Necrotrophic Exploitation and Subversion of Plant Defense: A Lifestyle or Just a Phase, and Implications in Breeding Resistance

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ABSTRACT

Breeding disease-resistant plants is a critical, environmentally friendly component of any strategy to sustainably feed and clothe the 9.8 billion people expected to live on Earth by 2050. Here, I review current literature detailing plant defense responses as they relate to diverse biological outcomes; disease resistance, susceptibility, and establishment of mutualistic plant–microbial relationships. Of particular interest is the degree to which these outcomes are a function of plant-associated microorganisms' lifestyles; biotrophic, hemibiotrophic, necrotrophic, or mutualistic. For the sake of brevity, necrotrophic pathogens and the necrotrophic phase of pathogenicity are emphasized in this review, with special attention given to the host-specific pathogens that exploit defense. Defense responses related to generalist necrotrophs and mutualists are discussed in the context of excellent reviews by others. In addition, host evolutionary trade-offs of disease resistance with other desirable traits are considered in the context of breeding for durable disease resistance.

Coevolution of plants and microbes likely accompanied the migration of plants onto land (de Vries and Archibald 2018; Gao et al. 2018). The earliest fossil evidence of land plant–microbial collusion dates to back to > 400 million years ago (Delaux et al. 2015; Upson et al. 2018). Over the millennia, selection pressure from microbial associates has fostered a suite of plant defense mechanisms that keep pathogens at bay but permit establishment of beneficial symbionts (Genre and Russo 2016; Plett and Martin 2018; Ponce de León and Montesano 2017; Su et al. 2018). Unlike animals that physically remove themselves from danger, plants are largely immobile and, instead, possess an array of secondary metabolites and preformed antimicrobial compounds that aid in warding off would-be pathogens. However, like animals, plants also mount active defense mechanisms termed pathogen-associated molecular pattern (PAMP)-triggered-immunity (PTI) and effector-triggered immunity (ETI) (Jones and Dangl 2006; Jones et al. 2016; Saijo et al. 2018). Here, I begin by describing key components of these active defense responses (ETI and PTI) and the lifestyles of the plant-associated microbes they target. I then introduce necrotrophic pathogens and (i) comprehensively review host-specific necrotrophs that exploit plant defense responses, (ii)

discuss the paucity of ETI against necrotrophic pathogens, (iii) summarize virulence mechanisms and host responses to generalist necrotrophs, and, finally, (iv) consider options for breeding or engineering of durable disease resistance effective against both biotrophic and necrotrophic pathogens.

PTI/ETI. PTI, a first line of defense against microbial invasion of hosts and nonhosts, is initiated by pathogen-recognition receptors (PRRs) that detect common microbial signatures, collectively called microbe-associated-molecular patterns (MAMPs) or PAMPs (Boutrot and Zipfel 2017; Saijo et al. 2018; Tang et al. 2017). Common MAMPs include bacterial flagella and lipopolysaccharides, fungal cell wall components such as chitin and galacturonic acids, and viral double-stranded ribonucleic acids (dsRNAs). Akin to MAMPs, damage-associated molecular patterns (DAMPs) are molecules such as oligogalacturonides (OGs) and small peptides (Choi and Klessig 2016; Lori et al. 2015; Ziemann et al. 2018) that are released from plant or pathogen cells as a result of microbial interaction with plants (Boutrot and Zipfel 2017; Gust et al. 2017). Upon MAMP (PAMP or DAMP) recognition, PRRs initiate a cascade of events involving rapid but transient calcium influx, mitogen-activated protein kinase (MAPK) cascades, reactive oxygen species (ROS) production, plant defense hormone regulation, and defense-associated transcription factor activation culminating in transcriptional reprogramming, callose deposition, and stomatal closure. PRRs are localized to the plant cell surface, may or may not have kinase domains—receptor-like kinases (RLKs) or receptor-like proteins (RLPs), respectively—and possess an ectodomain for ligand binding such as a leucine-rich-repeat (LRR) domain, a chitin-binding (LysM) domain (Miya et al. 2007), a lectin-binding, or a wall-associated

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domain (Bacete et al. 2018; Boutrot and Zipfel 2017; Brutus et al. 2010; He et al. 1996; Ranf 2017; Saijo et al. 2018). PRRs do not work alone but engage in fluid associations, disassociations, and transphosphorylations with coreceptors such as suppressor of Bir1-1 (SOBIR1), and somatic embryogenesis receptor kinases such as brassinosteroid coreceptor (BAK1) (Chinchilla et al. 2009; Hecht et al. 2001; Heese et al. 2007; Yasuda et al. 2017). PRR complexes further engage in intracellular signaling with receptor-like cytoplasmic kinases that lack ectodomains (RLCKs), such as Botrytis-induced kinase1 (BIK1) (Couto and Zipfel 2016; Veronese et al. 2006), and a review of RLCKs as central players in plant immunity, growth, and development is highly recommended (Liang and Zhou 2018).

Plant- and animal-associated microbes alike counter PTI by deploying virulence factors called effectors (Jones and Dangl 2006). Diverse repertoires of effectors that enhance pathogen virulence or symbiont establishment have been described for bacterial, oomycete, and fungal pathogens (Khan et al. 2018; Uhse and Djamei 2018; Varden et al. 2017). The functions of many effectors have been elucidated, several of which are redundant and converge on centers or “hubs” of the plant immune response (Carella et al. 2018; Mukhtar et al. 2011; Weßling et al. 2014) such as central components of PTI and, in some cases, ETI (Bourras et al. 2018; Macho et al. 2010). When hosts recognize effectors, a second round of defense, ETI, commences (Jones and Dangl 2006). Similar in nature to PTI but stronger, ETI results in localized cell death, or hypersensitive response (HR), and is often associated with single-gene resistance to pathogens. Resistance (*R*) genes confer qualitative pathogen immunity in contrast to the quantitative resistance typically associated with PTI. *R* genes most often encode nucleotide-binding (NB)-LRR proteins (NLRs) that interact with their cognate effectors directly, or indirectly by “guarding” and sensing perturbations of effector cellular targets (Dangl and Jones 2001). NLRs generally fall into two groups, those having coiled-coil domains or those having toll interleukin-like receptor domains (TNLs); however, interesting exceptions having integrated decoy domains (Le Roux et al. 2015; Nishimura et al. 2015, 2017; Sarris et al. 2016) and other atypical structures or functions have also been described (Baggs et al. 2017; Kourelis and van der Hoorn 2018; Nishimura et al. 2017; X. Zhang et al. 2017). Although *R* genes provide effective plant immunity, they also can be defeated by rapidly evolving pathogen effectors that evade their detection in an ongoing evolutionary arms race (Rouxel and Balesdent 2017; Yoshida et al. 2016). Furthermore, lines dividing PTI and ETI are somewhat blurred (Thomma et al. 2011). Several pathogen's effectors such as apoplastic effectors of *Cladosporium fulvum* (Postma et al. 2016) *Leptosporium maculans* (Ma and Borhan 2015), and *Verticillium dahliae* (Liebrand et al. 2013), to name a few, are detected by PRRs instead of NLRs, and Stotz et al. (2014) introduced the term effector-triggered-defense (ETD) to describe these responses. Similar to PTI, ETD is slower than ETI, dependent upon SOBIR1 and BAK1 (Liebrand et al. 2013; Ma and Borhan 2015; Postma et al. 2016), and may or may not result in hypersensitive cell death (Hammond-Kosack and Rudd 2008).

Pathogen lifestyles and phases. Pathogens are divided into lifestyle groups based on their preferred method for gaining nutrition; biotrophic pathogens require living tissues, necrotrophic pathogens kill tissue and invade dead or dying cells, and hemibiotrophic pathogens display both biotrophic and necrotrophic life phases. Although these trophic divisions are conceptually useful, it is becoming increasingly clear that they do not accurately describe all pathogens. For example, some pathogens considered to be necrotrophic actually have long “latent” periods and some endophytes are known to switch into necrotrophy when environmental conditions change (Delaye et al. 2013; Havis et al. 2014; Newton et al. 2010; Rodriguez et al. 2009). Even the archetypal necrotrophs *Botrytis* and *Sclerotinia* are now known to have short biotrophic phases (Liang and Rollins 2018; Shaw et al. 2016). The Z

model of plant innate immunity features a MAMP/PTI/effector/*R* gene/ETI sequence of events that works well in the context of biotrophic or hemibiotrophic pathogens and host coevolution (Jones and Dangl 2006) but, in reality, plants simultaneously discriminate among diverse members of their microbiomes: mycorrhizal and nodule-forming beneficial symbionts, endophytes, biotrophs, and necrotrophs. The complex processes governing these diverse relationships are not fully understood. In natural settings, plants have coevolved with their microbiota and thus, over time, have acquired mechanisms to accommodate them. In agricultural settings, the genetic diversity of domesticated plants represents only a fraction of the genetic potential of their wild plant ancestors because genotypes have been selected primarily based on yield (Gaut et al. 2018; E. Wang et al. 2008; Wright et al. 2005). Furthermore, plantings of monocultures grown in repetitively cultivated soil also lack microbial genetic diversity and may require inputs in the form of fertilizers, factors that collectively favor disease development (Berg and Koskella 2018; Toju et al. 2018). How plant breeders will utilize knowledge of plant innate immunity to incorporate growth-promoting symbionts, durable disease resistance effective against biotrophic and necrotrophic pathogens, and yield-related traits is our current challenge.

NECROTROPHS

Necrotrophic pathogens impart substantial economic losses in global fruit, vegetable, and grain production annually (Dean et al. 2012). Necrotrophs generally fall into two groups: broad-host-range generalists such as *Botrytis cinerea*, *Sclerotinia sclerotiorum*, and *Rhizoctonia* spp. or host-specific pathogens such as members of the fungal genera *Alternaria*, *Cochliobolus*, *Pyrenophora*, *Parastagonospora*, and *Periconia*. The gray mold pathogen *B. cinerea*, alone infects over 1,000 species (Fillinger and Elad 2016) and causes more than \$10 to 100 billion in losses per year, earning it the rank of the second most destructive pathogen worldwide (Dean et al. 2012). Losses due to *Cochliobolus* spp. in sorghum, wheat, rice, maize, cassava, and soybean are estimated to be \$10 billion worldwide annually (Bengyella et al. 2018). Host-specific necrotrophs have also been the culprits behind historical disease epidemics. The great Bengal famine of the 1940s resulted in the death of at least 2 million people (Greenough 1982) and was partially due (in addition to social and economic factors) to an epidemic of *Cochliobolus miyabaea* on rice at a time when rice constituted 75 to 85% of daily calorie intake. The southern corn leaf blight epidemic caused by the fungal pathogen *C. heterostrophus* in the 1970s was the most consequential crop epidemic in U.S. agricultural history, resulting in a great economic crisis (Ullstrup 1972). Widespread cultivation of a single plant genotype, male-sterile maize hybrids that were extremely sensitive to a necrotrophic effector (NE) produced by a previously unknown race of *C. heterostrophus* (T-toxin), precipitated the epidemic (Ullstrup 1972).

Exploitation of plant defense mechanisms by host-specific necrotrophs. Infection by a host-specific necrotroph is limited to plant species or genotypes that are sensitive to the host-selective toxins (HSTs), also called NEs, that the pathogen produces. Where biotrophic pathogens interact in a gene-for-gene relationships with their hosts (Flor 1956), host-specific necrotrophs interact in an inverse gene-for-gene manner in which disease susceptibility is conferred by a dominant host gene (*S*) that conditions sensitivity to HST or NE molecules produced by the pathogen (Wolpert et al. 2002). Host-specific pathogens and the HST or NEs they produce (referred to hereafter as NEs) have been reviewed by others and are not comprehensively addressed in this review (Friesen et al. 2008a; McDonald and Solomon 2018; Meena et al. 2017; Petrov et al. 2018; Wang et al. 2014). The actions of NEs are diverse and include causing plasma membrane depolarization, mitochondrial dysfunction, and

inhibition of histone deacetylation; however, for many NEs, mechanistic functions have not been determined (Petrov et al. 2018; Wang et al. 2014). Exploitation of host defense machinery (e. g., ETI, PTI, or salicylic acid [SA] production) resulting in cell death is attributed to a growing number of NEs produced by multiple pathogens (Faris et al. 2010; Hammond-Kosack and Rudd 2008; Lorang et al. 2012; Nagy and Bennetzen 2008; Shi et al. 2016) (Table 1). In these cases, resistance to biotrophic pathogens represents a trade-off with disease susceptibility to necrotrophic pathogens, the subtleties of which are detailed in this review.

C. victoriae. Victoria blight of oat, caused by *C. victoriae*, resulted in greater than 50% yield losses in the United States and Canada from 1945 to 1946 (Meehan and Murphy 1946). The historical context of Victoria blight emergence is the hallmark of this disease. Blight-susceptible oat genotypes (Victoria-type) were introduced from Uruguay as a source of resistance to the biotrophic oat rust pathogen *Puccinia coronata*, and were widely cultivated due to their robust, all-stage resistance conferred by the *Pc2* resistance gene. Victoria oat plants were subsequently found to contain a dominant gene, *Vb*, conditioning *C. victoriae*

TABLE 1
Inverse gene-for-gene interactions in which host defense contributes to disease susceptibility

Effector and fungus	Cellular target ^a	Susceptible gene or locus ^b	Defense type ^c	Host plant	Reference
Victorin, <i>Cochliobolus victoriae</i>	Thioredoxin?	Vb/Pc2 locus*	ETI?	<i>Avena sativus</i>	Wolpert and Lorang 2016
	Thioredoxins	LOV (an NLR)	ETI	<i>Arabidopsis</i> spp.	Lorang et al. 2007, 2012; Sweat and Wolpert 2007
	Thioredoxin?	PvLOV	ETI?	<i>Phaseolus vulgaris</i>	Lorang et al. 2018
	Thioredoxin?	HvLOV/MLA locus*	ETI?	<i>Hordeum vulgaris</i>	Lorang et al. 2010
<i>C. sativus</i>	?	Scs6/MLA locus*	ETI?	<i>H. vulgaris</i>	Leng et al. 2018
ToxA	ToxABP1 in chloroplast	Tsn1	ETI?	<i>Triticum aestivum</i>	Breen et al. 2017; Faris et al. 2010; Lu et al. 2014; Manning et al. 2007
<i>Pyrenophora tritici-repentis</i>	PR-1-5	(Serine/threonine protein kinase-NLR)	TaCAPE-dependent		
<i>Parastagonospora nodorum</i>	PR-1-5	Tsn1	ETI?	<i>T. aestivum</i>	Breen et al. 2017; Faris et al. 2010; Lu et al. 2014
			TaCAPE-dependent	<i>T. turgidum</i>	
<i>Bipolaris sorokiniana</i>	PR-1-5	Tsn1	ETI? TaCAPE-dependent	<i>T. aestivum</i>	Breen et al. 2017; Faris et al. 2010; Lu et al. 2014; Friesen et al. 2018
ChToxA-like, <i>C. heterostrophus</i>	?	Mitochondrial male sterility peptide	?	<i>Zea mays</i>	Lu et al. 2015
ToxB (MAX effector) <i>Pyrenophora tritici-repentis</i>	?	Tsc2 locus*	?	<i>T. aestivum</i>	Martinez et al. 2001; Strelkov and Lamari 2003; Nyarko et al. 2014
SnTox1, <i>Parastagonospora nodorum</i>	Chitin-binding	Snn1 Wall-associate kinase	PTI	<i>T. aestivum</i>	Liu et al. 2012; Shi et al. 2016
SnTox3, <i>P. nodorum</i>	PR proteins	Snn3 locus*	TaCAPE-dependent	<i>T. aestivum</i>	Breen et al. 2016, 2017; Liu et al. 2009
Pc-Tox, <i>Periconia circinata</i>	...	Pc NLR	ETI?	<i>Sorghum bicolor</i>	Nagy and Bennetzen 2008
AAL toxin, <i>Alternaria alternata</i> f. sp. <i>lycopersici</i>	Ceramide synthase	Asc1 (a longevity assurance gene homolog)	PCD	<i>Solanum lycopersicum</i>	Brandwagt et al. 2000

^a PR = pathogenesis related protein.

^b An asterisk (*) indicates gene mapped to locus but not isolated. NLR = nucleotide-binding leucine-rich repeat protein.

^c ETI = effector-triggered immunity, CAPE = C-terminally encoded peptide in tomato, PTI = pathogen-associated molecular pattern-triggered immunity, and PCD = programmed cell death.

susceptibility (Litzenberger 1949). All attempts to genetically separate *Pc2* and *Vb* failed and the two traits are assumed to share locus identity (Wolpert et al. 2002). Under this assumption, strong selection for juvenile (seedling) rust resistance precipitated the emergence of a new and formidable necrotrophic disease that aggressively kills all tissues, even emerging seedlings. The context of the epidemic emergence is somewhat reminiscent of that of southern corn leaf blight in that widespread cultivation of a single genotype with respect to disease susceptibility was causal to the severity of the epidemic in each case.

C. victoriae is considered host specific because only isolates that produce the cyclized pentapeptide toxin, victorin, are pathogenic and only host genotypes having a dominant *Vb* gene are susceptible to the pathogen (Wolpert et al. 2002). However, the original description of *C. victoriae* on oat noted that the fungus was first isolated from Timothy grass and also survives as an innocuous pathogen on soybean and seven weedy species (Meehan and Murphy 1946). Sensitivity to victorin has since been reported for species across diverse taxa, including *Arabidopsis*, barley, *Brachypodium* spp., rice, and common bean (Lorang et al. 2007, 2010, 2012, 2018; Wolpert and Lorang 2016). In contrast to the juvenile sensitivity on oat, in these other hosts, victorin sensitivity is mild and developmentally dependent, occurring only on the older leaves of adult plants. In barley and common bean, victorin sensitivity is a quantitative trait with clear genetic background effects (Lorang et al. 2010, 2018). These findings suggest that a *C. victoriae* blight could emerge in other hosts, as occurred for oat, if appropriate *R* genes or genetic backgrounds were unwittingly selected, and underscores the value of identifying genes and mechanisms by which necrotrophic pathogens usurp disease resistance responses. The oat *Vb/Pc2* locus has not been cloned but two other NLR-encoding genes that confer victorin sensitivity, an *Arabidopsis* “resistance gene” locus orchestrating victorin effects, *LOV* (Lorang et al. 2007), and the related *Phaseolus vulgaris* gene *PvLOV* (Lorang et al. 2018) have been cloned. Also, a major quantitative trait locus (QTL) contributing to victorin sensitivity in barley coaligns with *MLA*, a multi-*R*-gene locus that confers resistance to the biotrophic powdery mildew pathogen *Blumeria graminis* f. sp. *hordei* (Lorang et al. 2010). Together, these observations suggest that *Pc2/Vb* share identity and that *R* genes function as *S* genes for some pathogens with necrotrophic lifestyles. Interestingly, susceptibility to the barley leaf spot pathogen *C. sativus* (*Scs6*) was also mapped to a 125-kb interval at the *MLA* locus in barley cultivar Bowden-BC (Leng et al. 2018). Bowden-BC is not sensitive to victorin but it is feasible that *HvLOV* and *Scs6* are allelic variants conditioning sensitivities to victorin and a secondary metabolite, respectively, required to initiate spot blotch infection in Bowman (Condon et al. 2013; Leng et al. 2018). Alternatively *HvLOV* and *Scs6* may represent distinct genes at the *MLA* locus.

Further investigations of *C. victoriae* in *Arabidopsis* revealed that the *LOV* gene is under positive selection and functional in most *Arabidopsis* ecotypes, suggesting that it has been maintained for a resistance function (Sweat et al. 2008). Mutational analysis demonstrated that functional requirements of the *LOV* protein are similar to those of *RPM1*, an NLR that confers resistance to *Pseudomonas syringae*. Additional work demonstrated that the defense-related thioredoxin *ATTRXh5* is absolutely required for *LOV*'s victorin sensitivity function (Sweat and Wolpert 2007). Victorin covalently binds to thioredoxins and, together, victorin, *ATTRX5*, and *LOV* recapitulate the guard mechanism of ETI. In this regard, victorin is thought to mimic a biotrophic effector and, thus, hijack ETI and cause cell death, to *C. victoriae*'s necrotrophic advantage (Lorang et al. 2012).

Thioredoxins are conspicuous effector targets in both plants and animals. *ATTRX5* is a biotic stress-inducible thioredoxin that, along with the closely related *ATTRX3*, regulates the redox status of *NPR1*, allowing *NPR1* monomers to migrate from the cytoplasm

to the nucleus where they coordinate defense gene transcription in basal and systemic acquired resistance responses (Tada et al. 2008). In the animal pathogen *Salmonella enterica*, the virulence effector SirP targets mouse *TRX1* in the cytosol and a chaperonin *HSP40* in the endoplasmic reticulum (Bernal-Bayard and Ramos-Morales 2009; Bernal-Bayard et al. 2010). Crystal structures suggest that the active sites of thioredoxins are highly conserved protein domains (Collet and Messens 2010). Victorin covalently binds to the conserved active site cysteine of *ATTRX5* and is able to disrupt the redox function of both bacterial and plant thioredoxins (Lorang et al. 2012). Intuitively, evolutionarily constrained proteins would seem smart targets for biotrophic effectors because they are less able to evade effector recognition by mutation. In turn, indispensable and constrained effector targets would be best surveilled (guarded) by hosts. Several lines of evidence support the conjecture that *TRXs* are common components of plant immunity networks. (i) *ATTRX3* and *ATTRX5* interact not only with *NPR1* but, in yeast two-hybrid analysis, also with *Botrytis* susceptible1 interactor, an *Arabidopsis* RING domain-containing protein that confers resistance to *Botrytis cinerea* (Weßling et al. 2014) and *HARXL68*, a *Hyaloperonospora arabidopsis* effector protein (Mukhtar et al. 2011). (ii) *TRXh*s comprise integrated “decoy” domains of NLR pairs in rice, wheat, barley, and *Brachypodium* spp. (Brabham et al. 2018; Nishimura et al. 2015), strongly suggesting that they are effector targets in cereals. (iii) Two thioredoxins, the m-type thioredoxin *ZmTrm2* and *ZmTrxh*, an atypical thioredoxin with chaperone activity, both have roles in virus resistance in maize (Q. Liu et al. 2017; Shi et al. 2011). Thus, thioredoxins appear to be common features of defense responses.

Just as common or broad-spectrum targets of pathogen effectors and the *R* proteins that guard them are touted as promising candidates for engineering or breeding durable resistance to biotrophic pathogens (Petit-Houdenot and Fudal 2017), so targeting common components of ETI constitutes a safe bet for a necrotrophic pathogen that succeeds by inducing ETI-associated cell death. Because multiple, diverse plant species (brassicas, grasses, and legumes) are mildly sensitive to victorin at adult stages, and induction of ETI is the demonstrated mechanism of victorin-induced cell death (Lorang et al. 2012), it is intriguing to speculate that *C. victoriae* makes a living by invading a broad spectrum of hosts just before senescence and, thus, gets a competitive edge on other saprophytes. *C. victoriae* survival in natural settings has not been investigated; however, inducing ETI in juvenile plants as *C. victoriae* dies to oat would clearly be unsustainable because seedlings die before they reproduce and susceptible plant genotypes would rapidly be selected against. If not for intentional agricultural selection of robust juvenile rust resistance conferred by *PC2* and the subsequent emergence of Victoria blight on oat, *C. victoriae* would probably have remained an unimpressive and undescribed pathogen or saprophyte.

***Pyrenophora tritici-repentis*.** Tan spot caused by *Pyrenophora tritici-repentis* is an economically significant pathogen of wheat worldwide. Yield losses up to 50% can occur on susceptible genotypes if conditions are favorable, with highest yield reductions occurring when plants are infected at the adult stage (Rees and Platz 1983). The fungus was identified in Europe, the United States, and Asia around 1900. At the time, *P. tritici-repentis* was considered to be a saprophyte that occasionally caused disease outbreaks. Severe tan spot outbreaks emerged in the 1940s, potentially coinciding with *P. tritici-repentis*'s acquisition of a major virulence determinant, *ToxA*, by horizontal gene transfer (HGT) (Friesen et al. 2006), although the evolutionary history of the *ToxA* locus has not been confirmed (McDonald and Solomon 2018). In the 1970s, tan spot epidemics began to occur in North America, Australia, and South Africa around the same time agricultural practices (no-till) that favor survival of the fungus were implemented to reduce soil erosion.

P. tritici-repentis interacts with wheat in an inverse gene-for-gene relationship involving at least three gene pairs. Three *P. tritici-repentis* NEs (ToxA, ToxB, and ToxC) have been described (Ciuffetti et al. 2010; Effertz et al. 2002; Lamari and Strelkov 2010) and correspond to the dominant *S* genes *Tsn1*, *Tsc2*, and *Tsc1* on wheat chromosomes 5BL, 2BS, and 1AS (Faris et al. 2010, 2013; Singh et al. 2010). ToxA and ToxB are small, secreted proteins whose structures have been studied in considerable detail (Ciuffetti et al. 2010; Nyarko et al. 2014) and ToxC is a low-molecular-weight secondary metabolite that has not been further characterized (Effertz et al. 2002). ToxA and ToxC induce necrosis, whereas ToxB induces chlorosis. Based on presence or absence of ToxA, ToxB, or ToxC activity, a race structure for *P. tritici-repentis* was constructed (Lamari and Strelkov 2010; Lamari et al. 2003); however, at least one new race does not fit this structure (Ali et al. 2010; Faris et al. 2013). The race structure also does not correlate with genome level phylogeny, because ToxA-producing isolates do not cluster in phylogenetic analysis (Moolhuijzen et al. 2018). Several genetic studies of the host indicate that *Tsn1*, *Tsc2*, and *Tsc1* tell only part of the *P. tritici-repentis*-wheat story, because race-nonspecific resistance QTLs (Faris et al. 2013; Li et al. 2011; Patel et al. 2013), including a dominant, race-nonspecific resistance QTL on chromosome 3B that is epistatic to *ToxA-Tsn1*-induced susceptibility, have been identified (Kariyawasam et al. 2016). Manning and Ciuffetti (2015) also found that ToxA symptom development can be epistatic to other HST-induced symptoms, independent of host genetic background.

Prominent features of tan spot pathology clearly indicate that *P. tritici-repentis*, like *C. victoriae* on oat, exploits wheat defense responses to cause tan spot. (i) *Tsn1* (the only *P. tritici-repentis* *S* locus yet cloned) encodes a serine/threonine protein kinase-NLR, a protein resembling classic disease resistance genes (Faris et al. 2010). (ii) The crystal structure of ToxB resembles that of AvrPiz-t, a secreted avirulence protein produced by the rice blast fungus *Magnaporthe oryzae* (Nyarko et al. 2014). Both ToxB and AvrPiz-t are members of the MAX-effector (*Magnaporthe* AvrS and ToxB like) family. MAX effectors account for 5 to 10% of the estimated effector repertoire of *M. oryzae*, and are expressed during the early, biotrophic phase of infection (de Guillen et al. 2015). AvrPiz-t targets the RING E3 ubiquitin ligases APIP6 and APIP10 in rice to suppress PAMP immunity (Park et al. 2016) and APIP5, a bZIP-type transcription factor and negative regulator of cell death (Wang et al. 2016), but the target of ToxB is not yet known. APIP5 is recognized by the cognate R protein PIZ-T, an NLR (Zhou et al. 2006). (iii) Treatment of wheat with ToxA or ToxB causes transcriptional reprogramming, including upregulation of defense genes encoding WRKY transcription factors, RLKs, pathogenesis-related proteins (PRs), and components of the phenylpropanoid and jasmonic acid (JA) pathways. Furthermore, ROS accumulation and photosystem dysfunction are common downstream effects of ToxA and ToxB action. Taken together, these findings suggest that the NEs act as both virulence factors and elicitors of defense (Ciuffetti et al. 2010; Manning et al. 2009; Pandelova et al. 2009, 2012).

Fortunately, the cumulative knowledge of *P. tritici-repentis*-wheat pathology has provided useful tools for wheat breeders (Shankar et al. 2015). Purified NEs were utilized to show that *Tsn1*-ToxA, *Tsc2*-ToxB, and *Tsc1*-ToxC interactions all play significant roles in the development of tan spot in common wheat (hexaploid) (Faris et al. 2013; Kariyawasam et al. 2016), and *Tsc1* but not *Tsn1* is significant for tan spot development in durum wheat (tetraploid) (Virdi et al. 2016). Purified *P. tritici-repentis* NEs and molecular markers linked to the *P. tritici-repentis* *S* loci can now be used to remove these disease *S* loci from breeding populations (Abeysekara et al. 2009). Removal of *Tsn1* was recommended for minimizing impacts of not only tan spot (Z. Liu et al. 2017; See et al. 2018; Virdi et al. 2016) but also two other diseases of wheat, Septoria nodorum blotch (SNB) caused by *Parastagonospora nodorum* and spot

blotch caused by *Bipolaris sorokiniana*, both of which harbor ToxA genes that contribute to virulence of pathogens on *Tsn1* wheat (Ficke et al. 2018; Friesen et al. 2018; McDonald et al. 2018).

The ToxA locus present in *P. nodorum* (SnToxA) resides in a 14-kb region that shares 97% identity with *Pyrenophora tritici-repentis* ToxA (Friesen et al. 2006). The same region from *B. sorokiniana* shares 97% identity across all three fungi and, of two ToxA haplotypes, one is identical to that of *P. tritici-repentis* and the other harbors a single nonsynonymous nucleotide substitution (McDonald et al. 2018). *Parastagonospora nodorum* harbors diverse SnToxA haplotypes, whereas sequences among *Pyrenophora tritici-repentis* and *B. sorokiniana* are conserved (Ciuffetti et al. 2010; Friesen et al. 2006, 2018), suggesting that ToxA may have been transferred from *Parastagonospora nodorum* to the other fungi. However, sequencing of more *Pyrenophora tritici-repentis* ToxA loci would be required to confirm this notion. A ToxA gene is also present in *Parastagonospora avenaria* f. sp. *tritici*, a pathogen of wheat and oat and close relative of *P. nodorum*, and was likely acquired through interspecific hybridization (McDonald et al. 2013). Finally, a ToxA-like protein that acts as a virulence factor by inducing host-selective, light-dependent leaf necrosis on maize (as PtrToxA does on wheat) (Manning and Ciuffetti 2005), is produced by *C. heterostrophus* (Lu et al. 2015). The *C. heterostrophus* protein shows 64% similarity to PtrToxA and is predicted to adopt a similar three-dimensional structure, although it lacks the arginyl-glycyl-aspartic acid motif that PtrToxA requires for internalization into sensitive wheat mesophyll cells (Manning et al. 2008; Sarma et al. 2005). Taken together, these multiple occurrences of ToxA-like genes and evidence for HGT demonstrate the potential for emergence of new diseases caused by host-selective necrotrophs and should be a warning to breeders to choose recessive alleles of dominant *S* genes if and when they are known.

***P. nodorum*.** *P. nodorum* causes SNB, a severe foliar disease of common and durum wheats. The pathogen currently occurs in the United States, Canada, Western Australia, southern Germany, Switzerland, Latvia, Finland, and Norway and results in significant economic losses that can be in the hundreds of millions of dollars annually (Ficke et al. 2018; Murray and Brennan 2009). Like the other host-specific necrotrophs, the SNB host and pathogen operate in an inverse gene-for-gene manner, in which nine specific wheat *S* genes and their cognate NEs have been described, all of which play significant roles in the development of SNB (Friesen et al. 2006, 2007, 2008a, b, 2012; Gao et al. 2015; Liu et al. 2009, 2012; Shi et al. 2016; reviewed by McDonald and Solomon 2018). Two of the nine SNB *S* genes, *Tsn1* and *Snn1*, have been cloned. *Tsn1* is the same serine/threonine protein kinase-NLR (above) that confers PtrToxA-dependent cell death, and also confers SnToxA-induced cell death (Faris et al. 2010). *Snn1* encodes a wall-associated protein kinase (WAK) (Shi et al. 2016). *Snn1*-dependent SnTox1 activation of *TaMAPK3* occurs within 15 min of inoculation and is short lived and, therefore, is more indicative of a PTI than an ETI response, which usually requires longer activation periods and is typically sustained (Tsuda et al. 2013). This is significant in that *Snn1* represents the first known case of a pathogen utilizing an RLK and PTI to cause rather than to prevent disease.

Functions for the NEs corresponding to *Tsn1*, *Snn1*, and *Snn3* (SnToxA, SnTox1, and SnTox3, respectively) have all been described (Breen et al. 2016, 2017; Z. Liu et al. 2016; Lu et al. 2014; McDonald et al. 2018). SnToxA has a chitin-binding activity, a virulence function attributed to multiple effectors for various pathogens (Rodriguez-Moreno et al. 2018). Chitin binding suppresses PTI by preventing plant chitinases from degrading fungal cell walls and releasing chitin-derived OGs, which are known PAMPs. By tagging SnTox1 with green fluorescent protein, Z. Liu et al. (2016) showed that SnTox1 binds to the surface of *P. nodorum* hyphae at plant penetration foci, suggesting that chitin binding suppresses PTI. Indeed, *SnTox1* had a protective effect not

only on *P. nodorum* hyphae but also on three other fungal species in the presence of purified wheat chitinases (Z. Liu et al. 2016). NEs SnToxA and SnTox3 directly interact with multiple PRs (Breen et al. 2016). SnToxA interacts with the wheat PR1-5, and SnTox3 interacts with seven different PRs. PR1 is known for its ubiquitous and strong induction during plant pathogen infections but, more recently, PR1 was shown to act in a unique defense pathway through the C-terminally encoded peptide in tomato (CAPE1) protein, a signaling peptide hidden within PR1 and other proteins (Breen et al. 2017). Furthermore, exogenously applied TaCAPE1 increases susceptibility of wheat to SNB in an SnTox3-dependent manner. Thus, it seems that the *P. nodorum* NEs, like those for *Pyrenophora tritici-repentis* and victorin, have dual roles as virulence factors and defense-triggering effectors.

In summary of SNB, *Parastagonospora nodorum* causes disease by exploiting plant defense mechanisms resembling ETI in the case of Tsn1 and PTI in the case of Snn1. The NEs SNToxA, Tox1, and Tox3 display dual functions by both suppressing PTI as well as inducing ETI, PTI, or a TaCAPE-dependent pathway, respectively, to cause necrotrophic disease. Uncovering functions for the other SNB effectors, those associated with susceptibility at *Snn2*, *Snn4*, *Snn5*, *Snn6*, and *Snn7* (McDonald and Solomon 2018), is, of course, of great interest. Genome-wide association studies (GWAS) proved successful in locating SnToxA, SnTox3, and an unknown virulence locus in *P. nodorum* (Gao et al. 2016). A combination of GWAS and QTL analysis could also be used to identify the remaining SNB players in *P. nodorum* and in wheat (Phan et al. 2018).

A few remaining examples of host-selective necrotrophs that coopt plant immune machinery to promote virulence or induce programmed cell death (PCD) are *Periconia circinata*, causal agent of a root and crown rot of sorghum (milo disease), and *Alternaria alternata* f. sp. *lycopersici*, which causes stem canker of tomato. *P. circinata* produces a toxin (Pc) that mimics symptoms of milo disease and resembles an HR (Dunkle and Macko 1995). The semidominant sorghum *S* gene conferring milo disease and Pc-toxin sensitivity encodes an NB-LRR and resides at a complex genetic locus (Nagy and Bennetzen 2008). *A. alternata* f. sp. *lycopersici* produces AAL toxin, which is closely related to fumonisin B1 produced by *Fusarium* spp. These toxins inhibit ceramide synthase and, thus, increase accumulation of sphingoid bases, leading to PCD. The longevity assurance gene homolog of tomato *Asc-1* mediates resistance to *A. alternata* f. sp. *lycopersici* toxins and fumonisin B1 (Brandwagt et al. 2000) by preventing disruption of sphingolipid metabolism during AAL-toxin-induced PCD (Spasieva et al. 2002). In *Fusarium verticillioides* infection of maize, FB₁ enhances cell death and infection, presumably by activating SA defense; therefore, FB₁ could also be considered an NE (Arias et al. 2012). Other than causing PCD, a connection of these toxins to plant defense machinery is not clear but, in *Arabidopsis*, an inositol-phosphorylceramide synthase (ERH1) involved in regulating PCD acts as a suppressor of RPW8 mediated resistance to powdery mildew, implying a connection between sphingolipid metabolism and PCD during defense (W. Wang et al. 2008).

ETI AGAINST NECROTROPHS? NOT MUCH

Inverse gene-for-gene relationships characterized at the molecular level (above) can still be numerated on the digits of one's hands but many pathogen NEs and cognate *S* loci remain to be described (McDonald and Solomon 2018; Petrov et al. 2018; Wang et al. 2014). Classical gene-for-gene relationships, on the other hand, are commonly described for biotrophic disease interactions (Su et al. 2018) but are rare for necrotrophic pathogens. The first such example described *RLM3* in *Arabidopsis*, a single dominant gene encoding a toll interleukin 1 receptor NB protein that confers resistance to *L. maculans*, causal agent of black leg disease in

Brassica spp. *Arabidopsis* plants with mutant *rml* alleles lack resistance to *L. maculans* and are also more susceptible to the necrotrophic pathogens *Botrytis cinerea*, *A. brassicicola*, and *A. brassicae*. The *L. maculans* effector for *RLM3* has not been described but two genes that confer resistance to the same pathogen in *Brassica napus*, *LepR3* (encoding an RLP protein) (Larkan et al. 2013) and *Rlm2* (an allelic variant of *LepR3*) (Larkan et al. 2015) and the cognate effectors AVRML1 and AVRML2 have been characterized (Ghanbarnia et al. 2015; Gout et al. 2006). More recently, a *TNL* gene that cosegregates with the *Rlm9* locus in *B. napus* was shown to be under positive selection and is considered a candidate for *Rlm9* (Stotz et al. 2018). In wheat, the *Stb6* gene encoding a WAK-like protein controls gene-for-gene resistance to *Zymoseptoria tritici*, the economically important foliar pathogen that causes Septoria tritici blotch (Saintenac et al. 2018). The cognate effector gene in *Z. tritici*, *AvrStb6*, encodes a small cysteine-rich protein (Kema et al. 2018; Zhong et al. 2017). Interestingly, *Stb6* confers resistance in the absence of an HR and, together with *LepR3*-, *Rlm2*-, and *Rlm3*-conferred defense against *L. maculans*, are examples of an ETD response (Rudd et al. 2008; Stotz et al. 2014). One could imagine that, if *Stb6* were to induce cell death (HR), colonization of the resulting necrotic cells by *Z. tritici* might facilitate disease instead of resistance. Because *L. maculans* and *Z. tritici* are both "latent necrotrophs" that colonize the apoplast as endophytes prior to the induction of necrosis (Sánchez-Vallet et al. 2015), perhaps it is not surprising that either of these pathogens display gene-for-gene resistance. However, gene-for-gene resistance to the host-specific necrotroph *A. alternata* has also been described. The resistance was revealed in transgenic apple trees expressing antisense constructs for aldose-6-phosphate reductase (*A6PR*). Suppression of *A6PR* sorbitol synthesis led to down-regulation of NLRs, including the causal *R* gene, MdNLR16, and resulted in increased susceptibility to *A. alternata* (Meng et al. 2018).

Quantitative disease resistance to necrotrophic pathogens has also been associated with NLRs. NLRs present in QTLs for Ascochyta blight (*Ascochyta rabiei*) infection of chickpea, and a wheat NLR gene (*TaRCR1*) that confers partial resistance to sharp eyespot caused by *Rhizoctonia cerealis*, were both identified using comparative transcriptomics approaches (Sagi et al. 2017; X. Zhu et al. 2017). NLR genes present in QTLs for resistance against *Sclerotinia sclerotiorum* mapped to chromosomes A6, C7 (Li et al. 2015), and A9 (Mei et al. 2013) in the *B. napus* genome and are considered minor *R* gene candidates (Li et al. 2015; Mei et al. 2013). The NLRs described in all these cases (chickpea, wheat, and *B. napus*) confer quantitative resistance and corresponding pathogen effectors are not known. In this regard, one may or may not consider these gene-for-gene (ETI) resistance reactions, despite involvement of NLRs. Quantitative or partial-effect *R* loci have long been recognized as weaker, adult plant (AP) resistance (APR), or defeated *R* genes with residual effects (Li et al. 2006), and quantitative features of ETI due to genetic background effects have also been described (Iakovidis et al. 2016). Despite their minor effect, these NLRs, mechanistically, could be functioning in ETI-like processes during the brief biotrophic phases of these necrotrophic pathogens. Alternatively, X. Zhu et al. (2017) suggest that *TaRCR1* plays a regulatory role in normalizing levels of ROS to prevent a necrotrophic susceptibility response. In this regard, *TaRCR1* is similar to the case of *ZmCCoAOMT2* from maize, in which necrotrophic resistance is conferred by negatively impacting a biotrophic defense response (HR) (Yang et al. 2017). *ZmCCoAOMT2* encodes a caffeoyl-CoA O-methyltransferase associated with the phenylpropanoid pathway in maize. Resistance alleles of *ZmCCoAOMT2* act as general suppressors of the HR and confer partial resistance to three economically important, "mostly necrotrophic" diseases of maize: southern leaf blight (*C. heterostrophus*), gray leaf spot (*Cercospora zeae-maydis*), and northern leaf blight (*Setosphaeria turcica*) (Yang

et al. 2017). Because *ZmCCoAOMT2* and possibly *TaCR1* impart disease resistance by downregulating HR-like defenses, I like to call these interactions “inverse-inverse gene-for-gene responses”. Similarly, the rice blast fungus represses negative regulation of cell death during its necrotrophic phase, and resistance conferred by the NLR Piz-t results from the pathogen being unable to derepress cell death and enter the necrotrophic phase (Wang et al. 2016). In conclusion, cases of ETD, quantitative resistance associated with NLRs, and resistance to necrotrophic phases of pathogenicity through repression of HR have been described but only one clear case of ETI in resistance to a necrotrophic pathogen has been reported (Meng et al. 2018).

GENERALIST NECROTROPHS BALANCING ACT: TELL ME THIS DEATH THING IS JUST A PHASE

In contrast to a host-selective necrotroph's induction of gene-for-gene-induced ETI resulting in susceptibility (inverse gene-for-gene), or ETD described for latent necrotrophs (above), induction of ETI or ETD has not been observed for generalist necrotrophs such as *Botrytis* and *Sclerotinia* spp. Instead, these pathogens navigate a delicate balance of suppressing and inducing hormone-regulated defenses, ROS, and autophagic or apoptotic cell death (PCD). Each of these topics has been reviewed elsewhere and they are not comprehensively reviewed here (Berens et al. 2017; Dickman et al. 2017; Kabbage et al. 2017; Qi et al. 2017; Veloso and van Kan 2018). Defense responses mediated by SA and JA are generally considered antagonistic responses whereby SA mediates biotrophic defense, and JA and ethylene (ET) determine necrotrophic disease outcomes (Glazebrook 2005; Lal et al. 2018; Rahman et al. 2012). For example, ectopic expression of the grape aspartic protease VqAP13 promotes SA-dependent signaling that enhances resistance to powdery mildew but reduces resistance to *Botrytis cinerea* (Guo et al. 2016). However, several studies (Guerreiro et al. 2016; Jiang et al. 2016; L. Liu et al. 2016) now complicate this classical SA versus JA view (Glazebrook 2005; Lal et al. 2018; Rahman et al. 2012; Spoel and Dong 2008). In one case, JA signaling occurs in the biotrophic interaction of a downy mildew pathogen with grapevine (Guerreiro et al. 2016) and, in another, SA and JA pathways collaborate such that SA receptors activate JA signaling to promote ETI (L. Liu et al. 2016). In the latter case, the authors suggest that interplay between SA and JA may allow plants to defend against biotrophic pathogens without becoming vulnerable to necrotrophic pathogens. Furthermore, a comparative transcriptomic study of host resistance to *B. cinerea* and the biotrophic powdery mildew pathogen *Golovinomyces orontii* showed lower defense signaling (i.e., oxidative stress and ET-, JA-, and SA-responsive genes) in *B. cinerea* than in *G. orontii* but elevated expression of auxin-related and brassinosteroid pathway genes (Jiang et al. 2016). A fine-tuned balance in ROS production is also critical to necrotrophic disease outcomes. Small oxidative bursts are known to act as secondary messengers of defense but stronger ROS bursts kill cells and, thus, impede biotrophic infection while favoring necrotrophic pathogens (Girard et al. 2017; Govrin and Levine 2000; Mittler 2002). Plants and pathogens alike balance ROS by producing combinations of ROS-inducing factors such as oxalic acid or the NADPH oxidase RbohD (Kadota et al. 2015; Torres and Dangl 2005), or ROS quenching molecules such as vitamin B6 and the antioxidant enzymes catalase, peroxidase, and super oxide dismutase, at critical times during the infection process (Girard et al. 2017; Samsatly et al. 2018; Williams et al. 2011; Wu et al. 2016). Finally, a key pivotal point in necrotrophic disease outcomes is the execution of cell death by autophagy or apoptosis. Autophagy and apoptosis are considered to be mutually antagonistic mechanisms in plants and animals (Dickman et al. 2017). The capacity of necrotrophic generalists such as *Sclerotinia sclerotiorum* and

Botrytis spp. to suppress autophagy early in infection may determine the extent of their progression (Kabbage et al. 2013, 2017; Veloso and van Kan 2018). When autophagic and apoptotic signals are balanced, host cells remain alive and fungi are able to colonize plant cells asymptotically but, as the balance tips toward apoptosis, necrotrophic infection ensues.

Necrosis-inducing peptides: Necrosis- and ethylene-inducing-like peptides, cerato-platanins, cell-wall-degrading enzymes, and crinkling- and necrosis-inducing proteins. PCD in the necrotrophic stage of infection may be initiated by ROS or by necrosis-inducing peptides (NIPs) such as necrosis- and ethylene-inducing-like peptides (NLPs), cerato-platanins, (Azmi et al. 2018) cell-wall-degrading enzymes (CWDEs) independent of their enzymatic activity (Albert et al. 2015; Oome et al. 2014), or crinkling- and necrosis-inducing proteins (CRNs) in cases of the necrotrophic phase of oomycete hemibiotrophs (Amaro et al. 2017). NIPs also act as PAMPs in that they trigger a PTI response (Albert et al. 2015; Böhm et al. 2014; Zhang et al. 2014). A few recent examples of NIPs (among many not covered here) are the NLP1 protein from *Colletotrichum orbiculare* that enhances cucumber defense and impairs fungal virulence on cucumber (Azmi et al. 2018); the *S. sclerotiorum* cerato-platanin protein, SsCP1, that targets plant PR1 and contributes to virulence (Yang et al. 2018); and two genes encoding xyloglucanase of the GH12 family, PsXEG1 of *Phytophthora sojae* and BcXYG1 from *B. cinerea*, both of which contribute to virulence of these pathogens and their ability to trigger cell death and defense responses, independent of their enzymatic activity (Ma et al. 2015; W. Zhu et al. 2017). Interestingly, *Ssclp1*-expressing transgenic plants have increased SA and higher levels of resistance to *B. cinerea*, *Alternaria cola*, and *G. orontii* (Yang et al. 2018). CRNs, a large protein family found primarily in oomycetes such as *Pythium* and *Phytophthora* spp., like NLPs, include family members that may either induce or suppress cell death, are preferentially expressed in either biotrophic or necrotrophic phases of infection, and possess members for which virulence functions do not require cell death (Albert et al. 2015; Amaro et al. 2017). When NIP-induced PCD does occur and pathogens complete their life cycles by sporulating in dead tissue, it could be said they have exploited plant defense responses in so doing. However, the “necrotrophs” that produce NIPs also suppress these same defense responses at earlier phases of infection. A brilliant example of such biotrophic activity by a necrotrophic generalist is the suppression of host defenses by transkingdom transfer of sRNA from *B. cinerea* to its hosts (Wang et al. 2017; Weiberg et al. 2015). *B. cinerea* produces sRNAs that move into the host plant early in the infection process and manipulate RNAi machinery to silence host immunity genes (Weiberg et al. 2013). This leaves us to conjecture that trophic status (endophyte, biotroph, and necrotroph) and the outcomes of the defense responses they induce are a continuum dependent on subtle alterations in timing or stage of the infection process, as well as plant developmental stage (Häffner et al. 2015), a notion that has been expressed by others (Blacutt et al. 2018; Cook et al. 2015; De Wit 2016; Veloso and van Kan 2018). In conclusion, plants are able to respond to generalist necrotrophic pathogens displaying different life stages because immunity is a somewhat malleable balancing act in which, sometimes, the pathogen steals the show.

MUTUALISTS

Of equal relevance to the plasticity of defense is how plant defense plays out in mutualistic plant–microbial systems. Increased awareness of plant-associated microbiomes and the role of mutualists in sustainable agriculture has led to a flurry of related research, reviewed elsewhere (Bamisile et al. 2018; Busby et al. 2016, 2017; Finkel et al. 2017; Hacquard et al. 2017; Plett and

Martin 2018; Zipfel and Oldroyd 2017). The emerging consensus posits that plants utilize a common set of defense pathways such as PRRs to detect microbial presence and PTI to keep populations in check for pathogens, endophytes, and mutualists alike (Bamisile et al. 2018; Plett and Martin 2018; Toju et al. 2018; Zipfel and Oldroyd 2017). Subtle variations on a common defense theme allow plants to differentiate pathogenic and mutualistic secreted signals. For example, different LysM receptor kinases perceive either nodulation factors, arbuscular mycorrhizal lipochitooligosaccharides, or MAMPs and induce related but lifestyle-specific downstream signaling pathways (Bozsoki et al. 2017; Rey and Jacquet 2018). Plants may also monitor nutrient status to sense nearby pathogens or mutualists (Kiers et al. 2011), or sense ratios of MAMP/DAMP signals. Mutualists have evolved accordingly; for example, by producing fewer CWDEs and, therefore, fewer DAMPs (Benedetti et al. 2015; Kohler et al. 2015). However, because studies of this nature have been limited with respect to host species or genotypes, exactly what host variability exists in selection of nonpathogenic endophytes and mutualists requires further exploration (Plett and Martin 2018). Clearly, pathogens and mutualists induce overlapping defense pathways, and the potential of mutualists as not only growth promoting agents but also primers of defense should be further explored through genetic investigations of host and mutualist genotypic variability. Identifying and adding back compatible mutualists and other core microbiome constituents required for sustainable agroecosystems is also recommended (Toju et al. 2018).

EYES ON THE PRIZE: BREEDING FOR RESISTANCE AND OTHER GOOD THINGS

In this review, we have considered trade-offs between biotrophic pathogen resistance and susceptibility to host-selective necrotrophs, more subtle trade-offs of resistance or susceptibility to generalist necrotrophs, and a next-frontier, host genotype effect on selection of beneficial symbionts. A final and obvious consideration in developing sustainable disease resistance is the resistance–yield trade-off. Genetic bottlenecks for disease resistance and symbiont associations (Pérez-Jaramillo et al. 2017) were created when humans domesticated high-yielding plant genotypes (Gaut et al. 2018; E. Wang et al. 2008; Wright et al. 2005). Subsequent yield penalties from reintroduction of resistance (Karasov et al. 2017; Tian et al. 2003) as well as molecular mechanisms that explain these penalties are well known (Karasov et al. 2017; Lozano-Durán et al. 2013; Ning et al. 2017). Fortunately, achieving disease resistance without compromising yield is possible (Deng et al. 2017; Kumari et al. 2017; Xu et al. 2017). For example, in breeding elite rice cultivars for blast resistance, naturally occurring, epigenetic downregulation of an *R* gene in inflorescences (seed heads) but not in leaves resulted in effective immunity to the *M. grisea* with no yield penalty in the grain (Deng et al. 2017). “Going back” and tapping into the genetic richness of wild germplasm to find QTLs that contribute to resistance (Capistrano-Gossman et al. 2017; Mammadov et al. 2018; Mesarich et al. 2018; H. Zhang et al. 2017) without compromising yields should be more feasible today than ever, due to next-generation sequencing such as Illumina and single molecule real-time technologies, and exponential increases in computational power (Marri et al. 2018; Minio et al. 2017; Yuan et al. 2017). Combinations of comparative transcriptomics, GWAS, and QTL analysis of hosts and pathogens, alone or simultaneously (Lee and Lee 2018; Wang et al. 2018; Zhang et al. 2018), and genomic selection techniques (Bourke et al. 2018) will facilitate identification of more pathogen effectors and host genomic determinants of complex desirable traits. Advanced breeding methods such as use of multiparent populations (Huang et al. 2015; Ladejobi et al. 2016) and “speed breeding” are also hastening

discovery and deployment of these traits in desirable plant cultivars (Bourke et al. 2018; Li et al. 2018; Watson et al. 2018). Of course, accessing the full genetic potential of diverse crop plants and their wild progenitors will require that plant genetic diversity exists in seed banks or natural areas. Utilizing purified NE or biotrophic effector assays (Downie et al. 2018; McDonald and Solomon 2018; Mesarich et al. 2018; Toruño et al. 2016; Vleeshouwers and Oliver 2014), conventional field phenotyping, or digitally assisted (Lowe et al. 2017; Thomas et al. 2018) high-throughput (Araus et al. 2018; Willocquet et al. 2017) phenotyping will also facilitate identification of more *S* or *R* loci and effectors of mutualist, biotrophic, and necrotrophic interactors (Jones et al. 2018; Sperschneider et al. 2018). Using NEs to screen for and eliminate *S* loci to necrotrophic pathogens (Z. Liu et al. 2017; McDonald and Solomon 2018; See et al. 2018; Viridi et al. 2016) or knowledge of biotrophic defense targets to eliminate *S* genes to biotrophic pathogens (Engelhardt et al. 2018; Zaidi et al. 2018), while cautiously selecting *R* genes or QTLs that confer durable resistance to biotrophic pathogens (Mundt 2018), are sensible breeding strategies.

Multiple approaches for breeding (Li et al. 2018; Mundt 2018; Pilet-Nayel et al. 2017), engineering (Borrelli et al. 2018; Dangl et al. 2013; Kim et al. 2016; Molla et al. 2016; Xu et al. 2017), and deploying (Mundt 2018; Rimbaud et al. 2018) durable disease resistance have been proposed. All of these strategies should be considered in light of necrotrophic virulence mechanisms. Some methods designed to reduce selection for biotrophic pathogens that evade ETI or PTI could simultaneously reduce selection for virulent necrotrophs that target the same defense pathways, whereas others could have an opposite and detrimental effect. For example, pyramided *R* genes are defeated more slowly than singularly deployed *R* genes (Fukuoka et al. 2015) but, theoretically, pyramiding could also increase selection for a host-specific pathogen such as *Cochliobolus victoriae* that commandeers a potential “hub” of ETI (e.g., thioredoxins). Similarly, intentional selection for durability by choosing *R* genes that guard conserved or common effector targets, as proposed by Boutrot and Zipfel (2017), Clarke et al. (2015), and Dangl et al. (2013), if not chosen wisely, could increase the probability of “the next new blight” by a saprophyte or endophyte emerging as a formable pathogen, as occurred with Victoria blight on *Pc2* oat. *Cochliobolus* spp. have, in fact, expanded north over the past 30 years and are favored by warmer climate (Bengyella et al. 2018). For instance, in Uttar Pradesh, India, a new blight disease caused by *C. lunatus* on rice has emerged (Simon and Lal 2013). These authors suggest that a repeat of the great Bengali famine could be envisaged in Africa, because *Cochliobolus* is gradually gaining terrain against crops of different gene pools. Engineering durable resistance by integrating common effector-target decoys into *R* proteins (Kim et al. 2016) invites similar risks. Engineering pathogen-inducible PTI (Boutrot and Zipfel 2017; Dangl et al. 2013) may provide broad-spectrum disease resistance but, as in at least one case, a host-selective necrotroph, *Parastagonospora nodorum*, hijacks PTI and CAPE-dependent immunity to cause disease (McDonald and Solomon 2018; Shi et al. 2016). All of these approaches to engineer disease resistance are potential win-lose strategies when considering both biotrophic and host-selective necrotrophic pathogens. Altering or eliminating plant genes involved in pathogen susceptibility is a strategy that could be a win-win for controlling both biotrophic (Engelhardt et al. 2018; Zaidi et al. 2018) and necrotrophic disease (Z. Liu et al. 2017; See et al. 2018; Viridi et al. 2016). Another strategy, pyramiding minor *R* genes or APR genes, may also be effective for control of diverse pathogens. At least in the case of *C. victoriae*, plants having AP sensitivity to victorin in bean, barley, *Brachypodium* spp., and rice were not highly susceptible to the fungus (Lorang et al. 2010, 2012, 2018). For *P. nodorum*, both juvenile and AP sensitivity genes incrementally contribute to yield loss but earlier infections increase inoculum potential more than AP

susceptibility (Ficke et al. 2018). Both juvenile and adult plants can be infected by *Pyrenophora tritici-repentis*, and one study showed 13% losses by early season disease, 35% by later disease, and 48% in combined early and late disease (Rees and Platz 1983). These cases suggest that APR genes may constitute a compromise that could keep both biotrophic and necrotrophic diseases at acceptable levels. APR genes that provide durable resistance to biotrophs, however, may also confer plant phenotypes that favor necrotrophic pathogens. The *Lr34* gene confers broad-spectrum, durable, and quantitative resistance to multiple biotrophic pathogens in wheat but also causes leaf-tip necrosis and may function through senescence-associated processes (Krattinger et al. 2009). The recessive *mlo* gene confers durable resistance to the powdery mildew pathogen *Blumeria graminis* f. sp. *hordei* in barley but also causes rapid necrosis at infection sites and increased susceptibility to *M. grisea* (Büschges et al. 1997) *Bipolaris sorokiniana* (Kumar et al. 2001), and *Ramularia collo-cygni* (McGrann et al. 2014) but not to *Rhynchosporium secalis* or *Pyrenophora teres* (Makepeace et al. 2007). Despite these potential risks, the fact that *Lr34*, *mlo*, and other APR genes are widely deployed and have successfully provided durable resistance without precipitating new necrotrophic disease for >50 years is encouraging. Deployment strategies such as varietal mixtures, mosaic plantings, and crop rotations reduce

inoculum, slow epidemic development, and reduce selection pressure on biotrophic pathogens such as cereal rusts (Burdon et al. 2016; Mundt 2002, 2018; Zhu et al. 2000). These same strategies could also reduce necrotrophic disease incidence and selection for virulence when potential pathogens are present (Ayanru and Browning 1977). In the near future, plant breeders and growers will likely continue to use familiar varieties and *R* genes that address the most imminent of pathogens; however, keeping the risks associated with necrotroph–biotroph trade-offs in mind would be prudent.

LITERATURE CITED

- Abeysekara, N. S., Friesen, T. L., Keller, B., and Faris, J. D. 2009. Identification and characterization of a novel host-toxin interaction in the wheat–*Stagonospora nodorum* pathosystem. *Theor. Appl. Genet.* 120:117–126.
- Albert, I., Böhm, H., Albert, M., Feiler, C. E., Imkamp, J., and Wallmeroth, N. 2015. An RLP23-SOBIR1-BAK1 complex mediates NLP-triggered immunity. *Nat. Plants* 1: Article 15140.
- Ali, S., Gurung, S., and Adhikari, T. B. 2010. Identification and characterization of novel isolates of *Pyrenophora tritici-repentis* from Arkansas. *Plant Dis.* 94:229–235.
- Amaro, T. M. M., Thilliez, G. J. A., Motion, G. B., and Huitema, E. 2017. A perspective on CRN proteins in the genomics age: Evolution, classification, delivery and function revisited. *Front. Plant Sci.* 8:99.
- Araus, J. L., Kefauver, S. C., Zaman-Allah, M., Olsen, M. S., and Cairns, J. E. 2018. Translating high-throughput phenotyping into genetic gain. *Trends Plant Sci.* 23:451–466.
- Arias, S. L., Theumer, M. G., Mary, V. S., and Rubinstein, H. R. 2012. Fumonisin: Probable role as effectors in the complex interaction of susceptible and resistant maize hybrids and *Fusarium verticillioides*. *J. Agric. Food Chem.* 60:5667–5675.
- Ayanru, D. K. G., and Browning, J. A. 1977. Effect of heterogeneous oat populations on the epiphytic development of Victoria blight*. *New Phytol.* 79:613–623.
- Azmi, N. S. A., Singkaravanit-Ogawa, S., Ikeda, K., Kitakura, S., Inoue, Y., and Narusaka, Y. 2018. Inappropriate expression of an NLP effector in *Colletotrichum orbiculare* impairs infection on cucurbitaceae cultivars via plant recognition of the C-terminal region. *Mol. Plant-Microbe Interact.* 31: 101–111.
- Bacete, L., Mérida, H., Miedes, E., and Molina, A. 2018. Plant cell wall-mediated immunity: Cell wall changes trigger disease resistance responses. *Plant J.* 93:614–636.
- Baggs, E., Dagdas, G., and Krasileva, K. 2017. NLR diversity, helpers and integrated domains: Making sense of the NLR IDentity. *Curr. Opin. Plant Biol.* 38:59–67.
- Bamisile, B. S., Dash, C. K., Akutse, K. S., Keppanan, R., and Wang, L. 2018. Fungal endophytes: Beyond herbivore management. *Front. Microbiol.* 9: 544.
- Benedetti, M., Pontiggia, D., Raggi, S., Cheng, Z., Scaloni, F., and Ferrari, S. 2015. Plant immunity triggered by engineered in vivo release of oligogalacturonides, damage-associated molecular patterns. *Proc. Natl. Acad. Sci. USA* 112:5533–5538.
- Bengyella, L., Yekwa, E. L., Nawaz, K., Iftikhar, S., Tambo, E., and Alisoltani, A. 2018. Global invasive *Cochliobolus* species: Cohort of destroyers with implications in food losses and insecurity in the twenty-first century. *Arch. Microbiol.* 200:119–135.
- Berens, M. L., Berry, H. M., Mine, A., Argueso, C. T., and Tsuda, K. 2017. Evolution of hormone signaling networks in plant defense. *Annu. Rev. Phytopathol.* 55:401–425.
- Berg, M., and Koskella, B. 2018. Nutrient- and dose-dependent microbiome-mediated protection against a plant pathogen. *Curr. Biol.* 28:2487–2492.E3.
- Bernal-Bayard, J., Cardenal-Muñoz, E., and Ramos-Morales, F. 2010. Salmonella type III secretion effector SlrP targets the human chaperone ERdj3. *J. Biol. Chem.* 285:16360–16368. link
- Bernal-Bayard, J., and Ramos-Morales, F. 2009. Salmonella type III secretion effector SlrP is an E3 ubiquitin ligase for mammalian thioredoxin. *J. Biol. Chem.* 284:27587–27595.
- Blacutt, A. A., Gold, S. E., Voss, K. A., Gao, M., and Glenn, A. E. 2018. *Fusarium verticillioides*: Advancements in understanding the toxicity, virulence, and niche adaptations of a model mycotoxigenic pathogen of maize. *Phytopathology* 108:312–326.
- Böhm, H., Albert, I., Oome, S., Raaymakers, T. M., Van den Ackerveken, G., and Nürnberger, T. 2014. A conserved peptide pattern from a widespread microbial virulence factor triggers pattern-induced immunity in Arabidopsis. *PLoS Pathog.* 10:e1004491.

Seven conclusions and future considerations

- Significant progress has been made in understanding NEs and their associated *R* or *S* genes, but many NEs and *S* loci have yet to be described. Continued characterization of NEs and their cognate *S* loci will facilitate elimination of *S* genes from breeding populations, when possible.
- Trophic divisions for plant pathogens (i.e., biotroph, necrotroph, endophyte, and mutualist) are conceptually useful but actually describe only life phases of plant-associated microbes and not the microorganisms themselves.
- Early time points of infection, before necrotrophic pathogens enter a necrotic phase, warrant continued investigation. In fact, any aspect of biotrophic defenses that influence necrotrophic resistance or susceptibility or successful establishment of mutualists is of interest.
- “Omics” is hastening identification of determinants for disease resistance but environmental factors, epistasis, and genetic background effects that complicate breeding for resistance to biotrophic pathogens also confound breeding for resistance to necrotrophic pathogens.
- The full potential of genomics will only be realized if plant genotypic diversity exists in seed banks or wild populations.
- Because history can repeat itself, novel necrotrophic diseases may emerge in the future (i) through HGT of NEs, (ii) as crops and pathogens geographically shift with changing climate, or, last but not least, (iii) if intensified breeding or engineering for biotrophic disease resistance results in plant phenotypes that are exploitable by necrotrophic pathogens for disease susceptibility.
- Strategies proposed for sustainable, durable reduction of biotrophic disease such as targeted alteration of *S* genes and use of APR genes implemented in combination with select, qualitative resistance and diverse genotype plantings (e.g., rotations and mosaics) should also be considered for minimizing the probability of novel and possibly catastrophic necrotrophic pathogen epidemics.

- Borrelli, V. M. G., Brambilla, V., Rogowsky, P., Marocco, A., and Lanubile, A. 2018. The enhancement of plant disease resistance using CRISPR/Cas9 technology. *Front. Plant Sci.* 9:1245.
- Bourke, P. M., Voorrips, R. E., Visser, R. G. F., and Maliapaard, C. 2018. Tools for genetic studies in experimental populations of polyploids. *Front. Plant Sci.* 9:513.
- Bourras, S., Praz, C. R., Spanu, P. D., and Keller, B. 2018. Cereal powdery mildew effectors: A complex toolbox for an obligate pathogen. *Curr. Opin. Microbiol.* 46:26-33.
- Boutrot, F., and Zipfel, C. 2017. Function, discovery, and exploitation of plant pattern recognition receptors for broad-spectrum disease resistance. *Annu. Rev. Phytopathol.* 55:257-286.
- Bozsoki, Z., Cheng, J., Feng, F., Gysel, K., Vinther, M., and Andersen, K. R. 2017. Receptor-mediated chitin perception in legume roots is functionally separable from Nod factor perception. *Proc. Natl. Acad. Sci. USA* 114: E8118-E8127.
- Brabham, H. J., Hernández-Pinzón, I., Holden, S., Lorang, J., and Moscou, M. J. 2018. An ancient integration in a plant NLR is maintained as a trans-species polymorphism. *bioRxiv Article* 239541.
- Brandwagt, B. F., Mesbah, L. A., Takken, F. L. W., Laurent, P. L., Kneppers, T. J. A., and Hille, J. 2000. A longevity assurance gene homolog of tomato mediates resistance to *Alternaria alternata* f. sp. *lycopersici* toxins and fumonisin B1. *Proc. Natl. Acad. Sci. USA* 97:4961-4966.
- Breen, S., Williams, S. J., Outram, M., Kobe, B., and Solomon, P. S. 2017. Emerging insights into the functions of pathogenesis-related protein 1. *Trends Plant Sci.* 22:871-879.
- Breen, S., Williams, S. J., Winterberg, B., Kobe, B., and Solomon, P. S. 2016. Wheat PR-1 proteins are targeted by necrotrophic pathogen effector proteins. *Plant J. Cell. Mol. Biol.* 88:13-25.
- Brutus, A., Sicilia, F., Macone, A., Cervone, F., and De Lorenzo, G. 2010. A domain swap approach reveals a role of the plant wall-associated kinase 1 (WAK1) as a receptor of oligogalacturonides. *Proc. Natl. Acad. Sci. USA* 107:9452-9457.
- Burdon, J. J., Zhan, J., Barrett, L. G., Papaix, J., and Thrall, P. H. 2016. Addressing the challenges of pathogen evolution on the world's arable crops. *Phytopathology* 106:1117-1127.
- Busby, P. E., Ridout, M., and Newcombe, G. 2016. Fungal endophytes: Modifiers of plant disease. *Plant Mol. Biol.* 90:645-655.
- Busby, P. E., Soman, C., Wagner, M. R., Friesen, M. L., Kremer, J., and Bennett, A. 2017. Research priorities for harnessing plant microbiomes in sustainable agriculture. *PLoS Biol.* 15:e2001793.
- Büsches, R., Hollricher, K., Panstruga, R., Simons, G., Wolter, M., and Frijters, A. 1997. The barley *Mlo* gene: A novel control element of plant pathogen resistance. *Cell* 88:695-705.
- Capistrano-Gossmann, G. G., Ries, D., Holtgräwe, D., Minoche, A., Kraft, T., Frerichmann, S. L. M. 2017. Crop wild relative populations of *Beta vulgaris* allow direct mapping of agronomically important genes. *Nat. Commun.* 8: Article 15708.
- Carella, P., Evangelisti, E., and Schornack, S. 2018. Sticking to it: Phytopathogen effector molecules may converge on evolutionarily conserved host targets in green plants. *Curr. Opin. Plant Biol.* 44:175-180.
- Chinchilla, D., Shan, L., He, P., de Vries, S., and Kemmerling, B. 2009. One for all: The receptor-associated kinase BAK1. *Trends Plant Sci.* 14:535-541.
- Choi, H. W., and Klessig, D. F. 2016. DAMPs, MAMPs, and NAMPs in plant innate immunity. *BMC Plant Biol.* 16:232.
- Ciuffetti, L. M., Manning, V. A., Pandelova, I., Betts, M. F., and Martinez, J. P. 2010. Host-selective toxins, Ptr ToxA and Ptr ToxB, as necrotrophic effectors in the *Pyrenophora tritici-repentis*-wheat interaction. *New Phytol.* 187:911-919.
- Clarke, C. R., Studholme, D. J., Hayes, B., Runde, B., Weisberg, A., and Cai, R. 2015. Genome-enabled phylogeographic investigation of the quarantine pathogen *Ralstonia solanacearum* race 3 biovar 2 and screening for sources of resistance against its core effectors. *Phytopathology* 105:597-607.
- Collet, J.-F., and Messens, J. 2010. Structure, function, and mechanism of thioredoxin proteins. *Antioxid. Redox Signal.* 13:1205-1216.
- Condon, B. J., Leng, Y., Wu, D., Bushley, K. E., Ohm, R. A., and Otiilar, R. 2013. Comparative genome structure, secondary metabolite, and effector coding capacity across *Cochliobolus* pathogens. *PLoS Genet.* 9:e1003233.
- Cook, D. E., Mesarich, C. H., and Thomma, B. P. H. J. 2015. Understanding plant immunity as a surveillance system to detect invasion. *Annu. Rev. Phytopathol.* 53:541-563.
- Couto, D., and Zipfel, C. 2016. Regulation of pattern recognition receptor signalling in plants. *Nat. Rev. Immunol.* 16:537-552.
- Dangl, J. L., Horvath, D. M., and Staskawicz, B. J. 2013. Pivoting the plant immune system from dissection to deployment. *Science* 341:746-751.
- Dangl, J. L., and Jones, J. D. G. 2001. Plant pathogens and integrated defence responses to infection. *Nature* 411:826-833.
- Dean, R., Kan, J. L. V., Pretorius, Z. A., Hammond-Kosack, K. E., Pietro, A. D., and Spanu, P. D. 2012. The Top 10 fungal pathogens in molecular plant pathology. *Mol. Plant Pathol.* 13:414-430.
- de Guillen, K., Ortiz-Vallejo, D., Gracy, J., Fournier, E., Kroj, T., and Padilla, A. 2015. Structure analysis uncovers a highly diverse but structurally conserved effector family in phytopathogenic fungi. *PLoS Pathog.* 11: e1005228.
- Delaux, P.-M., Radhakrishnan, G. V., Jayaraman, D., Cheema, J., Malbreil, M., and Volkening, J. D. 2015. Algal ancestor of land plants was preadapted for symbiosis. *Proc. Natl. Acad. Sci. USA* 112:13390-13395.
- Delays, L., García-Guzmán, G., and Heil, M. 2013. Endophytes versus biotrophic and necrotrophic pathogens—Are fungal lifestyles evolutionarily stable traits? *Fungal Divers.* 60:125-135.
- Deng, Y., Zhai, K., Xie, Z., Yang, D., Zhu, X., and Liu, J. 2017. Epigenetic regulation of antagonistic receptors confers rice blast resistance with yield balance. *Science* 355:962-965.
- de Vries, J., and Archibald, J. M. 2018. Plant evolution: Landmarks on the path to terrestrial life. *New Phytol.* 217:1428-1434.
- De Wit, P. J. G. M. 2016. Apoplastic fungal effectors in historic perspective: A personal view. *New Phytol.* 212:805-813.
- Dickman, M., Williams, B., Li, Y., de Figueiredo, P., and Wolpert, T. 2017. Reassessing apoptosis in plants. *Nat. Plants* 3:773-779.
- Downie, R. C., Bouvet, L., Furuki, E., Gosman, N., Gardner, K. A., and Mackay, I. J. 2018. Assessing European wheat sensitivities to *Parastagonospora nodorum* necrotrophic effectors and fine-mapping the Snn3-B1 locus conferring sensitivity to the effector SnTox3. *Front. Plant Sci.* 9: 881.
- Dunkle, L. D., and Macko, V. 1995. Peritoxins and their effects on sorghum. *Can. J. Bot.* 444-452.
- Effertz, R. J., Meinhardt, S. W., Anderson, J. A., Jordahl, J. G., and Francel, L. J. 2002. Identification of a chlorosis-inducing toxin from *Pyrenophora tritici-repentis* and the chromosomal location of an insensitivity locus in wheat. *Phytopathology* 92:527-533.
- Engelhardt, S., Stam, R., Hükelhoven, R., Engelhardt, S., Stam, R., and Hükelhoven, R. 2018. Good riddance? Breaking disease susceptibility in the era of new breeding technologies. *Agronomy (Basel, Switz.)* 8:114.
- Faris, J. D., Liu, Z., and Xu, S. S. 2013. Genetics of tan spot resistance in wheat. *Theor. Appl. Genet.* 126:2197-2217.
- Faris, J. D., Zhang, Z., Lu, H., Lu, S., Reddy, L., and Cloutier, S. 2010. A unique wheat disease resistance-like gene governs effector-triggered susceptibility to necrotrophic pathogens. *Proc. Natl. Acad. Sci. USA* 107: 13544-13549.
- Ficke, A., Cowger, C., Bergstrom, G., and Brodal, G. 2018. Understanding yield loss and pathogen biology to improve disease management: Septoria nodorum blotch—A case study in wheat. *Plant Dis.* 102:696-707.
- Fillinger, S., and Elad, Y., eds. 2016. Botrytis—The Fungus, the Pathogen and its Management in Agricultural Systems. Springer International Publishing, Cham.
- Finkel, O. M., Castrillo, G., Herrera Paredes, S., Salas González, I., and Dangl, J. L. 2017. Understanding and exploiting plant beneficial microbes. *Curr. Opin. Plant Biol.* 38:155-163.
- Flor, H. H. 1956. The complementary genic systems in flax and flax rust—Joint contribution from the Field Crops Research Branch, Agricultural Research Service, United States Department of Agriculture and the North Dakota Agricultural Experiment Station. Pages 29-54 in: *Advances in Genetics*. M. Demerec, ed. Academic Press, Cambridge, MA.
- Friesen, T. L., Chu, C., Xu, S. S., and Faris, J. D. 2012. SnTox5-Snn5: A novel *Stagonospora nodorum* effector-wheat gene interaction and its relationship with the SnToxA-Tsn1 and SnTox3-Snn3-B1 interactions. *Mol. Plant Pathol.* 13:1101-1109.
- Friesen, T. L., Faris, J. D., Solomon, P. S., and Oliver, R. P. 2008a. Host-specific toxins: Effectors of necrotrophic pathogenicity. *Cell Microbiol.* 10: 1421-1428.
- Friesen, T. L., Holmes, D. J., Bowden, R., and Faris, J. D. 2018. ToxA is present in the U.S. *Bipolaris sorokiniana* population and is a significant virulence factor on wheat harboring Tsn1. *Plant Dis.* 102:2446-2452.
- Friesen, T. L., Meinhardt, S. W., and Faris, J. D. 2007. The *Stagonospora nodorum*-wheat pathosystem involves multiple proteinaceous host-selective toxins and corresponding host sensitivity genes that interact in an inverse gene-for-gene manner. *Plant J.* 51:681-692.
- Friesen, T. L., Stukenbrock, E. H., Liu, Z., Meinhardt, S., Ling, H., and Faris, J. D. 2006. Emergence of a new disease as a result of interspecific virulence gene transfer. *Nat. Genet.* 38:953-956.
- Friesen, T. L., Zhang, Z., Solomon, P. S., Oliver, R. P., and Faris, J. D. 2008b. Characterization of the interaction of a novel *Stagonospora nodorum* host-selective toxin with a wheat susceptibility gene. *Plant Physiol.* 146: 682-693.

- Fukuoka, S., Saka, N., Mizukami, Y., Koga, H., Yamanouchi, U., Yoshioka, Y., Hayashi, N., Ebana, K., Mizobuchi, R., and Yano, M. 2015. Gene pyramiding enhances durable blast disease resistance in rice. *Sci. Rep.* 5: Article 7773.
- Gao, Y., Faris, J. D., Liu, Z., Kim, Y. M., Syme, R. A., and Oliver, R. P. 2015. Identification and characterization of the SnTox6-*Snn6* interaction in the *Parastagonospora nodorum*-wheat pathosystem. *Mol. Plant-Microbe Interact.* 28:615-625.
- Gao, Y., Liu, Z., Faris, J. D., Richards, J., Brueggeman, R. S., and Li, X. 2016. Validation of genome-wide association studies as a tool to identify virulence factors in *Parastagonospora nodorum*. *Phytopathology* 106: 1177-1185.
- Gao, Y., Wang, W., Zhang, T., Gong, Z., Zhao, H., and Han, G.-Z. 2018. Out of water: The origin and early diversification of plant *R*-genes. *Plant Physiol.* 177:82-89.
- Gaut, B. S., Seymour, D. K., Liu, Q., and Zhou, Y. 2018. Demography and its effects on genomic variation in crop domestication. *Nat. Plants* 4:512-520.
- Genre, A., and Russo, G. 2016. Does a common pathway transduce symbiotic signals in plant-microbe interactions? *Front. Plant Sci.* 7:96.
- Ghanbarnia, K., Fudal, I., Larkan, N. J., Links, M. G., Balesdent, M.-H., and Profotova, B. 2015. Rapid identification of the *Leptosphaeria maculans* avirulence gene AvrLm2 using an intraspecific comparative genomics approach. *Mol. Plant Pathol.* 16:699-709.
- Girard, I. J., Tong, C., Becker, M. G., Mao, X., Huang, J., and de Kievit, T. 2017. RNA sequencing of *Brassica napus* reveals cellular redox control of *Sclerotinia* infection. *J. Exp. Bot.* 68:5079-5091.
- Glazebrook, J. 2005. Contrasting mechanisms of defense against biotrophic and necrotrophic pathogens. *Annu. Rev. Phytopathol.* 43:205-227.
- Gout, L., Fudal, I., Kuhn, M.-L., Blaise, F., Eckert, M., and Cattolico, L. 2006. Lost in the middle of nowhere: The AvrLm1 avirulence gene of the Dothideomycete *Leptosphaeria maculans*. *Mol. Microbiol.* 60:67-80.
- Govrin, E. M., and Levine, A. 2000. The hypersensitive response facilitates plant infection by the necrotrophic pathogen *Botrytis cinerea*. *Curr. Biol.* 10:751-757.
- Greenough, P. R. 1982. Prosperity and Misery in Modern Bengal: The Famine of 1943-1944, first ed. Oxford University Press, New York.
- Guerreiro, A., Figueiredo, J., Sousa Silva, M., and Figueiredo, A. 2016. Linking jasmonic acid to grapevine resistance against the biotrophic oomycete *Plasmopara viticola*. *Front. Plant Sci.* 7:565.
- Guo, R., Tu, M., Wang, X., Zhao, J., Wan, R., Li, Z., Wang, Y., and Wang, X. 2016. Ectopic expression of a grape aspartic protease gene, AP13, in *Arabidopsis thaliana* improves resistance to powdery mildew but increases susceptibility to *Botrytis cinerea*. *Plant Sci.* 248:17-27.
- Gust, A. A., Pruitt, R., and Nürnberger, T. 2017. Sensing danger: Key to activating plant immunity. *Trends Plant Sci.* 22:779-791.
- Hacquard, S., Spaepen, S., Garrido-Oter, R., and Schulze-Lefert, P. 2017. Interplay between innate immunity and the plant microbiota. *Annu. Rev. Phytopathol.* 55:565-589.
- Häffner, E., Konietzki, S., Diederichsen, E., Häffner, E., Konietzki, S., and Diederichsen, E. 2015. Keeping control: The role of senescence and development in plant pathogenesis and defense. *Plants* 4:449-488.
- Hammond-Kosack, K. E., and Rudd, J. J. 2008. Plant resistance signalling hijacked by a necrotrophic fungal pathogen. *Plant Signal. Behav.* 3: 993-995.
- Havis, N. D., Nyman, M., and Oxley, S. J. P. 2014. Evidence for seed transmission and symptomless growth of *Ramularia collo-cygni* in barley (*Hordeum vulgare*). *Plant Pathol.* 63:929-936.
- He, Z. H., Fujiki, M., and Kohorn, B. D. 1996. A cell wall-associated, receptor-like protein kinase. *J. Biol. Chem.* 271:19789-19793.
- Hecht, V., Vielle-Calzada, J.-P., Hartog, M. V., Schmidt, E. D. L., Boutilier, K., and Grossniklaus, U. 2001. The *Arabidopsis* somatic embryogenesis receptor kinase 1 gene is expressed in developing ovules and embryos and enhances embryogenic competence in culture. *Plant Physiol.* 127:803-816.
- Heese, A., Hann, D. R., Gimenez-Ibanez, S., Jones, A. M. E., He, K., and Li, J. 2007. The receptor-like kinase SERK3/BAK1 is a central regulator of innate immunity in plants. *Proc. Natl. Acad. Sci. USA* 104:12217-12222.
- Huang, B. E., Verbyla, K. L., Verbyla, A. P., Raghavan, C., Singh, V. K., and Gaur, P. 2015. MAGIC populations in crops: Current status and future prospects. *Theor. Appl. Genet.* 128:999-1017.
- Iakovidis, M., Teixeira, P. J. P. L., Exposito-Alonso, M., Cowper, M. G., Law, T. F., and Liu, Q. 2016. Effector-triggered immune response in *Arabidopsis thaliana* is a quantitative trait. *Genetics* 204:337-353.
- Jiang, Z., Dong, X., and Zhang, Z. 2016. Network-based comparative analysis of *Arabidopsis* immune responses to *Gelovinomycetes orontii* and *Botrytis cinerea* infections. *Sci. Rep.* 6: Article 19149.
- Jones, D. A., Bertazzoni, S., Turo, C. J., Syme, R. A., and Hane, J. K. 2018. Bioinformatic prediction of plant-pathogenicity effector proteins of fungi. *Curr. Opin. Microbiol.* 46:43-49.
- Jones, J. D. G., and Dangl, J. L. 2006. The plant immune system. *Nature* 444: 323-329.
- Jones, J. D. G., Vance, R. E., and Dangl, J. L. 2016. Intracellular innate immune surveillance devices in plants and animals. *Science* 354: Article aaf6395.
- Kabbage, M., Kessens, R., Bartholomay, L. C., and Williams, B. 2017. The life and death of a plant cell. *Annu. Rev. Plant Biol.* 68:375-404.
- Kabbage, M., Williams, B., and Dickman, M. B. 2013. Cell death control: The interplay of apoptosis and autophagy in the pathogenicity of *Sclerotinia sclerotiorum*. *PLoS Pathog.* 9:e1003287.
- Kadota, Y., Shirasu, K., and Zipfel, C. 2015. Regulation of the NADPH Oxidase RBOHD during plant immunity. *Plant Cell Physiol.* 56:1472-1480.
- Karasov, T. L., Chae, E., Herman, J. J., and Bergelson, J. 2017. Mechanisms to mitigate the trade-off between growth and defense. *Plant Cell* 29: 666-680.
- Kariyawasam, G. K., Carter, A. H., Rasmussen, J. B., Faris, J., Xu, S. S., and Mergoum, M. 2016. Genetic relationships between race-nonspecific and race-specific interactions in the wheat-*Pyrenophora tritici-repentis* pathosystem. *Theor. Appl. Genet.* 129:897-908.
- Kema, G. H. J., Gohari, A. M., Aouini, L., Gibriel, H. A. Y., Ware, S. B., van den Bosch, F., Manning-Smith, R., Alonso-Chavez, V., Helps, J., Ben M'Barek, S., Mehrabi, R., Diaz-Trujillo, C., Zamani, E., Schouten, H. J., van der Lee, T. A. J., Waalwijk, C., de Waard, M. A., de Wit, P. J. G. M., Verstappen, E. C. P., Thomma, B. P. H. J., Meijer, H. J. G., and Seidl, M. F. 2018. Stress and sexual reproduction affect the dynamics of the wheat pathogen effector AvrStb6 and strobilurin resistance. *Nat. Genet.* 50: 375-380.
- Khan, M., Seto, D., Subramaniam, R., and Desveaux, D. 2018. Oh, the places they'll go! A survey of phytopathogen effectors and their host targets. *Plant J.* 93:651-663.
- Kiers, E. T., Duhamel, M., Beesetty, Y., Mensah, J. A., Franken, O., and Verbruggen, E. 2011. Reciprocal rewards stabilize cooperation in the mycorrhizal symbiosis. *Science* 333:880-882.
- Kim, S. H., Qi, D., Ashfield, T., Helm, M., and Innes, R. W. 2016. Using decoys to expand the recognition specificity of a plant disease resistance protein. *Science* 351:684-687.
- Kohler, A., Kuo, A., Nagy, L. G., Morin, E., Barry, K. W., and Buscot, F. 2015. Convergent losses of decay mechanisms and rapid turnover of symbiosis genes in mycorrhizal mutualists. *Nat. Genet.* 47:410-415.
- Kourelis, J., and van der Hoorn, R. A. L. 2018. Defended to the nines: 25 Years of resistance gene cloning identifies nine mechanisms for R protein function. *Plant Cell* 30:285-299.
- Krattinger, S. G., Lagudah, E. S., Spielmeier, W., Singh, R. P., Huerta-Espino, J., and McFadden, H. 2009. A putative ABC transporter confers durable resistance to multiple fungal pathogens in wheat. *Science* 323:1360-1363.
- Kumar, J., Huckelhoven, R., Beckhove, U., Nagarajan, S., and Kogel, K. H. 2001. A compromised Mlo pathway affects the response of barley to the necrotrophic fungus *Bipolaris sorokiniana* (teleomorph: *Cochliobolus sativus*) and its toxins. *Phytopathology* 91:127-133.
- Kumari, M., Rai, A. K., Devanna, B. N., Singh, P. K., Kapoor, R., and Rajashekara, H. 2017. Co-transformation mediated stacking of blast resistance genes Pi54 and Pi54rh in rice provides broad spectrum resistance against *Magnaporthe oryzae*. *Plant Cell Rep.* 36:1747-1755.
- Ladejobi, O., Elderfield, J., Gardner, K. A., Gaynor, R. C., Hickey, J., and Hibberd, J. M. 2016. Maximizing the potential of multi-parental crop populations. *Appl. Transl. Genomics* 11:9-17.
- Lal, N. K., Nagalakshmi, U., Hurlburt, N. K., Flores, R., Bak, A., and Sone, P. 2018. The receptor-like cytoplasmic kinase BIK1 localizes to the nucleus and regulates defense hormone expression during plant innate immunity. *Cell Host Microbe* 23:485-497.E5.
- Lamari, L., and Strelkov, S. E. 2010. Minireview/Minisynthese The wheat/*Pyrenophora tritici-repentis* interaction: Progress towards an understanding of tan spot disease. *Can. J. Plant Pathol.* 32:4-10.
- Lamari, L., Strelkov, S. E., Yahyaoui, A., Orabi, J., and Smith, R. B. 2003. The identification of two new races of *Pyrenophora tritici-repentis* from the host center of diversity confirms a one-to-one relationship in tan spot of wheat. *Phytopathology* 93:391-396.
- Larkan, N. J., Lydiate, D. J., Parkin, I. P., Nelson, M. N., Epp, D. J., and Cowling, W. A. 2013. The *Brassica napus* blackleg resistance gene LepR3 encodes a receptor-like protein triggered by the *Leptosphaeria maculans* effector AVRML1. *New Phytol.* 197:595-605.
- Larkan, N. J., Ma, L., and Borhan, M. H. 2015. The *Brassica napus* receptor-like protein RLM2 is encoded by a second allele of the LepR3/Rlm2 blackleg resistance locus. *Plant Biotechnol. J.* 13:983-992.
- Lee, T., and Lee, I. 2018. araGWAB: Network-based boosting of genome-wide association studies in *Arabidopsis thaliana*. *Sci. Rep.* 8: Article 2925.
- Leng, Y., Zhao, M., Wang, R., Steffenson, B. J., Brueggeman, R. S., and Zhong, S. 2018. The gene conferring susceptibility to spot blotch caused by

- Cochliobolus sativus* is located at the Mla locus in barley cultivar Bowman. Theor. Appl. Genet. 131:1531-1539.
- Le Roux, C., Huet, G., Jauneau, A., Camborde, L., Trémoulaye, D., and Kraut, A. 2015. A receptor pair with an integrated decoy converts pathogen disabling of transcription factors to immunity. Cell 161:1074-1088.
- Li, H., Rasheed, A., Hickey, L. T., and He, Z. 2018. Fast-forwarding genetic gain. Trends Plant Sci. 23:184-186.
- Li, J., Zhao, Z., Hayward, A., Cheng, H., and Fu, D. 2015. Integration analysis of quantitative trait loci for resistance to *Sclerotinia sclerotiorum* in *Brassica napus*. Euphytica 205:483-489.
- Li, X., Bai, H., Wang, X., Li, L., Cao, Y., and Wei, J. 2011. Identification and validation of rice reference proteins for Western blotting. J. Exp. Bot. 62: 4763-4772.
- Li, Z. K., Arif, M., Zhong, D. B., Fu, B. Y., Xu, J. L., Domingo-Rey, J., Vijayakumar, C. H. M., Yu, S. B., Khush, G. S. 2006. Complex genetic networks underlying the defensive system of rice (*Oryza sativa* L.) to *Xanthomonas oryzae* pv. *oryzae*. Proc. Natl. Acad. Sci. 103:7994-7999.
- Liang, X., and Rollins, J. A. 2018. Mechanisms of broad host range necrotrophic pathogenesis in *Sclerotinia sclerotiorum*. Phytopathology 108: 1128-1140.
- Liang, X., and Zhou, J.-M. 2018. Receptor-like cytoplasmic kinases: Central players in plant receptor kinase-mediated signaling. Annu. Rev. Plant Biol. 69:267-299.
- Liebrand, T. W. H., van den Berg, G. C. M., Zhang, Z., Smit, P., Cordewener, J. H. G., and America, A. H. P. 2013. Receptor-like kinase SOBIR1/EVR interacts with receptor-like proteins in plant immunity against fungal infection. Proc. Natl. Acad. Sci. USA 110:10010-10015.
- Litzenberger, S. C. 1949. Inheritance of resistance to specific races of crown rust, stem rust, and to Helminthosporium blight of oats. Iowa Agric. Home Economic Res. Stn. Res. Bull. 29: No. 370.
- Liu, L., Sonbol, F.-M., Huot, B., Gu, Y., Withers, J., and Mwimba, M. 2016. Salicylic acid receptors activate jasmonic acid signalling through a non-canonical pathway to promote effector-triggered immunity. Nat. Commun. 7: Article 13099.
- Liu, Q., Liu, H., Gong, Y., Tao, Y., Jiang, L., and Zuo, W. 2017. An atypical thioredoxin imparts early resistance to *Sugarcane mosaic virus* in maize. Mol. Plant 10:483-497.
- Liu, Z., Faris, J. D., Oliver, R. P., Tan, K.-C., Solomon, P. S., and McDonald, M. C. 2009. SnTox3 acts in effector triggered susceptibility to induce disease on wheat carrying the Snn3 gene. PLoS Pathog. 5:e1000581.
- Liu, Z., Gao, Y., Kim, Y. M., Faris, J. D., Shelver, W. L., and de Wit, P. J. G. M. 2016. SnTox1, a *Parastagonospora nodorum* necrotrophic effector, is a dual-function protein that facilitates infection while protecting from wheat-produced chitinases. New Phytol. 211:1052-1064.
- Liu, Z., Zhang, Z., Faris, J. D., Oliver, R. P., Syme, R., and McDonald, M. C. 2012. The cysteine rich necrotrophic effector SnTox1 produced by *Stagonospora nodorum* triggers susceptibility of wheat lines harboring Snn1. PLoS Pathog. 8:e1002467.
- Liu, Z., Zurn, J. D., Kariyawasam, G., Faris, J. D., Shi, G., and Hansen, J. 2017. Inverse gene-for-gene interactions contribute additively to tan spot susceptibility in wheat. Theor. Appl. Genet. 130:1267-1276.
- Lorang, J., Cuesta-Marcos, A., Hayes, P. M., and Wolpert, T. J. 2010. Identification and mapping of adult-onset sensitivity to victorin in barley. Mol. Breed. 26:545-550.
- Lorang, J., Kidarsa, T., Bradford, C. S., Gilbert, B., Curtis, M., Tzeng, S.-C., Maier, C. S., and Wolpert, T. J. 2012. Tricking the guard: Exploiting plant defense for disease susceptibility. Science 338:659-662.
- Lorang, J. M., Hagerty, C. H., Lee, R., McClean, P., and Wolpert, T. 2018. Genetic analysis of victorin sensitivity and identification of a causal nucleotide-binding site leucine-rich repeat gene in *Phaseolus vulgaris*. Mol. Plant-Microbe Interact. 31:1069-1074.
- Lorang, J. M., Sweat, T. A., and Wolpert, T. J. 2007. Plant disease susceptibility conferred by a "resistance" gene. Proc. Natl. Acad. Sci. USA 104: 14861-14866.
- Lori, M., van Verk, M. C., Hander, T., Schatowitz, H., Klauser, D., and Flury, P. 2015. Evolutionary divergence of the plant elicitor peptides (Peps) and their receptors: Interfamily incompatibility of perception but compatibility of downstream signalling. J. Exp. Bot. 66:5315-5325.
- Lowe, A., Harrison, N., and French, A. P. 2017. Hyperspectral image analysis techniques for the detection and classification of the early onset of plant disease and stress. Plant Methods 13:80.
- Lozano-Durán, R., Macho, A. P., Boutrot, F., Segonzac, C., Somssich, I. E., and Zipfel, C. 2013. The transcriptional regulator BZR1 mediates trade-off between plant innate immunity and growth. eLife 2:e00983.
- Lu, S., Faris, J. D., Sherwood, R., Friesen, T. L., and Edwards, M. C. 2014. A dimeric PR-1-type pathogenesis-related protein interacts with ToxA and potentially mediates ToxA-induced necrosis in sensitive wheat. Mol. Plant Pathol. 15:650-663.
- Lu, S., Gillian Turgeon, B., and Edwards, M. C. 2015. A ToxA-like protein from *Cochliobolus heterostrophus* induces light-dependent leaf necrosis and acts as a virulence factor with host selectivity on maize. Fungal Genet. Biol. 81:12-24.
- Ma, L., and Borhan, M. H. 2015. The receptor-like kinase SOBIR1 interacts with *Brassica napus* LepR3 and is required for *Leptosphaeria maculans* AvrLm1-triggered immunity. Front. Plant Sci. 6:933.
- Ma, Z., Song, T., Zhu, L., Ye, W., Wang, Y., Shao, Y., Dong, S., Zhang, Z., Dou, D., Zheng, X., Tyler, B. M., and Wang, Y. 2015. A *Phytophthora sojae* glycoside hydrolase 12 protein is a major virulence factor during soybean infection and is recognized as a PAMP. Plant Cell 27:2057-2072.
- Macho, A. P., Guevara, C. M., Tornero, P., Ruiz-Albert, J., and Beuzón, C. R. 2010. The *Pseudomonas syringae* effector protein HopZ1a suppresses effector-triggered immunity. New Phytol. 187:1018-1033.
- Makepeace, J. C., Oxley, S. J. P., Havis, N. D., Hackett, R., Burke, J. I., and Brown, J. K. M. 2007. Associations between fungal and abiotic leaf spotting and the presence of mlo alleles in barley. Plant Pathol. 56:934-942.
- Mammadov, J., Buyyarapu, R., Guttikonda, S. K., Parliament, K., Abdurakhmonov, I. Y., and Kumpatla, S. P. 2018. Wild relatives of maize, rice, cotton, and soybean: Treasure troves for tolerance to biotic and abiotic stresses. Front. Plant Sci. 9:886.
- Manning, V. A., Chu, A. L., Steeves, J. E., Wolpert, T. J., and Ciuffetti, L. M. 2009. A host-selective toxin of *Pyrenophora tritici-repentis*, Ptr ToxA, induces photosystem changes and reactive oxygen species accumulation in sensitive wheat. Mol. Plant-Microbe Interact. 22:665-676.
- Manning, V. A., and Ciuffetti, L. M. 2005. Localization of Ptr ToxA produced by *Pyrenophora tritici-repentis* reveals protein import into wheat mesophyll cells. Plant Cell 17:3203-3212.
- Manning, V. A., and Ciuffetti, L. M. 2015. Necrotrophic effector epistasis in the *Pyrenophora tritici-repentis*-wheat interaction. PLoS One 10:e0123548.
- Manning, V. A., Hamilton, S. M., Karplus, P. A., and Ciuffetti, L. M. 2008. The Arg-Gly-Asp-containing, solvent-exposed loop of Ptr ToxA is required for internalization. Mol. Plant-Microbe Interact. 21:315-325.
- Marri, P. R., Ye, L., Jia, Y., Jiang, K., and Rounsley, S. D. 2018. Advances in sequencing and resequencing in crop plants. Pages 11-35 in: Plant Genetics and Molecular Biology. R. K. Varshney, M. K. Pandey, and A. Chitkineni, eds. Advances in Biochemical Engineering/Biotechnology. SpringerNature, Switzerland, AG.
- Martinez, J. P., Ottum, S. A., Ali, S., Franci, L. J., and Ciuffetti, L. M. 2001. Characterization of the ToxB gene from *Pyrenophora tritici-repentis*. Mol. Plant-Microbe Interact. 14:675-677.
- McDonald, M. C., Ahren, D., Simpfendorfer, S., Milgate, A., and Solomon, P. S. 2018. The discovery of the virulence gene ToxA in the wheat and barley pathogen *Bipolaris sorokiniana*. Mol. Plant Pathol. 19:432-439.
- McDonald, M. C., Oliver, R. P., Friesen, T. L., Brunner, P. C., and McDonald, B. A. 2013. Global diversity and distribution of three necrotrophic effectors in *Phaeosphaeria nodorum* and related species. New Phytol. 199:241-251.
- McDonald, M. C., and Solomon, P. S. 2018. Just the surface: Advances in the discovery and characterization of necrotrophic wheat effectors. Curr. Opin. Microbiol. 46:14-18.
- McGrann, G. R. D., Stavrinides, A., Russell, J., Corbitt, M. M., Booth, A., and Chartrain, L. 2014. A trade off between mlo resistance to powdery mildew and increased susceptibility of barley to a newly important disease, Ramularia leaf spot. J. Exp. Bot. 65:1025-1037.
- Meehan, F., and Murphy, H. C. 1946. A new Helminthosporium blight of oats. Science 104:413-414.
- Meena, M., Gupta, S. K., Swapnil, P., Zehra, A., Dubey, M. K., and Upadhyay, R. S. 2017. *Alternaria* toxins: Potential virulence factors and genes related to pathogenesis. Front. Microbiol. 8:1451.
- Mei, J., Ding, Y., Lu, K., Wei, D., Liu, Y., and Disi, J. O. 2013. Identification of genomic regions involved in resistance against *Sclerotinia sclerotiorum* from wild *Brassica oleracea*. Theor. Appl. Genet. 126:549-556.
- Meng, D., Li, C., Park, H.-J., González, J., Wang, J., Dandekar, A. M. 2018. Sorbitol modulates resistance to *Alternaria alternata* by regulating the expression of an NLR resistance gene in apple. Plant Cell 30:1562-1581.
- Mesarich, C. H., Ökmen, B., Rovenich, H., Griffiths, S. A., Wang, C., and Karimi Jashni, M. 2018. Specific hypersensitive response-associated recognition of new apoplastic effectors from *Cladosporium fulvum* in wild tomato. Mol. Plant-Microbe Interact. 31:145-162.
- Minio, A., Lin, J., Gaut, B. S., and Cantu, D. 2017. How single molecule real-time sequencing and haplotype phasing have enabled reference-grade diploid genome assembly of wine grapes. Front. Plant Sci. 8:826.
- Mittler, R. 2002. Oxidative stress, antioxidants and stress tolerance. Trends Plant Sci. 7:405-410.
- Miya, A., Albert, P., Shinya, T., Desaki, Y., Ichimura, K., and Shirasu, K. 2007. CERK1, a LysM receptor kinase, is essential for chitin elicitor signaling in Arabidopsis. Proc. Natl. Acad. Sci. USA 104:19613-19618.

- Molla, K. A., Karmakar, S., Chanda, P. K., Sarkar, S. N., Datta, S. K., and Datta, K. 2016. Tissue-specific expression of *Arabidopsis* *NPR1* gene in rice for sheath blight resistance without compromising phenotypic cost. *Plant Sci.* 250:105-114.
- Moolhuijzen, P., See, P. T., Hane, J. K., Shi, G., Liu, Z., Oliver, R. P. 2018. Comparative genomics of the wheat fungal pathogen *Pyrenophora tritici-repentis* reveals chromosomal variations and genome plasticity. *BMC Genomics* 19:279.
- Mukhtar, M. S., Carvunis, A.-R., Dreze, M., Epple, P., Steinbrenner, J., and Moore, J. 2011. Independently evolved virulence effectors converge onto hubs in a plant immune system network. *Science* 333:596-601.
- Mundt, C. C. 2002. Use of multiline cultivars and cultivar mixtures for disease management. *Annu. Rev. Phytopathol.* 40:381-410.
- Mundt, C. C. 2018. Pyramiding for resistance durability: Theory and practice. *Phytopathology* 108:792-802.
- Murray, G. M., and Brennan, J. P. 2009. Estimating disease losses to the Australian wheat industry. *Australas. Plant Pathol.* 38:558-570.
- Nagy, E. D., and Bennetzen, J. L. 2008. Pathogen corruption and site-directed recombination at a plant disease resistance gene cluster. *Genome Res.* 18:1918-1923.
- Newton, A. C., Fitt, B. D. L., Atkins, S. D., Walters, D. R., and Daniell, T. J. 2010. Pathogenesis, parasitism and mutualism in the trophic space of microbe-plant interactions. *Trends Microbiol.* 18:365-373.
- Ning, Y., Liu, W., and Wang, G.-L. 2017. Balancing immunity and yield in crop plants. *Trends Plant Sci.* 22:1069-1079.
- Nishimura, M. T., Anderson, R. G., Cherkis, K. A., Law, T. F., Liu, Q. L., and Machius, M. 2017. TIR-only protein RBA1 recognizes a pathogen effector to regulate cell death in *Arabidopsis*. *Proc. Natl. Acad. Sci. USA* 114:E2053-E2062.
- Nishimura, M. T., Monteiro, F., and Dangel, J. L. 2015. Treasure your exceptions: Unusual domains in immune receptors reveal host virulence targets. *Cell* 161:957-960.
- Nyarko, A., Singarapu, K. K., Figueroa, M., Manning, V. A., Pandelova, I., Wolpert, T. J., Ciuffetti, L. M., and Barbar, E. 2014. Solution NMR structures of active *Pyrenophora tritici-repentis* ToxB and its inactive homolog reveal potential determinants of toxin activity. *J. Biol. Chem.* 289:25946-25956. [link](#)
- Oome, S., Raaymakers, T. M., Cabral, A., Samwel, S., Böhm, H., and Albert, I. 2014. Nep1-like proteins from three kingdoms of life act as a microbe-associated molecular pattern in *Arabidopsis*. *Proc. Natl. Acad. Sci. USA* 111:16955-16960.
- Pandelova, I., Betts, M. F., Manning, V. A., Wilhelm, L. J., Mockler, T. C., and Ciuffetti, L. M. 2009. Analysis of transcriptome changes induced by Ptr ToxA in wheat provides insights into the mechanisms of plant susceptibility. *Mol. Plant* 2:1067-1083.
- Pandelova, I., Figueroa, M., Wilhelm, L. J., Manning, V. A., Mankaney, A. N., and Mockler, T. C. 2012. Host-selective toxins of *Pyrenophora tritici-repentis* induce common responses associated with host susceptibility. *PLoS One* 7:e40240.
- Park, C. H., Shirsekar, G., Bellizzi, M., Chen, S., Songkumarn, P., and Xie, X. 2016. The E3 Ligase APIP10 Connects the Effector AvrPiz-t to the NLR Receptor Piz-t in Rice. *PLoS Pathog.* 12:e1005529.
- Patel, J. S., Mamidi, S., Bonman, J. M., and Adhikari, T. B. 2013. Identification of QTL in spring wheat associated with resistance to a novel isolate of *Pyrenophora tritici-repentis*. *Crop Sci.* 53:842-852.
- Pérez-Jaramillo, J. E., Carrión, V. J., Bosse, M., Ferrão, L. F. V., de Hollander, M., and Garcia, A. A. F. 2017. Linking rhizosphere microbiome composition of wild and domesticated *Phaseolus vulgaris* to genotypic and root phenotypic traits. *ISME J.* 11:2244-2257.
- Petit-Houdenot, Y., and Fudal, I. 2017. Complex interactions between fungal avirulence genes and their corresponding plant resistance genes and consequences for disease resistance management. *Front. Plant Sci.* 8:1072.
- Petrov, V., Qureshi, M. K., Hille, J., and Gechev, T. 2018. Occurrence, biochemistry and biological effects of host-selective plant mycotoxins. *Food Chem. Toxicol.* 112:251-264.
- Phan, H. T. T., Rybak, K., Bertazzoni, S., Furuki, E., Dinglasan, E., and Hickey, L. T. 2018. Novel sources of resistance to Septoria nodorum blotch in the Vavilov wheat collection identified by genome-wide association studies. *Theor. Appl. Genet.* 131:1223-1238.
- Pilet-Nayel, M.-L., Moury, B., Caffier, V., Montarry, J., Kerlan, M.-C., Fournet, S. 2017. Quantitative resistance to plant pathogens in pyramiding strategies for durable crop protection. *Front. Plant Sci.* 8:1838.
- Plett, J. M., and Martin, F. M. 2018. Know your enemy, embrace your friend: Using omics to understand how plants respond differently to pathogenic and mutualistic microorganisms. *Plant J.* 93:729-746.
- Ponce de León, I., and Montesano, M. 2017. Adaptation mechanisms in the evolution of moss defenses to microbes. *Front. Plant Sci.* 8:366.
- Postma, J., Liebrand, T. W. H., Bi, G., Evrard, A., Bye, R. R., and Mbengue, M. 2016. Avr4 promotes Cf-4 receptor-like protein association with the BAK1/SERK3 receptor-like kinase to initiate receptor endocytosis and plant immunity. *New Phytol.* 210:627-642.
- Qi, J., Wang, J., Gong, Z., and Zhou, J.-M. 2017. Apoplastic ROS signaling in plant immunity. *Curr. Opin. Plant Biol.* 38:92-100.
- Rahman, T. A. E., Oirdi, M. E., Gonzalez-Lamothe, R., and Bouarab, K. 2012. Necrotrophic pathogens use the salicylic acid signaling pathway to promote disease development in tomato. *Mol. Plant-Microbe Interact.* 25:1584-1593.
- Ranf, S. 2017. Sensing of molecular patterns through cell surface immune receptors. *Curr. Opin. Plant Biol.* 38:68-77.
- Rees, R. G., and Platz, G. J. 1983. Effects of yellow spot on wheat: Comparison of epidemics at different stages of crop development. *Aust. J. Agric. Res.* 34:39-46.
- Rey, T., and Jacquet, C. 2018. Symbiosis genes for immunity and vice versa. *Curr. Opin. Plant Biol.* 44:64-71.
- Rimbaud, L., Papaix, J., Rey, J.-F., Barrett, L. G., and Thrall, P. H. 2018. Assessing the durability and efficiency of landscape-based strategies to deploy plant resistance to pathogens. *PLOS Comput. Biol.* 14:e1006067.
- Rodriguez, R. J., White, J. F., Jr., Arnold, A. E., and Redman, R. S. 2009. Fungal endophytes: Diversity and functional roles. *New Phytol.* 182:314-330.
- Rodriguez-Moreno, L., Ebert, M. K., Bolton, M. D., and Thomma, B. P. H. J. 2018. Tools of the crook- infection strategies of fungal plant pathogens. *Plant J.* 93:664-674.
- Rouzel, T., and Balesdent, M.-H. 2017. Life, death and rebirth of avirulence effectors in a fungal pathogen of Brassica crops, *Leptosphaeria maculans*. *New Phytol.* 214:526-532.
- Rudd, J. J., Keon, J., and Hammond-Kosack, K. E. 2008. The wheat mitogen-activated protein kinases TaMPK3 and TaMPK6 are differentially regulated at multiple levels during compatible disease interactions with *Mycosphaerella graminicola*. *Plant Physiol.* 147:802-815.
- Sagi, M. S., Deokar, A. A., and Tar'an, B. 2017. Genetic analysis of NBS-LRR gene family in chickpea and their expression profiles in response to Ascochyta blight infection. *Front. Plant Sci.* 8:838.
- Saijo, Y., Loo, E. P.-I., and Yasuda, S. 2018. Pattern recognition receptors and signaling in plant-microbe interactions. *Plant J.* 93:592-613.
- Saintenac, C., Lee, W.-S., Cambon, F., Rudd, J. J., King, R. C., and Marande, W. 2018. Wheat receptor-kinase-like protein Stb6 controls gene-for-gene resistance to fungal pathogen *Zymoseptoria tritici*. *Nat. Genet.* 50:368-374.
- Samsatly, J., Copley, T. R., and Jabaji, S. H. 2018. Antioxidant genes of plants and fungal pathogens are distinctly regulated during disease development in different *Rhizoctonia solani* pathosystems. *PLoS One* 13:e0192682.
- Sánchez-Vallet, A., McDonald, M. C., Solomon, P. S., and McDonald, B. A. 2015. Is *Zymoseptoria tritici* a hemibiotroph? *Fungal Genet. Biol.* 79:29-32.
- Sarma, G. N., Manning, V. A., Ciuffetti, L. M., and Karplus, P. A. 2005. Structure of Ptr ToxA: An RGD-containing host-selective toxin from *Pyrenophora tritici-repentis*. *Plant Cell* 17:3190-3202.
- Sarris, P. F., Cevik, V., Dagdas, G., Jones, J. D. G., and Krasileva, K. V. 2016. Comparative analysis of plant immune receptor architectures uncovers host proteins likely targeted by pathogens. *BMC Biol.* 14:8.
- See, P. T., Marathamuthu, K. A., Iagallo, E. M., Oliver, R. P., and Moffat, C. S. 2018. Evaluating the importance of the tan spot ToxA-Tsn1 interaction in Australian wheat varieties. *Plant Pathol.* 67:1066-1075.
- Shankar, M., Mather, D., Jorgensen, D., Golzar, H., Chalmers, K., Hollaway, G. 2015. Germplasm enhancement for resistance to *Pyrenophora tritici-repentis* in wheat. Pages 193-199 in: *Advances in Wheat Genetics: From Genome to Field*. Y. Ogihara, S. Takumi, and H. Handa, eds. Springer Japan.
- Shaw, M. W., Emmanuel, C. J., Emilda, D., Terhem, R. B., Shafia, A., Tsamadi, D. 2016. Analysis of cryptic, systemic *Botrytis* infections in symptomless hosts. *Front. Plant Sci.* 7:625.
- Shi, G., Zhang, Z., Friesen, T. L., Raats, D., Fahima, T., and Brueggeman, R. S. 2016. The hijacking of a receptor kinase-driven pathway by a wheat fungal pathogen leads to disease. *Sci. Adv.* 2:e1600822.
- Shi, Y., Qin, Y., Cao, Y., Sun, H., Zhou, T., and Hong, Y. 2011. Influence of an m-type thioredoxin in maize on potyviral infection. *Eur. J. Plant Pathol.* 131:317-326.
- Simon, S., and Lal, A. A. 2013. A new blight disease of rice caused by *Curvularia lunata* from Uttar Pradesh. *Int. J. Agric. Sci. Res.* 3:13-16.
- Singh, P. K., Singh, R. P., Duveiller, E., Mergoum, M., Adhikari, T. B., and Elias, E. M. 2010. Genetics of wheat-*Pyrenophora tritici-repentis* interactions. *Euphytica* 171:1-13.
- Spassieva, S. D., Markham, J. E., and Hille, J. 2002. The plant disease resistance gene Asc-1 prevents disruption of sphingolipid metabolism during AAL-toxin-induced programmed cell death. *Plant J.* 32:561-572.

- Sperschneider, J., Dodds, P. N., Gardiner, D. M., Singh, K. B., and Taylor, J. M. 2018. Improved prediction of fungal effector proteins from secretomes with effectorP 2.0. *Mol. Plant Pathol.* 19:2094-2110.
- Spoel, S. H., and Dong, X. 2008. Making sense of hormone crosstalk during plant immune responses. *Cell Host Microbe* 3:348-351.
- Stotz, H. U., Harvey, P. J., Haddadi, P., Mashanova, A., Kukol, A., and Larkan, N. J. 2018. Genomic evidence for genes encoding leucine-rich repeat receptors linked to resistance against the eukaryotic extra- and intracellular *Brassica napus* pathogens *Leptosphaeria maculans* and *Plasmiodiophora brassicae*. *PLoS One* 13:e0198201.
- Stotz, H. U., Mitrousis, G. K., de Wit, P. J. G. M., and Fitt, B. D. L. 2014. Effector-triggered defence against apoplastic fungal pathogens. *Trends Plant Sci.* 19:491-500.
- Strelkov, S. E., and Lamari, L. 2003. Host-parasite interactions in tan spot [*Pyrenophora tritici-repentis*] of wheat. *Can. J. Plant Pathol.* 25: 339-349.
- Su, J., Spears, B. J., Kim, S. H., and Gassmann, W. 2018. Constant vigilance: Plant functions guarded by resistance proteins. *Plant J.* 93:637-650.
- Sweat, T. A., Lorang, J. M., Bakker, E. G., and Wolpert, T. J. 2008. Characterization of natural and induced variation in the LOV1 gene, a CC-NB-LRR gene conferring victorin sensitivity and disease susceptibility in *Arabidopsis*. *Mol. Plant-Microbe Interact.* 21:7-19.
- Sweat, T. A., and Wolpert, T. J. 2007. Thioredoxin h5 is required for victorin sensitivity mediated by a CC-NBS-LRR gene in *Arabidopsis*. *Plant Cell* 19: 673-687.
- Tada, Y., Spoel, S. H., Pajeroska-Mukhtar, K., Mou, Z., Song, J., and Wang, C. 2008. Plant immunity requires conformational changes [corrected] of NPR1 via S-nitrosylation and thioredoxins. *Science* 321:952-956.
- Tang, D., Wang, G., and Zhou, J.-M. 2017. Receptor kinases in plant-pathogen interactions: More than pattern recognition. *Plant Cell* 29:618-637.
- Thomas, S., Behrmann, J., Steier, A., Kraska, T., Muller, O., and Rascher, U. 2018. Quantitative assessment of disease severity and rating of barley cultivars based on hyperspectral imaging in a non-invasive, automated phenotyping platform. *Plant Methods* 14:45.
- Thomma, B. P. H. J., Nürnberger, T., and Joosten, M. H. A. J. 2011. Of PAMPs and effectors: The blurred PTI-ETI dichotomy. *Plant Cell* 23:4-15.
- Tian, D., Traw, M. B., Chen, J. Q., Kreitman, M., and Bergelson, J. 2003. Fitness costs of R-gene-mediated resistance in *Arabidopsis thaliana*. *Nature* 423:74-77.
- Toju, H., Peay, K. G., Yamamichi, M., Narisawa, K., Hiruma, K., and Naito, K. 2018. Core microbiomes for sustainable agroecosystems. *Nat. Plants* 4: 247-257.
- Torres, M. A., and Dangl, J. L. 2005. Functions of the respiratory burst oxidase in biotic interactions, abiotic stress and development. *Curr. Opin. Plant Biol.* 8:397-403.
- Toruño, T. Y., Stergiopoulos, I., and Coaker, G. 2016. Plant-pathogen effectors: Cellular probes interfering with plant defenses in spatial and temporal manners. *Annu. Rev. Phytopathol.* 54:419-441.
- Tsuda, K., Mine, A., Bethke, G., Igarashi, D., Botanga, C. J., and Tsuda, Y. 2013. Dual regulation of gene expression mediated by extended MAPK activation and salicylic acid contributes to robust innate immunity in *Arabidopsis thaliana*. *PLoS Genet.* 9:e1004015.
- Uhse, S., and Djamei, A. 2018. Effectors of plant-colonizing fungi and beyond. *PLoS Pathog.* 14:e1006992.
- Ullstrup, A. J. 1972. The impacts of the southern corn leaf blight epidemics of 1970-1971. *Annu. Rev. Phytopathol.* 10:37-50.
- Upson, J. L., Zess, E. K., Bialas, A., Wu, C.-H., and Kamoun, S. 2018. The coming of age of EvoMPMI: Evolutionary molecular plant-microbe interactions across multiple timescales. *Curr. Opin. Plant Biol.* 44:108-116.
- Varden, F. A., De la Concepcion, J. C., Maidment, J. H., and Banfield, M. J. 2017. Taking the stage: Effectors in the spotlight. *Curr. Opin. Plant Biol.* 38: 25-33.
- Veloso, J., and van Kan, J. A. L. 2018. Many shades of grey in Botrytis-host plant interactions. *Trends Plant Sci.* 23:613-622.
- Veronese, P., Nakagami, H., Bluhm, B., Abuqamar, S., Chen, X., and Salmeron, J. 2006. The membrane-anchored BOTRYTIS-INDUCED KINASE1 plays distinct roles in *Arabidopsis* resistance to necrotrophic and biotrophic pathogens. *Plant Cell* 18:257-273.
- Virdi, S. K., Liu, Z., Overlander, M. E., Zhang, Z., Xu, S. S., Friesen, T. L., and Faris, J. D. 2016. New insights into the roles of host gene-necrotrophic effector interactions in governing susceptibility of durum wheat to tan spot and Septoria nodorum blotch. *G3 Genes Genomes Genet.* 6:4139-4150.
- Vleeshouwers, V. G. A. A., and Oliver, R. P. 2014. Effectors as tools in disease resistance breeding against biotrophic, hemibiotrophic, and necrotrophic plant pathogens. *Mol. Plant-Microbe Interact.* 27:196-206.
- Wang, E., Wang, J., Zhu, X., Hao, W., Wang, L., and Li, Q. 2008. Control of rice grain-filling and yield by a gene with a potential signature of domestication. *Nat. Genet.* 40:1370-1374.
- Wang, M., Roux, F., Bartoli, C., Huard-Chauveau, C., Meyer, C., Lee, H., Roby, D., McPeck, M. S., and Bergelson, J. 2018. Two-way mixed-effects methods for joint association analysis using both host and pathogen genomes. *Proc. Natl. Acad. Sci. USA* 115:E5440-E5449.
- Wang, M., Thomas, N., and Jin, H. 2017. Cross-kingdom RNA trafficking and environmental RNAi for powerful innovative pre- and post-harvest plant protection. *Curr. Opin. Plant Biol.* 38:133-141.
- Wang, R., Ning, Y., Shi, X., He, F., Zhang, C., and Fan, J. 2016. Immunity to rice blast disease by suppression of effector-triggered necrosis. *Curr. Biol.* 26:2399-2411.
- Wang, W., Yang, X., Tangchaiburana, S., Ndeh, R., Markham, J. E., and Tsegaye, Y. 2008. An inositolphosphorylceramide synthase is involved in regulation of plant programmed cell death associated with defense in *Arabidopsis*. *Plant Cell* 20:3163-3179.
- Wang, X., Jiang, N., Liu, J., Liu, W., and Wang, G.-L. 2014. The role of effectors and host immunity in plant-necrotrophic fungal interactions. *Virulence* 5:722-732.
- Watson, A., Ghosh, S., Williams, M. J., Cuddy, W. S., Simmonds, J., and Rey, M.-D. 2018. Speed breeding is a powerful tool to accelerate crop research and breeding. *Nat. Plants* 4:23-29.
- Weiberg, A., Bellinger, M., and Jin, H. 2015. Conversations between kingdoms: Small RNAs. *Curr. Opin. Biotechnol.* 32:207-215.
- Weiberg, A., Wang, M., Lin, F. M., Zhao, H., Zhang, Z., Kaloshian, I., Huang, H. D., and Jin, H. 2013. Fungal small RNAs suppress plant immunity by hijacking host RNA interference pathways. *Science* 342:118-123.
- Wefling, R., Eppele, P., Altmann, S., He, Y., Yang, L., and Henz, S. R. 2014. Convergent targeting of a common host protein-network by pathogen effectors from three kingdoms of life. *Cell Host Microbe* 16:364-375.
- Williams, B., Kabbage, M., Kim, H.-J., Britt, R., and Dickman, M. B. 2011. Tipping the balance: *Sclerotinia sclerotiorum* secreted oxalic acid suppresses host defenses by manipulating the host redox environment. *PLoS Pathog.* 7:e1002107.
- Willcoquet, L., Savary, S., and Yuen, J. 2017. Multiscale phenotyping and decision strategies in breeding for resistance. *Trends Plant Sci.* 22:420-432.
- Wolpert, T. J., Dunkle, L. D., and Ciuffetti, L. M. 2002. Host-selective toxins and avirulence determinants: What's in a name? *Annu. Rev. Phytopathol.* 40:251-285.
- Wolpert, T. J., and Lorang, J. M. 2016. Victoria blight, defense turned upside down. *Physiol. Mol. Plant Pathol.* 95:8-13.
- Wright, S. I., Bi, I. V., Schroeder, S. G., Yamasaki, M., Doebley, J. F., and McMullen, M. D. 2005. The effects of artificial selection on the maize genome. *Science* 308:1310-1314.
- Wu, J., Zhao, Q., Yang, Q., Liu, H., Li, Q., and Yi, X. 2016. Comparative transcriptomic analysis uncovers the complex genetic network for resistance to *Sclerotinia sclerotiorum* in *Brassica napus*. *Sci. Rep.* 6: Article 19007.
- Xu, G., Yuan, M., Ai, C., Liu, L., Zhuang, E., and Karapetyan, S. 2017. uORF-mediated translation allows engineered plant disease resistance without fitness costs. *Nature* 545:491-494.
- Yang, G., Tang, L., Gong, Y., Xie, J., Fu, Y., and Jiang, D. 2018. A ceratoplatenin protein SsCP1 targets plant PR1 and contributes to virulence of *Sclerotinia sclerotiorum*. *New Phytol.* 217:739-755.
- Yang, Q., He, Y., Kabahuma, M., Chaya, T., Kelly, A., and Borrego, E. 2017. A gene encoding maize caffeoyl-CoA O-methyltransferase confers quantitative resistance to multiple pathogens. *Nat. Genet.* 49:1364-1372.
- Yasuda, S., Okada, K., and Saijo, Y. 2017. A look at plant immunity through the window of the multitasking coreceptor BAK1. *Curr. Opin. Plant Biol.* 38:10-18.
- Yoshida, K., Saunders, D. G. O., Mitsuoka, C., Natsume, S., Kosugi, S., and Saitoh, H. 2016. Host specialization of the blast fungus *Magnaporthe oryzae* is associated with dynamic gain and loss of genes linked to transposable elements. *BMC Genomics* 17:370.
- Yuan, Y., Bayer, P. E., Batley, J., and Edwards, D. 2017. Improvements in genomic technologies: Application to crop genomics. *Trends Biotechnol.* 35:547-558.
- Zaidi, S. S.-A., Mukhtar, M. S., and Mansoor, S. 2018. Genome editing: Targeting susceptibility genes for plant disease resistance. *Trends Biotechnol.* 36:898-906.
- Zhang, H., Mittal, N., Leamy, L. J., Barazani, O., and Song, B.-H. 2017. Back into the wild—Apply untapped genetic diversity of wild relatives for crop improvement. *Evol. Appl.* 10:5-24.
- Zhang, L., Huang, X., He, C., Zhang, Q.-Y., Zou, X., Duan, K. 2018. Novel fungal pathogenicity and leaf defense strategies are revealed by simultaneous transcriptome analysis of *Colletotrichum fructicola* and strawberry infected by this fungus. *Front. Plant Sci.* 9:434.
- Zhang, L., Kars, I., Essenstam, B., Liebrand, T. W. H., Wagemakers, L., and Elberse, J. 2014. Fungal endopolygalacturonases are recognized as microbe-associated molecular patterns by the *Arabidopsis* receptor-like protein RE-SPONSIVENESS TO BOTRYTIS POLYGALACTURONASES1. *Plant Physiol.* 164:352-364.

- Zhang, X., Dodds, P. N., and Bernoux, M. 2017. What do we know about NOD-like receptors in plant immunity? *Annu. Rev. Phytopathol.* 55:205-229.
- Zhong, Z., Marcel, T. C., Hartmann, F. E., Ma, X., Plissonneau, C., and Zala, M. 2017. A small secreted protein in *Zymoseptoria tritici* is responsible for avirulence on wheat cultivars carrying the Stb6 resistance gene. *New Phytol.* 214:619-631.
- Zhou, B., Qu, S., Liu, G., Dolan, M., Sakai, H., and Lu, G. 2006. The eight amino-acid differences within three leucine-rich repeats between Pi2 and Piz-t resistance proteins determine the resistance specificity to *Magnaporthe oryzae*. *Mol. Plant-Microbe Interact.* 19:1216-1228.
- Zhu, W., Ronen, M., Gur, Y., Minz-Dub, A., Masrati, G., and Ben-Tal, N. 2017. BcXYG1, a secreted xyloglucanase from *Botrytis cinerea*, triggers both cell death and plant immune responses. *Plant Physiol.* 175:438-456.
- Zhu, X., Lu, C., Du, L., Ye, X., Liu, X., and Coules, A. 2017. The wheat NB-LRR gene TaRCR1 is required for host defence response to the necrotrophic fungal pathogen *Rhizoctonia cerealis*. *Plant Biotechnol. J.* 15:674-687.
- Zhu, Y., Chen, H., Fan, J., Wang, Y., Li, Y., and Chen, J. 2000. Genetic diversity and disease control in rice. *Nature* 406:718-722.
- Ziemann, S., van der Linde, K., Lahrmann, U., Acar, B., Kaschani, F., and Colby, T. 2018. An apoplastic peptide activates salicylic acid signalling in maize. *Nat. Plants* 4:172-180.
- Zipfel, C., and Oldroyd, G. E. D. 2017. Plant signalling in symbiosis and immunity. *Nature* 543:328-336.