Review

Genetic Diversity of Weedy Rice and Its Potential Application as a Novel Source of Disease Resistance

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Genetic Diversity of Weedy Rice and Its Potential Application as a Novel Source of Disease Resistance

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Abstract: Weeds that infest crops are a primary factor limiting agricultural productivity worldwide. Weedy rice, also called red rice, has experienced independent evolutionary events through gene flow from wild rice relatives and de-domestication from cultivated rice. Each evolutionary event supplied/equipped weedy rice with competitive abilities that allowed it to thrive with cultivated rice and severely reduce yields in rice fields. Understanding how competitiveness evolves is important not only for noxious agricultural weed management but also for the transfer of weedy rice traits to cultivated rice. Molecular studies of weedy rice using simple sequence repeat (SSR), restriction fragment length polymorphism (RFLP) and whole genome sequence have shown great genetic variations in weedy rice population globally. These variations are evident both at whole genome and at single allele level, including *Sh4* (shattering), *Hd1* (heading and flowering), and *Rc* (pericarp pigmentation). The goal of this review is to describe the genetic diversity of current weedy rice germplasm and the significance of weedy rice germplasm as a novel source of disease resistance. Understanding these variations, especially at an allelic level, is also crucial as individual locus that control important traits can be of great target to rice breeders.

Keywords: Disease resistance; rice blast disease; sheath blight disease; weedy rice

1. Introduction

Rice (*Oryza sativa* L.) is one of the most important staple foods for humanity. Weedy rice is one of the most troublesome agricultural issues globally because it competes for nutrients, water, sunlight, and other crucial vital resources with cultivated rice, thus posing a great threat to food security [1,2]. Owing to its early flowering, enhanced photosynthesis and rapid grain filling, weedy rice can successfully outcompete cultivated rice [3–6]. Weedy rice is highly similar to cultivated rice but possess undesirable traits such as shattering [7,8], red pericarp pigmentation [9,10], seed dormancy [11], photoperiod sensitivity and flowering time variation, and increased plant height [12–15]. Moreover, some weedy rice biotypes possess awns that offer protections from predation[16]. Each year, weedy rice causes significant economic loss in rice production due to reduced quantity and grain quality [17,18]. Selective elimination of weedy rice from cultivated rice fields through application of herbicide has had limited success, since weedy and cultivated rice share morphological and physiological traits [19]. Understanding the biology of weedy rice is essential for weed management and can also benefit crop protection. Molecular markers such as microsatellite or simple sequence repeats (SSR), Amplified fragment length polymorphism (AFLPs), Random amplified polymorphism DNA (RAPDs), and DNA sequencing have developed and applied in the study of genetic variations and conservation studies by biologists in different plants species [20,21]. For instance, microsatellite markers have been used in conservation studies in endangered plants species such as *Calystegia soldanella* [22] and *Tricyrtis ishiiana* [23]. AFLP have been applied in genetic variations studies in plants such as *Jatropha curcas* [24] and *Rhodiola rosea* [25]. SSR is the most used molecular markers and are frequently used as allele-specific and co-dominant markers in genetic diversity and evolutionary relationships in wild and weedy rice [26,27]. In weedy rice apart from SSR

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markers, genome sequencing and quantitative trait loci analysis (QTL) have been used to implore the genetic diversity [28,29]. In this short review, we describe the genetic diversity at the allelic and genomic level in weedy rice and propose weedy rice as a novel source for

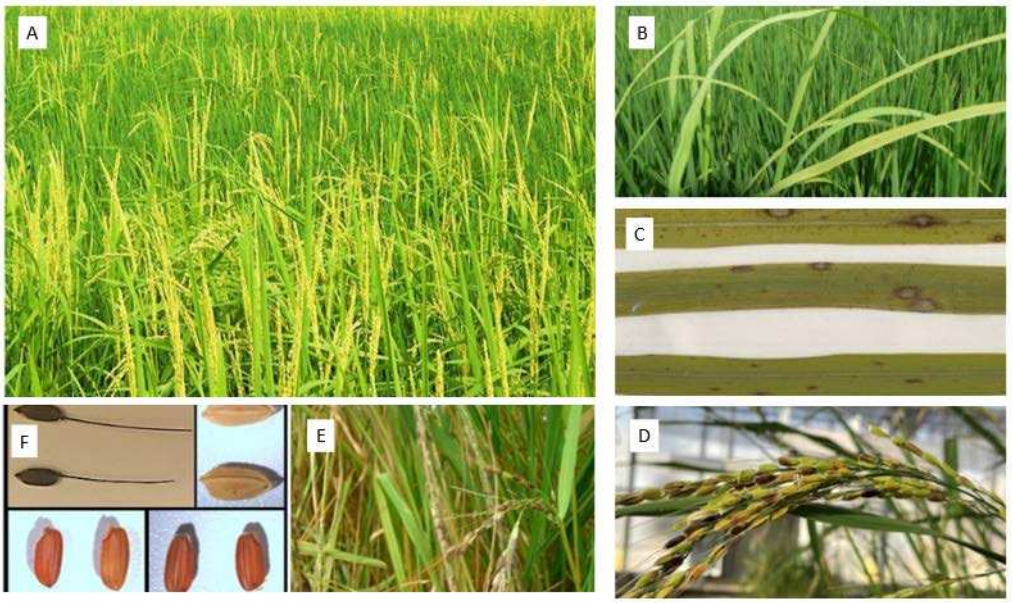

Figure 1. Weedy red rice in the USA. Weedy rice in a commercial rice field in Arkansas county (A). Blast reactions on leaves of weedy rice in a commercial Arkansas rice field (B) and enlarged leaves showing disease susceptibility (upper) and resistance (lower)(C), A black hull awned (BHA) weedy rice genotype grown in a greenhouse at DB NRRC, Stuttgart, Arkansas (D) and in a rice field (E), and seeds of both BHA and straw hull red rice from an Arkansas commercial rice field (F).

2. Diversity at an allelic level

2.1. Seed shattering (SH4)

Seed shattering allows plants to shed its seeds from the plant to the field and is crucial for dispersal [30]. Seed shattering is costly to farmers, as it leads to crop yield reduction and may cause continued presence of volunteer plants in cultivated fields [31,32] . Shattering of seeds by wild or weedy plants is considered a fitness mechanism that allows plants to evade collection by farmers for destruction. At maturity, shattering is sometimes crucial as it allow seeds to retain sufficient moisture for dormancy, thus enabling weeds to survive during winter and germinate during the cropping season[11,33,34]. Seed shattering is controlled by a complex genetic mechanism and involves proper formation and subsequent degradation of an abscission layer [35]. Quantitative trait loci (QTLs) involved in seed shattering have been identified on almost all the rice chromosome [36–41]. To date, major genes involved in rice seed shattering have been cloned. These genes include *qSH1*, located on chromosome 1, encodes a BEL1-type homeobox. A single nucleotide polymorphism (SNP) at the 5′ upstream regulatory region of *qSH1* that abolishes *qSH1* expression from the abscission layer, causing reduced shattering in cultivated rice [42]. *Sh-h*, that encodes a C-terminal domain phosphatase-like protein in cultivated rice, inhibited shattering in rice [43]. *SHAT*I, which encodes APETALA2 transcription factor, was demonstrated to be important for shattering by specifying the abscission zone formation [35]. While *Sh4*, a member of the trihelix family of transcription factors, controls shattering via hydrolyzing of AZ cells during the abscission process [44,45]. Among the four previously cloned genes, *Sh4* is located on chromosome 4 and is most responsible for reduced seed shattering in rice [45]. This gene was isolated from progeny derived from a cross between cultivated *O. sativa* subpopulation indica and a wild seed- shattering species of *O. nivara*. The *Sh4* gene was shown to be involved in the degradation of the abscission layer between the grain and the pedicel [45]. A nonsynonymous nucleotide substitution from G to T is present in the first exon of *Sh4* of

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cultivated rice. This substitution was reported to be the main reason for reduced sh4 function [45]. Functional genomic studies showed that when *Sh4* was silenced in cultivated rice, seed shattering was reduced [46]. Many cultivated rice varieties have been shown to develop shattering due to reversion to the wild rice populations through de-domestication (endoferality) [37,38].

Reduced shattering in cultivated rice has been linked to a T mutation in exon one of the *Sh4* gene; however, several studies on weedy rice have shown that the T mutation is not the sole reason for observed reduced shattering. Thurber et al. reported that despite possessing a T mutation at the *Sh4* locus like cultivated rice, most US weedy rice displays high shattering ability. The presence of non-shattering T mutations in US weedy rice as reported by Thurber et al. [49] suggests they can be a major unidentified locus or several minor loci responsible for shattering within *Oryza* that are hard to detect. Similarly, 20 out of 24 Italian weedy accessions had a G to T mutation at *sh4* locus and displayed high shattering ability [9]. Non-shattering *Sh4* genotype was also reported in Asian weedy rice but showed a shattering phenotype [8]. Other genetic studies showing that the G to T mutations at *Sh* locus caused reduced seed shattering in weedy rice [50,51]. Some diversity studies at the *Sh4* locus have shown weedy rice to contain both G, T, or heterozygous GT nucleotides. For example, Song et. al reported that Malaysia weedy rice displayed increased shattering and comprised accessions with fixed reduced shattering T and shattering G alleles [50]. Of 178 accessions, 104 (58.4%) were shown to be T homozygotes, 63 (35.4%) were homozygous for the ancestral G allele, and the remaining 11 (6.2%) displayed G/T heterozygosity. Similarly, phylogenetic analysis of South Asia weedy rice has shown large variations among the *Sh* alleles. These South Asia weedy rice were classified as wild-like and all had the ancestral G allele. The aus- and indica-type weedy rice (with only two exceptions) had the T allele [51]. However, according to Huang et. al [51], most of the South Asia weedy rice are of T allele with a few being of G allele, thus suggesting the majority of Asian weedy rice originated from cultivated aus and indica varieties through de-domestication. Furthermore, variation studies at the *Sh4* allele on Thai weedy rice revealed the existence of a dominant T allele in 95 of 111 accessions (85.6%). This T allele was present in all cultivated rice (59 of 59 accessions). Of the remaining 16 weedy rice accessions, one (14.4%) was heterozygous (G/T) and 15 were homozygous (G/G) [52], indicating that Thai weedy rice had multiple independent origins of *Sh4*.

2.2. Diversity at the Hd1 locus-

The *Hd1* locus has been implicated in many studies as being important for photoperiod sensitivity and flowering time variation in cultivated rice [12–15]. Most cultivated rice contains either *SNPs* or deletions in the *Hd1* locus that renders it to be nonfunctional, thus eliminating day length sensitivity and leading to later flowering under short days. The most common mutation is a 2-bp deletion in the exon which leads to a premature stop codon and is present in some indica and some japonica cultivars [14]. Between the two US weedy rice genotypes, the SH weedy rice was reported to flower earlier than the local tropical japonica cultivars while the BHA weedy rice flowered alongside or later than the cultivar [53,54]. The drastic difference in flowering exhibited by the SH and BHA was due to the *Hd1* alleles. The BHA weedy rice genotype has nonfunctional *Hd1* alleles, that lead to loss of day-length sensitivity and later flowering under short day conditions, while the SH weeds predominantly carry functional *Hd1* alleles and are day length sensitive resulting in early flowering under short-day conditions. Phenotypic traits such as height, emergence growth rate, average growth, flowering time, and tiller number grouped US weedy rice into four different haplotypes, SH, BHA (1 and 2) and BRH with their progenitors being indica, aus and hybridization of SH and BHA weeds (BRH) respectively [55]. The BHA (1and 2) plants were taller (BHA1-85 CM, BHA2-99 CM), and took a long time to flower (BHA1 126 days, BHA2 111days). Genetic diversity studies at the *Hd1* locus showed that the BHA genotypes are highly diverse compared to other weedy genotypes [55]. Although weedy rice infestation is a serious threat to rice production globally, the *Hd1* locus especially of US SH weedy rice genotype [53,54] can be exploited by breeders through biotechnology to develop commercial rice cultivars with short flowering time, thus reducing time periods required for seed production.

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2.3. Diversity at the Rc locus

Red pericarp is a prominent feature that distinguishes weedy rice from cultivated rice [10], and it is caused by the buildup of anthocyanins and proanthocyanidins in the pericarp [46]. Accumulation of anthocyanins and proanthocyanidins in the pericarp is a crucial physiological function for promoting seed dormancy [57]. Two loci (*Rc* and *Rd*) associated with red pericarp pigmentations in rice have been identified, which play a complementary role. The *Rc* locus is responsible for the accumulation of pigments, while the *Rd* gene increases the content of the pigment in pericarp [58]. For red pericarp pigmentations to occur both the *Rc* and *Rd* loci must be present. *Rc* alone produces brown seeds, while *Rd* without *Rc* has white pericarp phenotype [59]. The *Rc* gene is located on rice chromosome 7, contains eight exons, and encodes a basic helix-loop-helix transcription factor. This is an important gene for the regulation of proanthocyanidins biosynthesis [9,60]. Proanthocyanins accumulation result in red pericarp pigmentation and was shown to be dependent on functionality of the *Rc* allele [9]. Analysis of the *Rc* allele identified a 14-bp deletion in the seventh exon, this deletion is present in most white pericarp rice cultivars. The deletion causes a frameshift that results to a premature stop codon, which inactivates the DNA-binding domain, thus making the transcription factor nonfunctional [60]. Moreover, Sweeney et al reported *Rc*-s to be present in other white pericarp rice genotypes and is characterized by a C to A base transversion in the seventh exon [59]. Alleles *Rc* and *Rc-s* result in an inactive transcription factor, causing the pericarp to be white [59]. Some studies have reported the existence of red pericarp in rice cultivars and this phenotype is attributed by mutational reversion of the *Rc* nonfunctional allele to functional form. For instance, Brooks et. Al [61] showed that 1-bp deletion is present at 20 bp upstream of the origin 14-bp deletion in the *Rc* allele, this mutation restores reading from protein function, and the proanthocyanidin-pigmented in US red pericarp cultivar 'Wells'. Similarly, the Italian cultivar 'Perla' has red pericarp pigmentation as reported [62]. The red pericarp phenotype is due to the presence of 1-bp deletion located at the 44 bp upstream of the 14 bp deletion in *Rc* gene. These two studies [61,62] therefore indicate not all rice cultivars contain the nonfunctional *Rc* allele that has been selected for domestication.

Weedy rice, also called red rice, is found in many rice growing regions in the world. Previous genetic studies reported that red pericarp pigmentation is caused by a functional *Rc* gene in weedy rice resulting in the upregulation of proteins in the proanthocyanin biosynthetic pathway[9,10]. Although pericarp pigmentation is associated with the a 14-bp deletion at the *Rc* allele resulting in loss of function, in other studies, Italian weedy rice was classified into two haplotypes based on pericarp pigmentation. Haplotype 1 accessions had red pericarp without the 14-bp deletion at the *Rc* locus similar to the *Rc* allele in *O. rufipogon* suggesting these haplotypes could have originated from wild rice *O. rufipogon* population [9]. Haplotype 2 weedy rice accessions had a white pericarp with their *Rc* allele having the 14-bp deletion which was similar to that of japonica allele and an additional 1-bp deletion in the upstream region of the 14-bp gap. Thus haplotype 2 might have evolved from japonica rice cultivars. Moreover, a diversity study at the *Rc* locus in Malaysia weedy rice showed that 43 out of 52 had a red pericarp, while the remain 9 had white pericarps [63]. Direct Sanger sequencing of the exon 7 region at the *Rc* locus confirmed the presence of the 14-bp deletion in 8 of the 9 white pericarp Malaysian weedy rice. Phylogenetic tree[63] categorized these Malaysian weedy rice into three distinct groups. The largest group of Malaysian weeds (32 of 52 accessions) is in a large clade (labeled group 1), they were genetically closer to United States weeds, red-pericarp domesticated rice, and a few *O. rufipogon* accessions. The second clade (group 2) contains 7 Malaysian weeds that are grouped exclusively with *O. rufipogon* accessions. While the third group of Malaysian weeds (group 3) is characterized by haplotypes that either carry the *Rc* 14-bp deletion or have functional *Rc* sequences closely related to *Rc* genotype [63] Proanthocyanidins are important for numerous health benefit such as antioxidant, anticancer, antidiabetic, neuroprotective, and antimicrobial [64]. Furthermore, consumption of proanthocyanidins containing food products, such as red wine and chocolate, appeared to be associated with lower blood pressure, insulin resistance, and reverse endothelial dysfunction [65–67]. Attempt to increase proanthocyanidins content in red rice through crossing red pericarp 'Hong Xiang 1' ('HX1') and white pericarp rice 'Song 98-131' ('S98-

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131') has been undertaken [68]. However, this approach is not applicable for crossing weedy rice and cultivated rice as this could result in introgression of undesirable weedy traits in rice cultivars. Fortunately, with extensive genetic studies on weedy rice, alleles controlling pericarp pigmentation can individually be exploited. Therefore, weedy rice genotype without the 14-bp deletion at the *Rc* functional locus that have been reported to contain high levels of proanthocyanidins in their pericarp [9], their respective *Rc* locus can be introduced in rice varieties with low proanthocyanidins by breeders to generate rice varieties with higher or improved proanthocyanidins quantities

3. Diversity at the genome level

Molecular markers and whole genome sequencing have been used to study genetic variations in weedy rice. For example, Lu et. al [69] used InDel molecular markers and deployed principal component analysis to examine weedy rice in Asia. The study identified two different genetic weedy rice groups, the indica weedy rice accessions and the japonica weedy rice accessions. The indica varieties were found across latitudes between 5 to 40° N while the Japonica types were mostly confined to latitudes >35° [69]. Further analysis of the Asian weedy rice and common cultivated and wild rice by using Nei'genetic distance showed that japonica Asian weedy rice genotypes were genetically closer to the local japonica cultivars suggesting that these weedy rice accessions originating from japonica cultivars [52]. The indica weedy varieties are genetically closer to the common wild rice suggesting that they could have gradually originated from common wild rice or from natural cross hybrids of indica cultivars and common wild rice [69]. Analysis of genetic diversity and origin of North Asia weedy rice with SSR markers indicated that weedy rice in this region were highly diverse genetically with a heterozygosity of 0.434 and a high Shannon's information index of 0.748 [70]. Moreover, the use of SSR markers with the application of cluster analysis (UPGMA) and principal component analysis (PCA) to analyze genetic diversity of 30 weedy rice in Liaoning province in China by Cao et. al [71] showed a relatively high diversity in weedy population (He = 0.313, I = 0.572). Furthermore, molecular studies using SSRs identified two major genotypes of weedy rice in the USA. These were black hull with awn (BHA) with an estimated diversity of 0.76 and the Straw hull awnless (SH) with a diversity of 0.68 and were shown to have originated from cultivated Asian aus and indica progenitors, respectively [54]. The origin of these two US genotypes was confirmed using additional microsatellite and single-nucleotide polymorphism (SNP) molecular analysis [7,72]. SSR markers have also been used to study genetic diversity of Italian weedy rice, where the data of 19 SSR markers revealed that Italian weedy rice is highly diverse with the allelic average and heterozygosity of 3.368 and 0.295, respectively [73]. Weedy rice from Uruguay were classified into three distinct groups, A, B, and C, using AFLP molecular markers. Genetic diversity of these clusters was verified using dendrograms where A and C were purely weedy type, while cluster B included cultivated rice varieties [74]. Genome sequences were used to study the genetic diversity in weedy rice [54]. The whole genome sequences of 183 wild, cultivated, and weedy rice accessions were analyzed to assess the origins of weedy rice genotypes in the USA [75]. The origins of the US BHA weedy rice diverging from its crop ancestor aus was found to be much earlier than SH and Chinese weedy rice, whose ancestor is indica. Only a few genomic changes were identified that could lead to the formation of weedy forms. Distinct genomes of the SH and BHA weedy rice may have resulted from parallel evolution. Some genomic regions showing footprints of selection overlapped with other weedy genetic loci suggesting that parallel evolution has redefined the weedy rice genome. A mapping population derived from a cross of a BHA genotype with an aus was developed to evaluate the genetic basis of the competitiveness of weedy rice (Figure 2).

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Figure 2. Weedy rice mapping population derived from a cross of US BHA genotype with aus growing in a rice field at Dale Bumpers National Rice Research Center in Stuttgart, Arkansas. Plants were bagged for seed collection.

Whole genome sequencing analysis of 30 Korean weedy rice genotypes showed that Korean weedy rice did not originate from wild rice relatives since they were distinct and arose from either japonica or indica cultivated rice [76].

Table 1. Genetic diversity of weedy rice as detected by various molecular markers in different regions in the world.

Weedy rice	Region	Molecular marker used	Genetic diversity	Reference
Oryza sativa	Arkansas	SSR	Gradient Distance (GD)=07	[77]
Oryza sativa f. spontanea	Northern China	SSR	(He) = 0.313 (I) = 0.572	[71]
Oryza sativa L.	Italy	SSR	He = 0.295	[73]
Oryza sativa L.	Northeastern Asia	SSR	He = 0.748 I = 0.434	[70]
Red rice	Uruguay	RFP	25.6 bands per primer pair	[74]

4. Novel source of disease resistance

Rice blast disease caused by the filamentous fungus *Magnaporthe oryzae* and sheath blight disease caused by the fungus *Rhizoctonia solani* are two major diseases threatening rice production worldwide (Figure 3) [78].

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Figure 3. Graphic description of rice blast caused by *M. oryzae*, and sheath blight disease caused by *R. solani* of cultivated rice. Seedling blast disease (A) enlarged typical diamond shape lesion of leaf blast (B), panicle blast showing 90% crop loss (C) and sheath blight disease of rice showing typical symptom on sheath (D).

These two diseases have existed in commercial rice fields for hundreds of years and weedy rice has adapted and evolved to survive these two biological stressors. Resistance to *M. oryzae* is governed by race specific major resistance (*R*) genes and minor QTLs. Resistance to *R. solani* could be governed by QTLs. However, major *R* genes to *R. solani* have not been discovered in rice germplasm. Weedy rice, that competes with cultivated rice, possesses ancient untapped and novel *R* genes. For instance, Zhao et. al [79] studied blast resistant *Ptr* allele in black hull weedy rice. The *Ptr* gene, previously named as *Pi-ta2* in rice, encodes a protein with 4 armadillo repeats conferring a broad spectrum of resistance except for blast race IB33 [79]. Race IB33 is one of the most virulent blast races identified on the plant in our laboratory but not found in commercial fields. Sequence analysis of the *Ptr* allele from weedy rice, PtrBHA, identified a unique amino acid, glutamine (Gln) at protein position 874. This amino acid is absent in susceptible individuals. Minor changes in protein conformation of PtrBHA are predicted to create novel resistance to race IB33. Using genotyping by sequencing (GBS), a total of 28 resistance QTLs were identified in two US weedy rice ecotypes[80]. These resistance QTLs, some with large effects and others with small effects, suggest that US weedy rice has adapted to blast disease using both major *R* genes and QTLs. These *R* genes have not been found in cultivated rice varieties suggesting that they are newly evolved *R* genes. In another study, sheath blight resistance QTLs were identified using two recombinant inbred line mapping populations derived from crosses of an indica crop variety, Dee-Geo-Woo-Gen (DGWG), with progeny representing straw hull (SH) and black hull awned (BHA) [81]. A total of nine QTLs were identified, five of which were attributable to alleles for plant height and days to heading. Four sheath blight resistance QTLs were identified by treating these growth traits as covariates. Two of these QTLs, *qShB1-2* and *qShB4*, are new that were not identified in the study by Yan et. al [81]. *Pi-ta* is another effective *R* gene deployed to control rice blast disease in many rice growing regions of the world. Weedy rice genotypes containing the resistant *Pi-ta* allele showed a high level of resistance to two predominant US blast races, IB49 and IC17. The *Pi-ta* gene on rice chromosome 12 encodes a predicted nucleotide binding site and leucine rich domain which directly interacts with the product of *M. oryzae* avirulence gene *AVR-Pita1* during resistant responses [83–84]. The genome organization of the *Pi-ta* gene in weedy rice was investigated in a few studies to determine if gene flow between cultivated and weedy rice had occurred in the USA[82] The resistant *Pi-ta* allele was found in most of the investigated US weedy rice genotypes. The genomic region with the *Pi-ta* allele in US weedy rice was found to be very similar to that of cultivated rice [82]. The flanking sequences of the *Pi-ta* gene and SSR marker analysis revealed that the susceptible *pi-ta* allele and the non-resistant *Pi-ta* allele had been introgressed from

US cultivated rice to weedy rice through gene flow. This may be because the *Pi-ta* gene has not been widely deployed in the USA. In conclusion, these findings on rice blast and sheath blast diseases demonstrate that novel *R* genes from weedy rice can be used in combination with favorable growth traits to develop rice germplasm that are resistant to rice blast and sheath blast.

5. Conclusions and prospects

Weedy rice is one of the most damaging weeds for rice production. In this review, we summarized research on seed shattering, photoperiod sensitivity, flowering, and resistant to two major diseases Understanding genetic and molecular bases of these unique adaptive and competitive advantages for growth and disease resistance can be very useful in designing weed management strategies and breeding improved rice varieties under changing environments and production systems.

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