

Growth–Defense Tradeoffs in Plants: A Balancing Act to Optimize Fitness

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ABSTRACT Growth–defense tradeoffs are thought to occur in plants due to resource restrictions, which demand prioritization towards either growth or defense, depending on external and internal factors. These tradeoffs have profound implications in agriculture and natural ecosystems, as both processes are vital for plant survival, reproduction, and, ultimately, plant fitness. While many of the molecular mechanisms underlying growth and defense tradeoffs remain to be elucidated, hormone crosstalk has emerged as a major player in regulating tradeoffs needed to achieve a balance. In this review, we cover recent advances in understanding growth–defense tradeoffs in plants as well as what is known regarding the underlying molecular mechanisms. Specifically, we address evidence supporting the growth–defense tradeoff concept, as well as known interactions between defense signaling and growth signaling. Understanding the molecular basis of these tradeoffs in plants should provide a foundation for the development of breeding strategies that optimize the growth–defense balance to maximize crop yield to meet rising global food and biofuel demands.

Key words: plant immunity; plant hormone; salicylic acid; jasmonate; PAMP; plant growth.

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INTRODUCTION

While the deployment of defense mechanisms is imperative for plant survival, defense activation generally comes at the expense of plant growth (Figure 1). The ‘growth–defense tradeoff’ phenomenon was first observed in forestry studies of plant–insect interactions, and is based on the assumption that plants possess a limited pool of resources that can be invested either in growth or in defense (Coley et al., 1985; Simms and Rausher, 1987; Herms and Mattson, 1992). As plants must both grow and defend in order to survive and reproduce, growth–defense tradeoffs have important ecological, agricultural, and economic consequences. In nature, plants live in diverse and complex environments in which they constantly encounter a variety of pathogens and insect herbivores with a wide array of life styles and infection strategies. In adaptation to such natural conditions, plants have evolved sophisticated mechanisms to balance growth and defense (Herms and Mattson, 1992; Baldwin, 2001; Walling, 2009). However, in agricultural settings, crops have been bred for centuries

to maximize growth-related traits resulting in a loss of genetic diversity that often compromises defense (Strange and Scott, 2005). Understanding the molecular mechanisms used by plants to balance growth and defense can enrich plant breeding and engineering strategies for selection of elite genetic traits that will maximize plant fitness.

In this review, we discuss the evidence supporting the concept of growth–defense tradeoffs in plants as well as the recent advances in deciphering the molecular mechanisms underlying their occurrence. As numerous studies have implicated hormone crosstalk as having a fundamental role in fine-tuning the growth–defense process,

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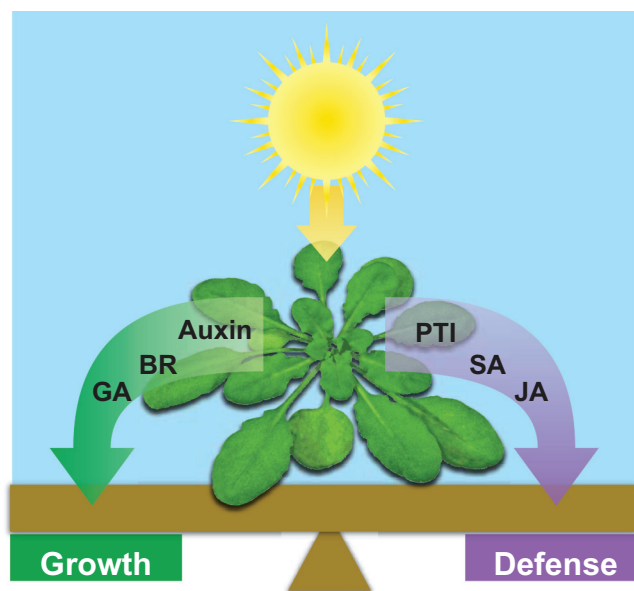


Figure 1 A diagram depicting the concept of growth–defense tradeoffs.

Plants use photosynthesis to convert light energy into chemical energy in the form of carbohydrates. These resources are then allocated towards growth or defense, depending on the presence or absence of specific stresses. This process is facilitated by hormone crosstalk and is referred to as the growth–defense tradeoff. BR, brassinosteroid; GA, gibberellin; PTI, pathogen-associated-molecular-pattern-triggered immunity; SA, salicylic acid; JA, jasmonates.

we provide brief descriptions of each defense and growth signaling pathway to introduce key players, and then discuss relevant hormone crosstalk. Due to space constraints, we focus our discussion on tradeoffs between defenses mediated by pathogen-associated-molecular-pattern (PAMP)-triggered immunity (PTI), salicylic acid (SA), and jasmonate (JA) versus growth mediated by auxin, brassinosteroids (BR), and gibberellins (GA), for which most progress has been made (Figure 1). Readers are referred to several recent reviews related to this topic, including discussions of the roles of ethylene (ET) and cytokinins (Bari and Jones, 2009; Robert-Seilaniantz et al., 2011a; Naseem and Dandekar, 2012; Bartoli et al., 2013; De Vleeschauwer et al., 2013; Denance et al., 2013; Yang et al., 2013). We conclude with a summary of concepts that may be drawn from current knowledge as well as several key areas where further research is needed.

DEFENSE SIGNALING

The ability to perceive and mount a rapid response to pathogen attack is critical for plant survival. Plants have evolved a sophisticated immune system that is initiated upon detection of highly conserved PAMPs by membrane-associated

pattern recognition receptors (PRRs), which leads to activation of PTI (Boller and Felix, 2009; Monaghan and Zipfel, 2012). While PTI is believed to provide sufficient defense against non-pathogenic microbes, pathogens have developed the ability to secrete virulence effectors into the plant cell to suppress PTI and promote disease (Boller and He, 2009; Dou and Zhou, 2012; Xin and He, 2013). Plants have evolved resistance (R) genes to recognize these effectors and activate a much stronger immune response, effector-triggered immunity (ETI), which often results in a type of programmed cell death response known as the hypersensitive response (HR) in pathogen-infected tissue (Chisholm et al., 2006; Jones and Dangl, 2006; Bent and Mackey, 2007; Caplan et al., 2008). ETI may also trigger secondary immune responses in distal, uninfected tissues and lead to so-called systemic acquired resistance (SAR) (Grant and Lamb, 2006; Fu and Dong, 2013).

Plant hormones are small organic molecules that are required by plants in low concentrations and regulate growth, development, reproduction, and immune responses. Changes in environmental signals—both abiotic and biotic—induce changes in the quantity and composition of these signal molecules to facilitate appropriate plant responses (Kazan and Manners, 2009; Santner and Estelle, 2009; Robert-Seilaniantz et al., 2011a; Denance et al., 2013). Plant defense hormones such as SA, JA, and ET play important roles in the precise regulation of plant immune responses both locally and systemically to coordinate plant defense against different types of pathogens and in different parts of the plant (Erb et al., 2012; Pieterse et al., 2012; Wasternack, 2013). SA signaling is primarily induced by and involved in defense against biotrophic pathogens, whereas JA signaling is primarily induced by and involved in defense against insect herbivores and, in conjunction with ET, against necrotrophic pathogens (Thomma et al., 1998; Glazebrook, 2005). SA and JA signaling pathways are generally antagonistic to each other (Pieterse et al., 2012). For example, elevated SA signaling in response to biotrophic pathogens is often correlated with reduced JA signaling and decreased resistance to necrotrophic pathogens (Spoel et al., 2007). The following sections provide brief summaries of PTI, SA, and JA signaling pathways relevant to this review.

PAMP-Triggered Immunity

As mentioned above, PTI is triggered following detection of PAMPs by PRRs (Monaghan and Zipfel, 2012). The best characterized PRRs are leucine-rich repeat receptor kinases (LRR-RKs) consisting of an extracellular LRR domain, which can vary in the number of repeats and is directly involved in ligand perception, a transmembrane domain, and an intracellular kinase domain (Nicaise et al., 2009). FLAGELLIN SENSING 2 (FLS2) and ELONGATION

FACTOR-TU RECEPTOR (EFR) are LRR–RKs that recognize bacterial flagellin and bacterial EF-Tu, respectively (Gomez-Gomez and Boller, 2000; Zipfel et al., 2004, 2006; Sun et al., 2013). Upon ligand perception, both FLS2 and EFR rapidly recruit a LRR–RK, BRI1-ASSOCIATED RECEPTOR KINASE 1 (BAK1), resulting in their transphosphorylation (Chinchilla et al., 2007; Heese et al., 2007; Schulze et al., 2010; Roux et al., 2011). Treatment with flg22, a bioactive 22-amino acid peptide derived from bacterial flagellin, activates the FLS2/BAK1 co-receptor complex and triggers a phosphorylation cascade, including the phosphorylation and displacement of BOTRYTIS-INDUCED KINASE 1 (BIK1) from the FLS2 complex to promote the immune response (Lu et al., 2010; Lin et al., 2014). Initial PTI responses occur within minutes to hours following PAMP perception, and include elevation of reactive oxygen species (ROS), calcium influx, activation of calcium/calmodulin-dependent kinase and mitogen-activated protein kinase signaling cascades, and transcriptional reprogramming (Boller and Felix, 2009; Dodds and Rathjen, 2010). PTI-associated transcriptional reprogramming is facilitated in part by the WRKY family of transcription factors, members of which are involved in both positive and negative regulation of PTI (Thilmony et al., 2006; Pandey and Somssich, 2009; Rushton et al., 2010). Later responses attributed to PTI activation include deposition of callose at the cell wall near the site of pathogen infection and seedling growth inhibition (Gomez-Gomez et al., 1999; Boller and Felix, 2009).

Salicylic Acid

SA is a phenolic hormone shown to affect many plant processes including growth, development, senescence, and stress responses (Vlot et al., 2009; Rivas-San Vicente and Plasencia, 2011). It is primarily recognized for its role in local defense induced against biotrophic and hemibiotrophic pathogens and in the establishment of SAR (Fu and Dong, 2013). After years of searching, two recent studies have proposed NONEXPRESSOR OF PATHOGENESIS RELATED PROTEINS 1 (NPR1) and its paralogs, NPR3 and NPR4, to act as SA receptors (Attaran and He, 2012; Fu et al., 2012; Wu et al., 2012). Multiple genetic screens led to the identification of NPR1, which is a key regulator of SA signaling (Cao et al., 1994; Delaney et al., 1995; Cao et al., 1997; Shah et al., 1997). Under non-induced conditions, NPR1 proteins oligomerize in the cytoplasm (Mou et al., 2003). SA accumulation in response to pathogen detection triggers the release of NPR1 monomers, which then translocate to the nucleus and activate defense gene expression (Kinkema et al., 2000; Mou et al., 2003; Tada et al., 2008). NPR1 regulates gene expression through physical interaction with TGA transcription factors, which bind to promoters of *PATHOGENESIS RELATED (PR)* genes to activate

expression in the presence of SA and repress expression in the absence of SA (Zhang et al., 2003b; Fu and Dong, 2013). *PR* genes encode small proteins, some of which have been shown to possess antimicrobial or antifungal properties *in vitro* (van Loon et al., 2006). Of the many *PR* genes identified, *PR1*, *PR2*, and *PR5* have been shown to be induced by SA and have long been used as markers of SA signaling (Fu and Dong, 2013). Other genes identified as direct targets of NPR1 include WRKY transcription factors and components required for the synthesis and secretion of PR proteins (Wang et al., 2006). WRKYs are involved in both NPR1-dependent and NPR1-independent SA signaling and, as in the case of PTI, include both positive and negative regulators of SA-mediated defense (Yu et al., 2001; Wang et al., 2006; Rushton et al., 2010; Fu and Dong, 2013).

Jasmonate

JAs are a group of lipid-derived hormones that regulate plant defense against necrotrophic pathogens and insect herbivores (Pieterse et al., 2012) and also affect several other physiological processes including abiotic stress responses, reproductive development, and primary and secondary metabolism (Wasternack, 2007; Browse, 2009). Jasmonoyl isoleucine (JA-Ile) is perceived by a co-receptor complex consisting of the F-box protein CORONATINE INSENSITIVE 1 (COI1) and the JASMONATE ZIM DOMAIN (JAZ) family of transcription repressors (Sheard et al., 2010). COI1 is required for almost all known JA-dependent responses (Feys et al., 1994; Xie et al., 1998; Browse, 2009). The JAZ-family proteins repress JA signaling by directly binding to the MYC family of transcription factors required for the expression of JA-responsive genes (Chini et al., 2007; Thines et al., 2007; Yan et al., 2007). Under normal growth conditions where JA-Ile levels are low, JAZ proteins recruit co-repressors, TOPLESS (TPL) or TPL-related proteins, either directly through their ETHYLENE RESPONSE FACTOR-ASSOCIATED AMPHIFILIC REPRESSION (EAR) motifs or indirectly through NOVEL INTERACTOR of JAZ (NINJA) protein to suppress MYC activities (Pauwels et al., 2010; Shyu et al., 2012). It was recently shown that physical association of JAZ proteins with MYC2 is required for the nuclear localization of JAZ repressors (Withers et al., 2012); however, the mechanism for JAZ repression of MYC activity is not clearly understood. Upon wounding or pathogen attack, JA-Ile is rapidly synthesized in both local and distal tissues (Staswick and Tiriyaki, 2004; Fonseca et al., 2009). An increasing concentration of JA-Ile promotes physical interaction between COI1 and JAZ proteins, which leads to ubiquitination and subsequent degradation of JAZs through the 26S proteasome, thereby relieving the repression on MYC transcription factors and initiating the expression of JA-responsive genes (Chini et al., 2007; Thines et al., 2007; Katsir et al., 2008).

GROWTH-PROMOTING HORMONE SIGNALING

Plant growth and development are coordinately regulated by a complement of hormones in order to optimize growth and reproduction (Depuydt and Hardtke, 2011). Growth hormones implicated in growth–defense tradeoffs are auxin, BRs, GAs, and cytokinins. As excellent reviews have been written on each of these hormones (Santner and Estelle, 2009; Sun, 2011; Zhao and Li, 2012), we will briefly describe what is known regarding the main signaling components for the three growth hormones relevant to this review.

Auxin

Auxins regulate many fundamental aspects of plant growth and development including stem and petiole elongation and root architecture in response to light, temperature, and gravity (Santner and Estelle, 2009; Vanneste and Friml, 2009; Kieffer et al., 2010; Kazan, 2013). Biosynthesis of indole-3-acetic acid (IAA), one of the primary auxins studied, occurs primarily in young leaves via multiple biosynthetic pathways and IAA is transported throughout the plant (Woodward and Bartel, 2005; Normanly, 2010). Once synthesized, accumulation of free IAA is regulated by GH3 proteins, which conjugate IAA with amino acids to yield metabolites for storage (IAA-alanine and IAA-leucine) or oxidation and degradation (IAA-aspartate and IAA-glutamic acid) (Ljung et al., 2002; Staswick et al., 2005; Ludwig-Muller, 2011). When auxin levels are low, auxin response genes are actively repressed by heterodimerization of the AUX/IAA family of transcriptional repressor proteins with the AUXIN RESPONSIVE FACTORS (ARF) family of transcription factors (Ulmasov et al., 1999; Tiwari et al., 2001; Liscum and Reed, 2002; Tiwari et al., 2004). The F-box proteins, TRANSPORT INHIBITOR RESISTANT 1 (TIR1) and AUXIN SIGNALING F-BOX (AFB), are substrate-recognition components of an SKP–Cullin–F-box (SCF) E3 ubiquitin ligase complex, SCF^{TIR1/AFB} (Gray et al., 1999, 2001). When auxin concentration reaches a threshold in the cell, auxin directly facilitates SCF^{TIR1/AFB} binding to AUX/IAA proteins, resulting in the ubiquitination and degradation of AUX/IAA repressors via the 26S proteasome thereby derepressing ARF-dependent transcription of auxin-regulated genes (Kepinski and Leyser, 2004; Dharmasiri et al., 2005; Kepinski and Leyser, 2005). Auxin-regulated genes include the AUX/IAA and GH3 gene families (Hagen et al., 1984; Abel et al., 1994), expression of which forms part of a feedback mechanism to reset auxin signaling homeostasis.

Brassinosteroids

BRs are polyhydroxylated steroid phytohormones that influence diverse developmental processes from seed

germination to plant senescence (Gruszka, 2013; Hao et al., 2013; Fariduddin et al., 2014). Plants that are insensitive to or deficient in BR signaling have severely stunted growth and are male infertile, whereas exogenous application of BR has a positive impact on the quality and quantity of crop yield (Khripach et al., 2000; Gruszka, 2013; Hao et al., 2013; Fariduddin et al., 2014). In the absence of BR, the glycogen-synthase-kinase-3-like kinase BRASSINOSTEROID INSENSITIVE 2 (BIN2) phosphorylates two nuclear-localized transcription factors, BRI1-EMS-SUPPRESSOR 1 (BES1) and BRASSINAZOLE-RESISTANT 1 (BZR1), to block activation of BR-responsive genes (He et al., 2002; Wang et al., 2002; Yin et al., 2002; He et al., 2005; Yin et al., 2005; Vert and Chory, 2006). The presence of BR stabilizes the BRASSINOSTEROID INSENSITIVE 1 (BRI1)/BAK1 co-receptor complex, causing activation of their respective kinase domains and subsequent transphosphorylation (Li and Chory, 1997; Li et al., 2002; Nam and Li, 2002; Wang and Chory, 2006; Hothorn et al., 2011; She et al., 2011). The resulting cascade of phosphorylation events leads to the phosphorylation and inactivation of BIN2 kinase and the dephosphorylation and activation of BES1 and BZR1 to promote the expression of BR-regulated genes (Mora-Garcia et al., 2004; Tang et al., 2011).

Gibberellins

GAs are tetracyclic diterpene acids that control seed development and germination, vegetative growth, and flower initiation and development (Sun, 2011). GA induces gene expression by relieving the repression of a family of transcriptional repressors known as DELLA proteins (Peng et al., 1997; Silverstone et al., 2001). In the absence of bioactive GAs, DELLAs bind to and inactivate PHYTOCHROME INTERACTING FACTORS (PIFs), a group of bHLH-family transcription factors (Sun, 2011). The presence of a growth signal stimulates the biosynthesis of GA, which is perceived by GA INSENSITIVE DWARF 1 (GID1) through direct binding. This leads to a conformational change of GID1, facilitating its binding to DELLA proteins (Murase et al., 2008). The formation of the GID1–DELLA complex enhances the interaction between DELLA and the F-box protein SLEEPY 1 in the SCF^{SLY1} E3 ubiquitin ligase complex, which results in DELLA ubiquitination and degradation that relieves PIF repression and promotes GA-mediated gene expression and growth (McGinnis et al., 2003; Dill et al., 2004; Achard et al., 2007; Sun et al., 2011).

IN DEFENSE OF THE GROWTH TRADEOFF

Implementation of defense imposes a substantial demand for resources, which has been suggested to reduce growth. This negative impact on growth could result from diminished photosynthesis, which would decrease the overall

pool of energy reserves, and/or from a diversion of resources away from growth and towards defense. As deficiencies in defense capabilities can result in pathogen-induced decimation of a plant population, a balance must be achieved between growth and defense to optimize plant fitness.

Finding Balance to Optimize Fitness

Fitness costs associated with defense have been clearly demonstrated (Heil and Baldwin, 2002; Tian et al., 2003; Heide et al., 2004; Zavala et al., 2004; Kempel et al., 2011; Meldau et al., 2012). For example, silencing components in JA-mediated defense signaling was shown to alleviate fitness costs observed in wild-type plants (Meldau et al., 2012). In the case of constitutive defense responses, reduced fitness may be due in part to unnecessary diversion of energy reserves away from growth in the absence of stress. Benzothiadiazole (BTH) is a synthetic analog of SA used commercially to enhance disease resistance by inducing SAR in crops (Gorlach et al., 1996; Lawton et al., 1996). Application of BTH to wheat was observed to negatively impact fitness in the absence of pathogens (Heil et al., 2000) and to increase fitness in the presence of the biotrophic fungus powdery mildew (Gorlach et al., 1996). Another fitness cost attributed to constitutive defense is the inability of the plant to respond appropriately to environmental conditions that limit energy production. In support of this, enhanced susceptibility to the hemi-biotrophic pathogen *Pseudomonas syringae* (*P. syringae*) and the necrotrophic pathogen *Botrytis cinerea* observed in shade-grown plants has been attributed to the need to prioritize growth under these light-restrictive conditions (Cerrudo et al., 2012; de Wit et al., 2013; Ballaré, 2014).

While it is easy to understand the costs associated with constitutive defense, fitness is also compromised in the absence of defense. Loss of NPR1-dependent, SA-mediated defense was shown to reduce the fitness of field-grown plants (Heide et al., 2004), whereas overexpression of *NPR1* was shown to enhance resistance to biotrophic and hemi-biotrophic pathogens without adversely affecting growth or fitness (Cao et al., 1998; Heide et al., 2004). This is most likely due to the fact that SA signaling is not constitutively active but rather primed for quicker response to pathogen detection in these plants (Cao et al., 1998). Together, these studies indicate that approaches used to achieve an enhanced primed state can ameliorate the fitness costs associated with constitutive defense, while optimizing the fitness benefits of rapid defense induction upon pathogen detection. They also emphasize the point that increased growth is not equivalent to enhanced fitness. Rather, plant fitness is optimized when growth and defense are appropriately prioritized in response to both environmental and developmental cues (Valverde et al., 2003; Heide et al., 2004).

Impacts on Photosynthesis

Pathogen/herbivore activity that results in damage to photosynthetic machinery, loss of photosynthetic tissue, and/or disruption of the vasculature affecting water and sugar transport has been shown to negatively impact photosynthesis (Aldea et al., 2005; Zou et al., 2005; Gutsche et al., 2009; Nabity et al., 2009; Kerchev et al., 2012). In addition, pathogen/herbivore attack has been shown to suppress components of photosynthesis at the levels of gene expression and of protein abundance (Zou et al., 2005; Jung et al., 2007; Denoux et al., 2008; Ishiga et al., 2009; Bilgin et al., 2010; Sugano et al., 2010; Chen et al., 2011b; Gohre et al., 2012; Guo et al., 2012; Borges et al., 2013). The negative impact of defense on photosynthesis has been best demonstrated in response to JA treatment, which results in a reduction of components essential for light harvesting and carbon fixation (Wierstra and Klopstech, 2000; Chen et al., 2011b; Shan et al., 2011; Guo et al., 2012) as well as a substantial decrease in photosynthetic activities and chlorophyll contents in *Arabidopsis* (Jung, 2004), supporting the need for energy acquisition to enable the defense response.

However, down-regulation of photosynthetic genes following defense activation does not always correlate with changes in protein profiles (Gohre et al., 2012), leading to the hypothesis that the stability of most photosynthetic proteins allows for a temporary halt at the transcriptional level without a significant impact on photosynthesis itself. This appears to be supported by some studies using chlorophyll fluorescence to measure photosynthetic rates following infection with biotrophic, hemi-biotrophic, or necrotrophic pathogens. A similar spatial pattern has been reported for each pathogen type where inhibition of photosynthesis is confined to infected cells and is offset by elevated photosynthesis in the surrounding cells whereas no impact is observed in distal, uninfected tissues (Chou et al., 2000; Berger et al., 2004; Bonfig et al., 2006; Berger et al., 2007). Also, proteomic and biochemical analyses of resistant and susceptible plants have shown that the ability to maintain photosynthesis during infection is a vital element of defense (Gutsche et al., 2009; Zhang et al., 2013). Furthermore, loss of RuBPCase activase (RCA), which has a critical role in carbon fixation, has been shown to diminish JA-mediated defenses (Mittra and Baldwin, 2014). Together, these studies indicate that the ability to appropriately maintain photosynthesis is crucial for defense. Whether or not the observed effects on photosynthesis are a programmed part of the defense response or merely a by-product remains to be determined.

Resource Diversion

In support of the growth–defense tradeoff theory, diversion of plant resources has been shown to occur at all levels,

including machinery involved in transcription, translation, and protein secretion from cells as well as prioritization of carbon and nitrogen towards production of defense compounds. Transcriptomic and proteomic studies have demonstrated transcriptional reprogramming and altered protein profiles upon pathogen/herbivore detection to promote defense at the expense of growth (Wang et al., 2006; Jung et al., 2007; Denoux et al., 2008; Bilgin et al., 2010; Sugano et al., 2010; Chen et al., 2011b; Gohre et al., 2012; Guo et al., 2012; Borges et al., 2013). Production and secretion of proteins with specific defensive properties, such as PR proteins, place a significant demand on the protein folding and secretory systems, which have also been shown to be required for defense (Wang et al., 2005; Kwon et al., 2008; Pajerowska-Mukhtar et al., 2012). Allocation of resources involved in protein folding and secretion towards defense has been proposed to be regulated in part by *TL1* BINDING TRANSCRIPTION FACTOR 1 (TBF1) (Pajerowska-Mukhtar et al., 2012). Many TBF1-regulated genes encode ER resident proteins involved in protein folding and secretion, and loss of *TBF1* was shown to compromise the unfolded protein response as well as to impair PTI and SAR (Pajerowska-Mukhtar et al., 2012). Furthermore, *tbfl* knockout mutants were shown to exhibit partial suppression of growth inhibition associated with defense activation, and transcriptional profiling of these mutants showed a general promotion of growth-related genes and repression of defense-related genes (Pajerowska-Mukhtar et al., 2012).

Studies using radiolabeled carbon or nitrogen have shown that pathogen/herbivore detection alters the normal metabolic flux to enable the incorporation of these resources into defense-related compounds (Engelsdorf et al., 2013; Ullmann-Zeunert et al., 2013). Reallocation of labeled nitrogen from ribulose-1,5-bisphosphate carboxylase/oxygenase (RuBisCO) into nicotine and phenolamide compounds following simulated herbivory was shown to rely on a functional JA pathway (Ullmann-Zeunert et al., 2013). Carbon availability has been shown to be important for SA-regulated defense, as starch-free mutants, which have a general reduction in carbohydrates compared with wild-type plants, showed a delayed production of SA-regulated defense compounds resulting in increased susceptibility to the hemi-biotrophic pathogen *Colletotrichum higginsianum* (Engelsdorf et al., 2013). Carbohydrates are produced in photosynthetic ‘source’ tissues and transported in the form of sucrose to non-photosynthetic ‘sink’ tissues (Roitsch and Gonzalez, 2004). Upon pathogen infection in the leaves, this process is disrupted by up-regulation of cell wall invertases, which cleave sucrose into glucose and fructose thereby preventing sucrose export from infected cells (Sturm, 1999; Roitsch and Gonzalez, 2004; Swarbrick et al., 2006; Kocal et al., 2008). Transgenic suppression of cell wall invertase activity results in elevated sucrose-to-hexose ratios accompanied by reduced and delayed callose deposition and inhibition of *PR* gene expression

following pathogen infection (Essmann et al., 2008; Kocal et al., 2008), whereas ectopic expression of a yeast cell wall invertase has been shown to activate defense responses in tobacco (Herbers et al., 1996). Comparison of resistant and susceptible barley interactions with the biotrophic fungal pathogen *Blumeria graminis* revealed a more robust activation of cell wall invertase in the resistant interaction resulting in accumulation of hexose sugars localized to regions of actively defending cells (Swarbrick et al., 2006). In addition, a recent study has shown cell wall invertase activity to be a possible virulence target of the biotrophic pathogen *Xanthomonas campestris* pv. *vesicatoria*, to promote disease in pepper (Sonnewald et al., 2012), providing further evidence supporting a role for cell wall invertases in redirecting carbon resources to enable plant defense.

Together, these studies begin to reveal some of the regulatory mechanisms underlying resource reallocation to mediate the growth–defense tradeoff in plants. Along with the co-opting of energy reserves and cellular machinery to produce compounds necessary for defense, transcriptional reprogramming induced by defense activation is often accompanied by repression of growth hormone signaling as a fundamental aspect of growth–defense tradeoffs. In the following sections, we discuss current knowledge regarding crosstalk between defense signaling and growth hormones.

PAMP-TRIGGERED IMMUNITY-MEDIATED DEFENSE VERSUS GROWTH

One of the most noticeable physiological consequences of prolonged or constitutively active PTI is growth inhibition, which is observed upon treatment of a plant with a PAMP (Gomez-Gomez et al., 1999; Zipfel et al., 2006). As discussed in the previous section, there is mounting evidence to support a mechanism whereby resources normally allocated towards growth are diverted to support defense and, as discussed below, hormonal crosstalk appears to play a major role in regulating the tradeoff between growth and PTI-mediated defense.

PAMP-Triggered Immunity Crosstalk with Auxin

Auxin has long been implicated in suppressing plant defense due to the fact that many pathogens, including *P. syringae* and *Agrobacterium tumefaciens*, can directly synthesize auxin or manipulate auxin synthesis and signaling in plants to promote disease (Yamada, 1993; Glickmann et al., 1998; O'Donnell et al., 2003; Chen et al., 2007; Kidd et al., 2011). Microorganisms primarily synthesize IAA from tryptophan and, in some cases, the genes encoding the enzymes required for this process are located on a pathogen virulence plasmid (Yamada, 1993). Analysis of plant transcriptional reprogramming following some pathogen infections has shown a general derepression of the auxin

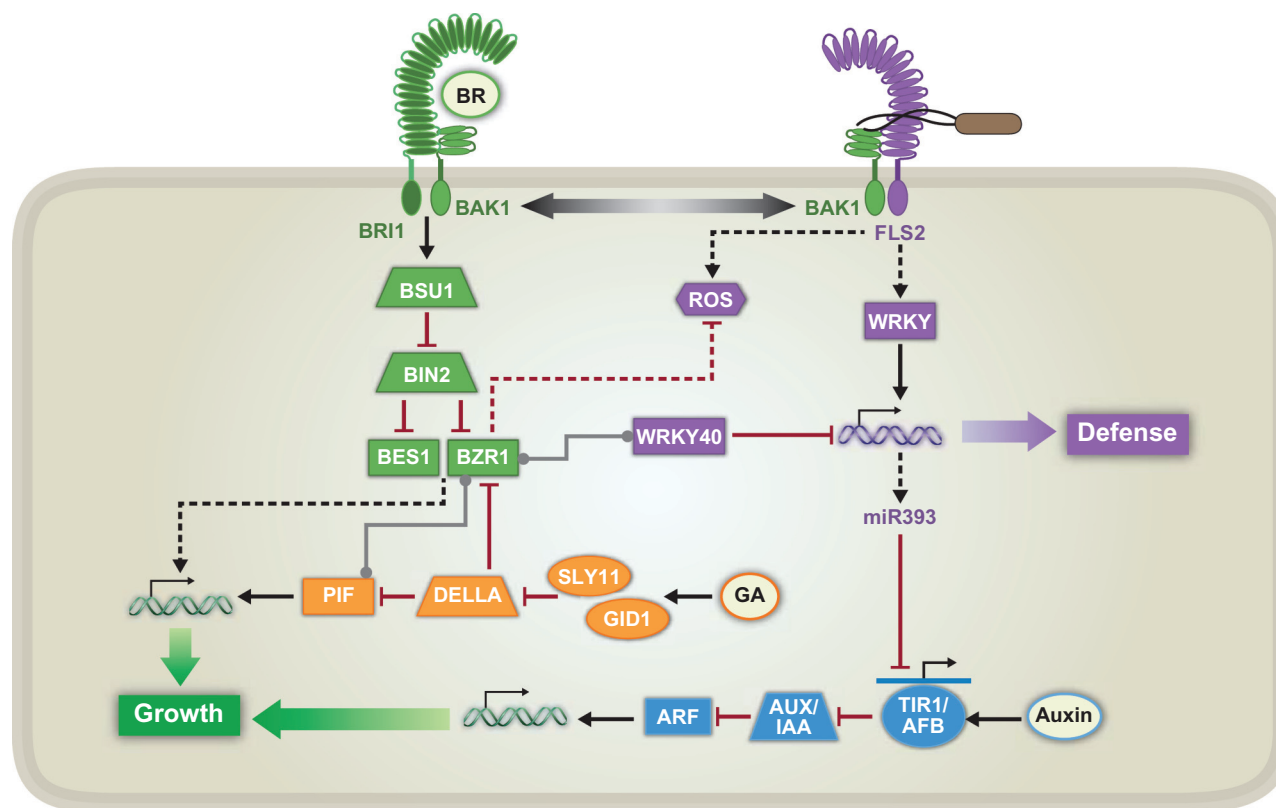


Figure 2 Known Signaling Contributing to Growth–Defense Tradeoffs between PTI-Mediated Defense and Auxin-, Brassinosteroid (BR)-, and Gibberellin (GA)-Mediated Growth.

Black arrows and red, blunted lines represent positive and negative regulation, respectively. Double helices with arrows represent global transcriptional reprogramming, and gray lines with dots at both ends indicate protein–protein interactions. Solid lines indicate a known connection between two components, whereas dashed lines indicate unknown connections or missing steps between two components. The solid blue line with an arrow represents expression of *TIR1/AFB* genes, the transcripts of which are targeted by miR393. FLS2, FLAGELLIN SENSING 2; ROS, reactive oxygen species; WRKY, WRKY DNA-BINDING PROTEIN; miR393, microRNA 393; TIR1, TRANSPORT INHIBITOR RESPONSE 1; AFB, AUXIN SIGNALING F-BOX; AUX/IAA, AUXIN-INDUCIBLE/INDOLE-3-ACETIC ACID INDUCIBLE; ARF, AUXIN RESPONSE FACTOR; BAK1, BRI1-ASSOCIATED RECEPTOR KINASE 1; BRI1, BRASSINOSTEROID INSENSITIVE 1; BSU1, BRI1 SUPPRESSOR 1; BIN2, BRASSINOSTEROID INSENSITIVE 2; BES1, BRI1-EMS-SUPPRESSOR 1; BZR1, BRASSINAZOLE-RESISTANT 1; SLY1, SLEEPY 1; GID1, GA INSENSITIVE DWARF 1A; DELLA, repressor protein; PIF, PHYTOCHROME INTERACTING FACTOR.

pathway including promotion of auxin biosynthetic genes and repression of *AUX/IAA* genes resulting in enhanced plant susceptibility (O'Donnell et al., 2003; Thilmony et al., 2006). Furthermore, virulence of the bacterial hemibiotrophic pathogen *P. syringae* pv. *tomato* DC3000 (*Pto* DC3000) can be enhanced by treatment with synthetic auxins prior to pathogen inoculation (Navarro et al., 2006; Chen et al., 2007).

To combat the effects of pathogen produced or induced auxin to promote disease, plants actively suppress auxin signaling during defense (Navarro et al., 2004). Following flg22-treatment, wild-type *Arabidopsis* plants show a reduction in both transcript and protein levels of the auxin F-box receptors, resulting in stabilization of AUX/IAA proteins and repression of auxin-responsive genes (Navarro et al., 2006). This suppression is partially due to the activity

of the microRNA miR393 (Figure 2), which is induced by flg22 and directly targets and cleaves *TIR1*, *AFB2*, and *AFB3* transcripts (Jones-Rhoades and Bartel, 2004; Sunkar and Zhu, 2004; Navarro et al., 2006). However, additional mechanisms such as transcriptional repression must also contribute to PTI inhibition of auxin signaling, as partial reduction in transcript levels is still observed in the *DICER LIKE 1* (*DCL1*) mutant, *dcl1-9*, which is required for miR393 function (Navarro et al., 2006). Also, the *AFB1* transcript is partially resistant to miR393 activity, and shows reduced transcript levels in both wild-type and *dcl1-9* mutant plants (Navarro et al., 2006).

Suppression of auxin signaling has been shown to be biologically relevant to PTI, as overexpression of *miR393* enhances resistance to virulent pathogens and overexpression of *AFB1* increases susceptibility relative to that observed

in wild-type plants, as measured by bacterial growth (Navarro et al., 2006). One study has shown that pathogen manipulation of auxin metabolism to generate higher levels of IAA-aspartate (IAA-Asp) promotes disease by positively regulating the expression of bacterial virulence genes rather than by directly suppressing PTI (González-Lamothe et al., 2012). This was shown to require the GH3.2 enzyme, as *gh3.2* knockout plants exhibited reduced susceptibility to *Pto* DC3000 (González-Lamothe et al., 2012). However, Mutka et al., (2013) were unable to reproduce these results, making the role of GH3.2 in this process unclear. If GH3.2 is involved, it cannot fully account for auxin-induced susceptibility because *gh3.2* knockout plants crossed with plants overexpressing the auxin biosynthetic gene, *YUCCA 1*, retained enhanced susceptibility (Mutka et al., 2013). Therefore, while there is much evidence to implicate auxin in promoting plant disease, the exact mechanism underlying this phenomenon remains unclear.

PAMP-Triggered Immunity Crosstalk with Brassinosteroids and Gibberellins

Unlike the mutually antagonistic interactions observed between PTI and auxin-mediated growth, negative crosstalk between PTI and BR-mediated growth is unidirectional (Albrecht et al., 2012; Belkhadir et al., 2012). Elevation of BR signaling in *Arabidopsis* using either transgenic modifications (Jaillais et al., 2011; Belkhadir et al., 2012) or exogenous application of BR (Albrecht et al., 2012) results in inhibition of flg22-mediated protection against *Pto* DC3000. Conversely, treatment with brassinazole, which inhibits BR biosynthesis, elevates ROS production in response to PAMP treatment (Lozano-Durán et al., 2013), indicating that endogenous levels of BR are sufficient to suppress PTI. Due to the association of BAK1 with both FLS2 and BRI1 receptors, it was hypothesized that FLS2 and BRI1 competition for BAK1 might facilitate BR-mediated suppression of PTI-mediated defense (Figure 2). However, while overexpression of BRI1 was shown to inhibit PTI responses in a BAK1-dependent manner (Belkhadir et al., 2012), neither exogenous BR nor expression of a hyperactive form of BRI1, BRI1^{sud1}, were shown to affect FLS2–BAK1 complex formation, transphosphorylation, or phosphorylation of downstream targets (Albrecht et al., 2012; Lozano-Durán et al., 2013).

A recent study by Lozano-Duran et al. (2013) has shown that constitutively active BZR1, but not BES1, is sufficient to block PAMP-triggered ROS burst, gene expression, and seedling growth inhibition (Figure 2). BZR1 inhibition of PTI appears to be mediated through its downstream targets, which include transcription factors known to promote BR responses and/or block defense (Lozano-Durán et al., 2013; Malinovsky et al., 2014). For example, a group of WRKY transcription factors known to negatively regulate PTI were identified as BR-induced BZR1 targets

(Lozano-Durán et al., 2013). Of these, WRKY40 was shown to have a role in suppression of PAMP-induced ROS production and seedling growth inhibition. It is possible that BZR1 and WRKY40 act together to suppress PTI, as co-immunoprecipitation experiments indicated that these two proteins physically interact (Figure 2), and analysis of publicly available gene expression data revealed that all WRKY40-regulated genes are also targets of BZR1 (Lozano-Durán et al., 2013). Another example of a BZR1 target involved in PTI suppression is *HBI1*, which encodes a bHLH transcription factor shown to promote BR-regulated cell elongation by inducing the expression of expansin genes (Bai et al., 2012a). In addition to enhanced growth phenotypes, overexpression of *HBI1* was shown to suppress PAMP-induced ROS and seedling growth inhibition downstream of FLS2–BAK1 complex formation (Malinovsky et al., 2014). While the mechanism for HBI1-mediated suppression of PAMP-responses is not known, identification of specific defense gene targets of BZR1-regulated transcription factors, including the WRKYs identified by Lozano-Duran et al. (2013), begins to shed light on the molecular mechanism behind BR suppression of PTI-mediated defense.

GA suppression of PAMP-induced seedling growth inhibition most likely occurs through promotion of BR signaling. BR- and GA-mediated signaling pathways work additively or synergistically to promote growth in response to environmental and developmental cues (Jaillais and Vert, 2012; Lilley et al., 2013). This cooperative relationship is facilitated in part by the formation of a BZR1/PIF4 heterodimer (Figure 2), which binds to the promoters of some 2,000 shared target genes to promote growth (Oh et al., 2012). DELLA proteins have been shown to inhibit both BZR1 and PIF4 proteins and may also target the BZR1/PIF4 heterodimer (De Lucas et al., 2008; Bai et al., 2012b; Gallego-Bartolome et al., 2012). While exogenous application of GA did not affect PAMP-induced seedling growth inhibition, chemical inhibition of GA synthesis completely blocked the effect of BR on seedling growth inhibition, and GA treatment in combination with BR resulted in an additive effect on PAMP-induced seedling growth inhibition (Lozano-Durán et al., 2013). This is most likely due to the effect of GA on DELLA stabilization. In the absence of GA, increased DELLA stabilization would result in BZR1 inhibition and loss of BR-mediated seedling growth inhibition (Figure 2). In support of this, flg22-induced stabilization of DELLA proteins has been shown to be a mechanism for PTI inhibition of GA-mediated growth (Navarro et al., 2008).

SALICYLIC ACID-MEDIATED DEFENSE VERSUS GROWTH

Suppression of growth by SA is best illustrated by constitutive defense mutants, which typically have a dwarf

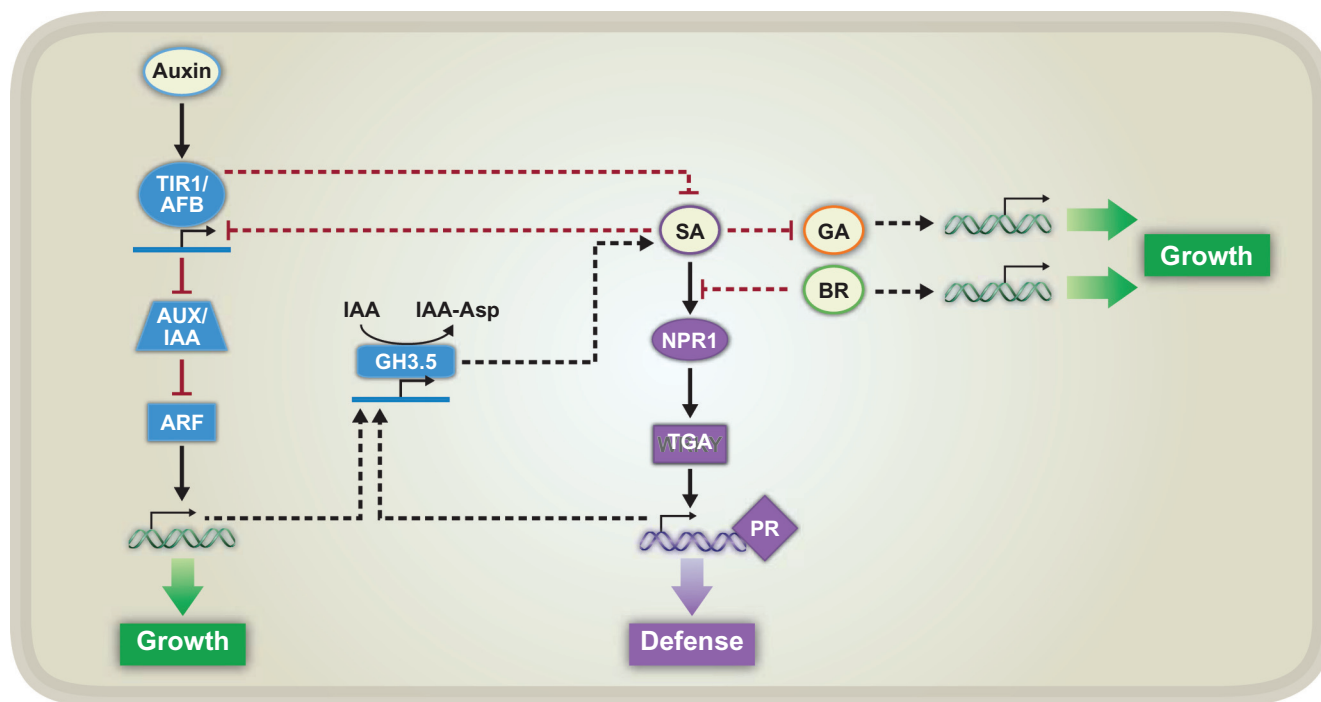


Figure 3 Known Signaling Contributing to Growth–Defense Tradeoffs between Salicylic Acid (SA)-Mediated Defense and Auxin-, Brassinosteroid (BR)-, and Gibberellin (GA)-Mediated Growth.

As in Figure 2, black arrows and red, blunted lines represent positive and negative regulation, respectively. Double helices with arrows represent global transcriptional reprogramming, and solid lines associated with arrows represent expression of TIR1/AFB and GH3.5 genes. Solid lines indicate a known connection between two components, whereas dashed lines indicate unknown connections or missing steps in between two components. NPR1, NONEXPRESSOR OF PR GENES 1; TGA, TGACG SEQUENCE-SPECIFIC BINDING PROTEIN; PR, PATHOGENESIS RELATED; IAA, INDOLE-3-ACETIC ACID; Asp, aspartate; TIR1, TRANSPORT INHIBITOR RESPONSE 1; AFB, AUXIN SIGNALING F-BOX; AUX/IAA, AUXIN-INDUCIBLE/IAA INDUCIBLE; ARF, AUXIN RESPONSE FACTOR.

plant phenotype due in part to elevated SA accumulation or signaling (Clarke et al., 2000; Zhang et al., 2003a); however, as these mutants may be perturbed in cellular processes other than SA defense, it is difficult to ascertain how SA itself is directly contributing to growth suppression in these plants. To demonstrate the effect of SA on plant growth, experiments employing chemical inducers or genetic manipulation to alter SA accumulation or perception have been used. Cold temperature-induced growth reduction in *Arabidopsis* has been shown to be due to endogenous elevation of SA as it was lost in plants compromised in SA accumulation (Scott et al., 2004). Also, repeated application of BTH reduced plant biomass in a reproducible and dose-dependent manner that was correlated with induction of SA-mediated defense responses (Canet et al., 2010a). Mutants isolated in a screen based on resistance to BTH-induced growth inhibition were compromised in SA-mediated disease resistance and were primarily identified as non-functional alleles of *NPR1* (Canet et al., 2010b). The mechanisms for SA-induced suppression of growth are most likely mediated by crosstalk with

growth hormone signaling pathways, as discussed in the following sections.

Salicylic Acid Crosstalk with Auxin

One of the primary ways SA has been shown to inhibit growth is by suppression of auxin signaling (Figure 3). A microarray study revealed that a number of auxin-responsive genes were affected by BTH treatment, namely 21 genes encoding proteins involved in auxin reception, import and export and signaling were down-regulated and two genes encoding GH3 enzymes were up-regulated (Wang et al., 2006, 2007). As GH3 enzymes are responsible for regulating auxin homeostasis by conjugating IAA with different amino acids (Staswick et al., 2005), the transcriptional profile indicates a general BTH-dependent repression of auxin homeostasis and signaling. A follow-up study confirmed this by investigating the effect of SA on auxin levels, uptake, sensitivity, and signaling (Wang et al., 2007). It was shown that SA does not affect auxin synthesis, but instead represses the expression of the *TIR1/AFB*

F-box genes (Figure 3), resulting in stabilization of AUX/IAA repressor proteins to decrease auxin signaling (Wang et al., 2007).

One of the two *GH3* genes identified in the microarray study encodes GH3.5 (Wang et al., 2006, 2007), which conjugates IAA with Asp (Staswick et al., 2005). The *gh3.5* knockout mutants were shown to be compromised in SAR while overexpression lines exhibited a dwarf phenotype, accumulated higher levels of SA, had elevated expression of *PR1*, and increased resistance to *Pto* DC3000 (Park et al., 2007; Zhang et al., 2007, 2008). IAA-Asp is an inactive form of auxin that is targeted for metabolism (Ostin et al., 1998; Ljung et al., 2002); therefore, it would seem logical to infer that GH3.5 directly facilitates the growth–defense tradeoff between SA and auxin by simultaneously elevating SA levels and reducing active IAA levels. However, the dwarf phenotype observed in several GH3.5 overexpression lines did not always correlate with a reduction in free IAA (Park et al., 2007; Zhang et al., 2007). As *GH3.5* expression is also induced by IAA to regulate its homeostasis (Hagen et al., 1984; Hagen and Guilfoyle, 2002), it is possible for GH3.5 to inhibit the auxin pathway directly by conjugating IAA and also indirectly by promoting SA biosynthesis and signaling, which then acts to block auxin responses (Figure 3).

SA-mediated defense has also been shown to be affected by auxin, as transgenic overexpression of the *AFB1* gene, which enhances auxin signaling, led to a reduction in pathogen-induced SA biosynthesis relative to wild-type plants (Figure 3) (Robert-Seilanianantz et al., 2011b). However, transgenic overexpression of the *YUCCA 1* gene showed that elevation of auxin levels alone can promote plant disease without affecting SA levels or signaling (Mutka et al., 2013). Auxin positively regulates expansins, which are involved in cell wall loosening, to promote growth (Cosgrove, 2005; Ding et al., 2008), and the ability of *Xanthomonas oryzae* pv. *oryzae* to induce expansins in rice was shown to be important in determining the outcome of the plant–pathogen interaction (Ding et al., 2008). Together, these studies indicate a dual function for auxin in direct interference with SA-mediated defense and in positive regulation of physiological changes that aid pathogen proliferation in the plant.

Salicylic Acid Crosstalk with Brassinosteroids and Gibberellins

There is much less known regarding the relationships between SA-mediated defense and BR- and GA-mediated growth. BR treatment was shown to block BTH-mediated resistance in rice, indicating suppression of SA signaling (De Vleeschauwer et al., 2012). Based on analysis of mutant plants affected in SA production or NPR1-mediated signaling, it was concluded that this antagonism occurs

downstream of SA biosynthesis and upstream of NPR1 signaling (Figure 3), but the mechanism for this suppression is unknown (De Vleeschauwer et al., 2012). A recent study showed that down-regulation of the gene encoding the hydroxycinnamoyl CoA (HCT) enzyme resulted in stunted plant growth that was directly correlated with lignin reduction and endogenous SA elevation (Gallego-Giraldo et al., 2011a). These same plants were also shown to be impaired in both GA accumulation and perception (Gallego-Giraldo et al., 2011a, 2011b). Crosses between *HCT* RNAi plants and plants defective in SA biosynthesis, accumulation, or perception by NPR1 revealed that loss of SA production and accumulation, but not NPR1-dependent SA perception, was responsible for growth suppression in these plants (Gallego-Giraldo et al., 2011a). Loss of SA accumulation was also shown to restore gene induction and growth enhancement in response to exogenous GA, implicating SA in repression of GA signaling and growth (Gallego-Giraldo et al., 2011a). As mentioned previously, BZR1 is directly targeted and suppressed by the DELLA family of growth-suppressing proteins (Gallego-Bartolome et al., 2012). SA-mediated suppression of GA would most likely result in increased DELLA stability, which may lead to suppression of BR-mediated signaling. Further studies are needed to both establish a molecular mechanism for SA-inhibition of GA signaling and to determine whether this suppression of GA results in loss or reduction in BR signaling.

JASMONATE-MEDIATED DEFENSE VERSUS GROWTH

It has long been known that activation of JA signaling by applying JA into the growth medium results in growth inhibition (Staswick et al., 1992). Correlated with growth inhibition, JA suppresses mitosis, arrests the cell cycle in G1 prior to the S transition, and delays the switch from the mitotic cell cycle to the endoreduplication cycle (Zhang and Turner, 2008; Noir et al., 2013). Transcriptomic analysis further confirmed that JA activates several critical regulators of endoreduplication and affects the expression of key determinants of DNA replication (Noir et al., 2013). As in the case of PTI and SA-mediated defense, the effects of JA on growth appear to be mediated by crosstalk with growth hormone signaling.

Jasmonate Crosstalk with Auxin and Brassinosteroids

The auxin signaling pathway has been implicated in JA-induced growth inhibition in *Arabidopsis* (Figure 4) (Wasternack and Hause, 2013). JA not only suppresses the expression of the auxin efflux carrier *PINFORMED 2* (*PIN2*),

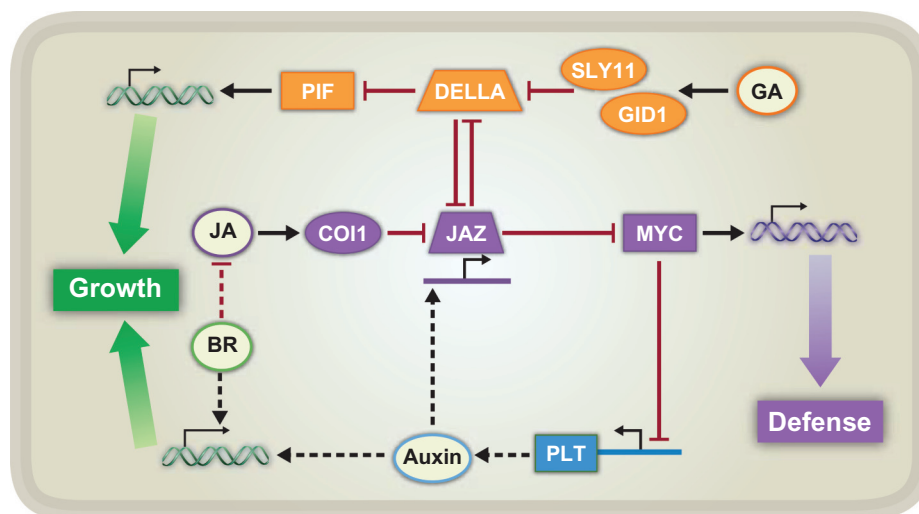


Figure 4 Known Signaling Contributing to Growth–Defense Tradeoffs between Jasmonate (JA)-Mediated Defense and Auxin-, Brassinosteroid (BR)-, and Gibberellin (GA)-Mediated Growth.

As in Figures 2 and 3, black arrows and red, blunted lines represent positive and negative regulation, respectively. Double helices with arrows represent global transcriptional reprogramming, and solid lines with arrows represent expression of JAZ and PLT genes. Solid lines indicate a known connection between two components, whereas dashed lines indicate unknown connections or missing steps in between two components. COI1, CORONATINE INSENSITIVE 1; JAZ, JASMONATE ZIM DOMAIN; MYC, transcription factor; SLY1, SLEEPY 1; GID1, GA INSENSITIVE DWARF 1A; DELLA, repressor protein; PIF, PHYTOCHROME INTERACTING FACTOR; PLT, PLETHORA.

but also inhibits PIN2 endocytosis and membrane accumulation (Sun et al., 2011). Consequently, the normal auxin distribution in roots is disrupted after JA treatment (Sun et al., 2011). Moreover, MYC2 has been shown to negatively regulate the expression of *PLETHORA* (*PLT1* and *PLT2*) transcription factors (Chen et al., 2011a), which are important regulators of auxin-mediated root stem cell development and auxin biosynthesis in roots (Figure 4) (Pinon et al., 2013). Taken together, it is postulated that JA changes the spatial and temporal distribution pattern of auxin in plants to suppress normal plant growth mediated by auxin. However, JA was also shown to increase auxin biosynthesis by inducing *ANTHRANILATE SYNTHASE* (*ASA1* and *ASB1*) and *YUCCA* (*YUC8* and *YUC9*) gene expression in certain plant tissues (Sun et al., 2009; Hentrich et al., 2013), and JA-induced auxin biosynthesis and lateral root formation were impaired in *yuc* knockout mutants (Hentrich et al., 2013). Conversely, auxin has been shown to induce expression of *JAZ1*, suggesting that auxin may suppress JA signaling through *JAZ1* (Figure 4) (Grunewald et al., 2009). These latter studies illustrate the complexity of the interaction between JA and auxin signaling pathways.

BR signaling has also been implicated in antagonizing JA-induced growth suppression (Figure 4) (Wasternack, 2013). The first indication of a connection between JA-mediated defense and BR-mediated growth was the identification of a *partially suppressing coi1* (*psc1*) mutant, which carries a mutation in a key enzyme involved in BR biosynthesis, *DWARF 4* (*DWF4*) (Ren et al., 2009).

In *Arabidopsis*, the *psc1* mutation partially suppresses the loss of JA-induced growth inhibition in the *coi1* mutant background (Ren et al., 2009) and displays increased JA-induced growth inhibition in the wild-type background (Huang et al., 2010). The negative impact of BR signaling on JA signaling has also been demonstrated in tomato, where BR was shown to antagonize several JA-dependent traits including trichome density and allelochemical content (Campos et al., 2009). Unlike in *Arabidopsis*, BR appears to act upstream of COI1 in tomato since loss of BR synthesis cannot suppress the tomato *coi1* mutation (Figure 4) (Campos et al., 2009). However, BR has also been shown to have positive effects on some JA-mediated traits, as JA-induced anthocyanin accumulation is reduced both in BR-biosynthetic mutants and a BR signaling mutant (Peng et al., 2011; Song et al., 2011). Thus, as in the case of the JA-auxin interaction, the crosstalk between JA and BR appears to be complicated.

Jasmonate Crosstalk with Gibberellins

A wave of recent studies has shown an important role for JA–GA signaling crosstalk in regulating the growth–defense tradeoff (Figure 4) (Hou et al., 2010; Wild et al., 2012; Yang et al., 2012; Heinrich et al., 2013). In *Nicotiana attenuata*, elevated JA has a negative effect on GA biosynthesis in stems resulting in growth inhibition (Heinrich et al., 2013). In several *Arabidopsis* mutants in which the DELLA transcriptional repressors are stabilized, MYC2-dependent

JA-responsive genes are hypersensitive to JA treatment resulting in increased growth inhibition (Hou et al., 2010). In addition, overexpression of a DELLA protein, RGA LIKE 3 (RGL3), which reduces GA-mediated growth, increases MYC2-dependent gene expression; whereas *rgl3* mutation reduces MYC2-dependent gene expression (Wild et al., 2012). MYC2 has also been shown to positively regulate *RGL3* by directly binding to the promoter of this gene, creating a positive feedback loop in JA signaling (Wild et al., 2012). Consistently with GA antagonism of JA signaling, DELLA repressor proteins have been shown to be positive regulators of JA-mediated disease resistance against necrotrophic pathogens, as JA-mediated defense is compromised in DELLA loss-of-function mutants and is enhanced by overexpression of *RGL3* (Navarro et al., 2008; Wild et al., 2012).

Direct physical interaction between JAZ and DELLA repressor proteins has been shown to be crucial for the JA–GA crosstalk in regulating growth and defense (Figure 4) (Hou et al., 2010; Wild et al., 2012; Yang et al., 2012). JAZ proteins interact with the GRAS domain of DELLA proteins, which is important for the interaction between DELLAs and growth-promoting PIF transcription factors (De Lucas et al., 2008). JAZ binding to DELLA proteins was shown to block the interaction between DELLAs and PIFs, thereby relieving the inhibition of DELLAs on PIFs and promoting GA-dependent growth in *Arabidopsis* (Yang et al., 2012). Accordingly, *Arabidopsis coi1* mutants, JAZ overexpression lines, and *COI1*-silenced rice plants show enhanced growth, whereas *Arabidopsis della* mutants and PIF overexpression lines are compromised in JA-induced growth inhibition (Yang et al., 2012). These results suggest that, in response to pathogen or herbivore attack, degradation of JAZ proteins makes more DELLA proteins available for interaction with and inhibition of PIF transcription factors as part of a mechanism to inhibit growth (Figure 4) (Yang et al., 2012; Kazan and Manners, 2013). Conversely, GA has also been demonstrated to have a positive effect on some JA-mediated traits such as sesquiterpene synthase gene expression (Hong et al., 2012). The RGA DELLA protein can interact with and repress MYC2 activity resulting in inhibition of JA-mediated terpene biosynthesis; in this case, GA-mediated degradation of DELLAs promotes a specific JA-mediated trait (Hong et al., 2012). Together, these findings suggest that interactions between JA and GA signaling pathways can occur at multiple levels and in different directions, illustrating the dynamic nature of JA–GA crosstalk in regulating the growth–defense tradeoff.

CONCLUSIONS AND FUTURE PERSPECTIVES

Pathogen and herbivore-induced damage is known to reduce plant yield, causing substantial economic losses

(Smedegaardpetersen and Stolen, 1981; Oerke, 2006). However, simply breeding plants to have constitutively active defense is not a viable solution, as there are known fitness costs associated with the induction of defense responses (Heil and Baldwin, 2002; Tian et al., 2003; Heidel et al., 2004; Kempel et al., 2011), as well as conditions under which growth must be prioritized in spite of pathogen or herbivore attack (Lozano-Durán et al., 2013; Ballaré, 2014). Plants have evolved mechanisms, such as hormone crosstalk, to optimize fitness in response to the dynamic environments in which they live. A critical step in harnessing this process for the improvement of crop performance is the identification of molecular targets responsible for implementing resource reallocation to facilitate prioritization of growth or defense.

Studies reviewed here and elsewhere have revealed a web of interconnected hormone signaling networks that enable fine-tuning of plant responses to environmental and developmental cues (Bari and Jones, 2009; Robert-Seilanianantz et al., 2011a; Naseem and Dandekar, 2012; Bartoli et al., 2013; De Vleeschauwer et al., 2013; Denance et al., 2013; Hao et al., 2013; Yang et al., 2013). However, it can be challenging to compare and integrate data collected using different experimental parameters, namely plant growth conditions and/or age. Untangling this web is also constrained by the tools and methods available. For instance, while ‘omic’ methods have enabled global visualization of changes in gene expression and protein profiles to some extent, the snapshots they provide are incapable of capturing the full range of dynamic temporal and spatial processes of growth–defense interactions. Also, tools currently available to isolate or amplify certain effects, such as the use of exogenous application of elicitors/hormones and stable genetic manipulation, may result in the identification of interactions that do not exist in nature or fail to identify those that do (Heil and Baldwin, 2002). Other issues include the limitations of using whole seedlings or tissues to investigate changes occurring on a sub-organismal scale, and the relatively few studies conducted to investigate the effects of multiple or variable stresses on growth–defense interactions.

Therefore, while the use of simple laboratory conditions is essential for establishing foundational knowledge of individual signaling pathways, it will also be necessary in the future to design experiments that more accurately reflect natural environments—fluctuating conditions, exposure to multiple stresses, and field studies—to identify network interactions and to test putative molecular mechanisms. As technology advances, the ability to observe plant growth and plant–pathogen/herbivore interactions at a cellular level and in a spatiotemporal manner will provide valuable insight towards elucidating the timing and subcellular localization of molecular interactions as well as to distinguish between local and global effects on plant growth and defense. Understanding the specific molecular interactions

that facilitate these tradeoffs will provide powerful tools to genetically tailor plants that optimize this balance to maximize crop yield in fluctuating environmental conditions.

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