REVIEW

Bacterial Type Two Secretion System Secreted Proteins: Double-Edged Swords for Plant Pathogens

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The type two secretion system (T2S) is important for virulence of a number of gram-negative bacterial plant pathogens. Most of the T2S-secreted proteins that have been characterized to date are involved in degrading different components of plant cell walls. Functional redundancy appears to exist among T2S-secreted proteins because significant effects on virulence are observed only in strains in which multiple secreted proteins are mutated. Several T2S-secreted proteins have been shown to induce plant defense responses, including hypersensitive response-like reactions. Bacterial pathogens can suppress these defense responses, and recent results indicate that suppression is mediated through the type three secretion system.

Additional keywords: cell wall-degrading enzymes, phytopathogenic bacteria, programmed cell death, pseudopilus, sec-dependent pathway.

Gram-negative bacteria employ a number of different secretion systems to transport proteins to the extracellular milieu (Henderson et al. 2004). One of these is the type two secretion system (T2S). In this review, we outline the dual role of T2S-secreted proteins in promoting virulence of plant-pathogenic bacteria and in the induction of plant defense responses with emphasis on recent studies. For more details about the T2S apparatus and its functioning, readers are referred to comprehensive reviews by Filloux (2004), Pugsley (1993), and Sandkvist (2001a).

Components of the T2S.

The T2S-secreted proteins are secreted from the cytosol to the extracellular milieu in a two-step process. In the first step, the secreted proteins are translocated across the cytoplasmic membrane using either the sec-dependent pathway (Pugsley 1993) or twin-arginine (Tat) pathway (Voulhoux et al. 2001), depending on the nature of the signal peptide. In the second step, the proteins are secreted from the periplasm across the outer membrane to the extracellular medium by the T2S apparatus, whose components are encoded by approximately 12 to 16 genes depending on the system (Filloux 2004; Sandkvist 2001b). The genes have been designated as genes A to O and S, and usually are organized in a gene cluster.

A number of gram-negative bacterial plant pathogens have been shown to encode a T2S. Representatives come from all major groups of bacterial plant pathogens, including the genera

Erwinia, *Pseudomonas*, *Xanthomonas*, *Xylella*, and *Ralstonia*. A notable exception is *Agrobacterium tumefaciens*, which does not appear to encode a T2S (Goodner et al. 2001; Wood et al. 2001). *Xanthomonas campestris* pv. *campestris* and *X. axonopodis* pv. *citri* appear to encode two complete T2S gene clusters, called *xcs* and *xps*, in their genomes (da Silva et al. 2002). The organization of genes encoding the T2S in different phytopathogenic bacteria is depicted in Figure 1.

Protein D is the major outer membrane component of the T2S and considered as the secretin (or pore) through which the secreted proteins are translocated to the extracellular space (Filloux 2004). Protein S is a small, outer-membrane lipoprotein which is present in some bacteria and may stabilize and promote protein D insertion into the outer membrane (Hardie et al. 1996; Shevchik et al. 1997). The exact functions of the inner-membrane proteins A and B (Filloux 2004; Sandkvist 2001b) are unknown, but they also may assist in translocation of protein D to the outer membrane (Ast et al. 2002). Protein G is the major prepilin-like protein and is believed to assemble into a pilus-like structure, called the pseudopilus, along with prepilin subunits protein H, I, and J (Filloux 2004). Sequence features of protein K indicate that the protein might be a prepilin subunit whose inclusion in the complex arrests pilus elongation. Protein O is a prepilin peptidase that also can methylate the new N-terminus produced after cleavage of the prepilin. The removal of the leader peptide by action of protein O is necessary for assembly of the prepilin subunits.

Protein E is located on the cytoplasmic side of the inner membrane and is predicted to be a “traffic ATPase” which provides the energy for translocation of pseudopilins across the inner membrane (Filloux 2004). Proteins F, L, M, and E are believed to form an inner membrane complex which serves as a platform on which the pseudopilus is built (Py et al. 2001). Proteins C and N are suggested (Filloux 2004; Sandkvist 2001a) to act as interconnectors between the outer membrane complex (composed of proteins D and S) and the inner membrane complex (proteins F, L, M, and E). A recent study indicates that protein C also mediates an interaction between protein G, the major pseudopilin, and protein D, the secretin (Lee et al. 2005b).

A number of similarities exist between components of the T2S and type IV pilus (T4P) (Peabody et al. 2003). Partly based on inferences drawn from T4P, one model for T2S action envisages that the pseudopilus serves as a piston to push the secreted proteins into the extracellular space through the secretin pore (Sandkvist 2001a). The controlled extension and retraction of the pseudopilus is considered to provide the force necessary for extrusion of the secreted proteins. The pseudopilus formed by T2S components probably does not ordinarily extend

beyond the cell surface under normal circumstances. However, an extended pseudopilus has been observed in cells that either contain the T2S gene cluster on a multicopy plasmid (Sauvonnnet et al. 2000) or overexpress protein G (Durand et al. 2003). Formation of the extended pseudopilus in *Pseudomonas aeruginosa* interferes with protein secretion through the T2S (Durand et al. 2003), presumably by blocking the passage through the secretin pore. Interestingly, *P. aeruginosa* cells that have an extended pseudopilus have an increased ability to form biofilms. The pseudopilus structure, therefore, might function in adherence of bac-

teria to the substratum (Durand et al. 2003). Increasing the level of expression of the major *P. aeruginosa* pseudopilin may allow either the assembly of a fully functional T2S or a fully extended pseudopilus, which then can participate in adhesion.

Proteins A, B, and S are not encoded in the T2S gene clusters of any phytopathogenic bacteria analyzed to date. Either other proteins, which are encoded elsewhere in the genome, can substitute for proteins A, B, and S or proteins A, B, and S are dispensable for T2S function in these bacteria. Proteins B and S are encoded nearby but not within the T2S gene clusters

Fig. 1. Schematic of the organization of type two secretion system (T2S) gene clusters from various phytopathogenic bacteria. Eca: *Erwinia carotovora* subsp. *atroseptica* (Bell et al. 2004); Ecc: *E. carotovora* subsp. *carotovora* (Reeves et al. 1993); Ech: *E. chrysanthemi* (He et al. 1991; Lindeberg and Collmer 1992); Psy: *Pseudomonas syringae* pv. *tomato* DC3000 (Buell et al. 2003); Rso: *Ralstonia solanacearum* (Salanoubat et al. 2002); Xac1 and Xac2: *xps* and *xcs* in *Xanthomonas axonopodis* pv. *citri*; Xcc1 and Xcc2: *xps* and *xcs* in *Xanthomonas campestris* pv. *campestris* (da Silva et al. 2002; Dums et al. 1991); Xfa: *Xylella fastidiosa* (Simpson et al. 2000); Xoo: *Xanthomonas oryzae* pv. *oryzae* (Lee et al. 2005a). C, D, E, F, G, H, I, J, K, L, M, N, and O represent genes encoding various components of T2S. The direction of arrows indicate the transcription orientation.

of *Erwinia chrysanthemi* (Condemine et al. 1992) and *E. carotovora* subsp. *atroseptica* (Bell et al. 2004). Protein O is encoded in the T2S gene clusters of *E. chrysanthemi* (Lindeberg and Collmer 1992), *E. carotovora* subsp. *carotovora* (Reeves et al. 1993), and *E. carotovora* subsp. *atroseptica* (Bell et al. 2004) but is not encoded in this gene cluster in other phytopathogenic bacteria. In *P. aeruginosa*, a prepilin peptidase in the T4P gene cluster serves in assembly of the T4P and the T2S (Strom et al. 1991). A prepilin peptidase encoded either in the T4P gene cluster or elsewhere in the genome also is likely to be involved in assembly of the T2S in several plant-pathogenic bacteria. A prepilin peptidase gene encoded in the T4P gene clusters of *X. campestris* pv. *campestris* (Hu et al. 1995) and *P. syringae* pv. *tomato* DC3000 (Roine et al. 1998) can complement the pilin assembly and exoprotein secretion defects of the *P. aeruginosa* prepilin peptidase mutant.

The two T2S gene clusters of *X. campestris* pv. *campestris* and *X. axonopodis* pv. *citri* are unrelated to each other in their nucleotide sequences, suggesting that each of these bacteria can assemble two different T2Ss (da Silva et al. 2002). Also, the lack of nucleotide similarity indicates that the two T2S gene clusters have not arisen by gene duplication and therefore are not paralogs. The T2S gene clusters of *X. campestris* pv. *campestris* display a high degree of nucleotide sequence similarity to their counterparts in *X. axonopodis* pv. *citri*, indicating that these are orthologs. Mutations in the *xps* gene cluster of *X. campestris* pv. *campestris* have been shown to result in virulence deficiency (Dow et al. 1987; Hu et al. 1992). Mutations have not yet been isolated in the *xcs* gene cluster of *X. campestris* pv. *campestris*, and the function of this T2S is unclear.

Why should these bacteria have two T2S gene clusters? *P. aeruginosa* has been shown to encode two functional T2Ss. The initially identified extracellular protein (Xcp) system is involved in secretion of various proteins, including lipases,

phospholipases, elastase, and the exotoxin A (Filloux et al. 1998). The alternate T2S (homologous to Xcp [Hxc]) is involved in secretion of a low molecular weight alkaline phosphatase (LAP), and gene expression analysis indicates that the Hxc is produced only under conditions of low phosphate (Ball et al. 2002). LAP is secreted only through Hxc and secretion is not affected by mutations in Xcp. The evidence, therefore, suggests that the two T2Ss are involved in the secretion of different substrates and that this provides flexibility for *P. aeruginosa* in adapting to different environmental conditions. Similarly, the presence of two different T2Ss may help *X. campestris* pv. *campestris* and *X. axonopodis* pv. *citri* adapt to different external environments. Interestingly, a single T2S gene cluster is encoded in the *X. oryzae* pv. *oryzae* genome (Lee et al. 2005a). Why a single T2S will suffice for this bacterium, while *X. campestris* pv. *campestris* and *X. axonopodis* pv. *citri* apparently require two T2Ss, is unclear.

T2S-secreted proteins in plant-pathogenic bacteria.

Mutations in T2S genes have been isolated in *E. carotovora* subsp. *carotovora* (Murata et al. 1990; Pirhonen et al. 1991; Reeves et al. 1993), *E. carotovora* subsp. *atroseptica* (Hinton et al. 1989), *E. chrysanthemi* (Andro et al. 1984; Thurn and Chatterjee 1985), *Ralstonia solanacearum* (Kang et al. 1994), *X. campestris* pv. *campestris* (Dow et al. 1987; Hu et al. 1992), and *X. oryzae* pv. *oryzae* (Ray et al. 2000). These mutants are virulence deficient, indicating that the T2S is important for virulence of these bacteria. As indicated above, in *X. campestris* pv. *campestris*, the role in virulence has been demonstrated for xanthomonas protein secretion and mutations have not yet been reported in the genes for xanthomonas caulobacterlike secretion. Mutations have not been reported in the T2S genes of *P. syringae* pv. *syringae*, *X. fastidiosa*, and *X. axonopodis* pv. *citri*.

The T2S-deficient mutants of plant-pathogenic bacteria have been found to be defective in secretion of a number of pro-

Table 1. Type two secretion system-secreted proteins in phytopathogenic bacteria

Name of the bacterium	Known effectors	References ^a
<i>Erwinia carotovora</i> pv. <i>carotovora</i>	Pectate lyases	1,2,3
	Cellulase/endoglucanase	1,2,3
	Polygalacturonase	1,2,3
<i>E. carotovora</i> pv. <i>atroseptica</i>	Pectate lyase	3
	Endoglucanase/cellulase	4
	Putative exported plant-proteoglycan hydrolase	4
	Putative cellulase	4
	Svx (homologous to AvrXca)	4
<i>E. chrysanthemi</i>	Pectate lyases	1,2,3,5
	Polygalacturonase	1,2,3,5
	Pectin methyl esterases	1,2,3,5
	Cellulase/endoglucanase	1,2,3,5
	Pectin acetyl esterases	2,3,5
	Rhamnogalacturonate lyase	5,6
	Avr-like protein (AvrL, homologous to AvrXca)	5
	FaeD esterase	5
<i>Ralstonia solanacearum</i>	Polygalacturonases	7
	Cellulase/endoglucanase	7
	Pectin methyl esterase	7
	Exo-cellobiohydrolase	8
<i>Xanthomonas campestris</i> pv. <i>campestris</i>	Polygalacturonate lyases	9,10,11
	Cellulase/endoglucanase	9,10,11
	Proteases	9,10,11
	α -Amylase	9,10,11
<i>X. oryzae</i> pv. <i>oryzae</i>	Xylanase	12
	Cellulase/endoglucanase	13,14,15
	Putative cysteine protease	13
	Putative cellobiosidase	15
	Lipase/esterase	16

^a 1 = Barras et al. 1994; 2 = Py et al. 1998; 3 = Thomson et al. 1999; 4 = Corbett et al. 2005; 5 = Kazemi-Pour et al. 2004; 6 = Laatu and Condemine 2003; 7 = Kang et al. 1994; 8 = Schell 2000; 9 = Dow et al. 1987; 10 = Dow et al. 1989a; 11 = Hu et al. 1992; 12 = Ray et al. 2000; 13 = Furutani et al. 2004; 14 = Sun et al. 2005; 15 = Jha et al. 2004; 16 = Rajeshwari et al. in press.

teins. A majority of these proteins are involved in degrading different constituents of the plant cell wall (Table 1). A T2S-secreted protein, Sv_x (secreted virulence factor from *Xanthomonas* spp.) of *E. carotovora* subsp. *atroseptica*, is homologous to AvrXca, an avirulence protein of *X. campestris* pv. *raphani* (Corbett et al. 2005). Introduction of the *avrXca* gene into compatible strains of *X. campestris* pv. *campestris* results in incompatible interactions with a number of *Arabidopsis thaliana* accessions (Parker et al. 1993). Although the function of the Sv_x protein is unclear, the presence of a zinc-binding signature found in metalloproteases has led to the suggestion that this protein may have an enzymatic activity in degrading plant cell walls (Corbett et al. 2005). Besides the proteins listed in Table 1, additional T2S-secreted proteins are likely to be identified that are expressed and secreted only during in planta growth. Several pectate lyases of *E. chrysanthemi* (Kelemu and Collmer 1993) have been shown to be induced during growth on potato tubers. A recent report indicates that the expression of several T2S-secreted proteins of *X. oryzae* pv. *oryzae* is induced in plant-mimic medium and that their expression is abrogated in *hrpX* mutants (Furutani et al. 2004). The HrpX protein is a transcriptional activator of plant-inducible genes of xanthomonads (Fenselau and Bonas 1995).

As discussed below, the T2S-secreted proteins are important virulence factors which also induce very potent plant defense responses. Therefore, the expression of these proteins must be very carefully regulated. The regulation of expression of the genes for T2S-secreted proteins has been investigated extensively in *Erwinia* spp. (Whitehead et al. 2001, 2002), *R. solanacearum* (Schell 2000; Whitehead et al. 2001), and *X. campestris* pv. *campestris* (Barber et al. 1997; Wang et al. 2004). These studies indicate that the expression of these genes is subject to multiple regulatory controls which presumably provide the fine tuning that is necessary to ensure that these proteins are expressed at the right place and the right time. A major theme that has emerged is that the expression of T2S-secreted proteins is controlled by various quorum-sensing systems, such that the proteins are made in maximal amounts at high cell densities. By adopting such a strategy, the bacteria may be ensuring that the host defense responses, which are induced by T2S-secreted proteins, are elicited only when the bacterial population is sufficient to cope with the host responses.

Role of T2S effectors in virulence of plant-pathogenic bacteria.

What is the contribution of individual T2S-secreted proteins toward virulence? This issue has been investigated extensively in studies on *Erwinia* spp. In general, mutations in genes for individual secreted proteins result only in either a partial or no loss of virulence (Barras et al. 1994; Laatu and Condemine 2003; Py et al. 1998). Host- and tissue-specific effects were observed when these mutants were assessed for virulence on different host plants as well as in the potato tuber maceration model, indicating that some of these enzymes are more important for virulence on certain hosts or tissues as opposed to others. The large repertoire of pectin-degrading enzymes of *E. chrysanthemi* may be important in the context of the wide range of host plants that this pathogen is capable of infecting. In *X. campestris* pv. *campestris*, a protease-deficient mutant exhibits reduced virulence when it is introduced into leaves through cut vein endings but not in some other tests of pathogenicity (Dow et al. 1990). Mutations in the gene for polygalacturonate lyase isozyme I of *X. campestris* pv. *campestris* have no effect on pathogenicity (Dow et al. 1989b), whereas mutations in the gene for the major secreted endoglucanase lead to a delay in the development of symptoms (Gough et al. 1988). An endoglucanase-deficient mutant of *R. solanacearum*

is slower at causing disease symptoms compared with the wild-type strain (Roberts et al. 1988).

Mutants that are defective in more than one T2S-secreted protein exhibit a more severe virulence deficiency, as observed in an *E. chrysanthemi* strain in which all five isoforms of pectate lyase were mutated (Ried and Collmer 1988). Similarly, in *R. solanacearum*, either endo-polygalacturonase (PehA) or exo-polygalacturonase (PehB) mutants were reduced for virulence, but the PehA-PehB double mutant exhibited a much greater virulence deficiency (Huang and Allen 1997). In *X. oryzae* pv. *oryzae*, lipase/esterase (LipA)- and xylanase (XynB)-deficient mutants exhibit slight virulence deficiencies, whereas the LipA-XynB double mutant exhibits a much more severe virulence deficiency (Rajeshwari et al. in press). Overall, these results suggest that there is a functional redundancy among individual T2S-secreted proteins with regard to their role in virulence. Functional redundancy can arise from the fact that individual cell wall-degrading enzymes are targeting different components of plant cell walls, and an inability to degrade one of these components might not seriously impede virulence. Alternatively, functional redundancy can be due to the presence of different isoforms of cell wall-degrading enzymes. For example, the genome of *X. campestris* pv. *campestris* is predicted to encode eight cellulases, five xylanases, and four pectate lyases, and the genomes of *X. axonopodis* pv. *citri* and *X. oryzae* pv. *oryzae* are each predicted to encode seven cellulases, four xylanases, and two pectate lyases (da Silva et al. 2002; Lee et al. 2005a).

Induction of host defense responses by T2S effectors.

Cell wall-degrading enzymes secreted by microbial pathogens have been shown to be elicitors of plant defense responses such as production of phytoalexins, fortification of cell walls by lignin deposition, oxidative burst, and so on (Darvill and Albersheim 1984; Ryan and Farmer 1991). A xylanase secreted by *E. chrysanthemi* causes cell death and tissue maceration in root cap cells and leaves, respectively, of several plant species (Braun and Rodrigues 1993). However, it is not clear whether death is due to damage caused to the cell wall or due to a plant programmed cell death response that is induced in response to the damage. Prior treatment of tobacco with purified preparations of *E. carotovora* subsp. *carotovora* pectate lyase and polygalacturonase induced the expression of defense genes and resistance against subsequent infection by the same pathogen (Palva et al. 1993). This effect is enhanced when the treatment includes pectic enzymes and cellulase (Vidal et al. 1998). Also, expression of an *E. carotovora* gene for pectate lyase in transgenic potato confers increased resistance to maceration caused by the pathogen (Wegener et al. 1996). An *E. chrysanthemi* EC16 pectate lyase, which is a T2S-secreted protein, elicits induction of a phytoalexin in soybean cotyledons (Kita et al. 1996). Site-directed mutations in this pectate lyase indicated that maceration activity and phytoalexin elicitation were not always correlated with in vitro pectinolytic activity, indicating that these are influenced in planta by unknown factors or conditions.

The culture filtrates of *E. carotovora* subsp. *carotovora* induce plant defense responses mediated by the jasmonic acid and ethylene pathways but not the salicylic acid pathway (Norman-Setterblad et al. 2000; Vidal et al. 1998). It is of interest to note that increased expression of an *Arabidopsis* homolog of allene oxide synthase, an enzyme involved in jasmonate biosynthesis, is observed following treatment with *E. carotovora* subsp. *carotovora* culture filtrates as well as oligogalacturonides, which are released by the action of pectinolytic enzymes (Norman et al. 1999). On the other hand, another pectinolytic enzyme of *E. chrysanthemi* strain 3937 is modi-

fied following secretion, and the matured form is able to elicit a rapid necrotic response akin to the hypersensitive response, along with production of capsidiol (the major tobacco phytoalexin) when infiltrated into tobacco leaves (Shevchik et al. 1998). Characterization of the elicitor activity from culture supernatants of strain 3937 indicated that it is a proteolytically processed form of PelI2, a T2S-secreted protein of *E. chrysanthemi*. The N-terminal 97 amino acids of PelI2 have been shown to be cleaved by extracellular proteases of strain 3937, both in vitro and in planta, to release a truncated form (PelI3) that has similar enzymatic activities (as assessed in vitro) as PelI2. However, PelI3, and not PelI2, is able to elicit a necrotic response when infiltrated into tobacco leaves. The smaller size and higher pI of PelI3 (24 kDa and pI 10.5) compared with PelI2 (34 kDa and pI 9) may contribute to the increased capacity of PelI3 to attack plant cell walls. Co-infiltration of PelI3 along with 1 mM lanthanum chloride (a calcium channel blocker) inhibited the necrotic response in tobacco leaves, indicating that an active plant response, as opposed to passive cell death, is involved. A PelI mutant of strain 3937 retains the capacity to elicit the necrotic response in tobacco, whereas a T2S-deficient mutant lacks this activity. This indicates that other, as yet unidentified T2S-secreted proteins can also serve as elicitors of this response.

Infiltration of rice leaves with any one of the *X. oryzae* pv. *oryzae* T2S-secreted proteins, cellulase, cellobiosidase, and lipase results in induction of a browning reaction that is akin to a hypersensitive reaction and is accompanied by lignin accumulation (Jha et al. 2004). These responses are similar to those that are induced upon infiltration of an incompatible *X. oryzae* pv. *oryzae* strain into rice leaves (Reimers and Leach 1991; Yang et al. 2000). Prior injection of any one of these three secreted proteins into midveinal regions of rice leaves induces resistance against subsequent challenge (20 h later) with *X. oryzae* pv. *oryzae*. Co-infiltration of rice leaves with these secreted proteins and wild-type *X. oryzae* pv. *oryzae* results in suppression of hypersensitive response-like symptoms and lignin deposition. A type three secretion system (T3S)-deficient mutant of *X. oryzae* pv. *oryzae* is unable to suppress the hypersensitive reaction-like symptoms and lignin deposition that are induced by the T2S-secreted proteins. Treatment of rice root cap cells and rice roots with T2S-secreted proteins causes cell death and DNA fragmentation as determined by propidium iodide uptake and positive reaction in a TUNEL (terminal deoxynucleotidyl transferase mediated dUTP nick-end labeling) assay, respectively. These effects are suppressed by wild-type bacteria in a T3S-dependent manner.

The elicitor activity of cell wall-degrading enzymes has been shown, in most cases, to be due to the oligosaccharides that are released by the action of these enzymes on plant cell walls. However, certain fungal xylanases have been demonstrated to elicit defense responses, including a hypersensitive cell death, when applied to plant tissues, but protein recognition appears to occur through a surface-exposed epitope and not through enzyme activity (Enkerli et al. 1999; Rotblat et al. 2002). In tomato, the receptor for xylanase has an extracellular leucine rich repeat domain, a transmembrane domain, and a domain that has a signal for receptor-mediated endocytosis (Ron and Avni 2004).

Can plant programmed cell death responses induced by T2S-secreted proteins be beneficial to bacterial pathogens?

Are the plant cell death responses that are induced by T2S-secreted proteins beneficial to the pathogen under certain circumstances? Infection by the necrotrophic fungal pathogen *Botrytis cinerea* has been shown to be facilitated by the hyper-

sensitive reaction (Govrin and Levine 2000). Host cell death responses induced by harpin (HrpN) and polygalacturonase (PehA) might be beneficial for a necrotrophic bacterial pathogen such as *E. carotovora* subsp. *carotovora* (Kariola et al. 2003). Abramovitch and Martin (2004) have proposed that, even for biotrophic bacterial pathogens, the ability to induce massive host cell death responses can be beneficial in later stages of infection, during which the pathogen might shift to a necrotrophic mode. The possible contribution of T2S-dependent plant programmed cell death responses in promoting bacterial pathogenesis needs to be investigated.

A proposal.

In our opinion, T2S-secreted proteins can induce dramatic changes in host cellular activity that rival those induced by the T3S-secreted proteins. Such being the case, we propose that the T2S-secreted proteins should be referred to as T2S effectors, as is done for the T3S effectors. Our suggestion is not merely cosmetic because we believe it would lead to a better appreciation of the role these proteins play in plant-pathogen interactions and provide further impetus for understanding the mechanistic basis of the defense responses they induce in plants.

Summary.

The T2S is important for virulence of many gram-negative bacterial plant pathogens. A majority of the characterized T2S-secreted proteins are involved in degrading different components of plant cell walls, and an apparent functional redundancy exists among them with regard to their role in virulence. T2S-secreted proteins also induce potent plant defense responses. Bacterial pathogens can suppress these defense responses and, at least in *X. oryzae* pv. *oryzae*, this suppression is mediated through the T3S. Although progress has been made in delineating the defense response pathways that are induced by T2S-secreted proteins, these studies are in the initial stages, and the mechanistic details and signal transduction pathways remain to be worked out. The mechanism by which these defense responses are suppressed, particularly the nature of the T3S effectors involved, and the mode of their action needs to be established.

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