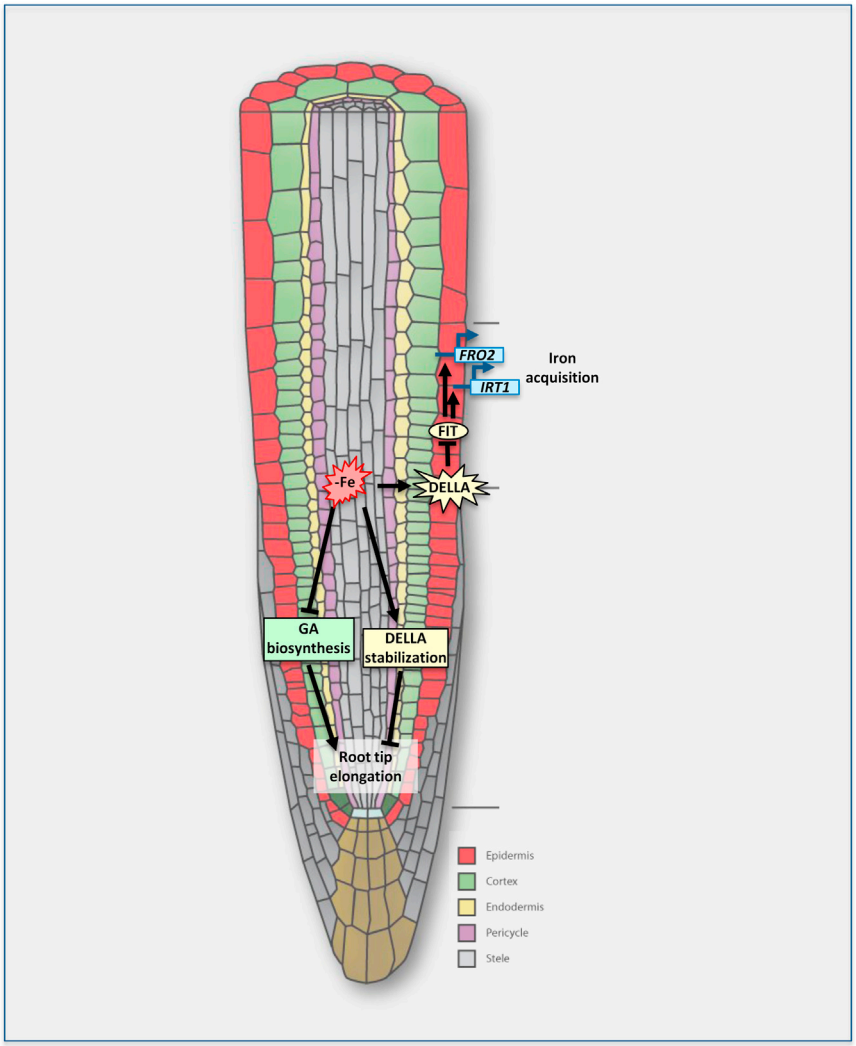

Figure 1. Schematic Representation of Divergent Outcomes of Crosstalk between Iron and GA Signaling Pathways in *Arabidopsis* Root Tip and Elongation Zones

has provided the basis for the green revolution through the creation of modern higher-yielding semi-dwarfed varieties (Hedden, 2003). Significantly, Wild et al. (2016) demonstrate that rice DELLA can interact with OsIRO2, an iron-inducible bHLH transcription factor closely related to AthbHLH38 and 39. Hence, these components appear to make up a highly conserved regulatory module in plants to optimize iron acquisition. Given these observations, the negative impact that DELLA stabilization may have on iron levels in semi-dwarfed cereal crops grown in low-iron soil conditions could be significant. Indeed, Fan et al. (2008) reported a decline in the concentration of iron (and several other micronutrients) in wheat grain collected during the long-term Broadbalk Wheat Experiment (Rothamsted, UK) that coincided with the introduction of semi-dwarf high-yielding cultivars.

Hence, could the crosstalk between GA and iron responses represent an Achilles' heel for modern dwarfed cereal varieties? In fact, the insights by Wild et al. could also provide a basis for improving iron acquisition in crops by, for example, limiting stabilized DELLA-mediated dwarfing to selected organs (i.e., shoot, not root) and/or expressing DELLA in specific tissues (e.g., endodermis) known to regulate GA-dependent organ growth (Ubeda-Tomás et al., 2008). This research therefore raises important societal concerns relating to micro-nutrient availability to the human diet from modern cereal varieties (White and Broadley, 2009), but also provides opportunities to better target the genetic manipulation of GA-regulated stature in crops.

REFERENCES

Fan, M.-S., Zhao, F.-J., Fairweather-Tait, S.J., Poulton, P.R., Dunham, S.J., and McGrath, S.P. (2008). J. Trace Elem. Med. Biol. *22*, 315–324.

Hedden, P. (2003). Trends Genet. *19*, 5–9.

Ivanov, R., Brumbarova, T., and Bauer, P. (2012). Mol. Plant *5*, 27–42.

Lingam, S., Mohrbacher, J., Brumbarova, T., Potuschak, T., Fink-Straube, C., Blondet, E., Genschik, P., and Bauer, P. (2011). Plant Cell *23*, 1815–1829.

Robinson, N.J., Procter, C.M., Connolly, E.L., and Guerinot, M.L. (1999). Nature *397*, 694–697.

Ubeda-Tomás, S., Swarup, R., Coates, J., Swarup, K., Laplaze, L., Beemster, G.T., Hedden, P., Bhalerao, R., and Bennett, M.J. (2008). Nat. Cell Biol. *10*, 625–628.

Vert, G., Grotz, N., Dédaldéchamp, F., Gaymard, F., Guerinot, M.L., Briat, J.F., and Curie, C. (2002). Plant Cell *14*, 1223–1233.

White, P.J., and Broadley, M.R. (2009). New Phytol. *182*, 49–84.

Wild, M., Davière, J.-M., Regnault, T., Sakvarelidze-Achard, L., Carrera, E., Lopez Diaz, I., Cayrel, A., Dubeaux, G., Vert, G., and Achard, A. (2016). Dev. Cell *37*, this issue, 190–200.

Yuan, Y., Wu, H., Wang, N., Li, J., Zhao, W., Du, J., Wang, D., and Ling, H.Q. (2008). Cell Res. *18*, 385–397.