At the Intersection of Plant Growth and Immunity

Wenfei Wang¹ and Zhi-Yong Wang²,*
¹Forestry and Biotechnology Center, Fujian Agriculture and Forestry University, Fuzhou 350002, China
²Department of Plant Biology, Carnegie Institution for Science, Stanford, CA 94305, USA
*Correspondence: zywang24@stanford.edu
http://dx.doi.org/10.1016/j.chom.2014.03.014

The tradeoff between growth and immunity is regulated by integrating hormonal cues, biotic signals, and developmental programs, and is fine-tuned to maximize organismal growth and survival. Four recent papers, including Chandran et al. (2014) in this issue of Cell Host & Microbe, provide insights into the underlying mechanisms in plants.

The ability to correctly and effectively switch between growth and defense is crucial for the wellbeing and survival of plants. When infected by a pathogen, the plant host not only activates its defense responses but also represses growth in order to focus the energy on fending off the pathogen. Plant immune responses are also modulated by abiotic signals such as light and temperature as well as the circadian clock (Hua, 2013). In the absence of perceived pathogens, however, the young tissues must suppress immune response to maximize growth, whereas mature organs can be more prepared for defense. Such fine-tuning of the tradeoff between growth and immunity requires integration of the growth and immune pathways with developmental programs.

Antagonistic interactions have been observed between many growth-promoting hormones and pathogen-triggered immune responses. For example, auxin inhibits immunity by suppressing salicylic acid (SA) biosynthesis and signaling as well as through a SA-independent mechanism. Reciprocally, signaling triggered by recognition of pathogen-associated molecular patterns (PAMPs) inhibits auxin signaling by microRNA-mediated suppression of auxin receptor TIR1 and by SA-mediated stabilization of the AUXIAA proteins that negatively regulate auxin signaling. On the other hand, virulent pathogens activate auxin biosynthesis to suppress host immunity (Robert-Seilaniantz et al., 2011). The molecular mechanisms through which auxin inhibits immunity are not fully understood.

Complex interactions have also been observed at the molecular level between the growth-promoting hormone brassinosteroid (BR) and PAMPs, which show antagonistic effects on growth and immunity (Wang, 2012). Both BR and flagellin are perceived by cell surface receptor kinases, namely BRI1 and FLS2, respectively, and crosstalks between BR and flagellin have been observed at many steps of the signal transduction pathways. First, BRI1 and FLS2 share a coreceptor kinase, BAK1, which is recruited to BRI1 by BR and to FLS2 by flagellin for activation of the ligand–binding receptor kinases through transphosphorylation. All three of these receptor kinases contain a leucine-rich repeat (LRR) extracellular domain, which is similar to the Toll-like receptors for innate immunity in animals. BR and FLS2 also share downstream substrate BSK1 and BIK1 kinases (Lin et al., 2013). However, conflicting sets of evidence suggest that these interactions at the receptor level appear to play only a minor role in the antagonism between the BR and PAMP pathways (Wang, 2012).

In contrast, several recent studies indicated that BR suppression of immunity is mainly mediated by signal integration at the level of transcriptional regulation (Lozano-Durán et al., 2013; Malinovsky et al., 2014; Fan et al., 2014). The BR-activated transcription factor BZR1 was shown to directly regulate many defense-related genes, including several BR-activated WRKY transcription factors that negatively regulate immune responses. BZR1 also interacts with WRKY40, which is required for full BR repression of PAMP-triggered reactive oxygen species production. It was proposed that BZR1 negatively regulates immunity through interaction with and transcriptional activation of different WRKY factors (Lozano-Durán et al., 2013). However, BZR1 itself is not affected by PAMP signaling, and thus unlikely to mediate PAMP-triggered seedling growth inhibition (Wang, 2012).

Two independent studies recently demonstrated that the downstream basic helix-loop-helix (bHLH) transcription factor, HB11, functions as a critical crosstalk node that mediates the antagonistic regulation of growth and immunity by growth hormones and PAMP signals (Malinovsky et al., 2014; Fan et al., 2014). BR induces expression of members of the PRE1 family of bHLH factors, which dimerize and inhibit another HLH factor, IBH1, which otherwise inhibits HB11 DNA binding (Fan et al., 2014). By contrast, PAMP signals rapidly repress HB11 expression, and constitutive overexpression of HB11 partly abolishes PAMP-induced growth inhibition and immune response (Malinovsky et al., 2014; Fan et al., 2014). A genome-wide study of HB11 target genes revealed that HB11 not only activates growth-related genes but also suppresses defense-related genes activated by PAMPs (Fan et al., 2014). As such, HB11 appears to function as a binary switch that mediates the hormone- and PAMP-controlled tradeoff between growth and immunity (Figure 1).

In addition to BR, other growth-promoting hormones such as auxin and gibberellin, as well as environmental signals such as shade and elevated temperature, can activate the expression of PRE family members (Fan et al., 2014), which should increase the activity of HB11, and thus inhibit immunity, through the PRE-IBH1-HB11 cascade. Further, increased expression levels of IBH1 in mature organs might contribute to inhibition of HB11 and derepression of the immune system in mature organs that have stopped growing. However, direct evidence for such roles of PREs and IBH1 in regulation of immunity by other hormones, environmental signals, and developmental programs is still lacking.
In this issue of *Cell Host & Microbe*, Chandran and colleagues reveal a mechanism by which a developmental program gauges immunity (Chandran et al., 2014). Plant organ development usually includes a cell proliferation phase followed by endoreduplication accompanying cell expansion and differentiation. This transition is mediated by the atypical E2F protein DEL1, which is a negative regulator of endocyte onset. DEL1 is an atypical E2F transcription factor. E2F factors are highly conserved in eukaryotes, with important roles in regulating DNA replication and cell proliferation. DEL1 promotes cell proliferation by repressing genes that promote endoreduplication onset. At late phase of organ development, DEL1 expression level drops, allowing endoreduplication. Consistent with this, the loss-of-function mutant del1-1 showed increased ploidy (Vlieghe et al., 2005).

Chandran et al. had previously observed that the biotrophic powdery mildew fungal pathogen *Golovinomyces orontii* induces endoreduplication of mesophyll cells underneath the fungal feeding structure, which correlates with pathogen growth and is thought to be important for feeding the pathogen (Chandran et al., 2013). Now, this research group tests the effects of mutation and overexpression of DEL1 on powdery mildew growth. Surprisingly, the del1-1 mutant plants were more resistant and the DEL1-overexpressing plants were more susceptible to *G. orontii*. Furthermore, leaf mesophyll cell ploidy was unaltered in del1-1 and increased in the DEL1-overexpressing plants. The discrepancy with a previous study (Vlieghe et al., 2005) was possibly due to different experimental conditions. Nevertheless, the powdery mildew phenotypes of del1-1 were not due to altered mesophyll ploidy. Microarray analysis indicated that del1-1 expressed elevated levels of genes involved in defense/stress responses, including genes related to SA accumulation, such as SA biosynthetic gene *ICS1*, and SA-regulated genes such as *Pathogenesis-related 1* (PR-1) (Chandran et al., 2014).

To determine whether elevated SA is responsible for the *G. orontii* resistance of del1-1, Chandran and colleagues created a del1 ics1 double mutant. The double mutant showed a normal level of PR-1 expression, and enhanced *G. orontii* susceptibility similarly to ics1 mutant, indicating that the enhanced resistance of del1-1 to *G. orontii* is SA dependent. Similar resistance phenotypes were observed with a bacterial pathogen. Furthermore, the small-size phenotype of del1-1 was also suppressed by ics1. The results demonstrate that both pathogen resistance and dwarf phenotypes of del1-1 are due to elevated SA production.

How does DEL1 repress SA accumulation? A search for the E2F binding site in the promoters of SA-related genes led to the identification of *Enhanced Disease Susceptibility 5* (*EDS5*) as a direct DEL1 target. *EDS5* encodes a SA transporter required for effective SA accumulation. Consistent with direct repression by DEL1, EDS5 expression was inversely correlated with the expression levels of DEL1 as leaves age. There are a high level of DEL1 and a low level of *EDS5* in young growing leaves, but a low level of DEL1 and high level of *EDS5* in older leaves. The results suggest that DEL1 suppresses SA accumulation and defense responses in growing tissues through repression of *EDS5* and *ICS1* expression (Chandran et al., 2014) (Figure 1). The decrease of DEL1 expression in mature tissues should contribute to increased preparedness for defense. This, however, is yet to be demonstrated experimentally. It will be interesting to test whether mature wild-type leaves are more resistant to pathogens than young growing leaves, and whether such difference is dependent on DEL1.

As illustrated by these recent studies, there are many molecular connections that ensure antagonistic regulation of growth and immunity in plants (Figure 1). In addition to developmental regulation, DEL1 expression is also activated by light (Berkman et al., 2011), which is known to modulate immunity through both photoreceptor signaling and photosynthesis (Hua, 2013). It is unclear whether regulation of DEL1 contributes to light regulation of SA production and immunity. In addition, light also enhances PAMP responses by antagonizing BR and gibberellin, which activate BZR1 and HBI1 (Lozano-Durán et al., 2013; Fan et al., 2014). It will be interesting to analyze how the multiple molecular connections operate in a coordinated manner under natural conditions.

**ACKNOWLEDGMENTS**

This study was supported by a grant from the National Institutes of Health (R01GM066258) to Z.-Y.W.

**REFERENCES**


Cell Host & Microbe 15, April 9, 2014 ©2014 Elsevier Inc. 401


