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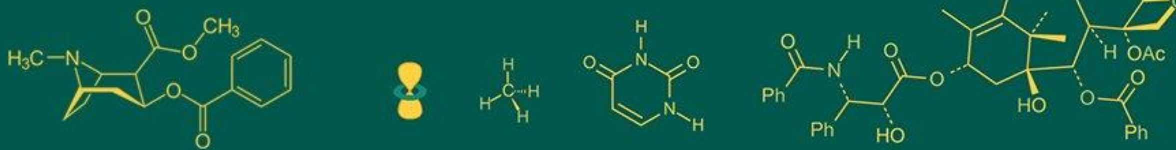

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Deciphering host manipulation strategies: Exploring Effector-target interactions in necrotrophic pathosystem

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Abstract
This comprehensive review delves into the intricate dynamics of host-pathogen interactions, focusing on three necrotrophic pathogens - *Pyrenophora tritici-repentis*, *Parastagonospora nodorum*, and *Zymoseptoria tritici* and their impact on wheat health. By dissecting infection processes, effector proteins, and susceptibility factor interactions, the review elucidates the strategies employed by these pathogens to colonize and thrive within wheat tissues. From the role of necrotrophic effectors like Ptr ToxA and SnTox1 in inducing programmed cell death to the genetic basis of susceptibility conferred by genes like Tsn1 and Snn1, each pathosystem unfolds a complex interplay between pathogen virulence and host defense. The review underscores the critical need for a nuanced understanding of these interactions to develop effective strategies for mitigating wheat diseases and ensuring global food security.

Keywords: Host-pathogen interactions, necrotrophic pathogens, wheat diseases, effector proteins, susceptibility genes, plant defense mechanisms

Introduction

Plant-fungal interactions are categorized into different types such as biotrophic, hemibiotrophic, and necrotrophic interactions, based on the pathogen's feeding behavior. Much of the scientific exploration in genetics and molecular biology has concentrated on the classical biotrophic feeding strategy. In this strategy, pathogens produce effector molecules that aid in colonization by manipulating the host. In response, plants have developed surveillance mechanisms to detect pathogen-related molecular patterns (Dodds and Rathjen, 2010) [11], (Thomma *et al*., 2011) [82], (Toruno *et al*., 2016) [85]. These mechanisms include pattern recognition receptors (PRRs) that recognize pathogen-associated molecular patterns (PAMPs), and effector-triggered immunity (ETI), which involves the recognition of pathogen-produced effector molecules. ETI often engages host resistance genes, particularly those encoding proteins with nucleotide-binding and leucine-rich repeat domains (NLR proteins). These conceptual models have significantly contributed to our understanding of host-pathogen interactions, exemplified by systems like the *Melampsora lini*-flax pathosystem proposed by H.H. Flor, which introduced the gene-for-gene hypothesis (Flor, 1942) [23], (Flor, 1955) [22], (Flor, 1971) [21]. To thrive and reproduce, pathogens must navigate around, inhibit, or influence the plant's innate defense mechanisms effectively. These mechanisms typically involve activating genes responsible for defense responses, increasing the production of pathogenesis-related (PR) proteins like chitinase and antimicrobial compounds, generating harmful levels of reactive oxygen species (ROS) through oxidative bursts, initiating defense pathways such as the phenylpropanoid pathway, and triggering the hypersensitive response (HR), a process that leads to controlled cell death in localized areas.

While all pathogens must manipulate elements of the defense response, necrotrophic pathogens have not been easily categorized within the established models of plant immunity designed for biotrophs. This article examines three necrotrophic pathogens - *Pyrenophora tritici-repentis*, *Parastagonospora nodorum*, and *Zymoseptoria tritici* - constituting the foliar

disease complex in wheat. It explores how these pathogens, despite inducing similar necrotic symptoms, have evolved both shared and distinct strategies for colonization aimed at achieving the ultimate goal of reproduction (sporulation). The discussion centers on the effectors produced by these pathogens and the corresponding receptors/targets in the host that mediate these necrotrophic interactions, leading to the development of three distinct wheat diseases of global significance. The review underscores the notion that each pathogen has independently evolved in concert with its specific host, resulting in a complex sequence of precisely timed interactions driven by the ongoing evolution of host-pathogen relationships.

Pyrenophora tritici-repentis - Wheat Pathosystem Infection Process

Tan spot, a significant disease in wheat production worldwide, is caused by *P. tritici-repentis* (Faris *et al*., 2013) [18]. Early studies utilized light microscopy to observe pathogen germination, penetration, and colonization patterns (Larez *et al*., 1986) [45], (Loughman and Deverall, 1986) [53]. These investigations revealed the formation of appressorium-like structures on epidermal cells, followed by penetration pegs entering these cells and developing vesicles. Secondary hyphae emerged from these vesicles and infiltrated the mesophyll layer within 24 hours, colonizing intercellularly without penetrating mesophyll cells. Interestingly, penetrated epidermal cells exhibited dark staining indicative of cell death once secondary hyphae reached the mesophyll layer (Loughman and Deverall, 1986) [53]. By 72 hours, the fungus disrupted mesophyll cell membranes beyond hyphal growth (Larez *et al*., 1986) [45], suggesting the secretion of molecules inducing programmed cell death ahead of mycelial advancement. Macroscopically, it induces lens-shaped lesions with necrotic centers and chlorotic borders. Initially, these symptoms were categorized as tan necrosis and extensive chlorosis (Lamari and Bernier, 1989a, 1989b) [40, 41]. Later, a genetically distinct symptom, localized chlorosis, was identified. The diverse symptomatology led to the classification of eight races based on combinations of necrotic and chlorotic symptoms (Lamari *et al*., 1995, 2003) [42, 43]. These symptoms were linked to necrotrophic effectors Ptr ToxA, Ptr ToxB, and Ptr ToxC (Ciuffeti *et al*., 2010), (Lamari and Strelkov, 2010) [44]. Susceptibility to each virulence component was genetically dominant, indicating an inverse gene-for-gene interaction (Lamari and Strelkov, 2010) [44].

Effector - Susceptibility factor Interaction

Tomas and Bockus (1987) [83] demonstrated that *P. tritici-repentis* culture filtrates induced necrotic symptoms in susceptible wheat lines but not in resistant ones. The necrosis-inducing component was identified as a small secreted protein (Balance *et al*., 1989), (Tomas *et al*., 1990) [84], later confirmed to be encoded by the single-copy ToxA gene, the first proteinaceous host-selective toxin found in any plant pathogen. Investigations into host metabolism and signaling revealed their necessity for ToxA-induced cell death, showcasing the pathogen's use of ToxA to trigger host-controlled programmed cell death, a mechanism typically associated with resistance to biotrophic pathogens (Kwon *et al*., 1998) [39]. An Arg-Gly-Asp (RGD) motif in Ptr ToxA was found to interact with an extracellular receptor, essential for inducing necrosis, as confirmed by mutagenesis studies. Ptr ToxA was internalized into sensitive wheat mesophyll cells, targeting chloroplasts and disrupting photo system processes, leading to light-dependent reactive oxygen species (ROS) accumulation and cell death (Manning *et al*., 2009) [54]. The susceptibility gene Tsn1 was identified as a dominant gene conferring sensitivity to ToxA, indicating its role in susceptibility to ToxA-producing *P. tritici-repentis* isolates (Faris *et al*., 1996) [14]. Transcriptional profiling studies revealed upregulation of defense-associated genes involved in signal transduction, phenylpropanoid pathway regulation, cell wall lignifications, ROS signaling, and pathogenesis-related (PR) proteins in ToxA-treated plants, reflecting the ToxA-Tsn1 interaction and resulting in sensitivity/susceptibility responses.

Ptr ToxB, a newly identified necrotrophic effector, was partially purified and characterized (Strelkov *et al*., 1998) [77]. It was found to induce chlorosis in a light-dependent manner by degrading chlorophyll through photo oxidation. This effector, consisting of a 6.61-kDa heat-stable protein, is encoded by a multicopy gene with a 261-bp open reading frame producing a 64-amino acid mature protein (Strelkov *et al*., 1999) [76], (Martinez *et al*., 2001) [57]. Its increased copy number and expression are speculated to correlate with enhanced virulence (Martinez *et al*., 2004) [56], (Strelkov and Lamari, 2003) [79], (Strelkov *et al*., 2002) [78]. Due to its stability and cysteine content, Ptr ToxB is believed to localize in the apoplast, showing resistance to protease digestion and high tolerance for apoplastic conditions. Fluorescent labeling demonstrated its apoplastic localization without internalization into cells (Figueroa *et al*., 2015) [20].

Structural analysis revealed similarities between Ptr ToxB and AvrPiz-t, an effector from *Magnaporthe oryzae* (Nyarko *et al*., 2014) [62]. This structural resemblance suggests Ptr ToxB might target biotrophic resistance mechanisms, inducing programmed cell death (PCD) and susceptibility, akin to AvrPiz-t in rice. The Ptr ToxB-Tsc2 interaction, which accounts for a significant portion of phenotypic variation, operates in an inverse gene-for-gene manner, with Tsc2 mapped to wheat chromosome 2B (Friesen and Faris, 2004). Transcriptional analysis of host responses to Ptr ToxB infiltration, compared to Ptr ToxA, revealed similar defense gene activation but with a delayed response (Pandelova *et al*., 2012) [66].

Less research has focused on the Ptr ToxC-Tsc1 interaction. Genetic assessment showed susceptibility to a chlorosis-inducing *P. tritici-repentis* strain, with a major QTL located on wheat chromosome 1A (Faris *et al*., 1997) [15]. Ptr ToxC, unlike Ptr ToxA and Ptr ToxB, is a small, polar molecule (Effertz *et al*., 2002) [14]. Sensitivity to Ptr ToxC also mapped to chromosome 1A, the same locus associated with susceptibility to Ptr ToxC-producing races (Effertz *et al*., 2001) [13], (Faris *et al*., 1997) [15].

Overall, the interactions between *P. tritici-repentis* and wheat necrotrophic effectors highlight diverse mechanisms of programmed cell death (PCD) in the pathogen's life cycle. Ptr ToxA, likely horizontally transferred from *P. nodorum*, rapidly induces necrosis by targeting an NLR resistance-like protein (Friesen *et al*., 2006) [30]. Ptr ToxB, structurally similar to avirulence effectors from *M. oryzae*, induces slower chlorosis. Ptr ToxC, a low-molecular-weight molecule, triggers extensive chlorosis. Despite their differences, all three effectors serve as virulence factors for the pathogen's necrotrophic life cycle.

Parastagonospora nodorum - Wheat Pathosystem Infection Process

Septoria nodorum blotch (SNB), caused by *P. nodorum*, and has posed a significant threat to foliar health globally (Faris and Friesen, 2020) [16], (Mehra *et al*., 2019) [59], (Murray and Brennan, 2009) [61], (Oliver *et al*., 2012) [64], (Singh *et al*., 2016) [74], (Xu *et al*., 2004) [87]. This wheat-specialized necrotrophic pathogen induces cell death in susceptible wheat lines to complete its life cycle. Studies have documented both direct epidermal and stomata penetration by *P. nodorum* (Baker and Smith, 1978) [2], (Bird and Ride, 1981) [5], (O'Reilly and Downes, 1986) [63]. The first indication of light-dependent repression of necrotrophic effector activity was observed by (Baker and Smith, 1978) [2], highlighting the significance of environmental cues in disease progression. Upon penetration, epidermal cells undergo rapid collapse and lignifications as mycelia advance into the mesophyll layer (Baker and Smith, 1978) [2], (Bird and Ride, 1981) [5]. Mesophyll cells undergo shape alterations, lignifications, and cytoplasmic degeneration, ultimately leading to complete collapse. Chloroplast deterioration and reduced photosynthetic rates indicate early host manipulation by the pathogen. Infection progresses rapidly, with mycelia reaching the mesophyll layer within days, followed by severe cellular collapse and eventual colonization. *P. nodorum* secretes a variety of cell wall-degrading enzymes (CWDEs) believed to aid in host tissue penetration (Lehtinen, 1993) [47], (Margo, 1984). While these enzymes display general toxicity to cell wall components, they lack host selectivity. Crude extracts containing toxic compounds from *P. nodorum* demonstrated selective action on wheat embryos, indicating the presence of necrotrophic effectors. This method was employed to differentiate resistance levels in breeding material, providing early evidence of *P. nodorum's* secreted necrotrophic effectors (Wicki *et al*., 1999) [86].

Effector - Susceptibility factor Interaction

SnTox1, a necrotrophic effector produced by *P. nodorum*, targets the wheat susceptibility gene Snn1 to facilitate its life cycle. This small secreted protein induces necrosis within 72 hours in wheat genotypes carrying Snn1, with sensitivity mapped to chromosome 1BS. The SnTox1-Snn1 interaction, accounting for up to 58% of disease variation, triggers host defense responses, including an oxidative burst, PR protein upregulation, and programmed cell death (PCD), promoting susceptibility (Liu *et al*., 2004a, 2004b) [50, 52]. SnTox1 expression peaks at 3 days, coinciding with sporulation initiation, and its infiltration or inoculation-induced necrosis is light-dependent (Liu *et al*., 2016, 2012) [48, 49]. Unlike other effectors, SnTox1 induces necrosis both upon infiltration and spraying onto the leaf surface, suggesting involvement in early penetration. SnTox1's prevalence across isolates suggests additional roles beyond Snn1 targeting (McDonold *et al*., 2013), (Richards *et al*., 2019) [68]. Structural similarity to plant chitin-binding proteins allows SnTox1 to bind chitin, protecting *P. nodorum* from wheat chitinase upregulated during SnTox1-Snn1 interaction (Liu *et al*., 2012) [49]. Snn1 encodes a WAK, a pattern recognition receptor (PRR) recognizing damage-associated molecular patterns (DAMPs), implying SnTox1's hijacking of a PRR-mediated defense pathway (Shi *et al*., 2016) [71]. TaMAPK3 upregulation upon SnTox1 inoculation suggests activation of plant immune responses, further validated by yeast two-hybrid experiments demonstrating SnTox1-Snn1 interaction. This interaction represents the first instance of a necrotrophic pathogen targeting a PRR, hijacking host defenses to facilitate its life cycle.

ToxA, the first proteinaceous necrotrophic effector identified, holds significance for three wheat pathogens (Ciuffetti *et al*., 2010) [9], (Friesen *et al*., 2018) [28], (McDonald *et al*., 2018) [58]. Initially discovered in *P. tritici-repentis*, its mode of action has been extensively studied. A homolog, SnToxA, was found in the *P. nodorum* genome, sharing high homology with PtrToxA. Diversity studies suggest ToxA originated in *P. nodorum* and transferred horizontally to *P. tritici-repentis* (Friesen *et al*., 2006) [30]. The ToxA-Tsn1 interaction confers susceptibility to *Septoria nodorum* blotch in both seedlings and adult plants (Faris and Friesen, 2009, 2020) [17, 16], (Friesen *et al*., 2009, 2006) [24, 30]. While Tsn1 contains domains typical of classical resistance genes, its direct interaction with ToxA or related proteins is unclear (Tai *et al*., 2007) [81]. However, Tsn1 appears involved in ToxA internalization. This discovery underscores how necrotrophic pathogens exploit host defense mechanisms for their benefit, highlighting a shift from classical gene-for-gene resistance to susceptibility in multiple pathosystems.

SnTox3, a proteinaceous necrotrophic effector, targets the wheat gene Snn3 (Friesen *et al*., 2008) [26], initially identified on chromosome 5B and later found on 5D (Zhang *et al*., 2011) [88]. This interaction significantly impacts disease susceptibility, ranging from 17% to 52% at the seedling stage and up to 24% in adult plants (Friesen *et al*., 2008) [26]. Allelic variation in Snn3-B1 may influence sensitivity to SnTox3, suggesting diverse disease outcomes (Shi *et al*., 2016) [73]. Cloning Snn3-D1 revealed S/TPK and MSP domains (Zhang *et al*., 2021) [89], both essential for SnTox3 sensitivity, highlight the broad arsenal of host-targeted genes by *P. nodorum* for inducing programmed cell death (PCD). The SnTox3 gene encodes a 693-bp intron-free sequence with no known homologs, expressed early during infection (Liu *et al*., 2009) [51]. Its pro-sequence, cleaved by Kex2, forms critical disulfide bonds, typical of apoplastic effectors. SnTox3 interacts with TaPR-1 proteins (Breen *et al*., 2016) [7], including the CAPE1 defense signaling peptide, enhancing susceptibility to SnTox3-producing isolates. SnTox3 disrupts host defense by preventing TaCAPE1 release from TaPR1, suppressing host immunity. Host responses to SnTox3 infiltration involve differential regulation of defense pathways, PCD-related processes, and phenylpropanoid accumulation, illustrating *P. nodorum's* strategy of hijacking defense mechanisms to complete its pathogenic life cycle (Sung *et al*., 2021) [80].

The interactions SnTox2-Snn2, SnTox6-Snn6, and SnTox7-Snn7 were identified and studied independently through host target mapping and sensitivity to necrotrophic effector activity (Friesen *et al*., 2007) [29], (Gao *et al*., 2015) [32], (Shi *et al*., 2015) [72]. These interactions contributed quantitatively to disease variation, with Snn2, Snn6, and Snn7 mapping to different loci. The proteins SnTox2, SnTox6, and SnTox7 were all small secreted proteins. A genomic study of *P. nodorum* revealed a single virulence locus associated with Snn2 and Snn6, indicating that SnTox2 and SnTox6 target both genes. Further analysis confirmed that Snn2, Snn6, and Snn7 are all targeted by the same protein, SnTox267. Snn2 and Snn6 were found to be

complementary genes in the same pathway required for sensitivity to SnTox267. Light dependency varied between the Snn2/Snn6 and Snn7 pathways, suggesting that SnTox267 targets separate pathways to facilitate the pathogen's life cycle (Richards *et al*., 2022) [67].

A tetraploid wheat mapping population was utilized to uncover the SnTox5-Snn5 interaction (Friesen *et al*., 2012) [25], where SnTox5, a small heat-stable protein, targeted Snn5, inducing necrosis to benefit the pathogen. This interaction was light-dependent and contributed significantly to disease variation, particularly when combined with other necrotrophic effectors like SnToxA-Tsn1, showing synergistic effects. SnTox5 encoded a 217-aa small secreted protein with six cysteine residues crucial for its activity, with a predicted signal peptide and pro-sequence aiding in folding (Kariyawasam *et al*., 2021) [34]. Besides targeting Snn5, SnTox5 aided mesophyll colonization, even without the presence of the Snn5 gene. Overall, *P. nodorum* employs various small secreted proteinaceous necrotrophic effectors, such as SnToxA (Friesen *et al*., 2006) [30], SnTox1 (Liu *et al*., 2012) [49], SnTox3 (Liu *et al*., 2009) [51], SnTox4 (Abeysekara *et al*., 2009) [1], SnTox267 (Richards *et al*., 2022) [67], and SnTox5 (Kariyawasam *et al*., 2021) [34], to target dominant susceptibility genes, inducing classical resistance responses that favor the pathogen's advantage. These host genes include an NLR (Faris *et al*., 2010) [19], a WAK (Shi *et al*., 2016) [71], and an S/TPK-MSP (Zhang *et al*., 2021) [89], each triggering typical resistance responses.

Zymoseptoria tritici - Wheat Pathosystem

Infection process

Z. tritici, the causative agent of septoria tritici blotch (STB), has been labeled a hemibiotroph, though it lacks biotrophic structures during the asymptomatic phase. Instead, it's proposed as a latent necrotroph, remaining undetected until triggering necrosis during symptomatic phases to access nutrients (Kema *et al*., 1996) [37], (Keon *et al*., 2007) [38], (Sanchez-Vallet *et al*., 2015) [70]. Infections begin with germination and stomata penetration as early as 12 hours post inoculation (hpi), progressing to mesophyll colonization by 48 hpi. From 2 to 8 days post inoculation (dpi), mycelia continue intercellular colonization while evading detection. Mesophyll cell collapse starts at 8 dpi, with rapid cell death increasing until 12 dpi, followed by heightened mycelial growth from host nutrient release. Incompatible interactions show attempted penetration and limited mesophyll colonization without HR (Kema *et al*., 1996) [37].

Effector Proteins in *Z. tritici*: Manipulating Host Defenses

Effector proteins in plant-pathogen interactions manipulate host defenses, aiding pathogen survival and reproduction. In the case of *Z. tritici*, effector-like proteins are secreted during asymptomatic colonization to evade detection and host defenses (Haueisen *et al*., 2019) [33], (Palma-Guerrero *et al*., 2017) [65]. Mg1LysM and Mg3LysM, two upregulated genes during asymptomatic infection, bind chitin and protect against host enzymes (Marshall *et al*., 2011) [55]. While disruption of Mg1LysM had no impact on virulence, ΔMg3LysM mutants failed to colonize leaves, preventing necrosis and sporulation. Additionally, Mg3LysM delays the wheat defense response, crucial for pathogen colonization. Wheat homologs of CERK1 and CEBiP, involved in PTI, were identified, with their silencing allowing ΔMg3LysM mutants to regain pathogenicity, highlighting Mg3LysM's role in evading wheat PTI (Lee *et al*., 2014) [46].

Unraveling Complexity in Z. tritici-Wheat Interactions

Simpler interactions can lead to progress due to easy understanding. In the *Z. tritici*-wheat system, numerous resistance genes (Stb genes) and quantitative trait loci (QTL) have been identified, suggesting a complex relationship. Qualitative and quantitative aspects, frequently combined, affect the virulence of *Z. tritici* (Kema *et al*., 2000) [36], (Meile *et al*., 2018) [60], (Stewart *et al*., 2018) [75]. ZtNIP1, a protein secreted by *Z. tritici*, triggers necrosis in wheat plants, potentially aiding in the transition from asymptomatic to necrotic phases of the pathogenic cycle by inducing programmed cell death (PCD). This suggests that multiple necrosis-inducing proteins could be involved in triggering plant defense responses.

Z. tritici populations were studied to pinpoint a single gene, AvrStb6, responsible for triggering avirulence in wheat plants carrying the Stb6 resistance gene (Brading *et al*., 2002) [6], (Chartrain *et al*., 2005) [8]. AvrStb6, a small cysteine-rich protein, didn't directly interact with Stb6 but initiated an avirulence response (Kema *et al*., 2018) [35], (Zhong *et al*., 2017) [90]. Stb6, identified as a wall-associated kinase (WAK) gene, didn't induce programmed cell death (PCD) upon interaction with AvrStb6 (Saintenac *et al*., 2018) [69]. Recent research revealed both major (qualitative) and minor (quantitative) loci influencing *Z. tritici* virulence across different wheat varieties. These effects were genotype-specific, with natural isolates showing various combinations of these loci. Avr3D1, a large-effect QTL, was identified as a host-specific avirulence factor targeted by the Stb7 resistance gene (Meile *et al*., 2018) [60]. Despite being present in all isolates, allelic variations allowed *Z. tritici* to evade recognition by Stb7, suggesting a fitness advantage. Avr3D1 expression peaks during the asymptomatic phase, aiding early colonization and evasion of host recognition. Table 1 presents characterized wheat genes/proteins in the pathosystem with *Pyrenophora tritici-repentis*, *Parastagonospora nodorum*, and *Zymoseptoria tritici*, while Table 2 details characterized pathogen genes/proteins in the same wheat pathosystem.

Table 1: Characterized Wheat Genes/Proteins in Pathosystem with *Pyrenophora tritici-repentis*, *Parastagonospora nodorum*, and *Zymoseptoria tritici*

Wheat genes	Activity	References
***Pyrenophora tritici-repentis*-wheat pathosystem**		
Tsn1	Targeted by Ptr ToxA to induce PCD	(Faris *et al*., 2010) [19]
***Parastagonospora nodorum*-wheat pathosystem**		
Tsn1	Targeted by SnToxA to induce PCD	(Faris *et al*., 2010) [19]
Snn1	Wall-associated kinase gene that is targeted by SnTox1	(Shi *et al*., 2016) [71]
Snn3-D1	Serine/threonine protein kinase, a primary target of SnTox3	(Zhang *et al*., 2021) [89]
***Zymoseptoria tritici*-wheat pathosystem**		
Stb6	Targets AvrStb6	(Saintenac *et al*., 2018) [69]
CERK1	Produces LysM protein, which attaches to and facilitates the identification of chitin.	(Lee *et al*., 2014) [46]
CEBiP	Produces LysM protein engaged in chitin detection and signaling	(Lee *et al*., 2014) [46]

Table 2: Characterized Pathogen Genes/Proteins in Wheat Pathosystem with *Pyrenophora tritici-repentis*, *Parastagonospora nodorum*, and *Zymoseptoria tritici*

Pathogen genes	Activity	References
***Pyrenophora tritici-repentis*-wheat pathosystem**		
ToxA	Triggers programmed cell death (PCD) via Tsn1	(Ballance *et al*., 1996) [3], (Ciuffetti *et al*., 1997) [10]
ToxB	Induces chlorosis through targeting Tsc2	(Martinez *et al*., 2001) [57], (Strelkov *et al*., 1999) [76]
***Parastagonospora nodorum*-wheat pathosystem**		
SnToxA	Necrotrophic effector directed at the NLR gene Tsn1	(Friesen *et al*., 2006) [30]
SnTox1	Necrotrophic effector directed at the WAK-like gene Snn1	(Liu *et al*., 2012) [49]
SnTox3	Necrotrophic effector directed both Snn3-B1 and Snn3-D1	(Liu *et al*., 2004) [50]
SnTox267	Necrotrophic effector directed at Snn2, Snn6, and Snn7	(Richards *et al*., 2022) [67]
SnTox5	Necrotrophic effector specifically targeting Snn5	(Kariyawasam *et al*., 2021) [34]
***Zymoseptoria tritici*-wheat pathosystem**		
ZtNIP1	Causes necrosis in Arabidopsis, yet its involvement in the *Z. tritici*-wheat pathosystem haven't been proven.	(Ben M'Barek *et al*., 2015) [4]
Avr3D1	Possibly involved in initial colonization but countered by Stb7, leading to resistance.	(Meile *et al*., 2018) [60]
AvrStb6	Targeted by Stb6 to induce early defense	(Kema *et al*., 2018) [35], (Zhong *et al*., 2017)
Mg3LysM	Attaches to chitin, postpones the defensive reaction	(Lee *et al*., 2014) [46], (Marshall *et al*., 2011) [55]
Mg1LysM	Attaches to chitin against chitinase, but no obvious role in avoiding recognition	(Lee *et al*., 2014) [46], (Marshall *et al*., 2011) [55]

Conclusion

Host-pathogen interactions are primarily understood through biotrophic systems, where fungal effectors manipulate plant defense responses to their advantage. Necrotrophic pathogens like *Z. tritici*, *P. tritici-repentis*, and *P. nodorum*, while distinct, share strategies to induce host susceptibility and colonization. *Z. tritici* notably remains unrecognized during early colonization, unlike its counterparts. Gene-for-gene recognition is observed in *Z. tritici*-wheat interactions, unlike in *P. tritici-repentis* and *P. nodorum*. Once the necrotrophic transition occurs, all three pathogens induce similar responses, triggering programmed cell death (PCD) and modulating antimicrobial components to obtain nutrients. Despite our understanding, gaps persist in how these pathogens evade host defenses, highlighting the need for comprehensive strategies to develop durable resistance.

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