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Classification and Function of Plant Disease Resistance Genes

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Plants are equipped with a variety of mechanisms to defend themselves against infection by fungi, viruses, bacteria, nematodes, insects, and even other plants. Following the rediscovery of Mendel's laws, plant breeders have used disease resistance (*R*) genes to produce more resistant varieties. It was proposed that plant defenses are activated by the specific interaction between the product of a disease resistance (*R*) gene in the plant and the product of a corresponding avirulence (*Avr*) gene in the pathogen (Flor, 1971). These *R* genes enable plants to recognize specific races of a pathogen and mount effective defence responses including a rapid induction of localized necrosis at the site of infection (the hypersensitive response), increasing expression of defense-related genes, production of anti-microbial compounds, lignin formation, and oxidative burst in many plant-patogen interactions.

Over the past seven years, numerous *R* genes were cloned from several plant species (Hammond-Kosack et al., 1977). These works have shown the structures of a number of plant *R* genes. A striking degree of similarity among these *R* genes has been observed. Based on the predicted protein structures, the cloned resistance genes can be grouped into five classes (Table 1). The first class is represented by the maize *Hm1* gene, the first cloned plant *R* gene, which encodes a reductase that inactivates the HC toxin from *Cochliobolous carbonum* race 1 (Johal and Briggs, 1992). However, this interaction does not conform to Flor's gene-for-gene hypothesis (Flor, 1971). Therefore, this gene is distinct from the interactions which involve *R* genes that may couple the recognition of specific pathogen races to expression of defense related genes. The second class of genes includes *Pto*, which confers resistance to the bacterial pathogen *Pseudomonas syringae* pv. *tomato*, containing *avrPto* (Martin et al., 1993). *Pto* encodes part of a small linked gene family and encodes a cytoplasmically located but potentially membrane-associated serine-threonine kinase. The third and most abundant class of *R* genes encodes a cytoplasmic receptor-like protein with a nucleotide binding site (NBS) and a leucine-rich repeat (LRR) domain. Resistance genes from *Arabidopsis* (*Rps2* and *Rpm1*), tobacco (*N*), flax (*L6*), and tomato (*Prf*) are members of this class (Bent et al., 1994; Grant et al., 1995; Lawrence et al., 1995; Salmeron et al., 1996; Whitham et al., 1994). *Xa1* is also the third class resistance gene encoding the cytoplasmic receptor-like protein with NBS and LRR domains (Yoshimura et al., 1998). Unlike any previously studied *R* genes, *Xa1* gene is induced by pathogen infection and wound. The fourth class is represented by the tomato *Cf* genes. These genes (*Cf-9*, *Cf-2*, *Cf-4*, and *Cf-5*) encode putative membrane-anchored proteins with the LRR motifs in the presumed extracellular domain and a short C-terminal tail in the intracellular domain (Dixon et al., 1996; Dixon et al., 1998; Jones et al., 1994; Thomas et al., 1997). $HS1^{pro-1}$ from sugar beet is also a member of this class (Baker et al., 1997). The fifth class is represented by the rice gene *Xa21*, conferring resistance to *Xanthomonas oryzae* pv. *oryzae* (Song et al., 1995). *Xa21* encodes a putative trans-membrane receptor with an extracellular LRR domain similar to that of the tomato CF-9 protein and an intracellular serine-threonine kinase domain similar to that of the *Pto* kinase. Therefore, the structure of *Xa21* implies an evolutionary link between two different classes of plant resistance genes. This review focuses on the classification and mode of action of disease resistance genes cloned to date. Several other recent reviews on the cloned R genes are available (Baker et al., 1997; Bent, 1996; Hammond-Kosack et al., 1997)

Classification of Resistance Genes

The *R* genes have been cloned using the methods of posi-

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Table 1. The five classes of cloned plant disease resistance genes

Class	*R* gene	Plant	Pathogen	*Avr* gene	Structure
1	*Hm1*	Maize	*Cochliobolus carbonum* (race 1)	None	HC-toxin reductase
2	*Pto*	Tomato	*Pseudomonas syringae* pv. *tomato*	*avrPto*	ser/thr protein kinase
3a	*RPS2*	Arabidopsis	*P. syringae* pv. *tomato*	*avrRpt2*	LZ-NBS-LRR
	RPM1	Arabidopsis	*P. syringae* pv. *maculicola*	*avrRpm1/avrB*	LZ-NBS-LRR
	Prf	Tomato	*P. syringae* pv. *tomato*	*avrPto*	LZ-NBS-LRR
	I2	Tomato	*Fusarium oxysporum* f. sp. *lycopersici*	Unknown	LZ-NBS-LRR
3b	*N*	Tobacco	Tobacco mosaic virus	TMV replicase?	TIR-NBS-LRR
	L6	Flax	*Melampsora lini*	AL^6	TIR-NBS-LRR
	RPP5	Arabidopsis	*Peronospora parasitica*	*avrPp5*	TIR-NBS-LRR
3c	*Xa1*	Rice	*Xanthomonas oryzae* pv. *oryzae*	Uknown	NBS-LRR
4	*Cf-9*	Tomato	*Cladosporium fulvum*	*Avr9*	LRR-TM
	Cf-2	Tomato	*C. fulvum*	*Avr2*	LRR-TM
5	*Xa21*	Rice	*X. oryzae* pv. *oryzae*	Unknown	LRR, protein kinase

[a]LZ: leucine zipper, NBS: nucleotide binding site, LRR: Leucine rich repeat, TIR: Toll/interleukin-1 receptor, TM: transmenbrane domain

tional cloning or transposon tagging (Hammond-Kosack and Jones, 1997). The first *R* gene was cloned through the transposon tagging of *Hm1* from maize. *Hm1* gene does not conform to Flor's gene-for-gene theory. The isolation and sequence analysis of other *R* genes involved in gene-for-gene recognition have shown that there are four related but distinct classes of *R* proteins involving *Avr* components in signal transduction pathway leading to the disease resistance. Table 1 lists the *R* genes isolated from many plants.

NBS/LRR class. This class encodes cytoplasmic receptor-like proteins that contain an NBS and an LRR. NBS/LRR class can be fallen into three subclasses. One contains leucine zipper (LZ) and the other possesses Toll and interleukin-1 receptor (TIR) at the amino terminal, respectively. The third subclass has neither LZ nor TIR.

LZ/NBS/LRR subclass. The family of genes encoding proteins with LZ/NBS/LRR motifs includes *RPS2* and *RPM1* from *Arabidopsis* and *Prf* from tomato. *RPS2* provides resistance to the strains of *Pseudomonas syringae* bacteria that carry the *avrRpt2* gene on their plasmids. *RPM1* confers resistance against *P. syringae* strains that express either of two nonhomologous *avr* genes, *avrB* or *avrRpm1* (Bent et al., 1994; Grant et al., 1995). The predicted proteins, 909 amino acids for *RPS2* and 926 amino acids for *RPM1*, carry a possible LZ at their amino termini, a potential NBS, and 14 or 15 imperfct LRRs at the carboxy termini, respectively.

Prf gene encodes an 1824-amino acid protein of 209.7 kDa with LZ, NBS, and LRR motifs of 23-amino acid length. Prf also possess a large amino-terminal half region, 860 residues in length, with no similarity to any known protein. The end of this region (amino acid position 716-758) comprises two direct repeats of 70 and 72 amino acids with 49% amino acid identity between two copies. LZ with five complete heptads spans residues 959-994. NBS region is composed of three domains: the P-loop (kinase 1a) occurs at residues 1120-1132 followed by the kinase domains 2 and 3a at 1195-1205 and 1224-1231, respectively. The LRR domain begins at residue 1398 with approximately 14-18 imperfect copies of the LRR motif with a consensus sequence of LXXLXXLXXLXLXXN/CXXLXXIPSX (Salmeron et al., 1996).

TIR/NBS/LRR subclass. This subclass includes *N* from tobacco, *L6* and *M* from flax, and *RPP5* from *Arabidopsis* (Hammond-Kosack and Jones, 1997; Lawrence et al., 1995; Whitham et al., 1994). The tobacco (*Nicotiana tabacum*) *N* gene is originally introgressed from *N. glutinosa* and provides resistance to most strains of tobacco mosaic virus. The amino acid sequence of *N* gene products reveals that the *N* gene encodes a protein with an amino-terminal domain similar to the cytoplasmic domains of the *Drosophila* Toll protein and the mammalian interleukin-1 receptor (IL-R) protein (20% and 16% identity, and 42% and 41% similarity, respectively). This region in plant *R* genes has been designated the TIR (*T*oll/*I*ntreleukin-1 *R*esistance) domain. This subclass also contains an NBS and an LRR region. Although *N* shows similar structural organization of RPS2 and RPM1, the amino terminal domain of *N* is distinct and contains TIR instead of LZ. Two forms of mRNA of the *N* gene result from alternative splicing (Whitham et al., 1994). The larger transcript of the *N* gene encodes an 1144-amino acid protein (N) with the TIR at the amino terminal, and the NBS comprising three motifs from amino acid 216 to 325 and the LRR region consisting of 14 imperfect tandem LRRs (23 amino acid length) at the carboxy terminal. The less abundant truncated transcript codes for a 652-amino acid protein (N^{tr}) that is identical to the amino terminal 616 amino acids of N except

for the carboxy terminal 1.5 LRRs followed by 36 amino acids. N protein does not contain a signal peptide or a potential transmembrane hydrophobic region, and thus N is a cytoplasmic protein.

The flax *L6* rust resistance gene confers resistance to strains of the rust fungus *Melampsora lini* that carry the *AL6* avirulence gene (Lawrence et al., 1995). Like *N*, the *L6* gene gives rise to two products of 1294 and 705 amino acids resulting from alternative spliced transcripts. The larger and predominant transcript contains the TIR domain with similarity to Toll and IL-1R (21% and 16% identity, and 50% and 41% similarity, respectively) within the amino terminus. This TIR domain is followed by an NBS, and 27 LRRs that fit 23-amino acid consensus but are highly imperfect in length. At the carboxy terminal 40% of the LRRs are encoded by two direct leucine-rich repeats of 146 and 149 amino acids with 74% identity containing 20% leucine residues. The alignment of the products between *L6* and *N* genes suggests that *L6* possesses at the extreme amino-terminus of an extra 60 amino acids, including a potential signal peptide that does not exist in the *N* gene product . The smaller trucated protein ($L6^{tr}$) is composed of a 705-amino acid that is identical to L6 for the first 676 amino acids and loses most of the LRR domain but contains a novel sequence of 29 amino acids of the C terminus.

NBS/LRR subclass. This subclass does not contain LZ or TIR at the amino terminal. *Xa1* belongs to this subclass. The rice *Xa1* gene provides resistance to race 1 of *Xanthomonas oryzae* pv. *oryzae*, the causal pathogen of bacterial blight. The predicted 1802 amino acid sequence of *Xa1* gene harbors several regions showing similarity to deduced protein domains of RPS2, RPM1, N, and L6 : three motifs of NBS amino acids 326-334 (P-loop), 399-408 (kinase 2a), and 438-449 (kinase 3a) and an LRR (amino acids 1093-1650). LRR of *Xa1* is composed of six almost perfect repeats, and each repeat contain 93 amino acids. Of the six direct repeat units, the first to fifth units are strikingly identical at the nucleotide sequence and amino acid levels (97-99% and 92-99%, respectively). The sixth unit shares less similarity with the other five units, showing 62-67% similarity at the amino acid and 73-75% at the nucleotide sequence level (Yoshimura et al., 1988).

LRR/TM class. This class does not contain the apparent NBS and thereby forms a second class within the LRR-containing *R* genes. This class contains *Cf-2*, *Cf-4*, *Cf-5* and *Cf-9* genes from tomato and $HS1^{pro-1}$ from sugar beet (Baker et al., 1997; Dixon et al., 1996; Dixon et al., 1998; Jones et al., 1994; Thomas et al., 1997). These predicted proteins possess putative transmembrane (TM) receptors with extracellular LRR domains. *Cf* genes, conferring resistance to the tomato leaf mold patogen *Cladosporium fulvum*, have been introgressed from various wild *Lycopersicon* species or land races into cultivated tomato *L. esculentum*. *Cf-2* and *Cf-9* were identified in *L. pimpinelliforium*, and *Cf-5* was identified in the land race *L. esculentum* var. *cerasiforme*. The *Cf-4* gene was orginated from *L. hirsutum*.

Cf-9 encodes an 863-amino acid membrane-anchored, predominantly extracytoplasmic glycoprotein containing 27 imperfect LRRs with average length of 24 amino acids. The 24-amino acid of these extracellular 23 amino terminal LRRs (domain 1) region differs from the predominantly intracellular 23-amino acid of 4 carboxy terminal LRRs (domain 3) by the insertion of a glycine in the consensus sequence LXXLXXLXXLXLXXNXLXGXIPXX. The hydrophobic domain (transmembrane domain), containing 37 amino acids, is located between these two terminal LRRs.

Cf-2 locus has two functional genes (*Cf2-1* and *Cf2-2*) that confer resistance to *Cladosporium fulvum* independently. Each *Cf-2* gene encodes a polypeptide of 1112 amino acids which differs from each other by three amino acids, and contains 38 LRR motifs. The LRRs of *Cf-2*s are nearly all exactly 24 amino acids in length, and 20 of LRRs have extremely conserved alternating repeats. When compared to other resistance genes, *Cf-2* gene has a similar overall structure to *Cf-9*. The C-terminus of *Cf-2* shares significant homology with the protein encoded by the unlinked *Cf-9* gene. Like the other Cf proteins, both Cf-2s have 31 putative NXS/T glycosylation sites and a putative signal peptide of 26 amino acids.

Cf-4 tightly linked to *Cf-9* is a predicted membrane-anchored extracellular LRR glycoprotein. *Cf-4* encodes an 806-amino acid protein with 25 LRRs sharing 91.5% identity with that of *Cf-9*. *Cf-4* differs from *Cf-9* by possessing two fewer LRRs, composed of 46 amino acids, and by a 10-amino acid deletion near the mature N terminus and a number of amino acid substitutions in the N terminal half of the protein. These differences may determine the recognition specificity of ligand binding in *Cf-4* and *Cf-9*.

Cf-5 gene encodes a largely extracytoplasmic protein of 968 amino acids containing 32 LRRs, and resembles the *Cf-2* gene having 38 LRRs. CF-5 is 90% identical and 93.3% similar to CF-2. Like CF-2, CF-5 can be divided into seven domains. Domain A is a putative signal peptide of 26 amino acids. Domain F is a potential membrane-spanning region of 24 uncharged amino acids.

Kinase class. This class does not have an LRR or an NBS. Kinase class includes the tomato *Pto* gene, conferring resistance to *P. syringae.* pv. *tomato* containing the *avr* gene *avrPto* (Martin et al., 1993). This was the first cloned race-specific *R* gene conforming gene-for-gene recognition. *Pto* encodes a 321-amino acid hydrophilic protein and has been shown to be a serine/threonine-specific protein kinase which is capable of autophosphorylation. *Pto* possesses 27

serine and 13 threonine residues and shows similarities with the catalytic domains of serine-threonine protein kinases in many plants, mammalians, and lower eukaryotes. Eleven subdomains and 15 invariant amino acids characteristic of protein kinases are present in the expected locations of *Pto*. Comparison of the deduced amino acid sequence of *Pto* with the other protein kinases reveals that *Pto* is in the same protein kinase class as the cytoplasmic domain of the gene *Brassica Srk6*, the mammalian serine-threonine kinases of signaling factor *Raf* family, the *Drosophila* pelle kinase, and the human IRAK kinase.

LRR/TM/kinase class. The rice *Xa21* belongs to this class. *Xa21* confers resistance to the bacterial pathogen *Xanthomonas oryzae* pv. *oryzae*. *Xa21* encodes an 1025-amino acid protein containing a signal peptide of 23 hydrophobic residues, 23 imperfect copies of 24 amino acid extracytoplasmic LRRs with numerous potential glycosylation sites, a single transmembrane domain of a 26-amino acid hydrophobic stretch, and an intracellular serine-threnine protein kinase catalytic domain of 297 amino acids (Song et al., 1995). Like *Pto*, this catalytic region carries the 11 subdomains and all 15 invariant amino acids, which is characteristic of protein kinases. The *Xa21* protein shares striking overall homology (54.7% similarity and 35.5% identity) with the *Arabidopsis* receptor-like ser/thr kinase *RLK5* and shows 54.9% similarity to *Cf-9* within the extracellular domain. Because *Xa21* possesses both the extracellular LRR feature of *Cf-9* protein and the intracellular *Pto*-like ser/thr kinase domain, *Xa21* may be an evolutionry link between LRR protein of *Cf* genes and the *Pto* kinase.

Other putative class of *R* gene. Recently, wheat *Lrk10* gene was cloned from wheat the leaf rust resistance gene *Lr10* locus (Feuillet et al., 1997). *Lrk10* encodes a polypeptide of 636 amino acids which is composed of a putative signal peptide of 25 amino acids, an extracellular domain of 251 amino acids, an transmembrane domain of 24 amino acids, highly charged domain of 43 amino acids, and a serine-threonine protein kinase domain of 291 amino acids. Unlike *Xa21*, *Lrk10* does not contain LRR but shows 30% identity to *Pto* and 25.4% identity to *Xa21* within kinase domain. Thereby *Lrk10* belongs to a new type of receptor-like kinase. The complete linkage of *Lrk10* and *Lr10* in the very distal telomeric region of chromosome 1AS demonstrates the possibility that *Lrk10* and *Lr10* are identical. But whether *Lrk10* is involved in resistance response has to be tested by transformation of *Lrk10* gene into wheat lines susceptible to leaf rust isolate avirulent on *Lr10*-containing wheat line.

From rice, disease resistance-like genes (*RLG4*, *RLG8*, *GRLG9*, and *GRLG13*) which have striking homogy with *Lrk10* gene were isolated (Yun et al., 1998). Each gene has a catalytic domain of serine-threonine protein kinase. The predicted protein sequences of *RLG4*, *RLG8*, *GRLG9*, and *GRLG13* show significant homology (85.1%, 78%, 83.2%, and 51.5%, respectively) to *Lrk10* within the protein kinase catalytic region. However, these putative *R* genes also should be testified by complementation test to know whether these genes confer resistance to susceptible lines

R Protein Motifs and Their Fuction

Although direct evidences are not known about the function of different *R* gene domains in the signaling pathway leading to the resistance response. The NBS, LRR, LZ, TIR, and kinase domains of *R* gene products are found in a number of eukaryotic proteins participating in signal transduction cascades.

NBS. Several resistance genes encoding LRR domain also encodes amino acid sequences with striking similarity to known NBS, which is found in many families of proteins such as the RAS proteins, adenosine triphosphatases (ATPases), ribosomal elongation factors, and heterotrimeric GTP-binding proteins (Saraste et al., 1990). The NBS-containing proteins are necessary for many fundamental eukaryotic cellular events such as cell growth, differentiation, cytoskeletal organization, vesicle transport, and defense (Bourne et al., 1991). Therefore, NBS domains have been the subject of structure-function analysis in other proteins. The consensus NBS of some proteins is composed of three regions: the kinase 1a (phosphate-binding loop) is followed by a kinase 2 domain, and then a kinase 3a domain locates (Traut, 1994).

The presence of NBS in some of the derived *R* gene products suggests that nucleotide triphosphate binding is indispensable for *R* gene function, although no biochemical evidence that NBS actually binds ATP or GTP is shown. Site-directed mutagenesis that alters key residues within the NBS domain eliminates the ability of *N* and *RPS2* to induce hypersensitive response upon pathogen infection (Baker et al., 1997). The mechanism of NBS domains in the activation of plant *R* genes leading to defense response remains unknown. Important challenges for the future will be to uncover the mechanistic role of nucleotide triphosphate binding in the activity of *R* gene products.

LRR. Plant *R* genes seem to encode receptors that can directly or indirectly interact with elicitors produced by pathogen *avr* genes. Except *Pto*, LRRs are common to all of the plant *R* genes cloned to date. Thereby the most obvious candidate motif for elicitor binding is the LRR domains. LRRs have been demonstrated in protein-protein interactions and ligand binding in signal-transducing eukaryotic proteins (Kobe and Deisenhofer, 1994). The LRRs consist of multiple, serial repeats of a motif of approximately 24 amino acids in length. The LRRs contain

leucines or other hydrophobic residues at regular intervals and can also contain regularly spaced prolines and asparagines. Comparison of the LRRs from many plant, animal, and fungal proteins has showed a conserved core motif of LXXLXLXX(N/C/T)XL within each LRR where an X represents an arbitrary amino acid sequence (Jones and Jones, 1997). The crystal structure for one LRR-containing protein, porcine ribonuclease inhibitor, has been determined. Based on comparison with this protein, the central XXLXLXX portions of each repeat are believed to form a parallel sheet flanked by parallel turns (Warren et al., 1998).

The LRR has functional importance in disease resistance response, because single amino acid changes in the LRR domain of RPS2, RPM1, RPS5, and N do not confer resistance (Baker et al., 1997; Kobe and Deisenhofer, 1995). This result suggests that the function of the LRR domain can be eliminated by minor modification. Mutations in the LRR may be particularly effective in identifying the ligand specificity regions which disrupt the resistance response to a pathogen, because the LRR may be required for the interaction with the AVR component of the pathogen. Elucidation of the role of LRR domain of *R* genes in the induction of defense responses will require characterization of proteins that interact with the LRR domain and determination of LRR structure.

LZ. Of the NBS/LRR class of *R* genes, *RPS2*, *RPM1*, and *Prf* encode probable leucine zipper (LZ) domain between the amino terminal and the NBS domain. The LZ of *RPS2* and *RPM1* have four and six contiguous heptad sequences, respectively, that match the consensus sequence (I/R)XDLXXX (Landschulz et al., 1988). *Prf* also includes a putative LZ, with five complete heptads, which spans residues 959-994 (Salmeron et al., 1996). The LZ is proposed for playing a role in homo- and heterodimerization of eukaryotic transcription factors but formation of similar coiled-coil structure interacts between proteins with other functions. Whether *R* gene products can undergo homodimerization using yeast two-hybrid system will be needed to identify other proteins that may interact with their LZ regions of *R* gene products (Fields and Song, 1989).

TIR (Toll/Interleukin-1 Receptor). *N*, *L6*, and *RPP5* belong to second group of NBS/LRR class of *R* genes in that they code for a large amino terminal domain showing a moderate similarity to the cytoplasmic signaling domain of the *Drosophila* Toll protein and mammalian interleukin-1 receptors (Lawrence et al., 1995; Whitham et al., 1994). The *Drosophila* Toll receptor protein is involved in the control of dorsal-ventral patterning in embryos (Morisato and Anderson, 1995). Transmembrane receptor Toll is activated by the binding of an extracellular protein ligand spätzle that has a cysteine-knot structure. Binding of spätzle to Toll may lead to the activation of a cytoplasmic protein tube. The activated tube in turn activates the cytoplasmic serine-threonine kinase pelle. The pelle activity controls the degradation of inhibitory protein cactus that is complexed with the transcription factor dorsal. The phosphorylation of cactus leads to its own degradation, and this permits dorsal to move into the nucleus and regulate transcription of genes controlling ventralization (Wasserman, 1993). The Toll, tube, pelle, cactus, and dorsal genes also appear to be inolved in *Drosophila* immune response (Paterson et al., 1995).

The human interleukin-1/interleukin-1 receptor protein system is also involved in both the inflammatory and immune responses (Sims et al., 1989). IL-1R activates the transcription factor NF-κB by releasing it from a cytoplasmically localized complex with the inhibitor protein IκB and require the protein kinase IRAK. Mutations in conserved amino acids in the cytoplasmic domain of Toll and IL-1R suggest that this domain is necessary for transcription factors NF-κB and Dorsal signal transductions. The presence of TIR domain in the amino terminal of some plant *R* genes indicates that this domain may trigger similar signal transduction pathway similar to Toll-Dorsal and IL-1R-NF-κB pathways.

Serine-threonine kinase. Of the plant *R* genes, only *Pto* and *Xa21* have serine-threonine protein kinase domain. Eleven subdomains and 15 invariant amino acid residues characteristic of protein kinase have been identified (Hanks et al., 1988). The derived amino acid sequence of the *Pto* gene contains these conserved domains. Because *Pto* is strikingly similar to the *Drosophila* protein kinase pelle required for Toll-mediated signaling, *Pto* kinase facilitates downstream signal transduction cascade leading to the hypersensitive response. Using yeast two hybrid system, several genes interacting with *Pto* were identified (Zhou et al., 1995). *Pto* interacts with another protein kinase called *Pti1* (*Pto*-interacting gene 1) and also a family of transcription factors (*Pti4*, *Pti5*, and *Pti6*) that activate transcription of PR proteins.

Xa21 encodes the apparent LRR receptor kinase which has extracellular amino terminal LRRs and a cytosolic serine-threonine protein kinase domain. LRR region of *Xa21* may act as the receptor domain for the elicitor secreted into the apoplast by *avr* gene of *X. oryzae* pv. *oryzae* strains and kinase domain may play a role as a *Pto* gene. Thus, *Xa21* seems to contain both perceiving and signaling domains

R Gene Families and Evolution

Many genes, which are members of multigene families, occur as as large arrays forming gene clusters. The *Cf-9*, *Cf-*

2, *I2*, and *Pto/Prf* loci of tomato, the *N* locus in tobacco, the *RPP5* locus in *Arabidopsis*, the *Xa21* gene family in rice, and the unlinked *L* and *M* loci of flax are each composed of at least five related genes (Simons et al., 1998). The tight clustering of *R* genes allows frequent recombination events leading to the generation of new specificities of resistance genes through unequal crossing over via meiotic mispairing, intra- and inter-genic recombination, and gene duplication. Many plant pathogens show a high mutation rate from avirulence to virulence that break down the effectiveness of plant *R* genes. Therefore, plants must develop novel resistance specificities that can recognize the modified Avr determinant of pathogen. The results of recombination events of plant *R* genes give plants a selective advantage against rapidly evolving pathogen populations (Baker et al., 1997).

Conclusions

The isolation and characterization of many avirulence and resistance genes have provided molecular support for Flor's gene-for-gene theory. The *R* genes can be isolated by map-based cloning, transposon tagging, and PCR-based strategy. The predicted R proteins incorporate several common structural motifs: nucleotide binding sites (NBS), leucine rich repeats (LRR), transmembrane domains (TM), and serine/threonine protein kinases (PK).

These are combined into several arrangements with the following classes: NBS/LRR, LRR/TM, kinase, and LRR/TM/kinase. There are several possible reasons for this divergence from the normal pattern. Some of the ligands, particularly those of bacterial origin, may be delivered to the inside of the plant cell by the *hrp* gene-based secretion mechanism (Hutcheson, 1998).

The discovery of structurally similar host *R* genes from evolutionarily diverse plant species encoding resistance to viral, bacterial, fungal, and nematode pathogens suggests that common signalling pathways leading to disease resistance exist among plants. These findings highlight the utilitiy of wild relatives of crop plants as a source for new *R* genes. The availabilty of cloned *R* genes now opens up possibilities for addition of new *R* genes to a plant line by genetic transformation to provide a promising strategy for the production of plants with superior disease resistance.

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