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Disease Resistance and Susceptibility Genes to Bacterial Blight of Rice

Tariq Mahmood and Frank F. White

Abstract

Rice (*Oryza sativa* L.) is a valuable resource for understanding the complex processes controlling yield and value-added traits. Bacterial blight (BB) is a vascular disease of rice, caused by strains of *Xanthomonas oryzae* pv. *oryzae* (Xoo) and provides insight, both practical and basic, into the concepts of susceptibility and resistance. Basic knowledge has been empirically and, more recently, intentionally exploited for broad and durable resistance to the disease. Bacterial blight involves representatives of most classes of resistance genes (*R* genes) and pathways for basal plant immunity. The study of BB also revealed novelties not observed in other models, possibly due to the long history of rice cultivation and the constant disease pressure. Conspicuous are the recessive *R* genes that target the notorious type III Transcription Activator-like effectors (TALs) of Xoo. Results indicate that pathogen and host are currently in a battle over a small patch of ground involving TALs function. At the same time, analyses of rice disease physiology are adding to a growing body of knowledge for plant disease processes and to how these processes are intertwined with disease susceptibility. The basic processes of BB present rich targets for the rapid advances in genome editing.

Keywords: *Xanthomonas oryzae* pv. *oryzae*, rice, recessive resistance, TAL effector, genome editing, CRISPR

1. Introduction

World population is expected to rise beyond 9 billion by 2050 [1]. Rice (*Oryza sativa*) is a staple food crop world-wide, providing about one fifth of the calories consumed by humans [2]. In particular, rice accounts for 35–75% of the calories consumed by more than 3 billion in Asian countries alone and planted on approximately 154 million hectares land annually [3]. Crop protection and food security go hand in hand, and breeding for resistance against crop diseases remains the essential ingredient for food security. Due to the labor-intensive nature of breeding, integrated disease control is often reduced to mere chemical control, leaving the very purpose of this environment-friendly approach in limbo. Advances in molecular tools in crop breeding, however, makes breeding an increasing sustainable effort in staying ahead of pathogen adaptation [4]. Bacterial blight (BB) of rice is a widespread vascular disease caused by *Xanthomonas oryzae* pv. *oryzae*

(*Xoo*). Epidemics can severely reduce grain yield due to collapse of the entire crop [5]. BB was first characterized in the late nineteenth century [6]. Introduction of resistance (*R*) genes into rice cultivars is considered as the best option for *Xoo* management. A total of 42 *R* genes have been identified in rice against *Xoo*, and the number continues to grow [7–9]. Due to co-evolution and selection pressure between *Xoo* and rice, these *R* genes are selective in their efficiency against specific *Xoo* strains or races, which are sets of strains that share incompatibility on defined sets of *R* genes [10].

2. Post genomic era and rice grain protection

Advancements in genomics, referring here to DNA and RNA analyses, is as beneficial to crop protection as is to other discipline of biology. Rice MetaSysB, an open source which provides detailed information about BB-responsive genes, is based on the global expression analysis. The database provided 7475 unique genes and 5375 simple sequence repeats, which were responsive to *Xoo* in rice [11]. Such information is based on the compatible and incompatible rice-*Xoo* interactions. In another example, 454 and 498 differentially expressed genes were reported as exemplified by the incompatible and compatible rice-*Xoo* interactions, respectively, using cDNA microarray [12]. Genomics also provides functional information of genes up- and downstream of candidate resistance genes in the defense signal pathway, as is done in near-isogenic rice lines introgressed with *Xa39*, an as yet uncharacterized BB resistance gene [13].

Multiple rice and *Xoo* genomes have been sequenced, either in draft or complete form [14–23], paving the way to identify functional connections between host and pathogen genes. The functional validation of the candidate genes is helping develop new rice varieties by introduction of the gene of interest through traditional breeding, marker assisted breeding, or genetic engineering approaches [3]. BB disease resistance is overcome by the emergence of more virulent strains of *Xoo*. Whole genome sequencing of 100 *Xoo* strains from India revealed that these strains were distinct from African and US *Xoo* strains [24]. Based on the reaction towards ten major resistance genes of rice, 46 out of the 100 strains were grouped into 11 pathotypes [24].

3. The genetic context of rice-*Xoo* interaction

Many BB-resistance genes in modern rice germplasm were selected long before the concepts of modern plant breeding were established, and a rich assortment of major dominant and recessive *R* genes has been identified by genetic and molecular studies (Table 1).

Perhaps the best known of these genes, *Xa21* represents the receptor kinase (RLK) class of *R* genes. *Xa21* was originally introgressed into rice from the related species *O. longistaminata* and confers resistance to a broad range of *Xoo* strains [25]. *Xa26*, another cloned member of RLK gene family, also confers broad resistance with a somewhat different strain profile [26]. The cognate elicitor for *Xa21* has been reported [27]. However, for *Xa26* has not been identified.

RLKs play a central role in disease immunity pathways in plants, largely via the characterization of the bacterial flagellin receptor FLS2 and the related receptor EFR in *Arabidopsis* [28, 29]. A typical RLK consists of an extracellular receptor domain comprising of leucine-rich repeats (LRRs), a transmembrane domain, and an intracellular kinase domain [30]. As a class, RLKs have great potential for

Gene	Class	Comments	Cognate elicitor/effector	Ref
<i>Xa21</i>	RLK ¹	extracellular, membrane and intracellular domains; kinase; broad resistance	RaxX	[25, 27]
<i>Xa26</i>	RLK	similar to <i>Xa21</i> ; same locus as <i>Xa3</i> ; broad resistance	Unknown	[26]
<i>Xa1</i> , <i>Xo1</i>	NBS-LRR ²	cytoplasm; narrow resistance	Multiple TALEs	[31–33]
<i>Xa4</i>	WAK ³	narrow	unknown	[40]
<i>Xa27</i> , <i>Xa23</i> , <i>Xa10</i>	TAL effector inducible	membrane and cell wall; novel protein; broad resistance	AvrXa27, AvrXa23, AvrXa10	[37–39]
<i>xa5</i>	Missense mutant of <i>TFIIAγ5</i> ; small subunit of TFIIA transcription factor complex	nuclear; broad resistance	TALe interference	[51, 53, 54]
<i>xa13</i>	promoter mutants of <i>OsSWEET11</i> ; nodulin 3 family	membrane; unresponsive to PthXo1	PthXo1	[42, 47]
<i>xa25</i> , <i>OsSWEET13^{Kit}</i>	promoter mutant of <i>OsSWEET13</i> , nodulin 3 family	TATA box polymorphisms; unresponsive to PthXo2	PthXo2	[44, 52]

¹RLK, receptor linked kinase.
²NBS-LRR, nucleotide binding site, leucine-rich repeat.
³WAK, wall-associated kinase.

Table 1.
Cloned R genes to bacterial blight of rice.

enhancing resistance to BB in rice and in other disease complexes of crop plants *Xa21*, *Xa26*, and other RLKs represent genetic components of the pathogen-associated molecular patterns (PAMPs)-triggered immunity (PTI) surveillance pathway in rice. Improvements in the rationale design of RLK receptor specificities, and screening for novel genes in germplasm or wild relatives could lead to general application for broad and durable resistance.

The nucleotide binding site-LRR (NBS-LRR) is another large class of *R* gene, represented in rice toward *Xoo* by *Xa1* and *Xo1* [31–33]. *XA1* and *XO1* recognize multiple TALE, and *Xoo* strains have adapted TALEs, the so-called iTALEs, that are truncated and inhibit the function of *XA1* and *XO1* [32, 34].

Specific TALE-dependent *R* genes governing dominant resistance in rice against *Xoo* are known as executor (*E*) genes. *E* genes are distinct from classical *R* genes, whose transcriptional activation by TALEs of *Xoo* trigger immunity, leading to dominant resistance [35]. *Xa27* represents the *E* genes class of dominant *R* genes and confers broad resistance to BB in rice [36]. Although not expressed in susceptible host, *Xa27* is expressed only upon inoculation with *Xoo* strains harboring the TALE gene *avrXa27* [37]. The protein is localized to apoplastic space, cell membrane and cell wall, and when expressed under a pathogen-nonspecific inducible rice *OsPR1* promoter, conferred constitutive resistance to both compatible and incompatible

strains alike [37]. The rice *R* genes *Xa10* and *Xa23* have similar requirements for the transcription activation domain and nuclear localization sequence (NLS) motifs of the corresponding TALs for their induction [38, 39].

Xa4 is the latest and, again, an unusual *R* gene of rice to be characterized. The protein is a wall-associated kinase (WAK) and provides attributes other than enhanced resistance. Rice plants with *Xa4* are shorter and stiffer in comparison to plants lacking the gene [40]. *Xa4* is race-specific, meaning many strains of *Xoo* are compatible on plants with *Xa4*. How *Xa4* functions in resistance is unknown at present.

3.1 SWEET genes and recessive resistance

A class of major TALE-dependent susceptibility (*S*) genes for BB in rice encodes sugar transporters, thereby named as SWEET gene family [41]. Specific TALs, referred to as major TALs, transcriptionally activate the corresponding SWEET genes in rice during infection to promote the disease in a gene-for-gene susceptibility manner [42]. Although at least five SWEET genes of the clade III members can function as an *S* gene in BB, only three members are known to be targeted by extant strains of *Xoo* [42–47]. A member of the SWEET gene family, *OsSWEET14*, is induced by multiple distinct TALs, which include AvrXa7, PthXo3, Tal5 and TalC and are present in strains of different geographic origins and genetic lineages [43, 45, 46]. Similarly, PthXo2 drives *OsSWEET13* expression in the susceptible rice variety IR24 [44], and *OsSWEET11* is induced by the cognate PthXo1 [42]. The typical TALE possesses a central repetitive domain, a nuclear localization signal domain, and a transcription activation domain. The repetitive domain is responsible for binding of the TALE to a sequence motif called the effector binding element (EBE), which is commonly located in the promoter region of the respective *S* gene.

Mutated *S* gene alleles are proposed to be potentially more durable than dominant *R* genes [48, 49]. Identifying the promoter variant alleles of major *S* genes has been proposed in breeding for BB resistance [42, 47, 50–53]. Recessive resistance is due to the cognate TALE cannot bind to the promoter variants of the *S* gene. The gene *xa13*, for example, is a recessive resistance insertion allele of 14.8 kb DNA fragment in the promoter of *OsSWEET11* [42, 47]. *OsSWEET11* encodes a protein related to *MtN3* encoding nodulin 3 (N3) protein of *Medicago truncatula*. The gene was originally named *Os8N3* due to its location on rice chromosome 8 and the similarity to *MtN3* [42]. The critical difference between resistant (*xa13/xa13*) and susceptible plants is the elevated expression of *OsSWEET11* during infection in otherwise susceptible plant genotypes [42]. RNAi-mediated silencing of *OsSWEET11* plants was similarly resistant to *Xoo* strains that are solely dependent on PthXo1 for SWEET induction. Silenced plants, but not promoter variants, showed low pollen viability, corroborating the fact that *Xoo* hijacked otherwise developmentally important genes in rice for pathogenicity [42, 47]. Similarly, the TALE PthXo2 cannot bind to the EBE of *xa25*, a recessive allele of *OsSWEET13*, or the EBE region of *OsSWEET13* in japonica rice cultivars, owing to single nucleotide polymorphisms in the respective EBEs [51, 52].

The gene *xa13* is a naturally occurring allele, actually a series of alleles that protects the plant from a genetic disease vulnerability in the plant developmental pathways [42, 47]. However, *xa13* is not a broad resistance provided in comparison to *Xa21*, *Xa27* and *xa5*), and many strains from China, Philippines, Japan and Korea are compatible on *xa13* lines [51]. Compatibility is derived by acquisition of major TALs that target alternative SWEET promoters [43]. As yet, not major TALE has been identified that replaces PthXo1 for *OsSWEET11* expression.

The gene *xa5* also affects TALE-dependent function but does not act at a specific SWEET gene. The recessive allele encodes a variant of the γ or small subunit of the transcription factor TFIIA [54, 55], which confers broad resistance. The gene differs from the susceptible allele by a single codon substitution of valine at position 39 to glutamic acid. TFIIA, consists of α , β , and γ subunits, and is involved in stabilizing the binding of the TATA box binding protein complex (TFIID) to the TATA box of gene promoters. The TFIIA components are highly conserved across the eukaryotes. Rice has two loci for *TFIIA γ* —one gene is on chromosome 5 (*TFIIA γ 5*, *xa5*) and another on chromosome 1 (*TFIIA γ 1*) [54]. The proteins are closely related but not identical. *xa5* provides broad BB resistance and functions in inhibiting TALE function [51, 56]. However, *xa5* is not effective against strains with the TALE PthXo1 [51].

Perhaps not all SWEET S genes are known or are not always induced in disease by *Xoo*. The Indian strain IX-80 was virulent but did not induce any known SWEET gene [57], suggesting an adaptation by the *Xoo* to relieve dependency on SWEET gene family. On the other hand, IX-80 remains TALE-dependent as the strain was not compatible on IR53 (*xa13/xa13*, *xa5/xa5*), a gene combination that blocks the *xa5*-compatible PthXo1 and all other major TALEs at *OsSWEET14* and *OsSWEET14* [51].

4. Implication of interactions between TALEs and the corresponding host genes

Due to the large reservoir of TALEs in each strain of *Xoo* and the diverse roles of TALEs in pathogenesis, the BB of rice represents an excellent plant/pathogen system for studying the biology of TALEs. The apparent reason for the broad activity of *Xa27* and *Xa23* is the presence of the cognate TALEs *avrXa27* and *avrXa23* in a large number of strains from southeast Asia, including Korea, China, Japan and the Philippines [37, 39]. On the other hand, the loss of *avrXa27*, *avrXa23*, or *avrXa10*, for that matter, does not appear to have an apparent fitness cost to the pathogen, and populations of *Xoo* may lose *avrXa27* if *Xa27* is widely deployed [37–39]. *AvrXa7* is an important virulence factor for some strains of *Xoo*, and strains with *AvrXa7* are incompatible on rice lines harboring the *Xa7*. In this case, loss of *avrXa7*, which is a major TALE for *OsSWEET14*, may result in strains that are weakly virulent or, essentially, nonpathogenic, if no other SWEET inducing TALEs are present [43, 58]. A variety of other TALE genes are present in *Xoo* populations that can restore full virulence to strains missing *avrXa7* [59]. Evasion of *Xa7*-mediated resistance is possible by loss of the gene, rearrangement of the central repeats or recombination among different TALE genes [60, 61]. However, despite rapid adaptation of bacteria by genetic changes and gene flow, field studies in the Philippines indicated that deployment of *Xa7* was durable in test plots for more than 10 years [62]. Therefore, strains may have other limitations due to geographical location or rice genotype. Nevertheless, pyramiding broadly effective *R* genes with cognate TALEs that are wide-spread in the pathogen populations should provide a degree of broad and durable resistance.

In the case of *xa13*, induction of the dominant allele *SWEET11* is mediated by the TALE PthXo1 [42]. However, strains of *Xoo* that solely rely on PthXo1 cannot induce *xa13* allele, and rice homozygous for *xa13* is symptomless. *xa13*-dependent recessive resistance is phenotypically and qualitatively different from resistance provided by the dominant *R* gene *Xa7* [42, 63]. Quantitatively, however, resistance mediated by *xa13* and *Xa7* are approximately equal with respect to bacterial growth and lesion length [42, 58, 64]. *Xa7* resistance is the result of the presence of the appropriate *AvrXa7* in the pathogen and dominant, while *xa13* resistance is dependent on the absence of an effective virulence factor and recessive. The mechanism of *XA7* mediated resistance is as yet unknown.

Type III effectors, in general, are hypothesized to interfere with host defense and defense signaling mechanisms. Strains of *Xoo* have other type III effectors, differing from TALEs, and, therefore, not entirely dependent on TALEs for suppression of host defenses [65]. *Xoo* strains lacking major TALEs are still capable of causing water-soaking, if syringe inoculated, which is in contrast to type III secretion system (Hypersensitive reaction/pathogenicity or Hrp⁻) mutants. Hrp⁻ mutant strains are incapable of secreting any type III effectors, including TALEs, and are virtually symptomless [66]. The mechanism by which SWEET transporters condition susceptibility is unknown. One hypothesis is that the transporters allow cells to leak sucrose, providing the pathogen with nutrients. SWEET function may interfere with normal plant defense functions or, possibly, allow transport of other nutrients or disease promoting compounds [41]. However, little empirical evidence for the nutrition model exists at present.

Sequencing of *Xoo* genomes has revealed the full complement of TALEs is now known [17–23]. The individual TALE genes are distinguishable on the basis of the number of repeats in the central repetitive region and by polymorphisms within each repeat sequence, particularly, at the 12th and 13th codons. Strains of the Asian lineage contain upwards of 16–19 TALE genes in each genome [18]. The large numbers of TALE genes in these species may reflect the evolutionary investment in utilizing the TALEs for virulence and are essential, to the ecological niche these bacteria occupy. The maintenance of a large repertoire of TALE genes may increase the frequency of recombination between, and diversity of TALE genes within the pathogen population [60]. Pathogen may then adapt faster to the changing host genotypes as exemplified by the appearance of *pthXo5*, which avoids Xa7 recognition and appears to be a hybrid between *avrXa7* and *pthXo6* [61].

Not all TALE genes of *Xoo*, however, are just substrates for new major TALEs. Two other TALE genes from PXO99 strain of *Xoo*, in addition to *pthXo1*, contribute to virulence, known to elevate the expression of two host genes distinct from *SWEET11*. *PthXo6* elevates the expression of *OsTFX1*, which contributes to approximately 35% of the disease [67]. Many strains induce *OsTFX1*. The gene *pthXo7* of PXO99 elevates the expression of *OsTFIIAγ1* and would appear to be an adaption to host genotypes containing the *xa5* allele of *TFIIAγ5* [67]. However, introduction of *pthXo7* to other strains does not restore full virulence on *xa5/xa5* plants and may provide only an incremental fitness benefit [67]. All Asian strains also carry a set of truncated TALEs, the inhibitory or iTALEs, which function to suppress Xa1-mediated resistance [32].

4.1 Executor *R* genes and super promoters

Xa10, *Xa23* and *Xa27* are representatives of the new class of E genes, so-named because the induction of these genes executes a response of programmed cell death (PCD) in the host. *Xa10* induced PCD in plant species rice and *N. benthamiana*, and mammalian HeLa cells [38]. No cognate S genes for AvrXa10, AvrXa23, or AvrXa27 in compatible host cultivars have been reported, though the presence of AvrXa27 and AvrXa23 in many extant strains of *Xoo* may portend either a defeated function or an unknown cryptic function in S gene expression. Nonetheless, E genes hold great potential for broad and durable resistance in rice against extant *Xoo* population. A super promoter consisting of multiple EBEs, corresponding to specific TALEs in extant population of *Xoo*, have been constructed (**Figure 1**). [68–70]. Addition of multiple EBEs to a pathogen strain specific rice BB resistance gene makes it effective against additional strains of *Xoo*. The EBEs of TALEs *PthXo1*, *PthXo6* and *Tal9a* when conjugated to E gene *Xa27*, showed resistance against PXO99 and a derivative strain lacking *AvrXa27* [68]. A similar scenario was

Figure 1.
Xoo TALE-dependent resistance and susceptibility in BB of rice. (A) Schematic of typical TALE from *Xoo* and (B) five types of TALE interactions affecting outcome of *Xoo* and rice interaction.

accomplished using E gene *Xa10* [69]. The study suggested that broad-spectrum and potentially durable resistance is possible by stable integration of an E gene engineered in a way to respond to multiple TALEs from different strains or even different pathogens. Design of a super promoter, however, needs to be done carefully. Risk that an added EBE might coincidentally contain a *cis* regulatory element could induce the E gene expression in response to particular stimuli and cause cell death without challenge by TALEs. Amended promoters should be tested thoroughly before deployment.

4.2 Targeted genome regulation and editing

Central to TALE function is the discovery of the DNA recognition cipher of TALEs [71, 72]. The central domain of a TALE, also known as binding domain, consists of variable number of tandem repeats, each consisting 33–35 amino acid residues. The 12th and 13th amino acid residues (known as repeat variable di-residues, RVDs)

of each repeat preferentially binds to the respective nucleotides in the EBEs of target gene, such that HD, NG, NI and NN bind to C, T, A, and G, respectively in the effector binding elements (EBEs) of the promoter of a target gene [71–73]. The TALE recognition code allowed custom-engineer of DNA binding domains, also called designer TALEs (dTALes), with novel specificity to the user-chosen DNA sequences [74–76]. dTALes provide a useful tool box to transiently activate host genes of interest for their functional analysis and assess the associated effect on host phenotype and physiology during rice-*Xoo* interaction. TALENs are fusions between dTALes and the nuclease domain of restriction enzyme FokI [77–80]. Other C-terminal domains have also been used [81]. Target site recognition and TALEN dimerization triggers a double-strand break (DSB) and generates small random insertions or deletions at the cleavage site, resulting in an edited sequence. CRISPR-Cas editing approaches have circumvented the need to construct dTALes and achieved wide general use, including editing of rice genes [82–84].

5. Prospects for engineered broad and durable resistance in rice to BB

Traditional resistance breeding has identified many useful *R* genes and introgressed the genes into elite cultivars. Further, development of molecular markers allows the pyramiding of multiple genes into single lines. The development of designer TALENs and CRISPR-Cas genome editing brings greater flexibility and rapidity to the development of resistant germplasm. A continuous provision of novel *R* genes in breeding programs is possible. Of course, the adoption and utility of different approaches is dependent on the regulatory climate. Introduction of novel or alien genes may be prohibitive in the foreseeable future. Classification of genome editing techniques will also vary depending on the individual country. In the rice system, our understanding allows numerous approaches for the enhancement of resistance beyond classical breeding. TALE biology, specifically, can be exploited (Figure 2). Least intrusive is targeted genome editing of *S* genes. *OsSWEET14* is targeted by unrelated TALEs, AvrXa7, PthXo3, Tal5 and TalC from different *Xoo* strains and which in some cases overlap their EBEs [43, 45, 46]. *OsSWEET14* was made unresponsive to TALEs AvrXa7 and Tal5, when their respective EBEs were mutated using TALENs in otherwise susceptible rice cv. Kitake [85, 86]. Thus, recessive resistance obtained by the genome editing of *OsSWEET14* is expected to be broad and contribute to durability given the apparent few major TALEs in the extant population. Future efforts will be to target all EBE/*S* gene combinations in single elite lines. Fusion of EBEs to a variety of *R* and *E* genes has

Figure 2. Super promoters: pyramiding of EBEs of multiple TALEs upstream of an *E* gene for broad and durable resistance. Subscript of each EBE corresponds to the respective TALEs. Blocks under each EBE represent the respective TALEs with blunt ends as their N termini, and arrowheads as their C-termini flanking the binding repeats in center.

been demonstrated to provide resistance [68, 87]. The functional specificity of an E gene can be broadened by linkage to general inducible defense genes [69, 88]. Approaches are not limited to TALE-associated responses. The RLK immunity receptor EFR from *Arabidopsis* [89, 90], as well as XA21/EFR fusion proteins function in rice [91]. Thus, the sky is the limit for the engineering of broad and durable resistance in rice to BB.

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References

- [1] Béné C et al. Feeding 9 billion by 2050—Putting fish back on the menu. *Food Security*. 2015;7(2):261-274
- [2] Kennedy G, Burlingame B. Analysis of food composition data on rice from a plant genetic resources perspective. *Food Chemistry*. 2003;80(4):589-596
- [3] Khush GS. What it will take to feed 5.0 billion rice consumers in 2030. *Plant Molecular Biology*. 2005;59(1):1-6
- [4] Collard BC, Mackill DJ. Marker-assisted selection: An approach for precision plant breeding in the twenty-first century. *Philosophical Transactions of the Royal Society, B: Biological Sciences*. 2007;363(1491):557-572
- [5] Mew T. Current status and future prospects of research on bacterial blight of rice. *Annual Review of Phytopathology*. 1987;25(1):359-382
- [6] Reddy A et al. Relationship of bacterial leaf blight severity to grain yield of rice. *Phytopathology*. 1979;69(9):967-969
- [7] Ou SH. *Rice Diseases*. IRRI; 1985
- [8] Kim SM et al. Identification and fine-mapping of a new resistance gene, Xa40, conferring resistance to bacterial blight races in rice (*Oryza sativa* L.). *Theoretical and Applied Genetics*. 2015;128(10):1933-1943
- [9] Busungu C et al. Identification and linkage analysis of a new rice bacterial blight resistance gene from XM14, a mutant line from IR24. *Breeding Science*. 2016;66(4):636-645
- [10] Mishra D et al. Pathotype and genetic diversity amongst Indian isolates of *Xanthomonas oryzae* pv. *oryzae*. *PLoS ONE*. 2013;8(11):e81996
- [11] Sureshkumar V et al. RiceMetaSysB: A database of blast and bacterial blight responsive genes in rice and its utilization in identifying key blast-resistant WRKY genes. In: Database. 2019
- [12] Li Q et al. Expression profiling of rice genes in early defense responses to blast and bacterial blight pathogens using cDNA microarray. *Physiological and Molecular Plant Pathology*. 2006;68(1-3):51-60
- [13] Zhang F et al. Comparative transcriptome profiling of a rice line carrying Xa39 and its parents triggered by *Xanthomonas oryzae* pv. *oryzae* provides novel insights into the broad-spectrum hypersensitive response. *BMC Genomics*. 2015;16:111
- [14] RGSP International. The map-based sequence of the rice genome. *Nature*. 2005;436(7052):793
- [15] Sun C et al. RPAN: Rice pan-genome browser for ~3000 rice genomes. *Nucleic Acids Research*. 2017;45(2):597-605
- [16] Ochiai H et al. Genome sequence of *Xanthomonas oryzae* pv. *oryzae* suggests contribution of large numbers of effector genes and insertion sequences to its race diversity. *Japan Agricultural Research Quarterly: JARQ*. 2005;39(4):275-287
- [17] Lee B-M et al. The genome sequence of *Xanthomonas oryzae* pathovar *oryzae* KACC10331, the bacterial blight pathogen of rice. *Nucleic Acids Research*. 2005;33(2):577-586
- [18] Salzberg SL et al. Genome sequence and rapid evolution of the rice pathogen *Xanthomonas oryzae* pv. *oryzae* PXO99A. *BMC Genomics*. 2008;9:204
- [19] Booher NJ et al. Single molecule real-time sequencing of *Xanthomonas oryzae* genomes reveals

a dynamic structure and complex TAL (transcription activator-like) effector gene relationships. *Microbial genomics*. 2015;**1**(4):1-22. DOI: 10.1099/mgen.0.000032

[20] Huguet-Tapia JC et al. Complete genome sequence of the African Strain AXO1947 of *Xanthomonas oryzae* pv. *oryzae*. *Genome Announcements*. 2016;**4**(1). DOI: 10.1128/genomeA.01730-15

[21] Quibod IL et al. Effector diversification contributes to *Xanthomonas oryzae* pv. *oryzae* phenotypic adaptation in a semi-isolated environment. *Scientific Reports*. 2016;**6**:34137. DOI: 10.1038/srep34137.

[22] Doucouré H et al. Functional and genome sequence-driven characterization of tal effector gene repertoires reveals novel variants with altered specificities in closely related Malian *Xanthomonas oryzae* pv. *oryzae* strains. *Frontiers in Microbiology*. 2018;**9**:1657

[23] Tran TT et al. Functional analysis of African *Xanthomonas oryzae* pv. *oryzae* TALomes reveals a new susceptibility gene in bacterial leaf blight of rice. *PLoS Pathogens*. 2018;**14**:1-25

[24] Midha S et al. Population genomic insights into variation and evolution of *Xanthomonas oryzae* pv. *oryzae*. *Scientific Reports*. 2017;**7**:40694

[25] Song WY et al. A receptor kinase-like protein encoded by the rice disease resistance gene, Xa21. *Science*. 1995;**270**(5243):1804-1806

[26] Sun X et al. Xa26, a gene conferring resistance to *Xanthomonas oryzae* pv. *oryzae* in rice, encodes an LRR receptor kinase-like protein. *The Plant Journal*. 2004;**37**(4):517-527

[27] Pruitt RN et al. The rice immune receptor XA21 recognizes a

tyrosine-sulfated protein from a Gram-negative bacterium. *Science Advances*. 2015;**1**(6):e1500245

[28] Gómez-Gómez L, Boller T. Flagellin perception: A paradigm for innate immunity. *Trends in Plant Science*. 2002;**7**(6):251-256

[29] Zipfel C et al. Perception of the bacterial PAMP EF-Tu by the receptor EFR restricts *Agrobacterium*-mediated transformation. *Cell*. 2006;**125**(4):749-760

[30] Shiu S-H, Bleecker AB. Plant receptor-like kinase gene family: Diversity, function, and signaling. *Science's STKE*. 2001;**2001**(113):re22

[31] Yoshimura S et al. Expression of Xa1, a bacterial blight-resistance gene in rice, is induced by bacterial inoculation. *Proceedings of the National Academy of Sciences*. 1998;**95**(4):1663-1668

[32] Ji Z et al. Interfering TAL effectors of *Xanthomonas oryzae* neutralize R-gene-mediated plant disease resistance. *Nature Communications*. 2016;**7**:13435. DOI: 10.1038/ncomms13435

[33] Triplett LR et al. A resistance locus in the American heirloom rice variety Carolina Gold Select is triggered by TAL effectors with diverse predicted targets and is effective against African strains of *Xanthomonas oryzae* pv. *oryzicola*. *The Plant Journal*. 2016;**87**(5):472-483

[34] Read AC et al. Suppression of Xo1-mediated disease resistance in rice by a truncated, non-dna-binding TAL effector of *Xanthomonas oryzae*. *Frontiers in Plant Science*. 2016;**7**(1516):eCollection

[35] Zhang J, Yin Z, White F. TAL effectors and the executor gene R genes. *Frontiers in Plant Science*. 2015;**6**:641

[36] Gu K et al. High-resolution genetic mapping of Xa27 (t), a new bacterial

- blight resistance gene in rice, *Oryza sativa* L. Theoretical and Applied Genetics. 2004;**108**(5):800-807
- [37] Gu K et al. geneR gene expression induced by a type-III effector triggers disease resistance in rice. Nature. 2005;**435**(7045):1122
- [38] Tian D et al. The rice TAL effector-dependent resistance protein XA10 triggers cell death and calcium depletion in the endoplasmic reticulum. The Plant Cell. 2014. DOI: 10.1105/tpc. 113.119255
- [39] Wang C et al. XA23 is an executor R protein and confers broad-spectrum disease resistance in rice. Molecular Plant. 2015;**8**(2):290-302
- [40] Hu K et al. Improvement of multiple agronomic traits by a disease resistance gene via cell wall reinforcement. Nature Plants. 2017;**3**:17009
- [41] Chen LQ et al. Sugar transporters for intercellular exchange and nutrition of pathogens. Nature. 2010;**468**(7323):527-532
- [42] Yang B, Sugio A, White FF. Os8N3 is a host disease-susceptibility gene for bacterial blight of rice. Proceedings of the National Academy of Sciences. 2006;**103**(27):10503-10508
- [43] Antony G et al. Rice xa13 recessive resistance to bacterial blight is defeated by induction of the disease susceptibility gene Os-11N3. Plant Cell. 2010;**22**(11):3864-3876
- [44] Zhou J et al. Gene targeting by the TAL effector PthXo2 reveals cryptic resistance gene for bacterial blight of rice. The Plant Journal. 2015;**82**(4):632-643
- [45] Streubel J et al. Five phylogenetically close rice SWEET genes confer TAL effector-mediated susceptibility to *Xanthomonas oryzae* pv. *oryzae*. The New Phytologist. 2013;**200**(3):808-819
- [46] Yu Y et al. Colonization of rice leaf blades by an African strain of *Xanthomonas oryzae* pv. *oryzae* depends on a new TAL effector that induces the rice nodulin-3 Os11N3 gene. Molecular Plant-Microbe Interactions. 2011;**24**(9):1102-1113
- [47] Chu Z et al. Promoter mutations of an essential gene for pollen development result in disease resistance in rice. Genes and Development. 2000;**20**(10):1250-1255
- [48] Gust AA, Brunner F, Nurnberger T. Biotechnological concepts for improving plant innate immunity. Current Opinion in Biotechnology. 2010;**21**(2):204-210
- [49] Iyer-Pascuzzi AS, McCouch SR. Recessive resistance genes and the *Oryza sativa*-*Xanthomonas oryzae* pv. *oryzae* pathosystem. Molecular Plant-Microbe Interactions. 2007;**20**(7):731-739
- [50] Hutin M et al. A knowledge-based molecular screen uncovers a broad-spectrum Os SWEET 14 resistance allele to bacterial blight from wild rice. The Plant Journal. 2015;**84**(4):694-703
- [51] Huang S et al. The broadly effective recessive resistance gene xa5 of rice is a virulence effector-dependent quantitative trait for bacterial blight. The Plant Journal. 2016;**86**(2):186-194
- [52] Liu Q et al. A paralog of the MtN3/saliva family recessively confers race-specific resistance to *Xanthomonas oryzae* in rice. Plant, Cell and Environment. 2011;**34**(11):1958-1969
- [53] Zaka A et al. Natural variations in the promoter of OsSWEET13 and OsSWEET14 expand the range of resistance against *Xanthomonas oryzae* pv. *oryzae*. PLoS ONE. 2018;**13**(9):e0203711

- [54] Iyer AS, McCouch SR. The rice bacterial blight resistance gene xa5 encodes anovel form of disease resistance. *Molecular Plant-Microbe Interactions*. 2004;**17**(12):1348-1354
- [55] Jiang G-H et al. Testifying the rice bacterial blight resistance gene xa5 by genetic complementation and further analyzing xa5 (Xa5) in comparison with its homolog TFIIA γ 1. *Molecular genetics and Genomics*. 2006;**275**(4):354-366
- [56] Yuan M et al. A host basal transcription factor is a key component for infection of rice by TALE-carrying bacteria. *eLife*. 2016;**5**
- [57] Carpenter SCD et al. A strain of an emerging Indian *Xanthomonas oryzae* pv. *oryzae* pathotype defeats the rice bacterial blight resistance gene xa13 without inducing a clade III SWEET gene and is nearly identical to a recent Thai isolate. *Frontiers in Microbiology*. 2018;**9**:2703
- [58] Bai J et al. *Xanthomonas oryzae* pv. *oryzae* avirulence genes contribute differently and specifically to pathogen aggressiveness. *Molecular Plant-Microbe Interactions*. 2000;**13**(12):1322-1329
- [59] Yang B, White FF. Diverse members of the AvrBs3/PthA family of type III effectors are major virulence determinants in bacterial blight disease of rice. *Molecular Plant-Microbe Interactions*. 2004;**17**(11):1192-1200
- [60] Yang Y, Gabriel DW. Intragenic recombination of a single plant pathogen gene provides a mechanism for the evolution of new host specificities. *Journal of Bacteriology*. 1995;**177**(17):4963-4968
- [61] Yang B, Sugio A, White FF. Avoidance of host recognition by alterations in the repetitive and C-terminal regions of AvrXa7, a type III effector of *Xanthomonas oryzae* pv. *oryzae*. *Molecular Plant-Microbe Interactions*. 2005;**18**(2):142-149
- [62] Cruz CMV et al. Predicting durability of a disease resistance gene based on an assessment of the fitness loss and epidemiological consequences of avirulence gene mutation. *Proceedings of the National Academy of Sciences*. 2000;**97**(25):13500-13505
- [63] Cao J et al. Dominant and recessive major geneR genes lead to different types of host cell death during resistance to *Xanthomonas oryzae* in rice. *Frontiers in Plant Science*. 2018;**9**:1711
- [64] Yang B et al. The virulence factor AvrXa7 of *Xanthomonas oryzae* pv. *oryzae* is a type III secretion pathway-dependent nuclear-localized double-stranded DNA-binding protein. *Proceedings of the National Academy of Sciences*. 2000;**97**(17):9807-9812
- [65] Song C, Yang B. Mutagenesis of 18 type III effectors reveals virulence function of XopZ(PXO99) in *Xanthomonas oryzae* pv. *oryzae*. *Molecular Plant-Microbe Interactions*. 2010;**23**(7):893-902
- [66] Zhu W, Magbanua MM, White FF. Identification of two novel hrp-associated genes in the hrp gene cluster of *Xanthomonas oryzae* pv. *oryzae*. *Journal of Bacteriology*. 2000;**182**(7):1844-1853
- [67] Sugio A et al. Two type III effector genes of *Xanthomonas oryzae* pv. *oryzae* control the induction of the host genes OsTFIIA γ 1 and OsTFX1 during bacterial blight of rice. *Proceedings of the National Academy of Sciences*. 2007;**104**(25):10720-10725
- [68] Hummel AW, Doyle EL, Bogdanove AJ. Addition of transcription activator-like effector binding sites to a pathogen strain-specific rice bacterial blight resistance gene makes it effective against

additional strains and against bacterial leaf streak. *The New Phytologist*. 2012;**195**(4):883-893

[69] Zeng X et al. Genetic engineering of the Xa10 promoter for broad-spectrum and durable resistance to *Xanthomonas oryzae* pv. *oryzae*. *Plant Biotechnology Journal*. 2015;**13**(7):993-1001

[70] Römer P, Recht S, Lahaye T. A single plant resistance gene promoter engineered to recognize multiple TAL effectors from disparate pathogens. *Proceedings of the National Academy of Sciences*. 2009;**106**(48):20526-20531

[71] Boch J et al. Breaking the code of DNA binding specificity of TAL-type III effectors. *Science*. 2009;**326**(5959):1509-1512

[72] Moscou MJ, Bogdanove AJ. A simple cipher governs DNA recognition by TAL effectors. *Science*. 2009;**326**(5959):1501

[73] Römer P et al. Promoter elements of rice susceptibility genes are bound and activated by specific TAL effectors from the bacterial blight pathogen, *Xanthomonas oryzae* pv. *oryzae*. *The New Phytologist*. 2010;**187**(4):1048-1057

[74] Morbitzer R et al. Regulation of selected genome loci using de novo-engineered transcription activator-like effector (TALE)-type transcription factors. *Proceedings of the National Academy of Sciences of the United States of America*. 2010;**107**(50):21617-21622

[75] Zhang F et al. Programmable sequence-specific transcriptional regulation of mammalian genome using designer TAL effectors. *Nature Biotechnology*. 2011;**29**(2):149

[76] Li T et al. Designer TAL effectors induce disease susceptibility and resistance to *Xanthomonas oryzae* pv. *oryzae* in rice. *Molecular Plant*. 2013;**6**(3):781-789

[77] Li T et al. Modularly assembled designer TAL effector nucleases for targeted gene knockout and gene replacement in eukaryotes. *Nucleic Acids Research*. 2011;**39**(14):6315-6325

[78] Christian M et al. Targeting DNA double-strand breaks with TAL effector nucleases. *Genetics*. 2010;**186**(2):757-761

[79] Cermak T et al. Efficient design and assembly of custom TALEN and other TAL effector-based constructs for DNA targeting. *Nucleic Acids Research*. 2011;**39**(12):e82

[80] Li T et al. TAL nucleases (TALNs): Hybrid proteins composed of TAL effectors and FokI DNA-cleavage domain. *Nucleic Acids Research*. 2011;**39**(1):359-372

[81] Chen K, Gao C. Targeted genome modification technologies and their applications in crop improvements. *Plant Cell Reports*. 2014;**33**(4):575-583

[82] Wiedenheft B, Sternberg SH, Doudna JA. RNA-guided genetic silencing systems in bacteria and archaea. *Nature*. 2012;**482**(7385):331

[83] Jinek M et al. A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. *Science*. 2012;**337**(6096):816-821

[84] Hsu PD, Lander ES, Zhang F. Development and applications of CRISPR-Cas9 for genome engineering. *Cell*. 2014;**157**(6):1262-1278

[85] Blanvillain-Baufumé S et al. Targeted promoter editing for rice resistance to *Xanthomonas oryzae* pv. *oryzae* reveals differential activities for SWEET14-inducing TAL effectors. *Plant Biotechnology Journal*. 2017;**15**(3):306-317

[86] Li T et al. High-efficiency TALEN-based gene editing produces

disease-resistant rice. *Nature Biotechnology*. 2012;**30**(5):390-392

[87] Hutin et al. Ectopic activation of the rice NLR heteropair RGA4/RGA5 confers resistance to bacterial blight and bacterial leaf streak diseases. *The Plant Journal*. 2016;**88**(1):43-55

[88] Tian D, Yin Z. Constitutive heterologous expression of avrXa27 in rice containing the *R* gene Xa27 confers enhanced resistance to compatible *Xanthomonas oryzae* strains. *Molecular Plant Pathology*. 2009;**10**(1):29-39

[89] Schwessinger B et al. Correction: Transgenic expression of the dicotyledonous pattern recognition receptor EFR in rice leads to ligand-dependent activation of defense responses. *PLoS Pathogens*. 2015;**11**(4):e1004872

[90] Lu F et al. Enhancement of innate immune system in monocot rice by transferring the dicotyledonous elongation factor Tu receptor EFR. *Journal of Integrative Plant Biology*. 2015;**57**(7):641-652

[91] Thomas NC et al. The rice XA21 ectodomain fused to the Arabidopsis EFR cytoplasmic domain confers resistance to *Xanthomonas oryzae* pv. *oryzae*. *PeerJ*. 2018;**6**:e4456