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Genetics and phylogenetics of rice domestication

Tao Sang¹ and Song Ge²

With genetically divergent cultivars and ecologically distinct wild progenitors, rice has posed a great challenge to the genetic and phylogenetic studies of the origin and evolution of crop species. A growing body of phylogenetic evidence suggested that the diverged genomic backgrounds of *indica* and *japonica* rice cultivars were derived independently from genetically distinct wild populations. However, a domestication gene, *sh4*, which was responsible for the reduction of grain shattering, seems to have originated only once, and it is now fixed in both cultivars. Two models have been proposed to reconcile these data. Whereas the 'combination model' emphasizes the importance of early introgression between independently domesticated cultivars, the 'snowballing model' emphasizes the importance of introgression from local populations of wild species into an ancestral domesticated population. In either case, the domestication of rice was a dynamic process.

Addresses

¹ Department of Plant Biology, Michigan State University, East Lansing, MI 48824, USA

² State Key Laboratory of Systematic and Evolutionary Botany, Institute of Botany, Chinese Academy of Sciences, Beijing 100093, China

Corresponding author: Sang, Tao (sang@msu.edu)

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Introduction

Rice (*Oryza sativa*) was domesticated approximately 10 000 years ago [1] and now provides staple food for half of the world's population. As a diploid crop with a relatively small genome, rice holds a great potential for understanding the genetic mechanisms of crop domestication and improvement. The completion of rice genome sequencing [2–4] has considerably accelerated the study of the history and process of rice domestication.

Unlike other major food crops such as maize and wheat, rice did not undergo drastic morphological modifications or genome duplications during domestication. There has been continuous gene flow between rice and its wild progenitors [5], which makes it challenging to trace the

origin of cultivated rice. Additionally, rice has two genetically divergent cultivars, *indica* and *japonica*, and ecologically distinct wild progenitors, *Oryza nivara* and *Oryza rufipogon* [6,7]. This diversity has spurred a long-standing debate over the origins of cultivated rice. Distinct cultivars were either independently domesticated or differentiated following a single domestication. In either case, there is no consensus on which wild species served as the direct progenitor of cultivated rice.

Only recently have phylogenetic studies with increased taxonomic sampling and genomic markers come together with population and molecular genetic analyses to reveal the dynamic process of rice domestication. The primary objectives of this paper are to review recent advances in the genetics and phylogenetics of rice domestication, and discuss major challenges for unraveling the complex evolutionary history of cultivated rice.

Wild progenitors

Molecular phylogenetic studies have confirmed that the closest wild relatives of cultivated rice were *O. nivara* and *O. rufipogon*, which are distributed from southeastern Asia to India. The two wild species are ecologically distinct. *O. nivara* is annual, photoperiod insensitive, self-fertilized, and adapted to seasonally dry habitats, whereas *O. rufipogon* is perennial, photoperiod sensitive, largely cross-fertilized, and adapted to persistently wet habitats [6]. *O. nivara* evolved from an *O. rufipogon*-like ancestor as a result of habitat shift ([8], Grillo *et al.* unpublished).

The identity of the species that served as the direct progenitor of cultivated rice remains controversial. The hypothesis of rice domestication from *O. nivara* was based on the phenotypic similarity between *O. nivara* and *O. sativa*, including an annual life history, self-fertilization, and high reproductive allocation [6–8]. Proponents of the hypothesis that *O. rufipogon* is the ancestor of cultivated rice emphasize the benefit of higher genetic diversity of an outcrossing progenitor [9].

Despite a growing number of phylogenetic analyses of cultivated rice with both wild species, researchers have been unable to unequivocally resolve the relationships among *O. sativa*, *O. nivara*, and *O. rufipogon*. Phylogenies based on a variety of molecular markers have been unable to place *O. nivara* and *O. rufipogon* accessions into well-supported monophyletic groups, or show a closer relationship of cultivated rice with one of the wild species [10–14,15**]. This lack of resolution may be a consequence of recent divergence between *O. nivara* and *O. rufipogon* and/or gene flow between the species.

Taxonomic inconsistency poses another problem to the phylogenetic analyses. While *O. nivara* was accepted as a separate species in the recent classification of *Oryza* [16,17], the argument of whether it should be treated as an ecotype or subspecies of *O. rufipogon* has continued [15^{••},18]. As a result, species names have been inconsistently assigned to the annual plants. A greater effort to correctly identify and distinguish these two ecologically distinct taxa should help better characterizing the wild progenitor of rice.

Domestication transitions

Regardless of which wild species was the direct wild progenitor, a basic set of morphological and physiological transitions known as the domestication syndrome must have occurred during rice domestication [19,20]. These included reduction in grain shattering and seed dormancy, synchronization of seed maturation, reduction in tiller number, increase in tiller erectness, increase in panicle length and branches, and reduction in coloration and awn length [21–25,26^{••}]. If rice was domesticated from *O. rufipogon* rather than from *O. nivara*, additional phenotypic changes involved in the switch from outcrossing to selfing mating systems and from perennial to annual habits would have had occurred.

When an *indica* cultivar was crossed with *O. nivara*, no segregation of the mating system or life history traits was observed in the F₂ population [26^{••}]. There were two explanations for this result. First, *indica* rice may have been domesticated from *O. nivara* so that their phenotypic similarity was genetically based. Alternatively, *indica* rice may have been domesticated from *O. rufipogon*, but the genes responsible for the independent origins of annual habit and self-fertilization in *O. nivara* and *O. sativa* were the same. This would imply that natural selection for annual life history and self-fertilization in the wild *O. nivara* and artificial selection for these traits in domesticated rice acted on the same gene targets. It is more parsimonious to consider the origin of *indica* rice from *O. nivara*.

While *O. nivara* could have been the primary genome donor for *indica*, it cannot be the sole genome donor for all rice cultivars. Cultivars with relatively strong photoperiod sensitivity and ability to grow in deep water conditions might have acquired *O. rufipogon* genes through introgression or independent domestication. Moreover, the comparison of *indica* and *japonica* genome sequences identified highly divergent linkage blocks, suggesting that more distantly related wild species might have also contributed to the domesticated rice gene pool through introgression probably assisted by breeders [27[•],28].

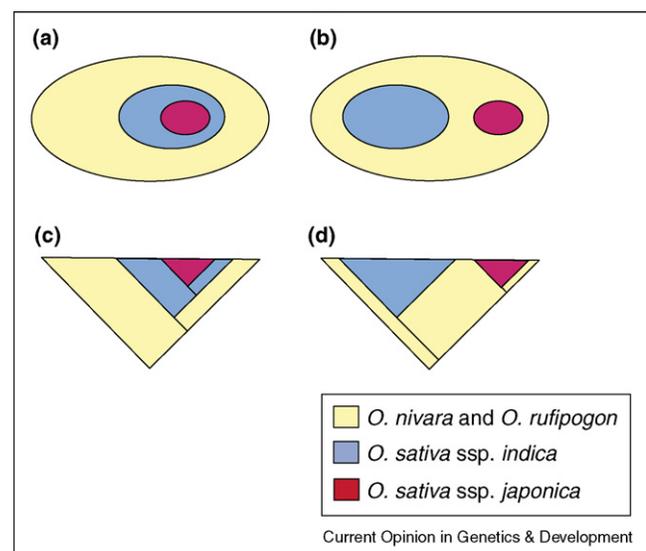
Rice cultivars

Two major types of rice cultivars have been recognized, namely *O. sativa* subspecies *indica* and subspecies

japonica. They are phenotypically and ecologically divergent and partially isolated by a postzygotic barrier [7,9]. The *japonica* rice can be grown in colder and drier environments at a higher altitude or latitude. Genetic substructures were further identified within each type of cultivar, including the division of *indica* into *aus* and *indica* subgroups and the division of *japonica* into *temperate japonica*, *tropical japonica*, and *aromatic* subgroups [29]. It was recently estimated that cultivated rice maintained less than 25% of the genetic diversity found in the wild progenitors, indicating a severe genetic bottleneck during domestication [15^{••}]. Additionally, *indica* has twice as much of genetic diversity as *japonica*, suggesting that the former had a larger founding population and/or went through a less severe bottleneck.

There have been two competing hypotheses regarding the origin of the rice cultivars, that is, independent domestication of *indica* and *japonica* versus the origin of *japonica* within *indica* [9,10] (Figure 1a and b). We would expect phylogenetic analyses to show *japonica* nested within *indica* if rice was domesticated just once (Figure 1c). By contrast, *indica* and *japonica* should form separate clades in a rice phylogeny if they were independently domesticated (Figure 1d). Recent molecular phylogenetic studies overwhelmingly supported the hypothesis of independent domestication of *indica* and *japonica* rice. They showed that *indica* and *japonica* fall into separate clades, each usually containing some accessions of the wild species

Figure 1



Schematic illustration of hypotheses and phylogenetics of rice domestication. (a) Hypothesis of the single origin of cultivated rice. *Oryza sativa* ssp. *indica* was domesticated from the wild species, and *O. sativa* ssp. *japonica* was derived within *indica*. (b) Hypothesis of independent domestication of *indica* and *japonica* rice. The larger size of ellipse representing *indica* indicates a higher genetic diversity of the cultivar in comparison with *japonica*. (c) Phylogeny supporting a single origin. (d) Phylogeny supporting independent domestication.

[12–14,30,31]. The *indica* rice was more often found intermixed with wild accessions, which is probably a result of deeper coalescence due to a larger founding population and/or a less severe genetic bottleneck.

Molecular dating of divergence time estimated that the genomes of *indica* and *japonica* have diverged for 0.2–0.4 million years [13,32,33], which considerably predates the time of rice domestication. The finding further supports the hypothesis that the genomes of *indica* and *japonica* rice were derived from those of wild populations that were already diverged at the time of rice domestication. A phylogeographic study suggested that *indica* was domesticated within a region south of the Himalayan mountain range including eastern India, Myanmar, and Thailand, whereas *japonica* was originated from southern China [34*].

Domestication genes

Recent molecular genetic dissection of important domestication traits provided new lines of evidence for rice domestication. This includes the cloning of two QTL, *sh4* and *qSH1*, for the reduction of grain shattering that was essential for effective field harvest. The functional mutation of *sh4* was confirmed to be a single nucleotide substitution in the first exon of a gene with a previously unknown function, which led to an amino acid substitution from lysine to asparagine in the predicted Myb3 DNA-binding domain [35**]. The nuclear localization of the *sh4* protein suggests that it is a transcription factor, and the single amino acid substitution observed in *sh4* could be a *trans*-regulatory mutation. The mutation causes incomplete development and partial function of the abscission zone between a grain and its pedicle. Consequently, this prevented easy shattering but still allowed manual separation of grains from pedicles, a part of rice harvest process known as threshing.

A survey of all five recognized subdivisions of cultivated rice revealed that all cultivars invariably carried the same functional mutation [35**,36]. When sequences of ~50 kb region surrounding *sh4* were compared between an *indica* variety (Guangluai 4) and a *japonica* variety (Nipponbare) with genome sequences, the average SNP density was 0.38 per kb. For the entire chromosome 4, the average SNP density was found to be 3.5 per kb between the two varieties ([37], B Han, pers. comm.). The nearly 10-fold reduction of sequence polymorphism surrounding the *sh4* locus indicates a strong selective sweep. Taken together, the evidence suggests that the non-shattering *sh4* allele, which is fixed in all rice cultivars surveyed so far, had a single origin.

Grains of *indica* are generally easier to thresh than those of *japonica*. *qSH1* was a major QTL accounting for the shattering difference between *indica* and *japonica* cultivars. A functional SNP was identified ~12 kb upstream of

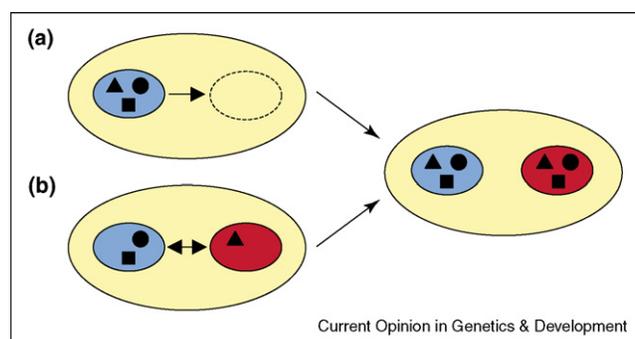
a homeobox gene homologous to replumless (RPL) that was involved in fruit dehiscence in *Arabidopsis* [38**]. The mutation eliminated or substantially reduced the expression of the gene and prevented abscission zone development in rice. This *cis*-regulatory mutation was found in the *temperate japonica* cultivar and was suggested to have been selected during the domestication of *japonica* rice [38**].

Two additional domestication-related genes, *Rc* and *Waxy*, responsible for the origins of white-grained and sticky rice, respectively, were also identified in the *japonica* varieties [39,40*,41**]. At the *Rc* locus, a 14-bp deletion in exon 6 of the gene knocked out its function as a potential regulator of anthocyanin biosynthesis that produces red color in rice pericarps. For *Waxy*, a nucleotide substitution at the 5' splice site of the first intron affected the function of the gene that encodes a granule-bound starch synthase. This led to the reduction of the amount of amylase in the endosperm and consequently the increase in grain stickiness when cooked.

Models for rice domestication and implications

The single origin of *sh4* implies that cultivated rice could also have originated only once. This contradicts the phylogenetic evidence for the independent domestication of *indica* and *japonica* cultivars. Two models were proposed to reconcile the apparently conflicting data [42*]. The snowballing model considers the single origin of cultivated rice (Figure 2a). In this model, the earliest cultivar fixed a combination of critical domestication alleles including *sh4*. When it was introduced to other regions of Asia, introgression occurred between the cultivar and local populations of *O. nivara* and *O. rufipogon*. The modern cultivars, *indica* and *japonica*, were derived from the hybrids between this early cultivar and genetically divergent wild populations. The core of the domestication alleles, once fixed in the founding cultivar, acted to facilitate cultivar diversification while it rolled through the wild gene pool.

Figure 2



Models for rice domestication. (a) Snowballing model. (b) Combination model. Shapes (triangle, square, and circle) inside of cultivated rice represent important domestication genes fixed in all cultivars.

The combination model considers multiple origins of cultivated rice (Figure 2b). In this model, rice domestication started from divergent wild populations. Rice was considered to be domesticated as long as it had fixed enough mutations that made cultivation worthwhile for the early farmers. For example, cultivars could be more resistant to shattering but produce a smaller number of grains per panicle and vice versa. Subsequent crosses among these semi-domesticated cultivars allowed farmers to select a combination of critical domestication alleles. The selection was so strong on domestication alleles, such as *sh4*, that they became quickly fixed in all cultivars.

Regardless of which model is correct, the fixation of common domestication alleles in the divergent genomes of cultivars could have been driven by a combined force of artificial and natural selections. Domestication alleles are under strong human selection, while most of the domesticated genome is under selection of environmental conditions to which the wild progenitor was adapted. Crosses among cultivars and between cultivars and wild relatives followed by artificial and natural selections provide opportunities for developing cultivars with a better combination of domestication traits and are more suitable for growing in new environments. The accumulation of excessive deleterious mutations in rice cultivars may be another signature of the interplay between artificial and natural selections on the self-fertilized crop [43].

Domestication genes that are fixed only in subset of rice cultivars, such as *qSH1*, *Rc*, and *Waxy*, might have been more recently derived, under weaker selection, or selected only in those cultivars. The universally fixed domestication genes define the essential difference between the cultivated and wild species, and the partially fixed genes account for the diversity observed among cultivars. Selection for new mutations and the change of frequencies of existing domestication alleles will continue to shape domestic organisms.

Challenges and prospects

Gene flow between rice cultivars and wild relatives coupled with taxonomic inconsistency poses a major challenge to trace the origin of cultivated rice through molecular phylogenetics. Introgression from cultivated rice to its wild progenitors has created an array of phenotypic intermediates known as weedy rice [22,44]. Although weedy rice is classified as a subspecies of cultivated rice, namely *O. sativa* ssp. *spontanae* or ssp. *fatua*, it has also been practically recognized as wild species, *O. rufipogon* or *O. nivara* [10,35^{••}]. No matter whether weedy accessions are named as cultivated or wild species, the mixed nature of their genomes yields misleading results in the phylogenetic analyses.

Phylogenetic reconstruction of recent speciation events, particularly in association with domestication, requires

extensive sampling of cultivated and wild accessions and utility of a large number of fast evolving molecular markers such as microsatellites [45,46]. This kind of analysis is the next logical step to further narrow down the geographic locations of rice domestication. Nevertheless, the increase in taxonomic and genomic sampling alone will not solve the problems caused by weedy accessions that are not correctly identified in the germplasm collections. This could be a common problem for crops that are morphologically similar and reproductively interfertile with wild progenitors. It would be helpful to grow and voucher sampled accessions in order to verify their taxonomic identification. Further, weedy rice should be excluded from phylogenetic analyses aimed at elucidating the domestication process.

With regard to domestication genes, it will be interesting to identify additional genes like *sh4* that were responsible for major domestication transitions and have been fixed in all rice cultivars. Cloning of these genes will help test the models of rice domestication. If the origins of the genes are traced back to the same or closely related wild populations in a geographic location, the snowballing model is supported. If the origins of the genes were derived from divergent wild populations at different geographic localities, the combination model is supported.

Although a relatively small number of domestication genes have been cloned so far, they have already yielded many novel insights into plant domestication [47]. With rapid technical advances in genetic mapping and genome analysis [48,49], the functional and population genetic studies of domestication genes will play an increasingly important role in our understanding of the history and genetic mechanisms of plant and animal domestication. This will in turn enable a more effective utilization of natural resources for cultivar improvement and new domestications, such as the domestication of energy crops [50], to meet the future needs of our society.

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