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REVIEW ARTICLE

The Evolution of Ethylene Signaling in Plant Chemical Ecology

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Abstract Ethylene is a key hormone in plant development, mediating plant responses to abiotic environmental stress, and interactions with attackers and mutualists. Here, we provide a synthesis of the role of ethylene in the context of plant ecology and evolution, and a prospectus for future research in this area. We focus on the regulatory function of ethylene in multi-organismal interactions. In general, plant interactions with different types of organisms lead to reduced or enhanced levels of ethylene. This in turn affects not only the plant's response to the interacting organism at hand, but also to other organisms in the community. These community-level effects become observable as enhanced or diminished relationships with future commensals, and systemic resistance or susceptibility to secondary attackers. Ongoing comparative genomic and phenotypic analyses continue to shed light on these interactions. These studies have revealed that plants and interacting organisms from separate kingdoms of life have independently evolved the ability to produce, perceive, and respond to ethylene. This signature of convergent evolution of ethylene signaling at the phenotypic level highlights the central role ethylene metabolism and signaling plays in plant interactions with microbes and animals.

Keywords Ethylene · Plant · Pathogen · Defense · Immunity · *Arabidopsis* · Tomato · Tobacco · *Pseudomonas* · *Botrytis* · Herbivore · Insect

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Introduction

Ethylene gas (C_2H_4) is studied mostly in the context of its role as a hormone and regulator of plant development and responses to biotic and abiotic stresses. Ethylene plays a central role in plant interactions with microbes and insects, which is exemplified by the fact that a variety of these organisms produce and perceive ethylene and use it as a signal. Furthermore, the origins of ethylene signaling are ancient and predate the evolution of the phytohormone jasmonic acid (JA), another key regulator of plant interactions with the environment. Ethylene's involvement in regulating this wide diversity of interactions has complicated the study of its mechanisms of action. Consequently, generalizations and predictions regarding the influence of ethylene on the outcome of multi-organismal interactions are difficult. Nonetheless, important general patterns do emerge, which we highlight below.

Aside from being produced in living cells, ethylene also is formed spontaneously in the environment under certain circumstances, and induces responses in a wide range of organisms in non-plant-based interactions spanning the diversity of life. For example, ethylene regulates cell aggregation and differentiation in the slime mold *Dictyostelium mucoroides* (Amagai and Maeda 1992), whereas it also can serve as an anaesthetic and hallucinogen in humans (Herb 1923). Remarkably, ethylene fumes released from a geological vent are speculated to have induced the trance-like state associated with the Pythia oracle of Delphi in the temple of Apollo in ancient Greece, which, according to myth, predicted future events (Spiller et al. 2002).

Here, we trace the evolutionary origins of biologically produced ethylene, and explore how the evolutionary context of ethylene production, perception, and signaling across diverse taxa relates to the interactions between plants and their biotic environment.

Evolutionary Origins of Ethylene and its Role in Biotic Interactions

Like cytokinin signaling, ethylene signaling is regulated by a two-component system co-opted from a prokaryotic common ancestor (Schaller et al. 2011). We provide an overview of the evolution of each compartment of ethylene signaling – biosynthesis, perception, and signal transduction – in plants, but also in the organisms with which plants interact. The most detailed understanding of ethylene biosynthesis and signaling in plants has been gained from studies on *Arabidopsis thaliana* (Arabidopsis), and we focus mostly on this species. Since the molecular mechanisms behind ethylene signaling have been reviewed extensively elsewhere (Bleecker 1999; Merchante et al. 2013; Wang et al. 2002; Yoo et al. 2009), we refer readers to these publications for more information on molecular and biochemical details.

Ethylene Biosynthesis Representatives from all major clades of photosynthetic organisms including cyanobacteria, algae, lichens, early-diverging land plants, gymnosperms, and angiosperms produce ethylene. Among other processes, ethylene signaling seems to be involved in the responses to environmental stress or symbiotic partners as a common denominator. Although the great majority of these species seem to produce ethylene, the genetic basis of ethylene biosynthesis varies among taxa.

In general, plants (including algae) produce ethylene from the amino acid methionine in two main steps (Plettner et al. 2005; Wang et al. 2002). In the first committed step, S-adenosylmethionine is converted into 1-aminocyclopropane-1-carboxylic acid (ACC), a reaction that is catalyzed by ACC synthase (ACS). During the next step, ethylene is synthesized from ACC by a second enzyme, the special 2-oxoglutarate ACC oxidase (ACO), leaving cyanide, water, and carbon dioxide as side products (Seo et al. 2011; Wang et al. 2002). The levels of ACS and ACO are upregulated by ethylene in a positive feedback loop known as the Yang cycle (Wang et al. 2002). In higher plants both the ACS and ACO enzymes are encoded by multi-gene families, whereas these genes are notably absent in the genomes of the early-diverging plant lineages *Physcomitrella patens* and *Selaginella moellendorffii* (Banks et al. 2011; Kawai et al. 2014; Rensing et al. 2008). Putative ACSs were identified only in the genome of *P. patens*, but this awaits confirmation (Rensing et al. 2008). The remaining lineages of vascular plants have evolved an intricate mechanism to finely regulate ethylene biosynthesis. Various ACSs and ACOs are expressed in a tissue-, developmental stage-, and environmental circumstance-specific manner (Barry et al. 1996; Tsuchisaka et al. 2009), and accumulation is further regulated at post-transcriptional and –translational levels (Merchante et al. 2013; Yoo et al. 2009).

Several plant lineages deviate from this general rule and produce ethylene independent of the ACC pathway. For example, in the aquatic angiosperm *Spirodela oligorrhiza* (Araceae), ethylene is synthesized via a distinct mechanism (Mattoo et al. 1986; Osborne et al. 1996). A lack of ACO activity also suggests that seed plants in the orders Ginkgoales and Cycadales use an ACC-independent synthesis route (Reynolds and John 2000). Since a functional ACC pathway has been found in several algal and lichen photobionts (both pro- and eukaryotes), active control over ethylene biosynthesis using this mechanism may have evolved early and subsequently been lost in some early-diverging land plant lineages (Blanc et al. 2010; John 1997; Ott et al. 2000; Plettner et al. 2005). Alternatively, the evolution of actively controlled ethylene biosynthesis could have involved lateral gene transfer.

Ethylene biosynthesis mostly has been studied in plants, but this trait is present in a wide range of bacteria and fungi (Hislop and Stahmann 1971; Ilag and Curtis 1968; Weingart and Völksch 1997; Weingart et al. 1999). Outside of plants, the presence of the ACC pathway has only rarely been observed (Jia et al. 1999). Exceptions are the slime mould *D. mucoroides* (Amagai and Maeda 1992), several lichen mycobionts (Ott et al. 2000; Ott and Zwoch 1992), and fungi in the genus *Penicillium* (Chalutz et al. 1977; Jia et al. 1999). Other fungi for which the ACC pathway is speculated to be present are from the genera *Saccharomyces* (Thomas and Spencer 1977), *Mucor* (Lynch 1974), and *Streptomyces* (Jia et al. 1999).

Three alternative ethylene biosynthesis routes have been characterized: 1) Methionine-based ethylene production can use α-keto-methylthiobutyric acid (KMBA), a transaminated methionine-derivative, as an intermediate instead of ACC. In this pathway, KMBA is then nonenzymatically oxidized to ethylene (Nagahama et al. 1994); 2) Ethylene is synthesized from 2-oxoglutarate by the ethylene-forming enzyme (EFE), which shows similarities to the higher plant ACOs and is a member of the Fe^{2+}/ascorbate oxidase superfamily. EFE needs the amino acids arginine or histidine as cofactors (Nagahama et al. 1994); 3) Ethylene is formed via peroxidation of lipids that are released after membrane damage induced by copper (Mattoo et al. 1986). The latter option is possibly used in *S. spirodela* and the non-seed plants (Mattoo et al. 1986; Osborne et al. 1996).

The KMBA pathway has been reported from *Escherichia coli* and other bacteria (Primrose and Dilworth 1976), but is also found in the fungus *Botrytis cinerea* (Chagué et al. 2002; Cristescu et al. 2002). The EFE biosynthesis route is seen in certain strains of *P. syringae* and *Ralstonia solanacearum*, and in the fungi *Fusarium oxysporum*, and *Penicillium*, *Phycomyces*, and *Streptomyces* spp. (Bignell et al. 2010; Chalutz et al. 1977; Hottiger and Boller 1991; Ott and Zwoch 1992; Weingart and Völksch 1997; Weingart et al. 1999). The *efe* gene in *Pseudomonas* and *Ralstonia* resides on a plasmid, which can be transferred laterally via conjugation (Nagahama et al. 1994; Watanabe et al. 1998; Zhao et al. 2005).

ACC Catabolism Plants use the enzyme ACC deaminase (ACD) to catabolize ACC and prevent ethylene formation, presumably to fine-tune the regulation of the ethylene pathway. In Arabidopsis, two copies of this enzyme have been characterized (McDonnell et al. 2009). As with ethylene biosynthesis, ACC catabolism is not restricted to plants, but is also found in bacteria. Most notably, the ACD-encoding gene *acdS* is present in many nitrogen-fixing bacteria and plant growth-promoting rhizobacteria (PGPR) including *Pseudomonas*, *Mesorhizobium* and *Rhizobium* spp. such as *P. fluorescens*, *P. putida*, *P. stutzeri*, and *M. loti* (Duan et al. 2013; Uchiumi et al. 2004; Yan et al. 2008). Like the *efe* gene for biosynthesis, ACD-encoding genes are also horizontally transferred among bacteria (Blaha et al. 2006; Hontzeas et al. 2005). Ethylene is at the heart of the establishment of mutualistic interactions between PGPR or endophytic fungi and plants (Camehl et al. 2010; Glick 2005). Bacterial ACC degradation likely functions to suppress ethylene-regulated plant immune responses to microbial mutualists in roots (Millet et al. 2010). However, some pathogenic strains of *Pseudomonas* and *Burkholderia* spp. seem to have co-opted ACD to dampen early host immune responses (Blaha et al. 2006).

In the case of the legume-rhizobia symbiosis, the exchange of multiple signaling molecules in subsequent rounds of communication, such as the bacterial Nod factor, activates nodule developmental signaling (Oldroyd 2013), which is under negative control by ethylene (Oldroyd et al. 2001). ACD prevents excessive ethylene formation and enhances nodulation (Ma et al. 2003). The fact that even non-host plants suppress local plant immunity in response to rhizobia shows the bacteria are targeting conserved root immune signaling mechanisms (Liang et al. 2013), of which ethylene is an integral part (Millet et al. 2010). For the plant, ethylene signaling is likely to be important to prevent “cheating” by the mutualistic microbes that could exploit the plant host (Kiers and Denison 2008). For example, ethylene-insensitive *Medicago truncatula* mutants become hyperinfected by symbiotic rhizobacteria (Penmetsa and Cook 1997), and bacteria that dampen ethylene signaling by secreting rhizobitoxine accrue fitness benefits by producing a storage lipid (poly-3-hydroxybutyrate) useful to them, but not their host (Ratcliff and Denison 2009).

ACC deaminase from PGPR and nitrogen-fixing bacteria not only helps to establish the mutualistic relationship between plant and microbe (Uchiumi et al. 2004), but also can influence interactions with third parties. Ethylene controls the morphology of crown galls induced by infection with *Agrobacterium tumefaciens*, thereby optimizing nutrient supply to the developing gall (Lee et al. 2009). ACD activity by PGPR decreases the development of crown galls induced by infection with *A. tumefaciens* (Hao et al. 2007), despite enhancing gene transfer from *A. tumefaciens* into plant cells (Nonaka et al. 2008a). In addition, an *A. tumefaciens* strain has been identified in which the acquisition of *acdS* rendered the pathogen avirulent (Hao et al. 2011).

Interestingly, in lichens, both the photobiont and the mycobiont use ethylene as a signaling molecule (Ott and Zwochj 1992; Ott et al. 2000). This may have parallels with the symbiosis between higher plants and mutualistic rhizobacteria.

Ethylene Perception The original plant ethylene receptor gene presumably was first transferred from the chloroplast genome, which is derived from an ancestral cyanobacterium (Bleecker 1999; Mount and Chang 2002; Rodriguez et al. 1999). In general, the basic ethylene receptor is a homodimer capable of binding ethylene. These homodimers may connect non-covalently into higher-order homomeric and heteromeric complexes (Gao et al. 2008). Such ethylene receptor clusters might be analogous to bacterial histidine kinase-linked chemoreceptor clusters (Baker and Stock 2007).

Ethylene binding to its receptors depends on a copper cofactor that is transported through RESPONSIVE TO ANTAGONIST1 (RAN1) (Rodriguez et al. 1999). This transporter is homologous to the mammalian Menkes/Wilson P-type ATPase copper transporter (Hirayama et al. 1999). RAN1 function is probably necessary for the formation and activity of all the ethylene receptors, of which there are five in Arabidopsis, divided in two clades: ETHYLENE RESPONSE1 (ETR1) and ETHYLENE RESPONSE SENSOR1 (ERS1) in the first, and ETR2, ERS2 and ETHYLENE INSENSITIVE4 (EIN4) in the second (Binder et al. 2010). In addition, seemingly only ETR1 relies on another protein (RTE1), which is highly conserved among eukaryotes, for proper functioning (Barry and Giovannoni 2006; Resnick et al. 2006). Since ethylene receptor function depends on copper made available through RAN1 and RTE1, the ethylene perception system in plants may have co-opted an ancient copper transport mechanism that protects the cell from the toxic effects of high copper concentrations. This idea is further supported by the fact that ethylene forms via lipid peroxidation after copper-induced damage to membranes (Mattoo et al. 1986).

In the moss *Physcomitrella patens*, seven putative ETR-like ethylene receptors have been identified (Ishida et al. 2010; Rensing et al. 2008), at least one of which has been found to bind ethylene as a substrate and to be needed for a full ethylene response (Yasumura et al. 2012). The genome of *Selaginella moellendorffii* on the other hand, seems to contain only the receptors of the first clade (Banks et al. 2011). This shows that the main ethylene perception machinery in plants was already present early on in land-plant evolution.

In non-photosynthesizing bacteria and fungi, ethylene is perceived differently. In *Pseudomonas* spp. ethylene perception seems to have been incorporated into a chemotaxis mechanism, and *P. aeruginosa*, *P. fluorescens* and *P. syringae* isolates show positive chemotaxis towards ethylene. Studies on *P. aeruginosa* isolate PAO1 have identified the ethylene chemoreceptor responsible: the methyl-accepting chemotaxis protein TlpQ (Kim et al. 2007).

In *P. syringae*, genes involved in chemotaxis are induced in epiphytic, but not apoplastic cells (Yu et al. 2013). However, the *P. syringae tlpQ* ortholog, encoded by the Psyr_2682 locus, was not induced *in planta*. Since *P. syringae* exhibits positive chemotaxis to host extracts (Cuppels 1988), the role of ethylene in this process warrants further examination. Together, these data suggest that *Pseudomonas* uses ethylene as a signal to localize plant hosts, although it has been reported that some strains may use ethylene as a carbon source (Kim 2006). In *A. tumefaciens*, ethylene suppresses the expression of virulence-associated genes over the course of infection, indicating that this bacterium also perceives ethylene albeit through an as yet unknown mechanism (Nonaka et al. 2008b).

In fungi, ethylene is perceived in several ways distinct from the plant and bacterial mechanisms. For example, the giant sporangiophore of the single-celled fungus *Phycomyces blakesleeanus* uses ethylene as an environmental cue for spatial orientation and shows an ethylene tropism (Campuzano et al. 1996). The perception of ethylene in this fungus relies on the blue light photoreceptor system (Campuzano et al. 1996), which is similar to the situation in plants, in which ethylene is necessary for the response to blue light (Pierik et al. 2004, 2006).

The fungus *Botrytis cinerea* perceives ethylene by a G-protein receptor, which activates fungal pathogenicity factors that enhance virulence in early stages of infection (Chagué et al. 2006). Interestingly, the ethylene-insensitive mutant *bcg1Δ* in the G-protein α subunit produces more ethylene than wild-type *B. cinerea*, analogous to the situation in plants where, for example, *etr1* ethylene-receptor mutants in wild and cultivated tobacco overproduce ethylene as well (Knoester et al. 1998; von Dahl et al. 2007). In another fungus, *Colletotrichum gloeosporioides*, ethylene promotes spore germination and subsequent appressorium formation (Flaishman and Kolattukudy 1994). These findings indicate that this fungus perceives ethylene, although its mechanism of perception remains unknown. Similarly, several metazoan species respond to and thus perceive ethylene, but again, the underlying mechanisms are unknown.

Studies of the marine sponge *Suberites domuncula* have provided more mechanistic insight into ethylene signaling in animals. Although an ethylene receptor gene has not been delineated, two ethylene-inducible genes have been identified indicating that this sponge perceives ethylene (Krasko et al. 1999). The first gene shares homology to plant ethylene- and stress-responsive genes, whereas the other encodes a putative $Ca^{2+/}$calmodulin-dependent protein kinase. The induction of the latter is related to the finding that in sponges, ethylene can induce a burst of cytosolic calcium (Custodio et al. 1998). The calcium burst generally is involved in activating downstream signaling during stress reponses. Ethylene is one of the major alkenes present in seawater, and is formed photochemically from dissolved organic matter. As such, ethylene could serve as a signal relaying information on the status of the surrounding seawater.

Ethylene Signaling Ethylene binding to plant receptors induces a signaling cascade that prevents proteasomal degradation of the central regulator EIN2 and downstream transcription factors EIN3 and EIN3-LIKE1 (EIL1). Degradation is regulated by the kinase CONSTITUTIVE TRIPLE RESPONSE1 (CTR1) and the F-box proteins EIN3 BINDING FACTOR1 (EBF1) or −2, and disrupting this process enhances EIN2, EIN3 and EIL1 stability (Merchante et al. 2013; Yoo et al. 2009). EBF1 and −2 in turn are regulated post-transcriptionally via the exoribonuclease EIN5, and post-translationally via proteasomal degradation (Merchante et al. 2013; Yoo et al. 2009). EIN2 is a membrane-bound protein, the N-terminus of which shows homology to members of the NRAMP metal transporter family, which includes transporters such as *Drosophila* Malvolio, mammalian DCT1, and yeast Smf1p (Alonso et al. 1999). This homology supports the hypothesis that the ethylene signaling machinery was co-opted from an ancient mechanism acting in metal ion metabolism.

Downstream of the positive regulators EIN3 and EIL1, transcription in response to ethylene is mediated further by members of several gene families, including MYB, NAC, WRKY, and ethylene response factor (ERF). The ERF transcription factor family consists of both positive and negative regulators of transcription in response to ethylene (McGrath et al. 2005), which allows another layer of fine-tuning a plant's ethylene response. In the genomes of the early-diverging land plants *Physcomitrella patens* and *Selaginella moellendorffii*, the presence of many signaling components has been confirmed. Both plants have genes encoding EBF1 and −2, EIN2, EIN3, EIL1, and ERF transcription factors (Banks et al. 2011; Ishida et al. 2010; Rensing et al. 2008), although the existence of *CTR1* in *P. patens* is less certain (Yasumura et al. 2012).

Central regulators of ethylene signaling are, thus, highly conserved among different plant species. Despite this observation, there still may be important variation in ethylene signaling within and between species. In an analysis of the evolutionary history of 27 defense genes in 96 accessions of Arabidopsis, the *ETR1* locus was identified as the best candidate for being a gene under transient balancing selection with the highest allelic divergence and a non-functional allele in one or two of the accessions (Bakker et al. 2008).

Furthermore, *EIN3* was found to likely have undergone a recent selective sweep. However, these findings were not confirmed in a more recent, independent study (Caldwell and Michelmore 2009), and more work will be required to resolve this discrepancy.

Potentially, more significant regulatory diversification may take place downstream, such as at the level of the ERF transcription factors, and their promoter binding sites. Comparison of ERF transcription factors between Arabidopsis and rice have revealed, however, that the major functional diversification has occurred already in an ancestral species (Nakano et al. 2006). Subsequently, divergent but still similar DNA-binding specificities have evolved resulting in distinct regulation of secondary metabolism by ERF transcription factors in various plant species (Shoji et al. 2013).

Ethylene is involved in regulating the biosynthesis of various defensive secondary metabolites. In Arabidopsis, ethylene regulates the production of camalexin, which is a major defense compound (Mao et al. 2011). Additionally, although not the topic of this review, cyanide that is formed as a by-product during ethylene production via the ACC biosynthetic route could play an important role in defense against various attackers (García et al. 2013; Seo et al. 2011; Stauber et al. 2012).

The mechanisms and role of ethylene in regulating the production of secondary metabolites is not restricted to plants, but also is found in fungi and other organisms. For example, plant host- or pathogen-derived ethylene induces a MAP kinase cascade in the fungus *Colletotrichum gloeosporioides* leading to cytokinesis and appressoria formation (Flaishman and Kolattukudy 1994; Kim et al. 2000). Additionally, ethylene inhibits aflatoxin biosynthesis in *Aspergillus parasiticus* grown on peanuts in a dose-dependent manner (Huang et al. 2009; Roze et al. 2004).

Summary of Ethylene Biosynthesis, Perception and Signaling Summarizing, mechanisms of ethylene biosynthesis, perception and signaling apparently have evolved at least three times independently in plants, fungi, and bacteria (Table 1). In plants, a progression towards increased sophistication in the regulation of plant metabolism by ethylene is clear (Fig. 1). However, the presence of the ACC biosynthetic route in certain algae and its absence in several gymnosperms obscure this picture. Future research should test whether the ACC biosynthetic route has been lost in many lineages of early-diverging land plants, or has been gained in certain algae, e.g., through lateral gene transfer.

Ethylene's Place in the Plant Immune Signaling Network

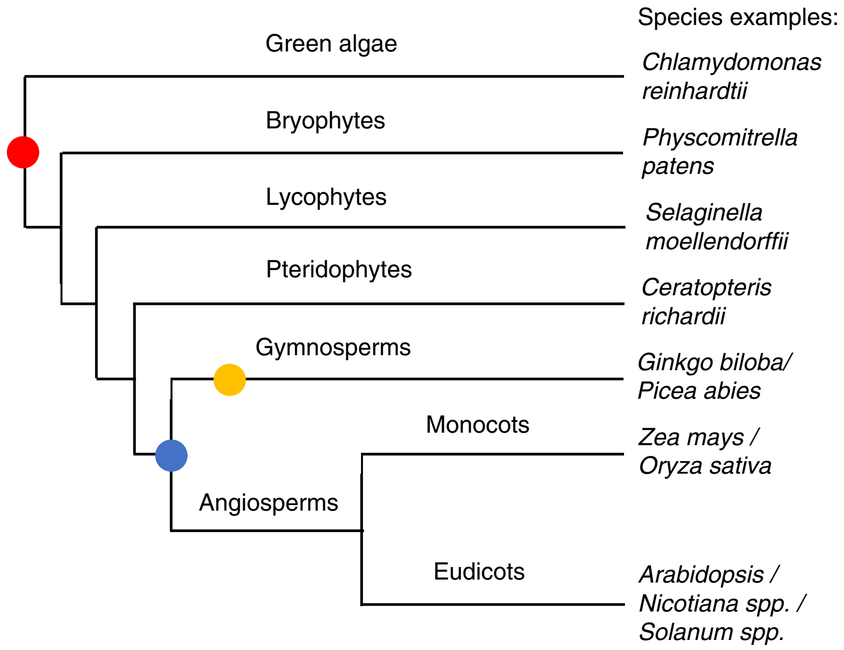
Plants perceive attack by natural enemies through at least two separate mechanisms (Jones and Dangl 2006). The first induces a general, relatively low-strength immune response, the second is induced more specifically, and leads to a more powerful response. These two mechanisms converge on the same downstream signaling network that tailors an appropriate immune response. The first mechanism is pattern-triggered immunity (PTI), in which plants sense the presence of conserved pathogen-, or damage-associated elicitors at the plasma membrane via leucine-rich repeat (LRR)-containing pattern-recognition receptors (PRRs). An example is FLS2, which is necessary for sensing a conserved epitope of the bacterial flagellar protein flagellin (Zipfel et al. 2004). In Arabidopsis, tomato, and other seed plants, ethylene signaling is induced early after pathogen perception, which depends on LRR co-receptors such as BOTRYTIS-INDUCED KINASE1 (BIK1) (Laluk et al. 2011). In Arabidopsis, ethylene is in turn necessary for the accumulation of FLS2 (Boutrot et al. 2010). Attackers use effectors to suppress PTI, and in the second layer of induced immunity, certain effectors or their activity can be recognized in specific, highly co-evolved plant-attacker contexts to spark a strong response that immunizes the plant against a broad range of attackers. This second layer has been labelled effector-triggered immunity (ETI), and often is accompanied by, but not reliant on, programmed cell death (PCD) to help restrict (hemi)biotrophic cellular pathogens, insects, nematodes, and viruses. Necrotrophic fungal pathogens, on the other hand, can benefit from the accompanying PCD and sometimes deliberately induce ETI to enhance access to nutrients (Lorang et al. 2012).

Experimental work complemented by recent computational approaches has shown that ethylene signaling forms an integral part of the plant immune signaling network (Kim et al. 2014; Pieterse et al. 2012; Robert-Seilaniantz et al. 2011; Tsuda et al. 2009; van Verk et al. 2011). When for simplicity the plant immune signaling network is visualized as having four sectors, the ethylene, JA, PHYTOALEXIN-DEFICIENT4 (PAD4), and salicylic acid (SA) signaling sectors (as proposed by Fumiaki Katagiri and co-workers) ethylene is a central contributor to network robustness controlling PTI against (hemi)biotrophic pathogens (Kim et al. 2014; Tsuda et al. 2009). The robustness-enhancing role of ethylene is mediated through its unique function as an inhibitor of the other three sectors (Fig. 2), which has been confirmed experimentally (Chen et al. 2009; Kim et al. 2014; Lorenzo et al. 2003, 2004; Tsuda et al. 2009). Other than synergizing with JA in the JA/ethylene branch of JA signaling, ethylene generally represses oxylipin-induced signaling regardless of the length of the oxylipin branch (Groen et al. 2013; López et al. 2011). Ethylene can also obviate the need for the central regulator of SA signaling NON-EXPRESSOR OF PATHOGENESIS-RELATED PROTEINS1 (NPR1) in crosstalk between SA and JA (Leon-Reyes et al. 2009), and make JA signaling insensitive to future suppression by SA (Leon-Reyes et al. 2010). Furthermore, ethylene-mediated

Table 1 Diversity of ethylene biosynthesis, perception and signaling across species

	Cyanobacteria	Early-diverging plants	Seed plants	Non-photosynthesizing bacteria	Fungi	Ecdysozoa	Other eumetazoa and porifera
Ethylene biosynthesis	Lipid peroxidation	Lipid peroxidation	ACC (lost in several gymnosperms)	EFE (ACC-like) KMBA	EFE (ACC-like) KMBA	Lipid peroxidation	Lipid peroxidation
ACC catabolism			ACD	acdS			
Ethylene perception	Ancestral ET receptor	Clade 1 ET receptors	Clade 1 and 2 ET receptors RTE1 RAN1	tlpQ	Blue light photoreceptor G-protein	RTE1 homolog RAN1 homolog	RTE1 homolog RAN1 homolog
Ethylene signaling components		MAP kinase (CTR1, MPKs) EIN2 EIN3/EIL1 ERF	MAP kinase (CTR1, MPKs) NRAMP (EIN2) EIN3/EIL1 ERF		MAP kinase	EIN2 homolog	EIN2 homolog
Ethylene-regulated responses	Chemotaxis, stress	Growth, development, stress, defense	Growth, development, stress, defense	Chemotaxis, pathogenesis	Growth, development, pathogenesis	Pheromone production	Calcium signaling
Oxylipin/JA and SA signaling	Oxylipins	Oxylipins, SA	Oxylipins, JA, SA (JA signaling lost in several gymnosperms)		Oxylipins	Oxylipins	Oxylipins
Species examples	*Synechocystis* strain 6803	*Chlamydomonas reinhardtii Physcomitrella patens Selaginella moellendorffii*	*Arabidopsis Nicotiana* spp. *Oryza sativa Solanum* spp.	*Pseudomonas* spp. *Ralstonia solanacearum*	*Botrytis cinerea Colletotrichum gloeosporioides Phycomyces blakesleeanus*	*Caenorhabditis elegans Drosophila melanogaster*	*Homo sapiens Mus musculus Suberites domuncula*

Fig. 1 Phylogeny of green plants showing putative ancestral states for key aspects of ethylene signaling in relation to jasmonic acid (*JA*) and salicylic acid (*SA*) signaling. Diagram adapted from Thaler et al. (2012). The red, blue, and yellow dots refer to the first occurrence of ethylene signaling, the gain of active control of ethylene biosynthesis via ACC oxidase and first evidence for SA/JA antagonism, and the loss of ACC oxidase in some lineages, respectively. Branch lengths do not convey additional information

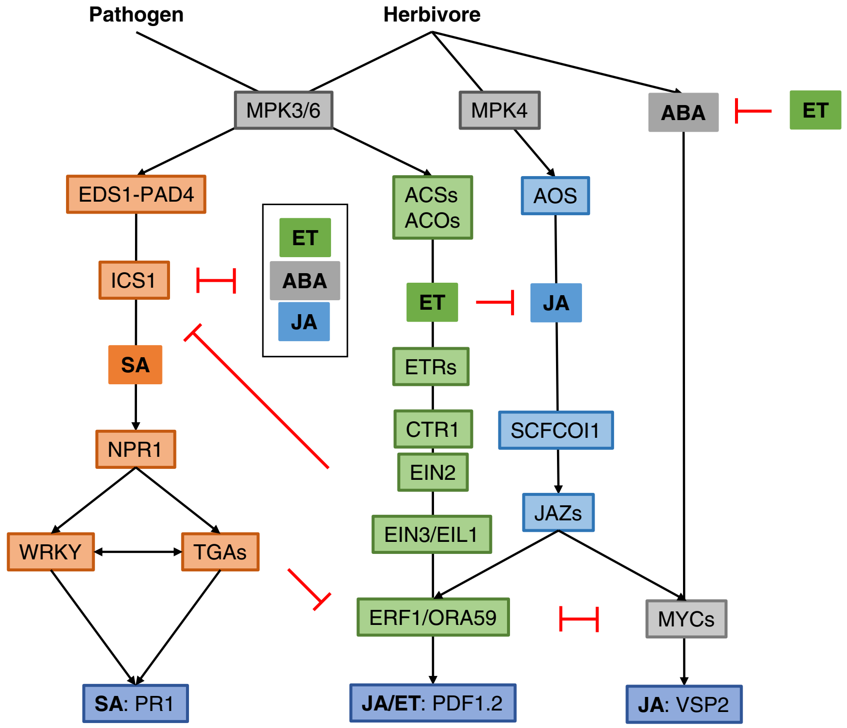


signaling via EIN5 seems to negatively regulate anti-viral RNA silencing (Gy et al. 2007), but not anti-insect defenses (Dong et al. 2004).

In response to necrotrophic pathogens, the role of ethylene seems to be different. Although ethylene is still an inhibitor of the MYC transcription factor-regulated branch of JA signaling (Lorenzo et al. 2004), as alluded to earlier, it synergizes with JA in regulating defense via the ERF transcription factor-regulated JA/ethylene branch (Lorenzo et al. 2003). These branches behave in a mutually antagonistic fashion (Lorenzo et al. 2004). JA/ethylene-mediated signaling regulate enhanced levels of defensive secondary metabolites, such as camalexin in Arabidopsis, and bring about changes in cell-wall architecture, which can severely hamper pathogen infectiveness (Knoester et al. 1998; Lloyd et al. 2011; Lorenzo et al. 2003; Mao et al. 2011; Thomma et al. 1999).

However, ethylene plays a dual role in in immune signaling. During ETI, ethylene shows compensatory relationships

Fig. 2 Schematic representation of plant immune signaling. The light blue squares at the bottom provide examples of marker genes, expression of which is commonly used to assess hormone signaling activity. Salicylic acid (*SA*) (orange)-, jasmonic acid (*JA*) (blue)-, ethylene (green)-, and abscisic acid (*ABA*) (purple)-dependent signaling are indicated. The square surrounding ABA-, JA-, and ethylene-dependent signaling indicates generally antagonistic interactions between signaling via these hormones and SA signaling. The black arrows indicate positive effects, and red inhibition lines represent negative effects. See text for details of individual genes in the signaling sectors. Diagram adapted from Pieterse et al. (2012)



in relation to the JA-, PAD4-, and SA-signaling sectors, which could explain the effectiveness of ETI and the difficulty for pathogens to perturb it (Tsuda et al. 2009). During ETI, typically a biphasic burst in ethylene production is observed. A first peak in ethylene production appears 1–4 h after the onset of infection, which is followed by a second, larger peak 6 h after the start (Mur et al. 2008). The occurrence of this second peak has been primed by the first and is followed by the deployment of PCD, the synthesis of secondary metabolites, and other defensive mechanisms that should restrict the growth of most biotrophic pathogens and viruses, unless the response is trailing the infection front (Jones and Dangl 2006; Mur et al. 2008; Takahashi et al. 2002). Mechanistically, the biphasic response in immune signaling may bear similarities to the biphasic response described for ethylene in plant growth, where low levels of ethylene have a positive effect on growth and high levels a negative effect (Pierik et al. 2006).

To complicate matters, ethylene signaling may actually aid attackers in some compatible interactions, especially hemibiotrophic pathogens. Many virulent hemibiotrophic pathogens either produce ethylene themselves or produce ethylene-inducing effectors such as the *Pseudomonas* spp. phytotoxin coronatine. This brings about a delayed second peak in ethylene production that enhances plant susceptibility to these pathogens and allows them to enter the necrotrophic phase of their pathogenesis cycle, which increases nutrient acquisition from senescing tissue (Hislop and Stahmann 1971; Huang et al. 2005; Kenyon and Turner 1992; Wi et al. 2012). For example, ethylene produced by the hemibiotrophic pathogen *Ralstonia solanacearum* modulates the expression of host-associated genes (Valls et al. 2006). Furthermore, delayed symptom development has been observed in *ein2* mutant Arabidopsis, indicating that pathogen-produced ethylene contributes to virulence (Hirsch et al. 2002). The issue of why ethylene is a defense activator against necrotrophic pathogens, but not against hemibiotrophic pathogens in the necrotrophic phase of their infection cycle has not yet been resolved.

Ethylene not only regulates local, but also systemic immune responses. As a gaseous hormone, it can overcome vascular constraints (Frost et al. 2007). This may be especially important in trees, where vascular signaling may be meters in distance but volatile signaling only centimeters. One of the systemic immune signaling mechanisms regulated by ethylene is induced systemic resistance (ISR), which is typically initiated in the roots (Pieterse et al. 1998). Both fungal (e.g., *Trichoderma* spp.) and bacterial (e.g., *Pseudomonas fluorescens* strains) microbes can induce ISR against a broad range of secondary attacks. Induced systemic resistance (ISR) induced by different microbes converges on the same signaling mechanism involving ethylene, JA, the transcription factor MYB72, and NPR1 (Korolev et al. 2008; Pieterse et al. 1998; Segarra et al. 2009), which is priming enhanced ethylene production that could strengthen early immunity upon secondary attacks (Hase et al. 2003).

Several additional systemic immune signaling mechanisms have thus far been characterized in leaves. In plant interactions with necrotrophic pathogens, the lipase-like protein GLIP1 is responsible for the productions of a systemic signal that immunizes distal tissues to secondary infection in an ethylene-dependent manner (Kim et al. 2013). Ethylene also plays an important role in local and systemic wound signaling, although its mechanism of signaling differs among species (León et al. 2001).

One important systemic, broad-spectrum immune response that ethylene does not always seem to be involved in is systemic acquired resistance (SAR) (Pieterse et al. 2012; Robert-Seilaniantz et al. 2011). After the initiation of an incompatible interaction with tobacco mosaic virus (TMV) in tobacco the establishment of SAR was partially dependent on ethylene (Verberne et al. 2003). However, this seemed not to be the case in Arabidopsis in experiments using an incompatible interaction with *P. syringae*, where ethylene signaling seemed to be redundant for effective SAR (Lawton et al. 1994).

Early photosynthesizing lineages already possessed an ethylene signaling system (Banks et al. 2011; Ponce de León and Montesano 2013; Rensing et al. 2008), as well as the machinery for several other stress-responsive plant hormone signaling mechanisms, such as oxylipin and SA signaling (Ponce de León et al. 2012; Scholz et al. 2012). These findings mean that signaling by ethylene and these other hormones likely predate the evolution of JA signaling, and thus the origins of the canonical JA-SA backbone of immune signaling (Fig. 1) (Ponce de León et al. 2012; Ponce de León and Montesano 2013; Scholz et al. 2012; Stumpe et al. 2010; Thaler et al. 2012). Therefore, the evolution of immune signaling by JA has to be seen in relation to the presence of signaling by these other hormones (Robert-Seilaniantz et al. 2011). Interestingly, in the early-diverging plants that do not produce JA, and in the gymnosperms that do not show the widespread antagonistic signaling between JA and SA, active control of ethylene production through the ACC biosynthetic is absent (Banks et al. 2011; John 1997; Rensing et al. 2008; Reynolds and John 2000; Stumpe et al. 2010; Thaler et al. 2012). More research is needed to determine whether this is a mere correlation, or whether causal mechanisms in one direction or the other are at play.

Because several lineages of early-diverging plants are non-vascular, the gaseous hormone ethylene would make a useful systemic signal. Very few studies have been conducted to elucidate immune signaling in early-diverging plants, and the role of ethylene in the immune systems of non-vascular plants such as the moss *P. patens* has not been clearly defined (Ponce de León and Montesano 2013). However, the fact that *P. patens* treatment with the ethylene precursor ACC induces the expression of the homologues of some genes involved in defense in angiosperm plants (Ponce de León and Montesano 2013) suggests that ethylene participates in immune signaling in non-vascular land plants as well. Furthermore, ethylene could still have had the robustness-enhancing effect on plant immune signaling in early-diverging plant lineages as in angiosperms, since it has a suppressive regulatory effect on signaling by SA and oxylipins (Chen et al. 2009; Groen et al. 2013; Kim et al. 2014; López et al. 2011; Tsuda et al. 2009).

Summary of Ethylene-Mediated Immune Signaling The colonization of land by early plants seems to have been accompanied by the evolution of an increasingly complex, interwoven network of plant immune signaling. For example, JA immune signaling may have evolved partially as a result of never-before experienced selection pressures by insects and novel fungal pathogens, and thus may have been embedded in an existing immune signaling network. In this ancestral network, ethylene likely played a role similar to its current central role. The ancient origin of the plant immune signaling network means that it has been an important factor in the co-evolutionary arms race between plants and their attackers for millions of years. Attackers must suppress pattern-triggered immunity (PTI) and effector-triggered immunity (ETI) by using effectors or by producing plant hormones or mimics thereof themselves to bring about “pathological hormone imbalances” (Robert-Seilaniantz et al. 2007). Several of these manipulating activities by plant attackers involve ethylene signaling, examples of which will be given below.

Both Parties may use Ethylene Signaling in Plant-Attacker Interactions

The role of ethylene in plant-attacker interactions has been reviewed elsewhere (Adie et al. 2007; Baldwin et al. 2006; Broekaert et al. 2006; von Dahl and Baldwin 2007; van der Ent and Pieterse 2012; van Loon et al. 2006), and below we integrate this body of knowledge with the available data on ethylene biosynthesis, perception, and signaling in the organisms that interact with plants.

Plant-Pathogen Interactions Ethylene plays a central role in regulating defense responses such as phytoalexin production and callose deposition both in the roots and in the shoots (Clay et al. 2009; Li et al. 2012; Mao et al. 2011; Millet et al. 2010). Because ethylene signaling is so conserved among plants, it is not surprising that numerous pathogen effectors have converged on targeting ethylene signaling to subvert plant immunity. Furhermore, pathogen effectors tend to target signaling hubs, and ethylene signaling is highly interconnected with these. Plants guard these high-value signaling hubs by using nucleotide binding site (NB)-LRR proteins that detect signs of pathogen subversion and activate ETI. As a consequence, both the pathogen effectors and the plant targets upon which they converge evolve faster than proteins not involved in the host-pathogen interactions, and they show the hallmarks of an evolutionary arms race (McCann et al. 2012; Mukherjee et al. 2013; Mukhtar et al. 2011; Murray et al. 2013).

Independently evolved effectors of geminiviruses (C2) and two hemibiotrophic plant pathogens, *P. syringae* and *Hyaloperonospora arabidopsidis* (29 distinct effectors), converge on targeting the plants 26S proteasome component CSN5a (Lozano-Durán et al. 2011; Mukhtar et al. 2011). Whereas negative regulators of signaling are targeted for degradation by the proteasome in signaling by several hormones (e.g., auxins, gibberellins, JA), in ethylene signalling, the positive regulator EIN2, and repressors of the negative regulators EBF1 and −2 are targeted (Merchante et al. 2013; Yoo et al. 2009). Thus, when the proteasome is disrupted by pathogen effectors, this will enhance ethylene signaling (Lozano-Durán et al. 2011). Another class of independently evolved virulence factors in viruses and hemibiotrophic plant pathogens are suppressors of RNA silencing. Several silencing suppressors cause enhanced ethylene signaling, such as *P. syringae* avrPto and avrPtoB and geminivirus C2 (Cohn and Martin 2005; Lozano-Durán et al. 2011; Navarro et al. 2008). The *P. syringae* effectors are of critical importance for successful infection (Kvitko et al. 2009). Several viral silencing suppressors even seem to have coopted ethylene signaling, as their function relies on the ethylene-inducible plant transcription factor RAV2 (Endres et al. 2010). However, a direct relationship between silencing suppression and the positive consequences of some of these effectors for ethylene signaling has not always been determined (Cohn and Martin 2005; Navarro et al. 2008). In general, RNA silencing mutants show enhanced ethylene signaling upon attack, as has been found for 26S proteasome mutants (Kettles et al. 2013; Pandey et al. 2008). The ensuing “pathological ethylene imbalance” could contribute to symptom formation and pathogen proliferation (Bent et al. 1992; Chen et al. 2013; Love et al. 2007; Lund et al. 1998; Robert-Seilaniantz et al. 2007; Weingart et al. 2001; Wi et al. 2012). For viruses and bacteria, there also could be effects on pathogen transmission by insect vectors, since the 26S proteasome and RNA silencing systems regulate anti-insect defenses, for example, via JA and ethylene signaling (Kettles et al. 2013; Westwood et al. 2013, 2014).

With respect to RNA silencing, the necrotrophic pathogen *B. cinerea*, to which ethylene induces resistance (Thomma et al. 1999), has no known silencing suppressors. This seems biologically realistic, because suppression of silencing would induce ethylene signaling. Instead, *B. cinerea* injects small RNAs into host cells that are coopted by the plant’s silencing machinery and are inadvertently used by the plant to suppress its own defenses (Weiberg et al. 2013). As alluded to earlier, it is therefore all the more surprising that *B. cinerea* does have the capacity to produce ethylene. However, it does not seem to produce ethylene in amounts that would influence plant defenses during infection (Chagué et al. 2002, 2006; Cristescu et al. 2002). To enhance infection *B. cinerea* produces abscisic acid (ABA), using enzymes encoded in a cytochrome P450-encoding gene cluster, which suppresses plant ethylene signaling (Anderson et al. 2004; Siewers et al. 2006). The pathogen likely only uses ethylene to regulate fungal developmental processes such as hyphal growth (Cristescu et al. 2002). Similar roles for ethylene signaling in fungal development have been found for other necrotrophic plant-pathogenic fungi, such as *Bipolaris sorokiana* (the anamorph of *Cochliobolus sativus*), *Colletotrichum musae*, *Fusarium oxysporum*, and *Verticillium dahliae* (Coleman and Hodges 1990; Daundasekera et al. 2003; Ioannou et al. 1977; Jones and Woltz 1969).

In summary, both hemibiotrophic and necrotrophic plants pathogens have the potential to produce ethylene themselves. However, in early infection stages, they do not seem to produce ethylene, since ethylene promotes early defense responses such as callose deposition (Clay et al. 2009; Millet et al. 2010). In later infection stages, hemibiotrohic pathogens may produce ethylene or deliver effectors or phytotoxins that manipulate the plant to produce ethylene to enter the necrotrophic stage of infection (Bent et al. 1992; Chen et al. 2013; Lund et al. 1998; Weingart et al. 2001; Wi et al. 2012). Again, a major unresolved issue is why ethylene is a defense activator against necrotrophic pathogens, but not against hemibiotrophic pathogens in the necrotrophic phase of their infection cycle.

Remarkably, comparative genomic studies of hemibiotrophic *P. syringae* strains have shown that even in these pathogens, ethylene production is not a widespread trait (Zhao et al. 2005). They have revealed that, except for a few “core” virulence factors, most factors are limited in distribution among pathovars of *P. syringae*, presumably due to a role in host specificity (Baltrus et al. 2011; Dudnik and Dudler 2014; Kvitko et al. 2009; Qi et al. 2011; Zhao et al. 2005). Indeed, the ethylene biosynthetic gene *efe* is not detected in many pathovars of *P. syringae*: *cannabina*, *glycinea*, *phaseolicola*, *pisi*, and *sesame* (Baltrus et al. 2011; Dudnik and Dudler 2014; Qi et al. 2011; Zhao et al. 2005). Interestingly, when present, the *efe* gene was associated with the presence of the type III effector avrRps4 (Baltrus et al. 2011). The pathovars containing both virulence factors are legume-specialized pathovars (Baltrus et al. 2011). AvrRps4 targets an unknown process in the chloroplast that suppresses host immunity (Li et al. 2014), and may synergize with ethylene production to contribute to virulence (Weingart et al. 2001). Indeed, ethylene-insensitive mutants of soybean are more susceptible to *P. syringae* (Hoffman et al. 1999). Similarly, ACD likely is involved in host specificity (Loper et al. 2012). Because some hemibiotrophic bacterial pathogens have both the capacity to synthesize ethylene and degrade ACC, it remains unclear whether these produce ACD to dampen early immunity and subsequently produce ethylene when the infection reaches the necrotrophic phase. An alternative is that these bacteria use ACD to metabolize ACC as a source of N (Penrose and Glick 2003).

Plant-Nematode Interactions Although lateral gene transfer regularly occurs between plant-parasitic nematodes and their hosts (Whiteman and Gloss 2010), none of these genes identified thus far have been involved directly in ethylene signaling (Danchin et al. 2010), nor have they been observed among nematode-associated bacteria (Vicente et al. 2012). For example, in a study on the pinewood nematode *Bursaphelenchus xylophilus*, bacteria producing ACD were expected to be associated with the nematodes, as the bacteria enhance root growth and could enhance nematode performance. Instead, these bacteria were absent (Vicente et al. 2012), and the likely explanation is that if present, these ACD-producing bacteria would enhance pine resistance to nematodes (Nascimento et al. 2013). The results are in line with findings with representatives of another clade of nematodes, the root-knot nematodes (*Meloidogyne* spp.). In tomato and Arabidopsis, ethylene induces resistance to root-knot nematode infection (Fudali et al. 2013; Mantelin et al. 2013). On the other hand, ethylene seems to enhance susceptibility to the sugar beet cyst nematode *Heterodera schachtii* when infecting Arabidopsis (Wubben et al. 2001).

Plant-Insect Interactions Analogous to plant-nematode and plant-(hemi)biotrophic pathogen interactions, ethylene has variable effects on the outcomes of plant-insect interactions. Ethylene mediates susceptibility to chewing herbivores in local, damaged tissue in Arabidopsis, maize, and native tobacco (Bodenhausen and Reymond 2007; von Dahl et al. 2007; Harfouche et al. 2006; Kahl et al. 2000; Verhage et al. 2011), but in tomato seems to regulate resistance (Abuqamar et al. 2008). However, ethylene mediates susceptibility in systemic tissue in tomato as in Arabidopsis (Groen et al. 2013; Tian et al. 2014). These findings are in line with the fact that ethylene suppresses signaling by JA, oxylipins and ABA, which also are involved in local and systemic resistance to chewing herbivores (Groen et al. 2013; Vos et al. 2013).

On the contrary, ethylene mediates resistance to aphid attack in Arabidopsis (Kettles et al. 2013). Again, tomato is the exception, and ethylene regulates susceptibility to aphid attack during compatible interactions (Mantelin et al. 2009). In Arabidopsis, however, the resistance-inducing role of ethylene to aphids is sometimes not apparent (Mewis et al. 2005). One hypothesis to explain this is the relative dependency of an effective defense response on callose deposition. In

Arabidopsis, ethylene has an important role in attack-induced callose deposition (Clay et al. 2009). Callose deposition can be an effective defense mechanism against phloem-feeders (Lü et al. 2013). In the regulation of callose deposition in Arabidopsis, ethylene signals synergistically with breakdown products of 4-methoxy-indol-3-ylmethylglucosinolate (Clay et al. 2009). However, these breakdown products themselves have a defensive role against phloem feeders (de Vos and Jander 2009; Westwood et al. 2013), and this could obscure the positive role ethylene has in mediating defense against aphids. Callose deposition also has the potential to explain another discrepancy, which is the positive role of ethylene signaling in mediating resistance against *Plutella xylostella* in Arabidopsis (Lü et al. 2013). First instar larvae of the specialist chewing herbivore *P. xylostella* are leaf-miners, and callose deposition can form an important barrier to first-instar leaf-miners, not only of *P. xylostella*, but also those of the dipteran herbivore *Scaptomyza flava* and other species (Lü et al. 2013; Whiteman et al. 2011; Groen and Whiteman, personal observations).

Although ethylene suppresses direct defenses against generalist chewing herbivores in a wide range of plant species, it does not interfere with the volatile-mediated attraction of parasitoids and predators as indirect defenses (Kahl et al. 2000), and even has a positive effect on volatile emissions (Ruther and Kleier 2005). In addition, the induction of ethylene signaling upon attack may be a mechanism for the plant to reduce the fitness costs associated with a strong immune response (Voelckel et al. 2001).

Other than regulating resistance, ethylene also has the capacity to influence insect behavior directly. A search of the literature and the pheromone database PheroBase (www.pherobase.com) revealed three plant-feeding insects that respond to ethylene directly, albeit via different mechanisms. One mechanism is that ethylene is used as a cue to activate reproductive behaviors in the corn earworm *Helicoverpa zea* (Lepidoptera, Noctuidae) (Raina et al. 1992). Using ethylene as a signal ensures that female *H. zea* wait until a suitable host plant has been found to produce and release sex pheromone (Raina et al. 1992). In a different mechanism, ethylene functions as an attractant to larvae of the Western corn rootworm *Diabrotica virgifera virgifera* (Coleoptera, Chrysomelidae) (Robert et al. 2012), whereas adults of a second beetle species, the olive bark beetle *Phloeotribus scarabaeoides* (Coleoptera, Scolytidae), are attracted to olive trees via foliar ethylene emissions (González et al. 1994; González and Campos 1996). Because ethylene has a critical regulatory role in fruit ripening, there is certainly potential for frugivores, and rotting fruit-inhabiting, microbe-feeding insects, such as *Drosophila melanogaster* (Diptera, Drosophilidae), or their predators or parasitoid wasps, to use ethylene as a cue to find larval substrates or hosts.

In several examples from the literature, ethylene is a hypothetical oviposition cue in *D. melanogaster* (Fluegel 1981); *D. melanogaster* larvae are speculated to respond to ethylene produced by fungal competitors (Rohlfs 2005); and in the Queensland fruit fly *Dacus tryoni* (Diptera, Tephritidae), excess ethylene has been proposed to contribute to repellence of females by volatiles emitted from infested fruit (Fitt 1984). Indeed, although *D. tryoni* adults were highly attracted to an ethylene-containing mixture of volatiles, ethylene did not seem to be responsible for this attractiveness (Morton and Bateman 1981). Despite these hypotheses, the behavioral responses of insects to ethylene remain obscure. The observation of behavioral responses to ethylene in two insect orders, Coleoptera and Lepidoptera, suggests that the ethylene response could either be evolutionary conserved, or it has evolved multiple times independently, and merits further study.

Community Perspective

Ethylene is used as a signal by many organisms that interact with plants, and it could have an important role in shaping a wide range of ecological interactions. Since plants under attack have the potential to relay an ethylene signal to neighboring plants (Arimura et al. 2002; Baldwin et al. 2006), ethylene could mediate community-wide interactions. However, here, we limit the discussion to the microbial and insect community of an individual plant, and point out a few interesting observations. We then narrow this further by focusing on interactions that involve *Pseudomonas* spp. bacteria, since these often clearly alter ethylene signaling and are so commonly associated with plants and herbivores (Humphrey et al. 2014).

Recent work on leaf microbiomes (phyllosphere microbial communities) has indicated that pseudomonads are commonly found in leaves of Brassicaceae, such as Arabidopsis (Bodenhausen et al. 2013), and *Cardamine cordifolia* (Humphrey et al. 2014). Laboratory experiments have revealed that ethylene signaling-inducing *P. syringae* induces systemic induced susceptibility (SIS) to secondary attack by conspecifics and chewing herbivores (Cui et al. 2005; Groen et al. 2013). The latter results have been replicated in the field on *C. cordifolia* (Humphrey et al. 2014), although in the field, a definitive role for ethylene remains to be confirmed. The field study with *C. cordifolia* further revealed interesting associations between bacteria and insects (Humphrey et al. 2014). In particular, it revealed positive associations between *P. syringae* infections in leaves and leaf-miner (*Scaptomyza nigrita*) abundance and negative associations between *P. fluorescens* infections in leaves and leaf-miner abundance.

Pseudomonads also form an integral part of the root microbiome (Bulgarelli et al. 2013), and can make important contributions to the disease-suppressive characteristics of the microbiome (Mendes et al. 2011). Furthermore, work on the wild barley *Hordeum spontaneum* in Israel's "Evolution Canyon" showed that the rhizosphere bacterial community of plants on stressful south-facing slopes produced more ACD rendering the plants there more stress tolerant (Timmusk et al. 2011). Enhanced drought tolerance is correlated with decreased ethylene and increased ABA signaling (Belimov et al. 2009). Lastly, ethylene-producing *Pseudomonas* spp. could stimulate inadvertent germination of parasitic plants in the genus *Striga* (Berner et al. 1999), thereby protecting surrounding plants from being parasitized.

These examples highlight just a few of the instances in which ethylene is shaping plant-attacker interactions, and conceptually similar mechanisms can be found in many other interactions between plants and their environment.

Conclusions

We can conclude that ethylene is a central regulator in the plant immune signaling network, and has likely played this role since the origin of land plants. The finding that organisms as diverse as bacteria, fungi, insects, sponges, and mammals can produce and/or respond to ethylene points to ancient origins of central components in ethylene signaling. Additionally, it highlights the important role ethylene could have in shaping interactions not only between plants and their environment, but even between non-photosynthesizing organisms. Elucidating the evolutionary history of ethylene signaling and its mechanistic role in shaping these numerous interactions will provide a scientific treasure trove that perhaps even the oracle of Delphi could not have foreseen.

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