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Fungal effectors at the crossroads of phytohormone signaling

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Phytohormone networks are crucial for maintaining the delicate balance between growth and biotic stress responses in plants. Jasmonic acid, salicylic acid, ethylene, and the associated signaling crosstalk are important for pathogen defense; whereas gibberellin and cytokinin function in growth and development in plants. Plant pathogenic fungi have evolved remarkable strategies to manipulate and/or hijack such phytohormone signaling cascades for their own benefit, thus leading to susceptibility and disease in host plants. Interestingly, these hormones are also targeted by fungal endosymbionts and mutualists during beneficial interactions with plants. We highlight current advances in our understanding of the role of fungal effectors in such antagonistic manipulation of phytohormones during pathogenic as well as symbiotic association with plant hosts. In addition to the aforementioned effector-based control, certain phytohormone mimics have recently emerged as a powerful molecular language in fungal manipulation of defense responses and innate immunity in plants.

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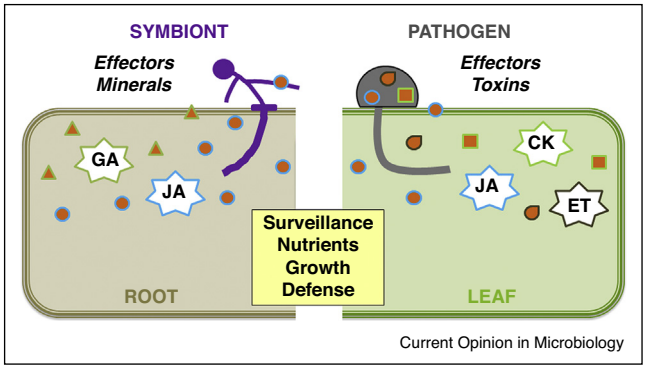
Introduction

Intricately regulated networks of phytohormones control growth, reproduction, defense, and nutrient homeostasis in plants. Both symbiotic and pathogenic fungi associate closely with plants to acquire nutrients for growth and development. However, symbiotic fungi provide growth-promoting minerals (e.g. phosphate, nitrogen, iron and sulphur) to plant roots in exchange for host-derived nutrients [1,2]. Pathogenic fungi on the other hand, deploy virulence factors and toxins to cause injury and cell death, before gaining access to essential nutrients in the host plants [3,4]. Such fungal pathogens and symbionts also subvert plant defense responses mediated by reactive oxygen species and/or phytohormones including jasmonic acid (JA), salicylic acid (SA) and ethylene (ET) [5–9]. In both instances, highly effective communication is important in establishing mutualistic as well as parasitic association between fungi and plants. Communication strategies with plants are particularly important during the initial stages of infection, wherein the colonizing fungus needs to avoid surveillance/detection by the host plants and at the same time overcome or suppress host defense responses. For example, detection of molecular patterns (e.g. long-chain chitins) in the fungal cell wall by specific host surface receptors activates and triggers the downstream basal defense responses [10–12]. In order to evade and overcome detection, fungal symbionts and pathogens need an effective molecular language to influence the host plants to reduce and/or stop the induction of the initial defense responses. Through constant interactions with plants, fungi have evolved a diverse range of secreted proteins and metabolites, referred to as effectors, to fulfil this need in efficient communication with plants (Figure 1) [13,14,15••,16••,17•,18–25]. Recent studies have uncovered an array of fungal effectors that target and modulate the host phytohormone signaling by altering it or by hijacking it for symbiont or pathogen benefit (Figures 2 and 3) [13,15••,16••,17•,22]. It is likely that the fungal strategy of secreting such phytohormone-related effectors rests on the ability of the plants to respond instantly to such extrinsic moieties that effectively forces host metabolism to down regulate basal immunity. This review provides insight into recent advances in fungal effector-based interkingdom signaling that targets the hormonal networks in host plants.

Symbiotic fungal effectors that target host phytohormone signaling

Association with symbiotic fungi has beneficial effects on plant growth and sustainability. For example, mutualistic symbionts such as the ectomycorrhizal (ECM) and arbuscular mycorrhizal (AM) fungi, provide host roots with essential minerals to promote growth, and in exchange acquire plant nutrients once symbiosis is successfully established [1,26,27]. Therefore, symbiotic fungi and hosts both benefit upon establishment of such nutrient-acquiring symbioses. Since host penetration and colonization can elicit strong defense responses, symbiotic fungi need to influence their hosts to effectively suppress such

Figure 1



Effectors function as an essential molecular language in fungus–plant communication. Beneficial fungi provide plant roots growth-promoting nutrients and minerals in exchange for shelter and host-derived nutrients (symbiont). Pathogenic fungi use virulence effectors and toxins to disable plant defenses to establish susceptibility and derive specific host nutrients. Pathogenic fungi target the hormonal signaling networks such as jasmonic acid (JA), ethylene (ET) and salicylic acid (SA) that are important for plant defense, whereas symbionts manipulate phytohormones related to 'growth' (GA, gibberellin) and 'stress' (JA). Much of plant metabolism is geared towards fungal detection or surveillance, nutrient homeostasis, and maintains an intricate balance in growth and defense. Both symbiotic and pathogenic fungi use effectors as an essential molecular language to convince their host to shift the metabolic balance in a way that favors their associations and nutrient acquisition. *Abbreviation*: CK, cytokinin.

responses during the initial entry and proliferation phases. An elegant strategy employed by symbiotic fungi is to secrete effector(s) that alter phytohormone signaling associated with host defense [13]. For instance, the ECM fungus *Laccaria bicolor* secretes MiSSP7 (Mycorrhiza-induced Small Secreted Protein 7) as a peptide effector to block JA signaling in *Populus trichocarpa*, thereby facilitating host colonization (Figure 2a) [13]. In Arabidopsis, JA signaling is initiated when a high level of jasmonoyl-L-isoleucine (JA-Ile), the active form of JA, is perceived by the JA receptor Coronatine Insensitive 1 (Coi1), which then binds to transcription repressors Jasmonate ZIM-domain (JAZ) proteins, thus targeting them for degradation [28–32]. Since JAZ proteins repress the expression of JA-related defense genes, their degradation transcriptionally activates Arabidopsis defense system [30,31]. A similar JA signaling pathway exists in poplar featuring PtJAZ6 and PtCOI1 [13]. The *L. bicolor* effector MiSSP7 blocks JA signaling in poplar through its interaction with the PtJAZ6, thus protecting it from JA-induced degradation by disrupting the PtJAZ6/PtCOI1 complex [13]. In this way, *L. bicolor* successfully prevents JA-dependent immune responses in poplar roots during establishment of its symbiotic association [13].

In addition to blocking host immunity, mutualistic symbiotic fungi also guide host root development in a way that favors establishment of their niche. Again, this is achieved by altering the host phytohormone signaling cascade. For instance, the AM fungus *Rhizophagus irregularis* manipulates *Medicago truncatula* gibberellin (GA) signaling to induce radial expansion of the root cortex to prepare the cortical cells therein for subsequent development of the mineral-delivering arbuscules (Figure 2b) [33••]. GA signaling is repressed by a subclass of GRAS transcriptional repressors collectively known as DELLA proteins; a high level of GA activates the signaling pathway by triggering degradation of DELLA proteins thus inducing the expression of GA-regulated genes [34–36]. In *M. truncatula*, GA signaling negatively controls root cortical expansion; GA treatment or DELLA deletion reduces root diameter. Conversely, inhibiting GA signaling, either through inhibitors or via a dominant DELLA mutation (the resultant DELLA protein is non-degradable by GA), increases root diameter [33••]. *R. irregularis* induces thickening in *M. truncatula* roots by stimulating the expression of a GRAS transcription factor, Mycorrhiza-induced GRAS 1 (Mig1), within the arbusculated cortical cells [33••]. Mig1 then interacts with the *M. truncatula* DELLA protein, DELLA1, and interferes with the GA signaling [33••]. Cortical cell size decreases whereas the percentage of smaller and distorted arbuscules increases in roots upon *MIG1* down regulation [33••]. Such phenotypic defects associated with *MIG1* knockdown, can be suppressed by disrupting GA signaling via a constitutive-active DELLA allele [33••]. Together, these new findings demonstrate how *R. irregularis* intersects host GA signaling to modulate host cortical cell size in a way that favors arbuscule development during AM endosymbiosis.

Remarkably, the establishment of such symbiosis requires molecular communication between AM fungi and their hosts before physical contact, with the involvement of the phytohormone strigolactone as the important signaling moiety [1,37–39]. Secretion of strigolactone by host plants activates AM fungal development as well as the corresponding secretion of diffusible signals, which in turn activate the common symbiosis signaling pathway required for the initial colonization of the root epidermis [1,37–40]. A recent study on *R. irregularis–M. truncatula* symbiosis identified such diffusible fungal signals to be short-chain chitin oligomers (COs), in particular CO4 and CO5, induced by the strigolactone analogue GR24, with the secreted COs effectively inducing the common symbiosis signaling pathway in the host (Figure 2c) [14]. Chitin oligomers are components of the fungal cell wall, with the long-chain chitins recognized as pathogen-associated molecular patterns (PAMPs) by the host defense machinery [10,11]. Therefore, it is intriguing that short-chain chitin oligomers are deployed by AM fungi as a molecular communication tool with their host during symbiotic association. Moreover, fungal cell wall components are also suggested to be strong inducers of *MIG1* expression [33••]. It would be most interesting to assess