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Spotlight

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Two titans finally meet each other under nitrogen deficiencies: FERONIA-TORC1 activation promotes plant growth

Plant growth is determined by well-defined developmental processes that integrate cell-intrinsic factors and external environmental cues, and it is largely dependent on the assimilation of macro- and micro-nutrients from the environment. Between the macro-nutrients, the inorganic nitrogen (e.g., nitrate and ammonium) and amino acids are essential for plant survival and productivity. Beyond acting as macro-nutrients and structural components of macro-molecules, these nitrogen-containing molecules could also act as signaling molecules to orchestrate diverse genetic programs (Wang et al., 2018). Plant nutritional cues that rapidly change over time and space in the soils are tightly linked to signaling pathways that execute fast cellular programs to adjust to a challenging environment. Plant Rapid Alkalinization Factors (RALFs) are secreted peptides that function as extracellular signals and bind to *Catharanthus roseus* receptor-like kinase 1-like family members such as FERONIA (FER) (Liao et al., 2017). RALF1–FER complexes are central regulators of plant growth that allow plants to respond to environmental changes (Du et al., 2016; Zhu et al., 2020). This interaction triggers the recruitment of RPM1-induced protein kinase (RIPK) and the phosphorylation of both FER and RIPK in a mutually dependent manner (Du et al., 2016), followed by the recruitment and activation via phosphorylation of an early translation initiation factor (eIF4E1) (Zhu et al., 2020). These findings highlighted that the RALF1–FER–RIPK pathway is an important hub to control plant cell growth under specific conditions.

In line with this, Target Of Rapamycin (TOR) is an evolutionarily conserved Ser/Thr protein kinase in all eukaryotic organisms that acts as a central growth regulator controlling metabolism and protein synthesis (Xiong and Sheen, 2014). The *Arabidopsis* TOR complex 1 (TORC1) is encoded by one *TOR* gene (*At*TOR), two *Regulatory-associated protein of TOR* (*RAPTOR 1A* and *1B*) genes, and two *Lethal with Sec thirteen 8* genes. Some canonical downstream targets of TOR are conserved in plants, such as the S6 kinase (S6K), which stimulates protein translation (Mahfouz et al., 2006). In plants, the TORC1 complex is activated by nutrient availability and inactivated by stresses that alter cellular homeostasis (Dobrenel et al., 2016). The TORC1 complex senses and integrates signals from the environment to coordinate developmental and metabolic processes including hormones (e.g., auxin), several nutrients (e.g., nitrogen), amino acids, and glucose (Schepetilnikov et al., 2017; Liu et al., 2021). It is known that FER and TOR kinase (along with its partners, RAPTOR1B and *Lethal with Sec thirteen 8*) both play major functions in cell growth, metabolism, and multiple stress responses in plants (Li and Zhang, 2014). For example, FER, when activated by RALF1 recognition, can phosphorylate ATL6, an E3 ubiquitin ligase that interacts and stabilizes 14-3-3 proteins in carbon/nitrogen responses (Xu et al., 2019). Although several molecular components were identified to be connected either with FER or TORC1 pathways, the underlying molecular mechanism by which both FER and TORC1 are involved in nutrient signaling remained unclear until now.

A recent study published in *Molecular Plant* led by Prof. Dr. Feng Yu describes a stress-response-adaptation mechanism that involves both FER kinase and TORC1, which promotes true leaves development under low-nutrient conditions (Song et al., 2022). As mentioned earlier, the FER kinase domain directly interacts and phosphorylates RIPK in response to RALF1 peptide to form the active phosphorylated complex FER/RIPK (Du et al., 2016). In this work, Song et al. (2022) showed that in plants grown under nitrogen-deficient conditions, RALF1 enhances the interaction between the complex FER/RIPK and TORC1 (Figure 1). In this way, TOR kinase physically interacts with FER kinase domain; meanwhile, RIPK phosphorylates TOR partner RAPTOR1B. Therefore, the activation of TOR–S6K regulatory hub increases to overcome the nitrogen deficiency stress in young leaves and stimulate the true leaf growth (Song et al., 2022). When plants are supplemented with individual amino acids, the FER–TOR interaction is also positively modulated via RALF1 under low-nutrient conditions. Gln/Asp/Gly specifically activates the TOR signaling pathway, the phosphorylation levels of S6K increase, and true leaves growth is promoted as well (Song et al., 2022). This research evidences a novel regulatory role of the RALF1–FER–RIPK–TOR pathway involved with nitrogen stress responses and cell metabolism (Figure 1).

The new discoveries reported by Song et al. (2022) represent the first direct link between the plasma membrane receptor FER and the cytoplasmic TORC1 complex, uncovering an important connection between environmental signal perception with the signal transduction pathways inside the plant cell. This work has opened new questions about how nitrogen as an inorganic or amino acid source directs RALF1 expression to activate the FER–RIPK–TORC1 pathway. It is unclear how specific or broad this pathway is during plant life cycle beyond true leaf development. Are other biological processes controlled by these signaling components? May numerous environmental signals such as nutrient availability (other than nitrogen), changes in temperature, or microbial partners that impact plant development

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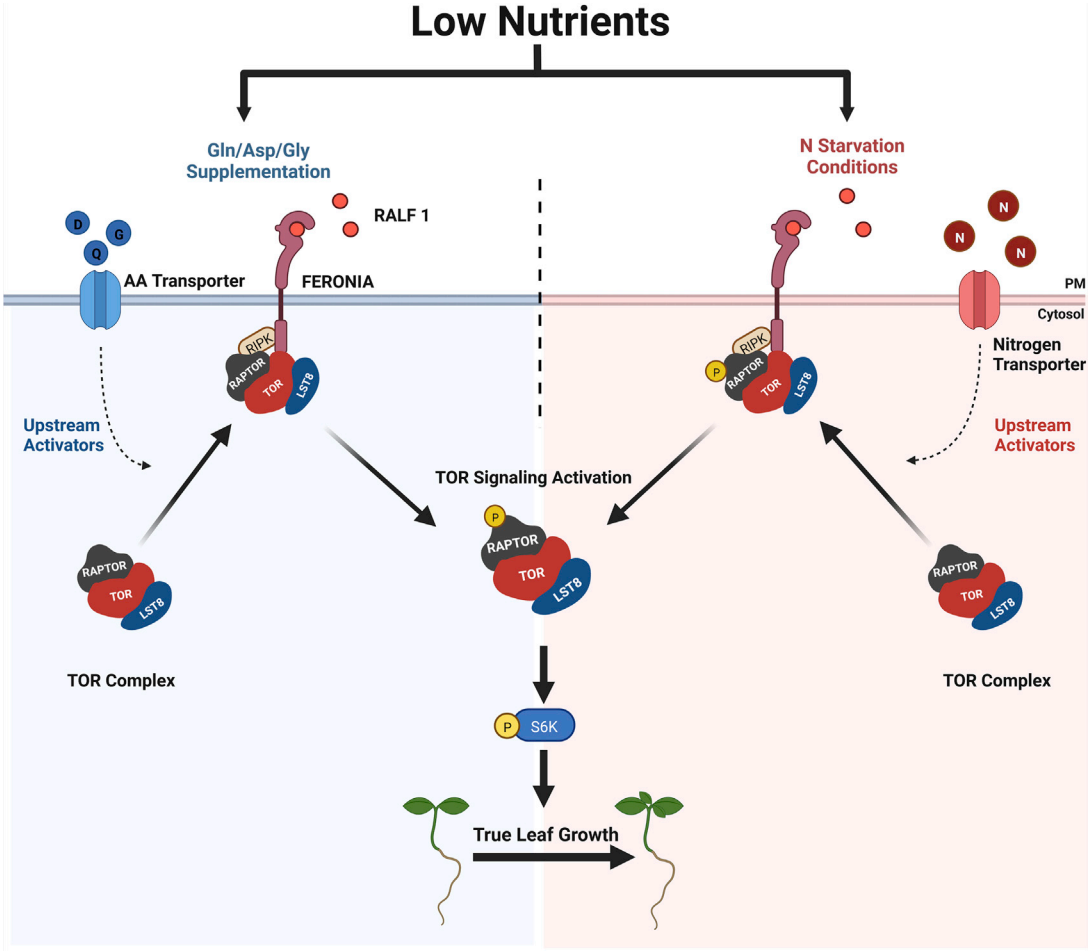

Figure 1. A regulatory pathway integrated by RALF1–FER–RIPK–TOR promotes true leaves growth and development under low-nutrient conditions.

In a nitrogen-deficient scenario (right panel), the RALF1 peptide enhances the interaction between the FERONIA receptor/RIPK interactor partner complex and TOR complex 1 (composed by TOR + RAPTOR1B + LST8). Consequently, the FER kinase domain and TOR kinase physically interact, and the kinase RIPK phosphorylates RAPTOR1B, thus activating the TOR signaling pathway and promoting the development of true leaves under low-nutrient conditions. The supplementation with specific amino acids (Gln/Asp/Gly, left panel) also increases the FER–TOR direct binding, TOR activity, and the true leaf growth under N-deficiency conditions. Nitrogen (as NO_3^- or NH_4^+) and amino acids could be imported into the leaf cells by members of the NPF/NRT family or AMTs and specific amino acid transporters (e.g., probably LHT1 or a related transporter), respectively. It still remains elusive how these upstream signals can specifically promote the FER–TOR interaction via RALF1 and the further activation of TOR signaling pathway toward a stress-response adaptation. Created with BioRender.com.

enhance or repress RALF–FER–TORC1 activation? In this direction, recently, it was shown that the RALF23–FER complex inactivates the FER–RHO-type GTPase of plants ROP2-related pathway (and linked reactive oxygen species production), and this enhanced the beneficial *Pseudomonas* presence in the complex rhizosphere microbiome (Song et al., 2021). This is a nice example of how closely interlinked the interface is between plant cell surface in roots and the soil microbiome environment.

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