REVIEW

Recessive Resistance Genes and the *Oryza sativa*–*Xanthomonas oryzae* pv. *oryzae* Pathosystem

Anjali S. Iyer-Pascuzzi and Susan R. McCouch

Department of Plant Breeding and Genetics, Cornell University, Ithaca, NY 14853, U.S.A.

Submitted 26 October 2006. Accepted 13 February 2007.

Though recessive resistance is well-studied in viral systems, little is understood regarding the phenomenon in plant-bacterial interactions. The *Oryza sativa*–*Xanthomonas oryzae* pv. *oryzae* pathosystem provides an excellent opportunity to examine recessive resistance in plant-bacterial interactions, in which nine of 30 documented resistance (*R*) genes are recessively inherited. Infestations of *X. oryzae* pv. *oryzae*, the causal agent of bacterial blight, result in significant crop loss and damage throughout South and South-east Asia. Two recently cloned novel recessive *R* genes, *xa5* and *xa13*, have yielded insights to this system. Like their viral counterparts, these bacterial recessive *R* gene products do not conform to the five commonly described classes of *R* proteins. New findings suggest that such genes may more aptly be viewed as mutations in dominant susceptibility alleles and may also function in a gene-for-gene manner. In this review, we discuss recent accomplishments in the understanding of recessively inherited *R* genes in the rice–bacterial blight pathosystem and suggest a new model for the function of recessive resistance in plant-bacterial interactions.

Extensive work on race-specific resistance has resulted in the identification of more than 40 cloned plant resistance (*R*) genes (Martin et al. 2003; McHale et al. 2006) to a wide variety of plant pathogens. Much of the focus in plant-bacterial interactions has centered around nucleotide binding site-leucine rich repeat (NBS-LRR) proteins, as these are the most common of the five classes of *R* proteins (Belkadir et al. 2004; Martin et al. 2003; McHale et al. 2006). Intriguingly, though six bacterial blight (BB) *R* genes have been cloned, only one, *Xa1*, encodes an NBS-LRR protein (Yoshimura et al. 1998). Although recessive resistance is relatively uncommon in plant-bacterial systems, nine of the approximately 30 *Xa* genes are recessive (Table 1). The recent isolation of two of these, *xa5* and *xa13*, suggests that there are several previously undescribed types of *R* genes and invites more questions. How do such *R* genes contribute to resistance? Is resistance mediated by recessive *R* genes equivalent to that mediated by dominantly inherited *R* genes? In this review, we offer a brief introduction to the disease and then discuss recent developments in the study of recessive genes of this pathosystem. Finally, we

discuss a new model for their function. Nino-Liu and associates (2006) have provided a comprehensive discussion of both *Xanthomonas oryzae* pv. *oryzae* and the *X. oryzae* pv. *oryzicola* history and biology.

Disease overview.

Rice BB, caused by *Xanthomonas oryzae* pv. *oryzae*, was first reported by farmers in 1884 in the southern region of Japan (Devadath 1992; Mizukami and Wakimoto 1969). Though the disease was common throughout that region by 1910, it was not a severe rice disease in northern Japan and other Asian nations until the 1960s and 1970s (Mizukami and Wakimoto 1969). Many countries, including Nepal, India, and Sri Lanka, trace the first reported outbreak of the disease to the introduction of new, high-yielding (or ‘modern’) varieties that occurred at this time (Adhikari et al. 1994b; Mew 1993; Mew et al. 1992) (Table 2).

Major BB epidemics resulted in intensive breeding for disease resistance at the International Rice Research Institute (IRRI) (Mew et al. 1992). By 1981 IRRI had identified more than 1,000 varieties with resistance to the common Philippine pathotype of *X. oryzae* pv. *oryzae* (at that time, race 1; Mew et al. 1981, 1992). By the early to mid 1980s, most released IRRI varieties carried BB resistance; these accounted for more than 90% of the rice planted in the Philippines (Mew et al. 1992). BB is still found throughout nearly every Asian country. Accurate estimates of average yield losses are difficult to obtain, as these vary extensively by geographic region and season, but Upadhyay (1985) estimated that, in India, losses of 15 to 20% were common and, occasionally, as much as 40% of the crop was lost to BB.

Disease epidemiology and symptoms.

X. oryzae pv. *oryzae* is a rod-shaped gram-negative bacterium that enters rice leaves through wounds, stomata, or hydathodes (Mew 1987). The bacteria multiply in the epitheme, the tissue connecting the hydathodes to the xylem, to which they subsequently move and further multiply to infect the plant (Shen and Ronald 2002). BB is most severe in highly managed systems such as irrigated paddies or those with high N fertilizer applications. The disease is aggravated by warm, humid, and wet conditions. Symptoms of BB include water-soaking or gray lesions down the leaf, which often dry and turn chlorotic. Leaves often curve inward. In severe infections, bacteria ooze out of cracks or hydathodes.

Cultural control methods are important, but the primary and most effective means of control is through planting resistant cultivars. There are approximately 30 known *R* genes to BB (Chu et al. 2006). To facilitate characterization of *Xa* genes and

Current address for A. S. Iyer: Department of Biology, Duke University, Durham, NC 27712, U.S.A.

Corresponding author: Susan R. McCouch; E-mail: srm4@cornell.edu; Telephone: +1.607.255.0420; Fax: +1.607.255.6683.

X. oryzae pv. *oryzae* isolates, IRRI developed a set of near-isogenic lines (NILs) in the 1980s. Each NIL contained a single *Xa* gene in the background of the susceptible cultivar IR24 (Ogawa et al. 1988). Using these isolines, six BB *R* genes have been cloned (*xa13*, Chu et al. 2006; *Xa27*, Gu et al. 2005; *xa5*, Iyer and McCouch 2004; *Xa21*, Song et al. 1995; *Xa1*, *Xa26*, Sun et al. 2004 and Yoshimura et al. 1998).

X. oryzae pv. *oryzae* virulence.

Like other gram-negative bacteria, *X. oryzae* pv. *oryzae* promotes disease and avirulence through type-III secreted effector proteins (Alfano and Collmer 2004; Gurlebeck et al. 2006). Based on similarity to known effector genes, eight homologs were identified in the recently sequenced *X. oryzae* pv. *oryzae* genome (Lee et al. 2005). Five were members of the *avrBs3/pthA* or TAL (transcription activator-like) family of effectors.

TAL effectors are found throughout the *Xanthomonas* genus and appear to be particularly important for *X. oryzae* pv. *oryzae* virulence. In a diverse set of *X. oryzae* pv. *oryzae* strains from various countries, several carried at least one of the four major virulence effectors: *avrXa7*, *pthXo1*, *pthXo2*, and *pthXo3* (Yang and White 2004). Loss of *avrXa7*, *pthXo1*, *pthXo2*, and *pthXo3* from *X. oryzae* pv. *oryzae* result in extremely reduced symptom development and bacterial growth (Bai et al. 2000; Swarup et al. 1991; Yang and White 2004).

Members of the TAL effector protein family are 90 to 97% identical and are typified by an N-terminal secretion signal and variable number of near-perfect repeats of a 34-amino acid sequence near the middle of the protein (Mudgett 2005). They have imperfect heptad leucine repeats, at least one nuclear localization signal (NLS), and an acidic activation domain (AAD) at the C terminus (Gurlebeck et al. 2006). Structure-function studies have examined the domains of the TAL family

Table 1. Recessively inherited rice bacterial blight resistance genes^a

Gene	Chm	Original donor	Resistance spectrum	Derived ^b	Comments/Durability	Cloned	Reference ^c
<i>xa5</i>	5	DZ192	PXO ^d races 1-3, 5	n	Stronger resistance in combination with other <i>Xa</i> genes	yes	Petpisit et al. 1977 Iyer and McCouch 2004
<i>xa8</i>	7	PI 231129	Moderately resistant to PXO races 1-3, resistant to PXO race 5	n	NA	no	Sidhu et al. 1978 Singh et al. 2002
<i>xa13</i>	8	BJ1 group	PXO race 6, susceptible to PXO races 1-5	n	Stronger resistance in combination with <i>Xa4</i> , <i>xa5</i> , <i>Xa21</i>	yes	Chu et al. 2006 Ogawa et al. 1987
<i>xa15</i>	NA ^e	M41(mutant of Harebare)	Japanese isolates	m	Also termed <i>xa(nm)</i>	no	Nakai et al. 1988, 1990; Ogawa 1996
<i>xa19</i>	NA	XM5	Japanese isolates	m	NA	no	Taura et al. 1991
<i>xa20</i>	NA	XM6	PXO races 1-6	m	NA	no	Taura et al. 1992
<i>xa24</i>	NA	DV85, DV86, Aus295	PXO race 6	n	NA	no	Khush and Angeles 1999
<i>xa26b</i>	NA	Nep Bha Bong To	MR PXO races 1-3, R PXO race 5	n	NA	no	Lee et al. 2003
<i>xa28</i>	NA	Lota Sail	PXO86, races 2 and 5	n	NA	no	Lee et al. 2003

^a Niño-Liu and associates (2006) provide a complete list of bacterial blight resistance genes.

^b n = Allele derived naturally, m = allele derived from an induced mutant.

^c References refer to first known identification and, if available, first cloning or mapping.

^d PXO = Philippine *Xanthomonas oryzae* pv. *oryzae* race.

^e NA = not available.

Table 2. Rice bacterial blight in selected Asian countries

Country or Region	First Reported Occurrence of BB	Average % disease loss/epidemics	Distribution throughout the country
China	At least by the 1950s (Mizukami and Wakimoto 1969)	'Severe' disease loss (Mew 1987)	Widespread since introduction of hybrids (Mew 1993)
India	Associated with introduction of TN-1 in 1965 in several states, first noticed in Maharashtra in 1951 (Sridhar 2002)	Most severe in the Northern states of Punjab and Uttar Pradesh. Major epidemics in the Punjab 1980s and in 1995 (Kang and Singh 1987, Raina et al. 1981)	Considered a problem everywhere except Assam, Kerala (Sridhar 2002; Upadhyay 1985)
Japan	1884 (Mizukami and Wakimoto 1969)	20 to 30% in moderately infected fields (Mizukami and Wakimoto 1969)	Throughout the country, in approximately 10% of total acreage grown to rice (Mizukami and Wakimoto 1969)
Nepal	1968, Kathmandu Valley (Adhikari et al. 1994a)	Major epidemics in 1979 and 1987, yield losses up to 26% (Adhikari et al. 1994a). In a survey of 32 districts, seven had average field infections greater than 50%, 6 had 25-50%, 16 between 10-25% and 2 less than 10% (Adhikari and Shrestha 1990)	Widespread (Adhikari and Shrestha 1990)
Pakistan	1976 (Mew and Majiid 1977)	Considerable yield loss (Akhtar and Akram 1987)	Widespread (Akhtar and Akram 1987)
Philippines	Since the 1950s (Mew et al. 1992)	Major epidemics in the 1960s, no large-scale or severe epidemics since the introduction of <i>Xa</i> genes (Mew et al. 1992)	Widespread (this study)
Sri Lanka	1950s (Ochiai et al. 2000)	Serious damage to rice production since 1967 (Ochiai et al. 2000)	Widespread (Ochiai et al. 2000)
Thailand	1963 in Pathum Thani Province (Eamchit and Mew 1981)	8 to 16% empty grains in central Thailand (Sirisantana et al. 1984)	NA
Vietnam	NA	Only severe in rainy season (van Kim et al. 1981)	Limited to certain regions (van Kim et al. 1981)

members that contribute to either virulence or avirulence. Results indicate that the AAD, NLS, and repeat regions are all important for both avirulence and virulence specificities (Szurek et al. 2001; Yang and White 2004; Yang et al. 2000). For example, mutations in the AAD were found to disrupt the avirulence activity of AvrXa10 in rice (Zhu et al. 1998, 1999), while loss of the NLS resulted in loss of avirulence and virulence activities of AvrXa7 (Yang et al. 2000).

Due to their transcription factor-like motifs, several studies have examined the possibility that these proteins play a role in host transcription (Marois et al. 2002; Szurek et al. 2001; Yang et al. 2000; Zhu et al. 1998, 1999). AvrXa10 and AvrXa7, both from *X. oryzae* pv. *oryzae* as well as AvrBs3 from *X. campestris* pv. *campestris* are localized to the nucleus (Szurek et al. 2001; Yang et al. 2000; Zhu et al. 1998). AvrXa10 can activate transcription in yeast and *Arabidopsis* (Zhu et al. 1998, 1999); AvrXa7 binds to AT-rich DNA sequences (Yang et al. 2000), and AvrBs3 interacts with nuclear transport protein importin alpha (Szurek et al. 2001) and can induce the transcription of several genes in pepper (Marois et al. 2002). Members of this family may also promote virulence through the suppression of plant defenses. AvrXa7 and AvrXa10 suppress the nonhost hypersensitive response (HR) in tobacco as well as the expression of certain *PR* (pathogen-responsive) genes (Fujikawa et al. 2006).

Recessive plant *R* genes.

Though most *R* genes in bacterial and fungal systems show dominant inheritance, recessive resistance is fairly common in viral systems, accounting for slightly less than half of all known viral *R* genes (Kang et al. 2005b). Strikingly, most of those isolated to date are homologs of the same gene, translation initiation factor *eIF4E* (Diaz-Pendon et al. 2004; Kang et al. 2005b). This gene provides resistance to several viruses in the family *Potyviridae* and has been identified in the dicots pepper (*pvr1*), pea (*sbm1*), lettuce (*mo1*), tomato (*pot1*), and melon (*nsv*) and in the monocot barley (*rym4/5*) (Kang et al. 2005b; Robaglia and Caranta 2006). Additionally, translation initiation factor *eIF4G* is responsible for resistance of rice to *Yellow mottle virus* (Albar et al. 2006) and in *Arabidopsis* to *Cucumber mosaic virus* and *Turnip crinkle virus* (Yoshii et al. 2004). Though the *R* genes mentioned above produce different resistance phenotypes (for example, inhibition of cell-to-cell movement or viral replication), several studies have shown that resistance is due to mutations in *eIF4E* or *eIF(iso)4E* (Diaz-Pendon et al. 2004; Kang et al. 2005b; Robaglia and Caranta 2006). Although the exact role of *eIF4E* in the potyvirus infection cycle is unknown, it is possible that *eIF4E* interacts with a small viral protein known as VPg (viral protein genome-linked) during infection and a lack of interaction results in the inability of the virus to complete its life cycle and successfully infect the plant (Kang et al. 2005a and b; Robaglia and Caranta 2006).

In bacterial and fungal plant-pathogen interactions, there are currently only four cloned recessively inherited *R* genes: barley *mlo* (Buschges et al. 1997), *Arabidopsis* *RRS1-R* (Deslandes et al. 2002), rice *xa13* (Chu et al. 2006), and *xa5* (Iyer and McCouch 2004; Jiang et al. 2006), all of which encode structurally different proteins. The *mlo* allele encodes a 60-kDa seven-transmembrane protein that provides broad-spectrum resistance to all known isolates of the powdery mildew pathogen *Blumeria graminis* f. sp. *hordei* (Buschges et al. 1997). *RRS1-R* is a unique member of the NBS-LRR class of *R* products, with a WRKY transcription factor domain in its C terminus (Deslandes et al. 2002). Though genetically defined as a recessive *R* gene in ecotype Niederzenz (Nd-1), *RRS1-R* behaves as a dominant *R* gene when transformed into *Arabidopsis* Colombia ecotype, and resistant plants transformed with

RRS1-S remain resistant, suggesting that *RRS1-R* is not a true recessive allele (Deslandes et al. 2002). In this review, we will focus on two examples of recessively inherited, race-specific resistance mediated by genes in the BB system.

Host plant resistance to BB: Not a 'typical' pathosystem?

xa5 encodes *TFIIA-gamma*. The *xa5* allele provides race-specific resistance to *X. oryzae* pv. *oryzae*. Based on candidate gene analysis, *xa5* appears to be unique among *R* genes because it does not fall into any of the predicted *R* gene product classes (Blair et al. 2003). Map-based cloning revealed that *xa5* encoded the small subunit of transcription factor IIA (*TFIIA* γ) (Iyer and McCouch 2004). A 2-nucleotide substitution at position 39 in the second exon of the gene resulted in an amino acid change from valine (V39) in susceptible cultivars to glutamic acid in resistant. Association analysis of 27 resistant and nine susceptible cultivars from the Aus-Boro group of rices identified a single haplotype among all resistant varieties tested and two haplotypes among the susceptible cultivars. All resistant cultivars contained glutamic acid at position 39; all susceptible cultivars contained valine, and some had an additional silent substitution (Iyer and McCouch 2004). There was no differential expression of either the *xa5* or *Xa5* allele in response to infection. Transformation of the dominant susceptible allele from IR24, an *indica*, into a resistant background resulted in diseased plants, as measured by lesion length and bacterial population growth (Jiang et al. 2006; A. Iyer-Pascuzzi and S. R. McCouch, *unpublished*). We will use the designation *Xa5^{RS}* to refer to the locus (containing either allele) and *xa5* or *Xa5* to refer specifically to the resistant or susceptible alleles, respectively.

Structure and function of TFIIA-gamma. *TFIIA* is one of several general transcription factors (GTF) that work with RNA polymerase II to transcribe DNA (Hampsey 1998; Orphanides et al. 1996; Roeder 1996). It is an extremely well-conserved protein, necessary for accurate development in both the animal and plant kingdoms (Aoyagi and Wassarman 2000; Burke et al. 1990). In yeast, *TFIIA* is composed of two subunits, Toa1 and Toa2, while in plants and animals, it has three: α and β (homologous to Toa1) and γ (homologous to Toa2). The α and β subunits are translated as one long polypeptide and are subsequently cleaved. *TFIIA* stimulates transcription (Kobayashi et al. 1998; Ozer et al. 1994, 1996; Stargell and Struhl 1995; Stargell et al. 2000), is involved in promoter selectivity (Hampsey 1998; Orphanides et al. 1996), and stabilizes the binding of transcription factor IID (*TFIID*; another GTF necessary for transcription by RNA polymerase II) to DNA (Chi et al. 1995; Lieberman and Berk 1994; Wang et al. 1992). *TFIIA* is an unusual GTF in that it is not necessary for activated transcription of all genes in typical conditions, and promoters vary in the degree to which they require this GTF (Liu et al. 1999; Ozer et al. 1998b). Structure analysis of the entire *TFIIA* protein (α , β and γ subunits) showed that it is composed of two domains: i) a β barrel that contacts DNA and the TATA-box binding protein (TBP) and ii) a four-helix bundle (4HB) that faces away from the DNA (Fig. 1) (Bleichenbacher et al. 2003; Geiger et al. 1996; Tan et al. 1996). Not unexpectedly, the 4HB is composed of four major α -helices, two within the large α/β subunit and two within the small γ subunit.

Mutational studies in yeast have shown that nucleotide changes in the 4HB region affect transcription and growth and disrupt interactions with transcription-associated factors (Kang et al. 1995; Kraemer et al. 2001; 2006; Liu et al. 1999; Ma et al. 1996; Robinson et al. 2005; Warfield et al. 2004). Intriguingly, the critical mutation for *xa5*-mediated resistance resides within an evolutionarily well-conserved hydrophobic patch within helix 3 of the 4HB in Toa2 (Fig. 1) (Kraemer et al.

2001; 2006). Though yeast carries glutamic acid at the corresponding position to OsTFIIA γ V39, mutation of this amino acid has no effect on *Saccharomyces cerevisiae* growth (Kang et al. 1995).

There are two copies of *TFIIA γ* in rice, one on chromosome 1 (*OsTFIIA γ 1*) and another on chromosome 5 (*OsTFIIA γ 5/* *Xa5^{RS}*). The coding regions of the *Xa5* and *OsTFIIA γ 1* alleles are 79% identical (86% identical at the protein level). The dupli-

Fig. 1. A, Model of the *Saccharomyces cerevisiae* crystal structure of TFIIA-TATA-box binding protein (TBP)-DNA (Bleichenbacher et al. 2003; Geiger et al. 1996; Tan et al. 1996). Blue = TBP, yellow = region of Toa1 homologous to the β chain of the large subunit in plants and animals, red = region of Toa1 homologous to the α chain of the large subunit, and purple = Toa2. The four-helix bundle (4HB) is composed of two helices from Toa1 and the two larger helices from the N terminus of Toa2. The amino acid homologous to the critical mutation in *Xa5* is starred; the side chain is shown. Modeled with SWISS PDB-view and coordinates from the protein data bank file 1NH2 (Bleichenbacher et al. 2003). **B**, Alignment of TFIIA γ from upper and lower eukaryotes. Secondary structures are denoted with underlines (H = α -helices) or arrows (S = β -strands). The two α helices and three β strands contributing to the 4HB and β -domains, respectively, are labeled in both this section and in section A. The critical mutation for *Xa5* is highlighted in red. Residues in contact with TBP are highlighted in gray (Geiger et al. 1996). Mutations in this region, particularly Y69 and W76, result in complex instability, transcription defects, or conditional viability or lethality, singly or in combination, in yeast (Ozer et al. 1996, 1998b; Stargell and Struhl 1995). The interaction with transcription-associated factors and other proteins typically occurs through the N terminus. Functionally important residues in this region, identified by single-point mutations to alanine or leucine in yeast, are starred (Kraemer et al. 2006; Ozer et al. 1996, 1998a; Warfield et al. 2004). In yeast, mutation of any 10 constitutive residues in Toa2 except the nonconserved region results in lethality. † indicates the TFIIA γ ortholog of *OsTFIIA γ 5* and ‡ indicates the TFIIA γ ortholog of *OsTFIIA γ 1*.

cation seems to be exclusive to monocots, as investigation of *TFIIA* γ expressed sequence tags and cDNAs in GenBank revealed that dicots, such as *Arabidopsis* and citrus, have only one copy, while all monocots examined (rice, barley, oat, maize, wheat, and sorghum) have at least two copies (A. Iyer-Pascuzzi and S. R. McCouch, *unpublished*). Additionally, all plant *TFIIA* γ predicted proteins examined, including *OsTFIIA* γ 1, are similar to the susceptible allele product *Xa5* in that they contain valine or a conservative substitution such as leucine or isoleucine at the variable amino acid position.

Phylogenetic analysis suggests that *Xa5*^{*RS*} may be ancestral to *OsTFIIA* γ 1. The evidence is based on the fact that *Xa5*^{*RS*} is more closely related to the small subunit of *Arabidopsis TFIIA* than to the rice paralog on chromosome 1 (Jiang et al. 2006). In further support of this, using the published X-ray crystal structure (Bleichenbacher et al. 2003) of the human *TFIIA*-TBP-DNA complex as a template, Jiang and associates (2006) used homology modeling to predict the X-ray crystal structure of *Xa5*^{*RS*} and *OsTFIIA* γ 1. The structures of *Xa5* and *xa5* were very similar, with a root mean square deviation (rms) of only .024 nm. However, they differed more from the *OsTFIIA* γ 1 structure (rms = .056 nm for *Xa5*) than from human *TFIIA* γ (rms = .0405 and .0397 nm, for *Xa5* and *xa5*, respectively). This was despite higher amino acid sequence similarity between *Xa5*^{*RS*} and *OsTFIIA* γ (86%) than between *Xa5*^{*RS*} and human *TFIIA* γ (approximately 47%) (Jiang et al. 2006). These results all indicate that *Xa5*^{*RS*} is ancestral to *OsTFIIA* γ 1.

Function of *xa5*. Whether *Xa5*^{*RS*}, *TFIIA* γ 1, or both function as the small subunit of *TFIIA* is not yet known, though the observation that the functional single-copy *Saccharomyces cerevisiae* allele carries glutamic acid at the corresponding position to the *xa5* resistant allele suggests that this amino acid does not disrupt its essential function. Further, reverse transcription-polymerase chain reaction analysis of *TFIIA* γ 1 and *Xa5*^{*RS*} expression in different organs of the rice plant showed that both genes were expressed in leaves, stems, and roots, but only *Xa5*^{*RS*} was expressed in panicles (Jiang et al. 2006). This suggests that *Xa5*^{*RS*} may play a critical role in DNA transcription, particularly at or after the reproductive stage.

How might *xa5*, as *TFIIA* γ , provide resistance to *X. oryzae* pv. *oryzae*? Jiang and associates (2006) suggested that the resistant allele product *xa5* may bind to transcriptional activators more tightly than to repressors, allowing the activation of genes important for defense, while the susceptible *Xa5* allele product may preferentially bind to activators of defense silencing genes. Alternatively, *TFIIA* γ was recently shown to play a role in the oxidative stress response in yeast (Kraemer et al. 2006). Since this response is an important part of the plant defense response, it is possible that *xa5* mediates resistance in part through this pathway. However, based on recent results from our lab (A. Iyer-Pascuzzi and S. R. McCouch, *unpublished*), we propose that *xa5*-mediated resistance is a passive process that relies on secondary or basal defenses. In this scenario, we hypothesize that the valine to glutamic acid substitution in *xa5* would prevent it from productively interacting with any bacterial proteins, but the susceptible allele product *Xa5* would do so. This interaction could lead to the activation of genes that indirectly promote disease, such as those involved in nutrient, sugar, or iron metabolism. Based on evidence regarding *X. oryzae* pv. *oryzae* proteins in the AvrBs3 family, it is tempting to speculate that such a *Xa5* interactor could be a transcriptional activator of eukaryotic genes.

Indeed, *TFIIA* γ has been reported to bind to transcriptional activators (Kraemer et al. 2006; Kobayashi et al. 1995). As mentioned above, *TFIIA* helps stabilize the *TFIID*-DNA complex (Chi et al. 1995; Lieberman and Berk 1994; Wang et al. 1992). The stability of this complex is important for gene tran-

scription and, thus, provides a good target for transcriptional regulators (Kashanchi et al. 1996; Kobayashi et al. 1995; Stargell and Struhl 1995; Xie et al. 2000). In yeast, *TFIIA* γ directly interacts with transcriptional activators like the basic leucine zip factor Yap1 (Kraemer et al. 2006), herpes simplex virus VP16, and Epstein-Barr virus Zta (Kobayashi et al. 1995). *TFIIA* has also been reported to be involved in tissue-specific gene expression. In *Drosophila* spp., an isoform of *TFIIA* γ is involved in photoreceptor development (Zeidler et al. 1996).

Because rice has two copies of *TFIIA* γ , it is of interest to determine whether only one or whether both paralogs are implicated in the disease response. Recently, Sugio and colleagues (2005) identified *OsTFIIA* γ 1 in a screen for genes upregulated by the virulent Philippine race PXO99^A. Infection of rice with *X. oryzae* pv. *oryzae* PXO99^A results in the upregulation of *TFIIA* γ 1 but not *Xa5*^{*RS*}, while inoculation of *xa5*-containing rice with *X. oryzae* pv. *oryzae* race PXO86 results in no change in expression level of either *TFIIA* γ 1 or *TFIIA* γ 5 (*Xa5*^{*RS*}) (Iyer and McCouch 2004; Jiang et al. 2006). This raises the possibility that PXO99^A targets *TFIIA* γ 1 to promote disease. These exciting results suggest that there may be a complex relationship between the paralogs and the disease response.

Could *TFIIA* mediate resistance to other *Xanthomonas* species that infect plants or animals? Thus far, a role for *TFIIA* γ in disease resistance has not been reported in any other system. Interestingly, a 10-amino acid peptide of the large *TFIIA* subunit, mutated in one amino acid, activated T-cells in patients with celiac disease, an autoimmune disorder in which patients cannot absorb the gliadin proteins found in specific cereals (Kumar et al. 2002). This mutant peptide was created in the lab and is not found in native human populations. Nonetheless, this study showed that a mutation in the large subunit of *TFIIA* could activate the human immune system, suggesting that *TFIIA* may be involved in pathways other than RNA polymerase II transcription. Further, a human isoform of the large subunit *TFIIA*-ALF is expressed specifically in male testis (Upadhyaya et al. 1999), and an isoform of the *Drosophila* small subunit plays a role in photoreceptor development (Zeidler et al. 1996). Work in yeast has shown that some *TFIIA* γ mutations result in a wild-type phenotype (Kang et al. 1995; Warfield et al. 2004). Hence, although *TFIIA* γ is a single-copy gene in humans, some mutations might provide additional functionality without disrupting its essential function. These findings are significant in light of the observed similarities between animal immunity and plant resistance (Ausubel 2005; Fluhr and Kaplan-Levy 2002; Nurnberger and Brunner 2002; Nurnberger et al. 2004; Staskawicz et al. 2001; Zipfel and Felix 2005). Together, these reports indicate that *TFIIA* is not a typical GTF and suggest the possibility that *TFIIA* γ might play a role in disease resistance other than rice BB.

***xa13*.** The recessive gene *xa13*, derived from the BJ1 group of rices, provides resistance to race 6 *X. oryzae* pv. *oryzae*, PXO99^A, the same broadly virulent Philippine race described above in relation to *OsTFIIA* γ 1 (Ogawa et al. 1987). Resistant (*xa13*) and susceptible (*Xa13*) alleles each encode unique 307-amino acid plasma membrane-localized proteins (Chu et al. 2006) that show 68% sequence similarity to the MtN3 protein induced by *Rhizobium* spp. in legume nodule development.

Examination of gene expression in leaves showed that *Xa13* is upregulated upon pathogen infection but not when mock-inoculated with water. Promoter- β -glucuronidase fusions demonstrated that *Xa13* was expressed in the parenchyma cells that surround xylem elements of leaves. *Xa13* induction leads to susceptibility, as the recessive resistant allele was not upregulated upon pathogen challenge. In uninoculated plants, both alleles were expressed predominantly in the panicles and an-

thers, suggesting a role for *Xa13^{RS}* in developmental processes. One amino acid substitution was found between the susceptible and resistant proteins of the susceptible variety IR24 and its resistant NIL IRBB13 (which carries *xa13*). Examination of proteins encoded by other *Xa13* and *xa13* alleles suggested that this amino acid was not the functional amino acid polymorphism (Chu et al. 2006). Further investigation identified a variable area in the -69 to -86 region of the promoter. All 11 *xa13*-carrying lines examined had an insertion, deletion, or substitution (compared with *Xa13* lines) in this area. Mutations in this region appeared to eliminate the induction of *Xa13* during pathogen inoculation (Chu et al. 2006). Thus, expression levels of the alleles appear to be key to resistance. In support of this, silencing the dominant susceptible allele resulted in resistance, while silencing the recessive resistant allele yielded even higher levels of resistance, as measured by reduced lesion length. Additional work showed that this locus is critical to viable pollen development, as plants silenced for either allele were male-sterile (Chu et al. 2006). Understanding how the developmental and disease-resistant pathways intersect is the next exciting step in this system.

Recessive resistance or dominant susceptibility?

Are *xa5* and *xa13* really resistant genes or are they simply mutant forms of susceptibility alleles? This is an important distinction, as it has implications regarding plant defense and disease control. For example, if susceptibility is an active process in which a host gene is targeted by a bacterial protein to induce susceptibility, then recessive resistance may be a passive response defined more by the lack of susceptibility than the activation of defense signaling pathways.

If this were the case with *xa5* and *xa13*, we might expect responses to these genes to differ from those commonly observed in *R* gene systems. Indeed, though investigations of *xa5* and *xa13* resistance mechanisms are still in the early stages, several points of evidence already suggest that these genes have atypical *R* gene responses. First, neither gene shows a typical hypersensitive response in the resistant reaction. A delayed and somewhat weak HR becomes apparent 48 to 72 h after infiltration of *X. oryzae* pv. *oryzae* PXO86 in rice leaves expressing *xa5* (A. J. Bogdanove, *personal communication*). Inoculation of IRBB13, which carries only the *xa13* gene for BB resistance, with the incompatible *X. oryzae* pv. *oryzae* PXO99^A does not result in the browning seen after inoculation with an incompatible PXO99^A strain carrying the effector *avrXa7-sacB50* (Yang et al. 2006). Second, at least for *xa13*, defense gene expression is altered. *POX22.3*, a peroxidase gene usually highly induced in the rice defense response, is not induced in IRBB13 when inoculated with incompatible PXO99^A but is induced in the interaction with the incompatible PXO99^A(*avrXa7-sacB50*) strain (Yang et al. 2006). Additionally, several genes not previously associated with defense pathways showed differential expression in the *xa13* response (Chu et al. 2004). Resistant responses due to *xa5* are currently under investigation.

These atypical reactions suggest that at least some recessive *R* genes might more aptly be thought of as mutations of dominant susceptibility ('S') alleles. Indeed both *Xa13* and *Xa5* may act as susceptibility alleles. When transformed into homozygous resistant lines, each causes disease, and bacteria are more virulent as evaluated by lesion length on plants expressing *Xa5* or *Xa13* than on plants expressing the resistant alleles (Chu et al. 2006; A. Iyer-Pascuzzi and S. R. McCouch, *unpublished*). Moreover, recent exciting work by Yang and colleagues (2006) suggests that susceptibility alleles like *Xa13* might be targeted by type III effectors in a gene-for-gene manner. We postulate that there are two classes of recessive *R* genes, those like *RRS1-R* that do not have corresponding 'S' alleles (dis-

cussed above) and those like *xa5* and *xa13* that are likely to be mutated forms of 'S' genes. Further, we hypothesize that i) 'S' genes are necessary for pathogen virulence, ii) 'S' genes may function in a gene-for-gene manner with bacterial effectors, and iii) 'S' genes are likely to be essential host proteins.

In a search for host susceptibility genes induced by *X. oryzae* pv. *oryzae*, Yang and colleagues (2006) used whole-genome-based microarray analysis of rice cultivar Nipponbare (subpopulation *japonica*) inoculated with the highly virulent race PXO99^A and a PXO99^A mutant, ME2. PXO99^A carries the TAL effector gene *pthXo1*, and strains mutated in this gene, such as ME2, are severely reduced in virulence (Yang and White 2004). One gene, *Os8N3*, was induced more than 100-fold in Nipponbare leaves inoculated with PXO99^A, as compared with those inoculated with the ME2 mutant, and was not induced when mock-inoculated with water. Plants silenced for *Os8N3* were resistant to PXO99^A. Additional analysis showed that *Os8N3* was allelic to *Xa13*. Examination of the isolines IR24 and IRBB13 showed that PXO99^A, which is highly virulent to IR24 but incompatible with IRBB13, could induce *Os8N3* in IR24 but not in IRBB13 or in other cultivars containing *xa13*. This induction and compatibility was dependent on the effector *pthXo1*, as the mutant ME2 could not induce *Os8N3* in IR24 and was only weakly virulent. Reintroduction of *pthXo1* restored both virulence and *Os8N3* upregulation to ME2, when inoculated on IR24. Further, introduction of the TAL effector *avrXa7* [ME2(*avrXa7*)], a major virulence factor for *X. oryzae* pv. *oryzae* PXO86 (Bai et al. 2000; Yang et al. 2000), restored full virulence of ME2 on IR24 and IRBB13 but did not result in the upregulation of *Os8N3*. *Xa13/Os8N3*, therefore, appears to be a gene-for-gene 'S' allele.

Yang and colleagues (2006) also demonstrated that the resistance affected by *Xa7* is 'dominant' to the susceptibility induced by *Xa13*. PXO99^A(*avrXa7*) could induce *Os8N3/Xa13* yet triggered a HR on plants carrying *Xa7*. Surprisingly, PXO99^A(*avrXa7*) was also virulent to IRBB13. Therefore, the resistance due to *xa13* can be overcome by the addition of a virulence factor rather than the loss of an avirulence allele, further supporting the conclusion that *xa13* is not a typical *R* gene (Yang et al. 2006).

Recessive resistance due to a mutation in an essential host protein?

Intriguingly, both *xa5* and *xa13*, though completely different in function, encode essential host proteins. TFIIA γ is an evolutionarily conserved protein necessary for efficient transcription across plant and animal kingdoms and for effective responses to oxidative stress (Aoyagi and Wassarman 2000; Kraemer et al. 2006; Orphanides et al. 1996). *Xa13* is essential for pollen development and, hence, reproduction in this self-pollinating species, as silencing of *Xa13^{RS}* results in abortive pollen (Chu et al. 2006). Thus, for both *xa5* and *xa13*, resistance is the result of a mutation affecting a vital host gene that has acquired a new function (resistance) but most likely still functions in its 'normal' capacity.

Fraser (1986, 1990) hypothesized that recessive viral *R* genes were due to a mutation in a host protein necessary for viral multiplication. Adapting Fraser's concept to plant-bacterial interactions yields the hypothesis that plant recessive *R* genes are due to a mutation in an essential host protein necessary for bacterial virulence. This hypothesis suggests that the probability of gaining a new function while retaining an original, essential function via a single mutation is a very rare event. This helps explain why there are fewer known recessively inherited genes. Even in viral systems, most recessive *R* genes appear to encode isoforms of just one or two proteins (discussed above).

Are recessive *R* genes durable?

R genes that have been successfully used for many years in a large population over a large area conducive for disease development are thought to be durable (Johnson 1984). Unfortunately, many *R* genes 'break down', in part due to mutation of effector genes (Leach et al. 2001). Understanding how to prevent this by identifying potentially durable *R* genes is key to preventing disease outbreaks on *R*-gene-containing cultivars. Might recessive *R* genes be a place to start? Since dominant *S* genes appear to be important for bacterial virulence, mutations in corresponding effector genes may carry a fitness cost (Leach et al. 2001). This may result in durable recessive *R* genes.

Unfortunately, little information exists as to the durability of *xa5* or *xa13* when used alone in rice cultivars. However, several studies have shown that when used in combination with other *R* genes, both *xa5* and *xa13* provide stronger and broader levels of resistance than when used alone (Huang et al. 1997; Shanti et al. 2001; Singh et al. 2001; Sridhar et al. 1999; Yoshimura et al. 1995). For example, though the most common *X. oryzae* pv. *oryzae* haplotype identified in Eastern India could overcome *Xa3*, *Xa4*, and *xa5* when deployed individually and several pathotypes were also virulent to *xa13* and *Xa21*, cultivars with gene combinations of *Xa4+xa5*, *xa5+Xa21*, or *Xa4+xa5+Xa21* were resistant to all isolates tested (Shanti et al. 2001). Complementary gene action among two or more of the *Xa4*, *xa5*, *Xa21*, or *xa13* genes has been observed in four additional studies (Adhikari et al. 1999; Huang et al. 1997; Sridhar et al. 1999; Yoshimura et al. 1995). In all four studies, cases in which *xa5* was used with *xa13*, *Xa21*, or *Xa4* resulted in increased resistance (in terms of number of isolates, degree of infection severity, or both) to *X. oryzae* pv. *oryzae* strains.

Perspectives.

Work on the molecular mechanisms of plant recessive gene-for-gene resistance to bacterial pathogens is just beginning. Though the identification of *xa5* and *xa13* has stimulated research in this area, much more data are needed. Biochemical, genetic, and cell biology studies will be important for understanding how *xa5* and *xa13* lead to resistance. The isolation of additional recessive *R* genes will reveal whether they are typically variants of 'S' alleles essential for a host function and will address whether most fall into one of the classic well-characterized *R* gene classes or encode new classes of proteins. The observation that an *S* gene can act in a gene-for-gene manner suggests that these alleles might be direct targets for bacterial manipulation and may yield clues to pathogen control. Eventually it may be possible to predict which genes might be susceptibility alleles. The identification of natural variants in wild germplasm or through manipulation in the lab could then lead to novel disease-prevention strategies. Alternatively, combinations of recessive *R* genes may provide durable resistance. Future work will hopefully center around the mechanisms by which these intriguing loci function in both resistance and susceptibility.

LITERATURE CITED

- Adhikari, T., and Shrestha, S. M. 1990. Distribution of bacterial blight (BB) in Nepal. *Int. Rice Res. Notes* 15:4, 22-23.
- Adhikari, T. B., Mew, T. W., and Teng, P. S. 1994a. Progress of bacterial blight on rice cultivars carrying different *Xa* genes for resistance in the field. *Plant Dis.* 78:73-77.
- Adhikari, T. B., Mew, T. W., and Teng, P. S. 1994b. Phenotypic diversity of *Xanthomonas oryzae* pv. *oryzae* in Nepal. *Plant Dis.* 78:68-72.
- Adhikari, T. B., Basnyat, R. C., and Mew, T. W. 1999a. Virulence of *Xanthomonas oryzae* pv. *oryzae* on rice lines containing single resistance genes and gene combinations. *Plant Dis.* 83:46-50.
- Akhtar, M. A., and Akram, M. 1987. Evaluation of national uniform rice yield trial 1985 against bacterial blight (BB) in Pakistan. *Int. Rice Res. Notes* 12:6, 12.
- Albar, L., Bangratz-Reyser, M., Hebrard, E., Ndjondjop, M. N., Jones, M., and Ghesquiere, A. 2006. Mutations in the eIF(iso)4G translation initiation factor confer high resistance of rice to *Rice yellow mottle virus*. *Plant J.* 47:417-26.
- Alfano, J. R., and Collmer, A. 2004. Type III secretion system effector proteins: Double agents in bacterial disease and plant defense. *Annu. Rev. Phytopathol.* 42:385-414.
- Aoyagi, N., and Wassarman, D. A. 2000. Genes encoding *Drosophila melanogaster* RNA polymerase II general transcription factors: A diversity of TFIIA and TFIID components contributes to gene-specific transcriptional regulation. *J. Cell Biol.* 150:F45-50.
- Ausubel, F. M. 2005. Are innate immune signaling pathways in plants and animals conserved? *Nature Immunol.* 6:973-979.
- Bai, J., Choi, S. H., Ponciano, G., Leung, H., and Leach, J. E. 2000. *Xanthomonas oryzae* pv. *oryzae* avirulence genes contribute differently and specifically to pathogen aggressiveness. *Mol. Plant-Microbe Interact.* 13:1322-1329.
- Belkhadir, Y., Subramaniam, R., and Dangl, J. L. 2004. Plant disease resistance protein signaling: NBS-LRR proteins and their partners. *Curr. Opin. Plant Biol.* 7:391-399.
- Blair, M. W., Garris, A. J., Iyer, A. S., Chapman, B., Kresovich, S., and McCouch, S. R. 2003. High resolution genetic mapping and candidate gene identification at the *xa5* locus for bacterial blight resistance in rice (*Oryza sativa* L.). *Theor. Appl. Genet.* 107:62-73.
- Bleichenbacher, M., Tan, S., Richmond, T. J. 2003. Novel interactions between the components of human and yeast TFIIA/TBP/DNA complexes. *J. Mol. Biol.* 332:783-93.
- Burke, C., Yu, X. B., Marchitelli, L., Davis, E. A., and Ackerman, S. 1990. Transcription factor IIA of wheat and human function similarly with plant and animal viral promoters. *Nucleic Acids Res.* 18:3611-3620.
- Buschges, R., Hollricher, K., Panstruga, R., Simons, G., Wolter, M., Frijters, A., van Daelen, R., van der Lee, T., Diergaarde, P., Groenendijk, J., Topsch, S., Vos, P., Salamini, F., and Schulze-Lefert, P. 1997. The barley *Mlo* gene: A novel control element of plant pathogen resistance. *Cell* 88:695-705.
- Chi, T., Lieberman, P., Ellwood, K., and Carey, M. 1995. A general mechanism for transcriptional synergy by eukaryotic activators. *Nature* 377:254-257.
- Chu, Z., Ouyang, Y., Zhang, J., Yang, H., and Wang, S. 2004. Genome-wide analysis of defense-responsive genes in bacterial blight resistance of rice mediated by the recessive *R* gene *xa13*. *Mol. Genet. Genomics* 271:111-120.
- Chu, Z., Yuan, M., Yao, J., Ge, X., Yuan, B., Xu, C., Li, X., Fu, B., Li, Z., Bennetzen, J. L., Zhang, Q., and Wang, S. 2006. Promoter mutations of an essential gene for pollen development result in disease resistance in rice. *Genes Dev.* 20:1250-1255.
- Deslandes, L., Olivier, J., Theulieres, F., Hirsch, J., Feng, D. X., Bittner-Eddy, P., Beynon, J., and Marco, Y. 2002. Resistance to *Ralstonia solanacearum* in *Arabidopsis thaliana* is conferred by the recessive *RRS1-R* gene, a member of a novel family of resistance genes. *Proc. Natl. Acad. Sci. U.S.A.* 99:2404-2409.
- Devadath, S. 1992. Bacterial blight of paddy. Pages 158-185 in: *Plant Diseases of International Importance: Diseases of Cereals and Pulses*. U. S. Singh, A. N. Mukhopadhyay, J. Kumar, and H. S. Chaube, eds. Prentice-Hall, Inc., Englewood Cliffs, NJ, U.S.A.
- Diaz-Pendon, J. A., Truniger, V., Nieto, C., Garcia-Mas, J., Bendahmane, A., and Aranda, M. A. 2004. Advances in understanding recessive resistance to plant viruses. *Mol. Plant Pathol.* 5:223-233.
- Eamchit, S., and Mew, T. W. 1981. Comparison of virulence of *Xanthomonas campestris* pv. *oryzae* in Thailand and the Philippines. *Plant Dis.* 66:556-559.
- Fluhr, R., and Kaplan-Levy, R. N. 2002. Plant disease resistance: Commonality and novelty in multicellular innate immunity. *Curr. Top. Microbiol. Immunol.* 270:23-46.
- Fraser, R. S. 1986. Genes for resistance to plant viruses. *CRC Crit. Rev. Plant Sci.* 3:257-294.
- Fraser, R. S. 1990. The genetics of resistance to plant viruses. *Annu. Rev. Phytopathol.* 28:179-200.
- Fujikawa, T., Ishihara, H., Leach, J. E., and Tsuyumu S. 2006. Suppression of defense response in plants by the *avrBs3/pthA* gene family of *Xanthomonas* spp. *Mol. Plant-Microbe Interact.* 19:342-349.
- Geiger, J. H., Hahn, S., Lee, S., and Sigler, P. B. 1996. Crystal structure of the yeast TFIIA/TBP/DNA complex. *Science* 272:830-836.
- Gu, K., Yang, B., Tian, D., Wu, L., Wang, D., Sreekala, C., Yang, F., Chu, Z., Wang, G. L., White, F. F., and Yin, Z. 2005. *R* gene expression induced by a type-III effector triggers disease resistance in rice. *Nature* 435:1122-1125.
- Gurlebeck, D., Thieme, F., and Bonas, U. 2006. Type III effector proteins

- from the plant pathogen *Xanthomonas* and their role in the interaction with the host plant. *J. Plant Physiol.* 163:233-255.
- Hampsey, M. 1998. Molecular genetics of the RNA polymerase II general transcriptional machinery. *Microbiol. Mol. Biol. Rev.* 62:465-503.
- Huang, N., Angeles, E. R., Domingo, J., Magpantay, G., Singh, S., Zhang, G., Kumaravel, N., Bennett, J., and Khush, G. S. 1997. Pyramiding of bacterial blight resistance genes in rice: Marker-assisted selection using RFLP and PCR. *Theor. Appl. Genet.* 95:313-320.
- Iyer, A. S., and McCouch, S. R. 2004. The rice bacterial blight resistance gene *xa5* encodes a novel form of disease resistance. *Mol. Plant-Microbe Interact.* 17:1348-1354.
- Jiang, G. H., Xia, Z. H., Zhou, Y. L., Wan, J., Li, D. Y., Chen, R. S., Zhai, W. X., Zhu, L. H. 2006. Testifying the rice bacterial blight resistance gene *xa5* by genetic complementation and further analyzing *xa5* (*Xa5*) in comparison with its homolog *TFIIAgamma1*. *Mol. Genet. Genomics.* 275:354-66.
- Johnson, R. 1984. A critical analysis of durable resistance. *Annu. Rev. Phytopathol.* 22:309-330.
- Kang, B. C., Yeam, I., Frantz, J. D., Murphy, J. F., and Jahn, M. M. 2005a. The *pvr1* locus in *Capsicum* encodes a translation initiation factor eIF4E that interacts with Tobacco etch virus VPg. *Plant J.* 42:392-405.
- Kang, B. C., Yeam, I., and Jahn, M. M. 2005b. Genetics of plant virus resistance. *Annu. Rev. Phytopathol.* 43:581-621.
- Kang, J. J., Auble, D. T., Ranish, J. A., and Hahn, S. 1995. Analysis of the yeast transcription factor TFIIA: Distinct functional regions and a polymerase II-specific role in basal and activated transcription. *Mol. Cell Biol.* 15:1234-1243.
- Kang, M. S., and Singh, I. 1987. Some pathological and physiological diseases of rice in the Punjab. *Int. Rice Research Notes* 12:6, 24.
- Kashanchi, F., Khleif, S. N., Duvall, J. F., Sadaie, M. R., Radonovich, M. F., Cho, M., Martin, M. A., Chen, S. Y., Weinmann, R., Brady, J. N. 1996. Interaction of human immunodeficiency virus type 1 Tat with a unique site of TFIIID inhibits negative cofactor Dr1 and stabilizes the TFIIID-TFIIA complex. *J. Virol.* 70:5503-10.
- Khush, G. S., and Angeles, E. R. 1999. A new gene for resistance to race 6 of bacterial blight in rice, *Oryza sativa*. *Rice Genetics Newsl.* 16:92-93.
- Kobayashi, N., Boyer, T. G., and Berk, A. J. 1995. A class of activation domains interacts directly with TFIIA and stimulates TFIIA-TFIIID-promoter complex assembly. *Mol. Cell Biol.* 15:6465-6473.
- Kobayashi, N., Horn, P. J., Sullivan, S. M., Triezenberg, S. J., Boyer, T. G., and Berk, A. J. 1998. DA-complex assembly activity required for VP16C transcriptional activation. *Mol. Cell Biol.* 18:4023-4031.
- Kraemer, S. M., Ranallo, R. T., Ogg, R. C., Stargell, L. A. 2001. TFIIA interacts with TFIIID via association with TATA-binding protein and TAF40. *Mol. Cell Biol.* 21:1737-1746.
- Kraemer, S. M., Goldstrohm, D. A., Berger, A., Hankey, S., Rovinsky, S. A., Scott, Moye-Rowley, W., Stargell, L. A. 2006. TFIIA plays a role in the response to oxidative stress. *Eukaryot. Cell* 5, :1081-90.
- Kumar, R., Eastwood, A. L., Brown, M. L., and Laurie, G. W. 2002. Human genome search in celiac disease: Mutated gliadin T-cell-like epitope in two human proteins promotes T-cell activation. *J. Mol. Bio.* 319:593-602.
- Leach, J. E., Vera Cruz, C. M., Bai J., and Leung, H. 2001. Pathogen fitness penalty as a predictor of durability of disease resistance genes. *Annu. Rev. Phytopathol.* 39:187-224.
- Lee, B. M., Park, Y. J., Park, D. S., Kang, H. W., Kim, J. G., Song, E. S., Park, I. C., Yoon, U. H., Hahn, J. H., Koo, B. S., Lee, G. B., Kim, H., Park, H. S., Yoon, K. O., Kim, J. H., Jung, C. H., Koh, N. H., Seo, J. S., and Go, S. J. 2005. The genome sequence of *Xanthomonas oryzae* pv *oryzae* KACC10331, the bacterial blight pathogen of rice. *Nucleic Acids Res.* 33:577-586.
- Lee, K. S., Rasabandith, S., Angeles, E. R., and Khush, G. S. 2003. Inheritance of resistance to bacterial blight in 21 cultivars of rice. *Phytopathology* 93:147-152.
- Leonard, S., Chisholm, J., Laliberte, J. F., Sanfacon, H. 2002. Interaction in vitro between the proteinase of Tomato ringspot virus (genus *Nepovirus*) and the eukaryotic translation initiation factor iso 4E from *Arabidopsis thaliana*. *J. Gen. Virol.* 83:2085-2089.
- Lieberman, P. M., and Berk, A. J. 1994. A mechanism for TAFs in transcriptional activation: Activation domain enhancement of TFIIID-TFIIA--promoter DNA complex formation. *Genes Dev.* 8:995-1006.
- Liu, Q., Gabriel, S. E., Roinick, K. L., Ward, R. D., and Arndt, K. M. 1999. Analysis of TFIIA function in vivo: Evidence for a role in TATA-binding protein recruitment and gene-specific activation. *Mol. Cell Biol.* 19:8673-8685.
- Ma, D., Olave, I., Merino, A., and Reinberg, D. 1996. Separation of the transcriptional coactivator and antirepression functions of transcription factor IIA. *Proc. Natl. Acad. Sci. U.S.A.* 93:6583-6588.
- Marois, E., Van den Ackerveken, G., and Bonas, U. 2002. The *Xanthomonas* type III effector protein AvrBs3 modulates plant gene expression and induces cell hypertrophy in the susceptible host. *Mol. Plant-Microbe Interact.* 15:637-646.
- Martin, G. B., Bogdanove, A. J., and Sessa, G. 2003. Understanding the functions of plant disease resistance proteins. *Annu. Rev. Plant Biol.* 54:23-61.
- McHale, L., Tan, X., Koehl, P., and Michelmore, R. W. 2006. Plant NBS-LRR proteins: Adaptable guards. *Genome Biol.* 7:212.
- Mew, T. W. 1987. Current status and future prospects of research on bacterial blight of rice. *Annu. Rev. Phytopathol.* 25:359-382.
- Mew, T. W. 1993. *Xanthomonas oryzae* pathovars on rice: Cause of bacterial blight and bacterial leaf streak. Pages in 30-39 in: *Xanthomonas*. J. G. Swings and E. L. Civerolo, eds. Chapman and Hall, London.
- Mew T. W., and Majid, A. 1977 Bacterial blight of rice in Pakistan. *IRRN* 2:1, 5.
- Mizukami T., and Wakimoto S. 1969. Epidemiology and control of bacterial leaf blight of rice. *Annu. Rev. Phytopathol.* 7:51-72.
- Mew T. W., Vera Cruz C. M., and Reyes R. C. 1981. Characterization of resistance in rice to bacterial blight. *Ann. Phytopath. Soc. Japan* 47:58-67.
- Mew, T. W., Vera Cruz, C. M., and Medalla, E. S. 1992. Changes in race frequency of *Xanthomonas oryzae* pv. *oryzae* in response to rice cultivars planted in the Philippines. *Plant Dis.* 76:1029-1032.
- Mudgett, M. B. 2005. New insights to the function of phytopathogenic bacterial type III effectors in plants. *Annu. Rev. Plant. Biol.* 56:509-531.
- Nakai, H., Nakamura, S., Kuwahara, S., and Saito, M. 1988. Genetic studies of an induced rice mutant resistant to multiple races of bacterial leaf blight. *Rice Genetic Newsl.* 5:101.
- Nakai, H., Nakamura, K., Kuwahara, S., and Saito, M. 1990. A new gene developed through mutagenesis for resistance of rice to bacterial blight *Xanthomonas campestris* pv. *oryzae*. *J. Agricul. Sci.* 114:219-224.
- Nino-Liu, D. O., Ronald, R., and Bogdanove, A. 2006. *Xanthomonas oryzae* pathovars: Model pathogens of a model crop. *Mol. Plant Path.* 7:303-324.
- Nurnberger, T., and Brunner, F. 2002. Innate immunity in plants and animals: Emerging parallels between the recognition of general elicitors and pathogen-associated molecular patterns. *Curr. Opin. Plant Biol.* 5:318-324.
- Nurnberger, T., Brunner, F., Kemmerling, B., and Piater, L. 2004. Innate immunity in plants and animals: Striking similarities and obvious differences. *Immunological Rev.* 198:249-266.
- Ochiai, H., Horino, O., Miyajima, K., and Kaku, H. 2000. Genetic diversity of *Xanthomonas oryzae* pv. *oryzae* strains from Sri Lanka. *Phytopathology* 90:415-421.
- Ogawa, T. 1996. Monitoring race distribution and identification of genes for resistance to bacterial leaf blight. Pages 456-459 in: *Rice Genetics III, Proceedings of the Third International Rice Genetics Symposium*. G. S. Khush, ed. International Rice Research Institute, Manila, Philippines.
- Ogawa, T., Lin, L., Tabien, R. E., and Khush, G. S. 1987. A new recessive gene for resistance to bacterial blight of rice. *Rice Genetic Newsl.* 4:98-100.
- Ogawa, T., Yamamoto, T., Khush, G. S., Mew, T. W., and Kaku, H. 1988. Near-isogenic lines as international differentials for resistance to bacterial blight of rice. *Rice Genetic Newsl.* 5:106-109.
- Orphanides, G., Lagrange, T., and Reinberg, D. 1996. The general transcription factors of RNA polymerase II. *Genes Dev.* 10:2657-2683.
- Ozer, J., Moore P. A., Bolden A. H., Lee A., Rosen C. A., and Lieberman P. M. 1994. Molecular cloning of the small (gamma) subunit of human TFIIA reveals functions critical for activated transcription. *Genes Dev.* 8:2324-2335.
- Ozer, J., Bolden, A. H., and Lieberman, P. M. 1996. Transcription factor IIA mutations show activator-specific defects and reveal a function distinct from stimulation of TBP-DNA binding. *J. Biol. Chem.* 271, 11182-11190.
- Ozer, J., Mitsouras, K., Zerby, D., Carey, M., and Lieberman, P. M. 1998a. Transcription factor IIA derepresses TATA-binding protein (TBP)-associated factor inhibition of TBP-DNA binding. *J. Biol. Chem.* 273:14293-14300.
- Ozer, J., Lezina, L. E., Ewing, J., Audi, S., and Lieberman, P. M. 1998b. Association of transcription factor IIA with TATA binding protein is required for transcriptional activation of a subset of promoters and cell cycle progression in *Saccharomyces cerevisiae*. *Mol. Cell. Biol.* 18:2559-2570.
- Petpisit, V., Khush, G. S., and Kauffman, H. E. 1977. Inheritance of resistance to bacterial blight in rice. *Crop Sci.* 17:551-554.
- Raina, G. L., Sidhu, G. S., and Saini, P. K. 1981. Rice bacterial blight status in the Punjab, India. *International Rice Research Notes* 6:5, 12.
- Robaglia, C., and Caranta, C. 2006. Translation initiation factors: A weak link in plant RNA virus infection. *Trends Plant Sci.* 11:40-45.

- Robinson, M. M., Yatherajam, G., Ranallo, R. T., Bric, A., Paule, M. R., Stargell, L. A. 2005. Mapping and functional characterization of the TAF11 interaction with TFIIA. *Mol. Cell Biol.* 25:945-57.
- Roeder, R. G. 1996. Role of general and gene-specific cofactors in the regulation of eukaryotic transcription. *Trends Biochem. Sci.* 21:327-335.
- Shanti, M. L., George, M. L. C., Vera Cruz C. M., Bernardo M. A., Nelson R. J., and Leung H. 2001. Identification of resistance genes effective against rice bacterial blight pathogen in Eastern India. *Plant Dis.* 85:506-512.
- Shen, Y., and Ronald, P. 2002. Molecular determinants of disease and resistance in interactions of *Xanthomonas oryzae* pv. *oryzae* and rice. *Microbes Infect.* 4:1361-1367.
- Sidhu, G. S., Khush, G. S., and Mew, T. W. 1978. Genetic analysis of bacterial blight resistance in seventy-four cultivars of rice, *Oryza sativa* L. *Theor. Appl. Genet.* 53:105-111.
- Singh, K., Vikal, Y., Singh, S., Leung, H., Dhaliwal, H. S., and Khush, G. S. 2002. Mapping of bacterial blight resistance gene *xa8* using microsatellite markers. *Rice Genet. Newsl.* 19:94-96.
- Singh S., Sidhu J. S., Huang N., Vikal Y., Li Z., Brar D. S., Dhaliwal H. S., and Khush G. S. 2001. Pyramiding three bacterial blight resistance genes (*xa5*, *xa13* and *xa21*) using marker-assisted selection into *indica* rice cultivar PR106. *Theor. Appl. Genet.* 102:1011-1015.
- Sirisantana, W., Nilpanit, N., Phawichit, S., Kiatsuranont, P., and Disthaporn, S. 1984. Yield loss to bacterial blight (BB) in central Thailand. *International Rice Res. Notes* 9:6, 10, 11.
- Song, W., Wang, G., Chen, L., Kim, H., Pi, L., Holsten, T., Gardner, J., Wang, B., Zhai, W., Zhu, L., Fauquet, C., and Ronald P. 1995. A receptor kinase-like protein encoded by the rice disease resistance gene, *Xa21*. *Science*:1804-1806.
- Sridhar, R. 2002. Use of molecular tools for understanding bacterial blight pathogen populations of rice and usefulness of disease resistance genes. *Indian Phytopathol.* 55:417-429.
- Sridhar, R., Reddy, J. N., Singh, U. D., and Agrawal, P. K. 1999. Usefulness of combinations of bacterial blight resistance genes at Cuttack, Orissa, India. *Rice Genet. Newsl.* 16:24-25.
- Stargell, L. A., and Struhl K. 1995. The TBP-TFIIA interaction in the response to acidic activators *in vivo*. *Science* 269:75-78.
- Stargell, L. A., Moqtaderi, Z., Dorris, D. R., Ogg, R. C., and Struhl K. 2000. TFIIA has activator-dependent and core promoter functions *in vivo*. *J. Biol. Chem.* 275:12374-12380.
- Staskawicz, B. J., Mudgett, M. B., Dangl, J. L., and Galan, J. E. 2001. Common and contrasting themes of plant and animal diseases. *Science* 292:2285-2289.
- Sugio, A., Yang, B., and White, F. F. 2005. Characterization of the *hrpF* pathogenicity peninsula of *Xanthomonas oryzae* pv. *oryzae*. *Mol Plant-Microbe Interact* 18:546-554.
- Sun, X., Cao, Y., Yang, Z., Xu, C., Li, X., Wang, S., and Zhang, Q. 2004. *Xa26*, a gene conferring resistance to *Xanthomonas oryzae* pv. *oryzae* in rice, encodes an LRR receptor kinase-like protein. *Plant J.* 37:517-527.
- Swarup, S., De Feyter, R., Brlansky, R. H., and Gabriel, D. W. 1991. A pathogenicity locus from *Xanthomonas citri* enables strains from several pathovars of *Xanthomonas campestris* to elicit canker-like lesions on citrus. *Phytopathology* 81:802-809.
- Szurek, B., Marois, E., Bonas, U., and Van den Ackerveken, G. 2001. Eukaryotic features of the *Xanthomonas* type III effector AvrBs3: Protein domains involved in transcriptional activation and the interaction with nuclear import receptors from pepper. *Plant J.* 26:523-534.
- Tan, S., Hunziker, Y., Sargent, D. F., and Richmond, T. J. 1996. Crystal structure of a yeast TFIIA/TBP/DNA complex. *Nature* 381:127-134.
- Taura, S., Ogawa, T., Yoshimura, A., Ikeda, R., and Omura, T. 1991. Identification of a recessive resistance gene in induced mutant line XM5 of rice to rice bacterial blight. *Japan J. Breed.* 43:427-432.
- Taura, S., Ogawa, T., Yoshimura, A., Ikeda, R., and Iwata, N. 1992. Identification of a recessive resistance gene to rice bacterial blight of mutant line XM6, *Oryza sativa* L. *Japan J. Breed.* 42:7-13.
- Upadhyay, R. K. 1985. Rice disease status in India. *International Rice Res. Notes* 10:5, 17-18.
- Upadhyaya, A. B., Lee, S. H., and DeJong, J. 1999. Identification of a general transcription factor TFIIA alpha/beta homolog selectively expressed in testis. *J. Biol. Chem.* 274:18040-18048.
- van Kim, P., Thi Nghiem, N., Len, L., and Ngoc Kinh, D. 1981. Survey of rice diseases in the Vietnamese Mekong Delta from 1978 to 1980. *IRRN* 6:5, 14-15.
- Wang, W., Gralla, J. D., and Carey, M. 1992. The acidic activator GAL4-AH can stimulate polymerase II transcription by promoting assembly of a closed complex requiring TFIID and TFIIA. *Genes Dev.* 6:1716-1727.
- Warfield, L., Ranish, J. A., and Hahn, S. 2004. Positive and negative functions of the SAGA complex mediated through interaction of Spt8 with TBP and the N-terminal domain of TFIIA. *Genes Dev* 18: 1022-34.
- Xie, J., Collart, M., Lemaire, M., Stelzer, G., and Meisterernst, M. 2000. A single point mutation in TFIIA suppresses NC2 requirement *in vivo*. *EMBO (Eur. Mol. Biol. Organ.) J.* 19:672-682.
- Yang, B., and White, F. F. 2004. Diverse members of the AvrBs3/PthA family of type III effectors are major virulence determinants in bacterial blight disease of rice. *Mol. Plant-Microbe Interact.* 17:1192-1200.
- Yang, B., Zhu, W., Johnson, L. B., and White, F. F. 2000. The virulence factor AvrXa7 of *Xanthomonas oryzae* pv. *oryzae* is a type III secretion pathway-dependent nuclear-localized double-stranded DNA-binding protein. *Proc. Natl. Acad. Sci. U.S.A.* 97:9807-9812.
- Yang, B., Sugio, A., and White, F. F. 2006. *Os8N3* is a host disease-susceptibility gene for bacterial blight of rice. *Proc. Natl. Acad. Sci. U.S.A.* 103:10503-10508.
- Yoshii, M., Nishikiori, M., Tomita, K., Yoshioka, N., Kozuka, R., Naito, S., and Ishikawa, M. 2004. The *Arabidopsis* Cucumovirus multiplication 1 and 2 loci encode translation initiation factors 4E and 4G. *J. Virol.* 78:6102-6111.
- Yoshimura, S., Yoshimura, A., Iwata, N., McCouch, S. R., Abenes, M. L., Baraoidan, M. R., Mew, T. W., and Nelson, R. J. 1995. Tagging and combining bacterial-blight resistance genes in rice using RAPD and RFLP markers. *Mol. Breed.* 1:375-387.
- Yoshimura, S., Yamanouchi, U., Katayose, Y., Toki, S., Wang, Z. X., Kono, I., Kurata N., Yano, M., Iwata, N., and Sasaki T.1998. Expression of *Xa1*, a bacterial blight-resistance gene in rice, is induced by bacterial inoculation. *Proc. Natl. Acad. Sci. U.S.A.* 95:1663-1668.
- Zeidler, M. P., Yokomori, K., Tjian, R., and Mlodzik, M. 1996. *Drosophila* TFIIA-S is up-regulated and required during Ras-mediated photoreceptor determination. *Genes Dev.* 10:50-59.
- Zhu, W., Yang, B., Chittoor, J. M., Johnson, L. B., and White, F. F. 1998. AvrXa10 contains an acidic transcriptional activation domain in the functionally conserved C terminus. *Mol. Plant-Microbe Interact.* 11:824-832.
- Zhu, W., Yang, B., Wills, N., Johnson, L. B., and White, F. F. 1999. The C terminus of AvrXa10 can be replaced by the transcriptional activation domain of VP16 from the Herpes simplex virus. *Plant Cell* 11:1665-1674.
- Zipfel, C., and Felix, G. 2005. Plants and animals: A different taste for microbes? *Curr. Opin. Plant Biol.* 8:353-360.