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REVIEW

Harnessing neo-domestication of wild pigmented rice for enhanced nutrition and sustainable agriculture

Ray Singh Rathore[1] · **Wenjun Jiang**[1] · **Khalid Sedeek**[1] · **Magdy Mahfouz**[1]

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Abstract

Advances in precision gene editing have enabled the rapid domestication of wild crop relatives, a process known as neo-domestication. During domestication, breeding rice for maximum productivity under optimal growth conditions reduced genetic diversity, eliminating variants for stress tolerance and grain nutrients. Wild rice varieties have rich genetic diversity, including variants for disease resistance, stress tolerance, and grain nutritional quality. For example, the grain of pigmented wild rice has abundant antioxidants (anthocyanins, proanthocyanidins, and flavonoids), but low yield, poor plant architecture, and long life cycle limit its cultivation. In this review, we address the neo-domestication of wild pigmented rice, focusing on recent progress, CRISPR-Cas editing toolboxes, selection of key candidate genes for domestication, identifying species with superior potential via generating genomic and multi-omics resources, efficient crop transformation methods and highlight strategies for the promotion and application pigmented rice. We also address critical outstanding questions and potential solutions to enable efficient neo-domestication of wild pigmented rice and thus enhance food security and nutrition.

Introduction

Approximately 10,000–12,000 years ago, our ancestors shifted from hunting and gathering to farming, fundamentally transforming food acquisition. Early farmers selected and altered many wild plant species, resulting in domesticated cultivars tailored to their needs. This process, known as domestication syndrome, led to crops with larger grains, higher yields, more upright growth, non-shattering seeds, increased apical dominance, coordinated flowering, and loss of seed dormancy (Doebley 2006; Gross and Olsen 2010). Comprehensive demographic analysis indicates that domestication has occurred in approximately 2,500 species, with only 250 species undergoing extensive trait domestication (Meyer and Purugganan 2013). Among these, major staple crops like rice (*Oryza sativa*), maize (*Zea mays*), and wheat (*Triticum aestivum*) exhibit the highest productivity and cultivation areas globally (Jeyasri et al. 2021; Nutan et al. 2020).

Rice is the primary food source for more than half of the global population, sustaining both affluent and impoverished communities (Song et al. 2025). The domestication of rice occurred independently in Asia and Africa (Meyer et al. 2016; Wing et al. 2018). Asian-cultivated rice (*O. sativa*) was domesticated from *O. rufipogon* in Asia around 9,000 years ago, resulting in two subspecies: *O. sativa* ssp. *japonica* and ssp. *indica* (Chen et al. 2019a; Gross and Zhao 2014). African-cultivated rice (*O. glaberrima*) was domesticated from *O. barthii* in West Africa approximately 3,000 years ago (Meyer and Purugganan 2013). Extensive domestication in diverse geographical regions has produced rice varieties with distinct plant characteristics, grain qualities, and cultivation patterns (Meyer and Purugganan 2013). However, rice domestication has primarily focused on productivity and grain quality, often compromising beneficial traits related to nutrition, biotic and abiotic stress tolerance (Fig. 1a). Additionally, domesticated rice requires high inputs of water, fertilizer, and agrochemicals. With the global population projected to reach 10 billion by 2050, developing crops with enhanced nutritional value and increased tolerance to biotic and abiotic stress is crucial for food security (Acosta-Motos et al. 2024). This necessitates a significant boost in crop productivity to meet future

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✉ Magdy Mahfouz
magdy.mahfouz@kaust.edu.sa

[1] Laboratory for Genome Engineering and Synthetic Biology, Division of Biological Sciences, King Abdullah University of Science and Technology (KAUST), Thuwal, Saudi Arabia

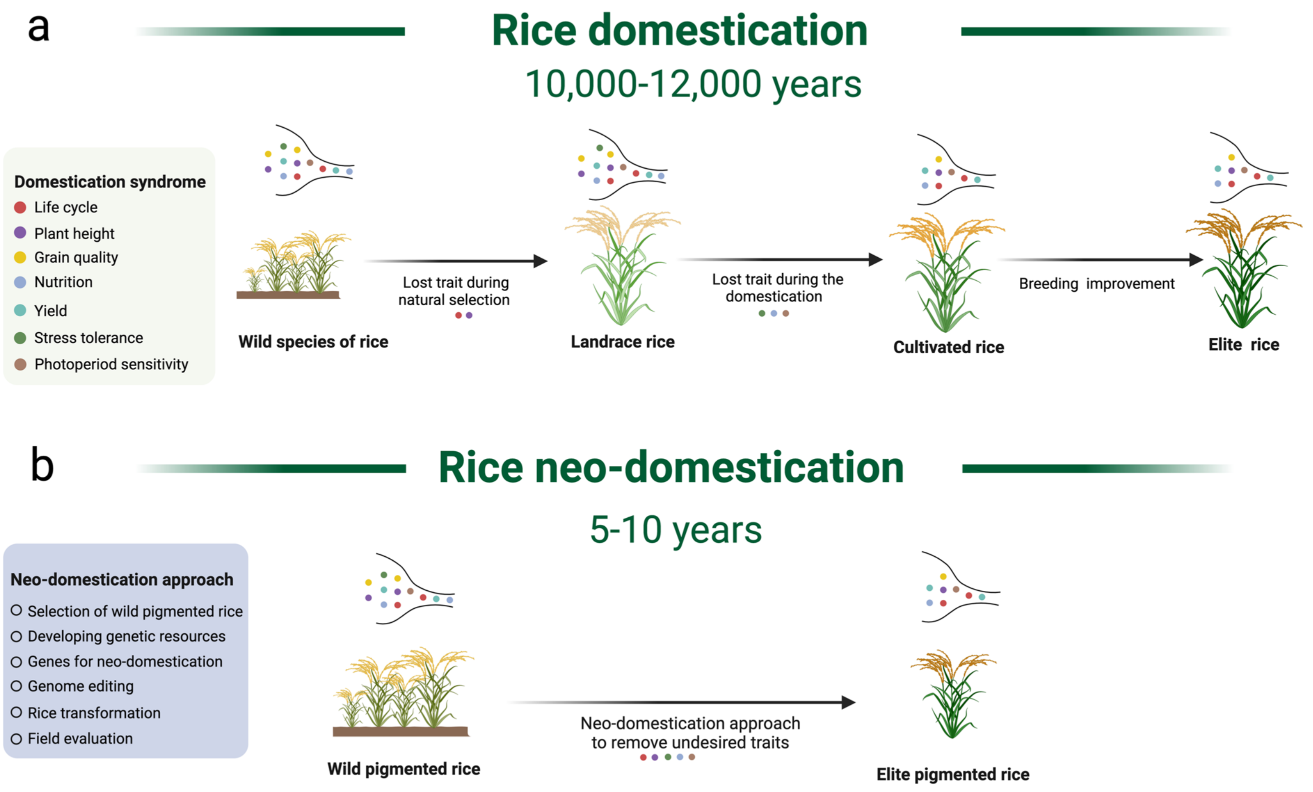


Fig. 1 Strategies for traditional and neo-domestication approaches for the domestication of wild vs. pigmented rice. **a** Representation of the domestication process and subsequent loss of genetic variation. This illustration depicts the domestication process, highlighting the gradual loss of useful genetic variation that has resulted from selective breeding and the selection of a limited number of alleles. Over time, as humans have selected specific desirable traits such as increased yield or uniformity, the genetic diversity in cultivated rice populations has decreased, leading to a reduction in the pool of available alleles. **b** Neo-domestication approaches for wild pigmented rice. This illustration depicts the proposed and currently practiced neo-domestication approaches for wild pigmented rice, aimed at addressing future agricultural challenges. These approaches focus on expediting the selection and domestication of elite pigmented rice varieties, while retaining genetic diversity and the associated elite traits. By leveraging advanced breeding techniques and genomic tools, these neo-domestication strategies offer promising avenues for developing improved pigmented rice varieties capable of both meeting evolving agricultural needs and preserving genetic diversity

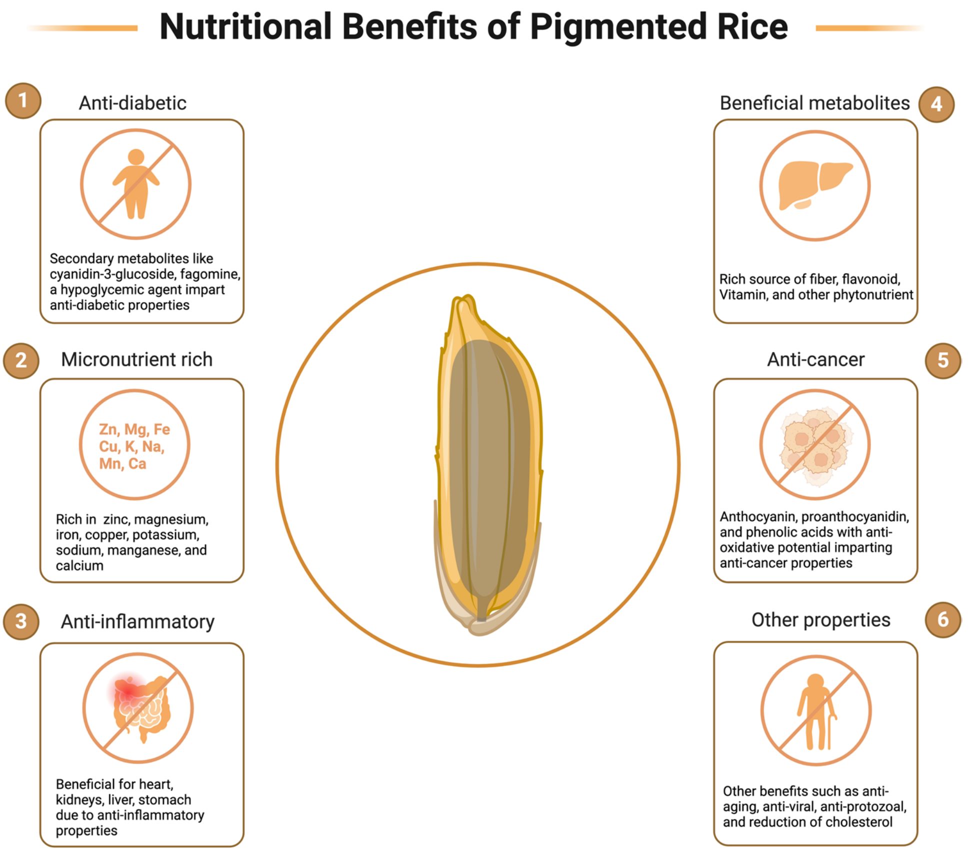
demands. Looking toward wild rice, particularly pigmented varieties, are nutritious and adapted to various climatic conditions, making them a potential solution for nutrition and food security in sustainable agriculture.

Pigmented rice varieties, such as black, red, and brown rice, have a rich history of cultivation and consumption, traditionally black rice is reserved for Chinese royalty and is often referred to as "forbidden rice" or "imperial rice" (Oikawa et al. 2015). These varieties are now gaining attention for their potential to improve human health and enhance food security due to their superior nutritional profiles compared to white rice (Sedeek et al. 2023). Pigmented rice exhibits potent antioxidant properties owing to its high content of anthocyanins and proanthocyanidins that help reduce oxidative stress and inflammation, which are linked to chronic diseases such as cardiovascular diseases, diabetes, and certain cancers (Table 1) (Avinash et al. 2024; Laokuldilok et al. 2011). Anthocyanins, responsible for the red, purple, and blue hues, exhibit significant antioxidant activity, neutralizing free radicals, reducing oxidative stress, and lowering the risk of chronic diseases (Avinash et al. 2024; Laokuldilok et al. 2011). Their anti-inflammatory properties aid in mitigating chronic inflammation, a key factor in conditions like arthritis and cardiovascular diseases (Fig. 2) (Callcott et al. 2019; Pomilio et al. 2024). Additionally, anthocyanins enhance endothelial function, reduce blood pressure, prevent platelet aggregation, and potentially protect against neurodegenerative diseases like Alzheimer's and Parkinson's (Sivasinprasasn et al. 2024; Yadav and Appukuttan 2019). Proanthocyanidins protect cells from oxidative damage, support cardiovascular health by improving blood vessel function, lowering blood pressure, and reducing LDL cholesterol levels (Qi et al. 2023; Sivasinprasasn et al. 2024). Their anti-inflammatory and anticancer activities enhance their health benefits, contributing to the management of conditions like arthritis and the inhibition of cancer cell growth and tumor spread (Fig. 2) (Qi et al. 2023; Sivasinprasasn et al. 2024; Yadav and Appukuttan 2019). Black rice

Table 1 Comparison of the average metabolite abundance among pigmented rice varieties

Nutrient component (Average relative abundance)	Pigmented rice			Human health benefits
	Black (n = 24)	Red (n = 35)	Brown (n = 4)	
Carbohydrates	3.446	1.815	1.276	The main body energy source
Amino acid	1.468	1.158	1.456	Synthesis of body protein and hormones, essential in cell repair and growth
Secondary metabolites	6.642	0.957	0.663	Antioxidant and anti-inflammatory properties, modulate the body health, and maintaining biological processes
Lipids	2.550	0.974	2.206	Energy storage, cell membrane building, and integrity
Cofactors	1.441	1.492	1.206	Crucial for enzyme activities in metabolic pathways
Hormones	1.276	1.256	1.562	Regulate body functions
Flavonoids	12.259	0.904	0.569	Antioxidant properties, and reduces risk of chronic diseases
Peptides	1.906	0.692	0.769	Needed for muscle growth and repair, and slow down the aging process
Anthocyanin	177.998	0.410	0.058	Antioxidant properties, and reduces risk of chronic diseases
Proanthocyanidins	1.527	4.437	0.336	Antioxidant properties that protect the heart and cardiovascular system
Terpenoids	2.501	1.114	0.827	Have anticancer, antimicrobial, anti-inflammatory, antioxidant, and antiallergic properties
Vitamin B1	1.771	0.804	2.876	Needed for skin, hair, muscles, and brain health, essential for nerve function
Vitamin B2	1.911	0.866	0.563	Support various cellular functions, body growth and development
Vitamin B6	6.199	5.169	4.355	Helps make red blood cells, and improve immune function
Vitamin C	1.053	0.963	1.019	Antioxidant properties and lower the risk for some cancers
Vitamin E	5.254	5.098	4.748	Antioxidant properties, and protects vitamin A and certain lipids from damage

Pigmented rice measurements were taken from Sedeek et al. (2023)



Secondary metabolites like cyanidin-3-glucoside, fagomine, a hypoglycemic agent impart anti-diabetic properties

Rich in zinc, magnesium, iron, copper, potassium, sodium, manganese, and calcium

Beneficial for heart, kidneys, liver, stomach due to anti-inflammatory properties

Rich source of fiber, flavonoid, Vitamin, and other phytonutrient

Anthocyanin, proanthocyanidin, and phenolic acids with anti-oxidative potential imparting anti-cancer properties

Other benefits such as anti-aging, anti-viral, anti-protozoal, and reduction of cholesterol

Fig. 2 The importance of pigmented rice in providing a variety of nutraceutical benefits for human health. The importance of pigmented rice varieties lies in their diverse range of health benefits, disease resistance, and abiotic stress tolerances. These rice varieties contain natural compounds that have been proven to positively impact cardiovascular health, regulate blood sugar levels, boost the immune system, and provide antioxidant protection. They also possess anti-inflammatory properties and are rich in essential nutrients contains higher levels of vitamins, fiber, and iron compared to non-pigmented counterparts, supporting immune function and digestive health (Tables 1 and 2) (Sedeek et al. 2023; Tiozon et al. 2023a). Red rice consumption has been associated with reduced cholesterol levels and better cardiovascular health due to monacolin K, a naturally occurring statin. The high fiber content in pigmented rice varieties aids in glycemic control and contains the antidiabetic compound fagomine, making them beneficial for individuals with diabetes (Sedeek et al. 2023; Zhao et al. 2024).

Pigmented rice is also a major source of amino acids, secondary metabolites, lipids, cofactors, hormones, flavonoids, phenylpropanoids, terpenoids, and vitamins like B1, B2, B6, C, and E that play crucial roles in maintaining human health and preventing various diseases (Table 1). Amino acids support muscle growth, immune function, and overall metabolism (Laokuldilok et al. 2011). Secondary metabolites, including flavonoids, phenylpropanoids, and terpenoids, act as antioxidants, anti-inflammatory agents, and antimicrobial compounds, preventing chronic diseases such as cancer, heart disease, and neurodegenerative disorders (Laokuldilok et al. 2011; Qi et al. 2023; Sivasinprasasn et al. 2024). Phytosterols in pigmented rice inhibit cholesterol absorption and regulate undesirable lipoprotein levels. Carotenoids like lutein and zeaxanthin, predominantly found in the bran, contribute to reducing cholesterol levels and protecting eye health (Mbanjo et al. 2020; Melini et al. 2019). Lipids support brain function, reduce inflammation, and improve heart health (Deng et al. 2013). Cofactors, including vitamins and minerals, are necessary for enzyme function and metabolic processes, enhancing metabolic efficiency, supporting energy production, and promoting overall health (Tiozon et al. 2023a). Vitamins such as B1, B2, B6, C, and E are essential for various bodily functions, including metabolism, skin, eye health, brain function, immune support, and protection against oxidative stress (Mbanjo et al. 2020; Melini et al. 2019). Pigmented rice varieties also contain an abundance of metal ions, such as potassium, sodium, calcium, iron, zinc, manganese, magnesium, copper, cobalt, selenium, chromium, silver, and molybdenum, contributing to their nutritional value and health benefits (Table 2). These elements and secondary metabolites play vital roles in improving human health by acting as antitumor, cholesterol-lowering, immunosuppressant, antiprotozoal, anthelmintic, antiviral, and anti-aging agents (Vaishnav and Demain 2011) (Fig. 2). The rich nutrient profile of pigmented rice contributes to its numerous health benefits.

In terms of food security, pigmented rice is often more resilient to environmental stresses, both biotic and abiotic, reducing the risk of crop failure and ensuring a stable food supply. Moreover, wild pigmented rice, with its distinctive agronomic traits and specific farming practices, offers numerous advantages for farmers compared to cultivated white rice (Table 3). However, it also exhibits negative traits such as a long life cycle, low yield, and higher plant height, which make it more prone to lodging (Sedeek et al. 2024, 2023) (Table 3). Addressing these negative traits is crucial for the successful integration of pigmented rice into mainstream agriculture. The neo-domestication approach, leveraging advancements in biotechnology like precise genome

Table 2 Metal ion profiling of the pigmented rice

Metal ion content	Pigmented rice			Human health significance
	Black (n = 24) μg/g	Red (n = 35).μg/g	Brown (n = 4) μg/g	
Potassium (K)	5573	5438	5296	Maintain fluid and electrolyte balance, and supports cardiovascular health
Sodium (Na)	98.9	107.7	71.4	Maintain fluid and electrolyte balance, supports nerve and cognitive function
Calcium (Ca)	235	237	260	Bone health, muscle contraction, and osteoporosis prevention
Iron (Fe)	47.3	29.2	30.1	Hemoglobin formation and prevents anemia
Zinc (Zn)	46.2	50.8	50.9	Essential for growth and recovery, and immune system function
Manganese (Mn)	67.0	48.2	35.7	Brian function, energy metabolism, protein synthesis, and Improve heart health
Magnesium (Mg)	2203	2365	2266	Muscle activity, protein, fat, and carbohydrate metabolism
Copper (Cu)	8.5	8.0	12.0	Electron carrier, and supports immune and brain function
Cobalt (Co)	0.117	0.140	0.025	Part of vitamin B12 and essential for cell function and nervous system
Selenium (Se)	0.208	0.430	0.000	Antioxidant, reduces inflammation, and enhances immunity
Chromium (Cr)	3.070	1.384	0.764	Carbohydrate metabolism, and controlling glucose level
Silver (Ag)	0.009	0.006	0.003	Antimicrobial properties
Molybdenum (Mo)	2.823	2.176	4.246	a key component of several important enzymes, and support the respiratory system

Pigmented rice measurements were taken from Sedeek et al. (2023)

Table 3 Agronomic trait comparison between cultivated white rice and wild pigmented rice

Agronomic trait	Cultivated white rice	Wild Pigmented Rice
Growth Conditions	Optimal in warm, temperate climates	Adaptable to diverse climates, often found in harsher environments
Soil Requirements	Prefers well-drained, fertile soils	Tolerant of various soil types, often grows in less fertile soils
Water Requirements	Requires consistent, abundant water	Require less or frequent irrigation
Plant Height	Typically 80–120 cm	Variable, shorter or highly tall
Maturity Period	90–150 days	120–180 days, varies with environment
Yield	High yield, often 4–8 tons/ha	Lower yield, generally 1–4 tons/ha
Pest and Disease Resistance	Moderate resistance to common pests	High resistance to pests and diseases
Nutrient Requirements	Standard nutrient requirements	Low nutrient requirements, can grow in poor soils
Harvesting Method	Mechanized and efficient	Often harvested manually due to uneven growth
Post-Harvest Processing	Standard milling processes	Traditional or manual milling, often more labor-intensive
Climate Adaptability	Limited to specific climate ranges	Highly adaptable, can grow in a range of climates
Environmental Impact	Moderate, depends on agricultural practices	Generally lower due to traditional farming methods
Sustainability	Dependent on modern agricultural practices	Often cultivated using traditional, sustainable practices

editing with CRISPR/Cas9, offers solutions by incorporating desirable traits while eliminating or minimizing undesirable characteristics in rice. These advanced tools can rapidly transform wild pigmented rice into commercially viable cultivars with enhanced agronomic and nutritional traits (Fig. 1b) (Anilkumar et al. 2022; Varshney et al. 2021). In addition, genetic diversity within pigmented rice cultivars offers significant potential for breeding programs aimed at developing new varieties with enhanced nutritional qualities and greater adaptability to changing climatic conditions. However, transferring beneficial traits from pigmented rice to modern cultivated rice is challenging due to complex genetic interactions and linkage drag (Meyer and Purugganan 2013). This resilience and adaptability make pigmented rice a vital crop for supporting sustainable agricultural practices and contributing to global food security. Additionally, the cultural significance and traditional value of pigmented rice in many regions can drive consumer acceptance and market demand, further promoting its cultivation and consumption. Therefore, focusing on pigmented rice not only addresses nutritional deficiencies and health concerns but also supports agricultural sustainability and food security. Given its role in sustainable agriculture, pigmented rice presents a compelling case for increased focus and research.

This review outlines current progress and presents a comprehensive plan for the neo-domestication of wild pigmented rice. Key questions addressed include: What we learn from domestication, what are the successful examples of CRISPR neo-domestication in crop species, and how can these be applied to wild pigmented rice? What CRISPR-based molecular suites are available for generating various types of genetic edits? Which domestication genes are amenable to CRISPR engineering in wild pigmented rice, and what potential traits can be improved through gene editing? How should appropriate wild-type varieties of pigmented rice be selected based on phenotypic characteristics, nutritional values, and resilience to biotic and abiotic factors? What is the amenability of wild pigmented rice varieties to tissue culture, transformation, and regeneration, and what genomic, metabolomic, and sequencing resources are available or needed? How can making pigmented rice available and affordable in low-income areas provide health benefits and solve local nutritional problems for both producers and consumers? How does the neo-domestication of wild pigmented rice impact human health and food security, and why is a multipronged approach necessary for its successful implementation?

CRISPR breeding and editing toolbox for neo-domestication

Lessons from traditional domestication and milestones in neo-domestication

Throughout history, phenotype-targeted selection has served as the fundamental basis of crop domestication and advancement. At the initiation of domestication, various crops underwent convergent alterations in phenotypic traits associated with the domestication syndrome (Doebley 2006; Meyer and Purugganan 2013; Pickersgill 2018). These significant morphological changes seem to have been primarily caused by a restricted number of large-effect QTLs (Doebley 2006; Lenser and Theissen 2013; Meyer and Purugganan 2013). The identification of genes responsible for domestication in current crops has led to intriguing discoveries concerning the nature of the relevant mutations. Meyer and Purugganan (2013) analyzed 60 characterized domestication genes and found that 28 genes had loss-of-function mutations, such as frameshifts and splicing defects resulting in premature truncations of translated proteins. Additionally, cis-regulatory mutations were found in 15 out of 60 genes, and 10 domestication genes showed either loss-of-function or cis-regulatory mutations. These findings revealed that fundamental aspects of human-oriented crop domestication are focused on loss-of-function mutations or mutations that alter the expression of key genes. Similar studies by Gross and Olsen (2010) and Osterberg et al. (2017) supported this hypothesis. Moreover, a recent study by Chen et al. (2020) revealed that among 17 domestication-related rice QTLs with clear origins, the alleles selected at 11 of the 17 QTLs (65%) are loss-of-function mutations, 4 (23%) are cis-regulatory mutations, and 2 (12%) involve both loss-of-function mutations and cis-regulatory mutations. These reports suggest that loss-of-function mutations have played a more critical role than cis-regulatory mutations in rice domestication.

Building upon these foundational insights, researchers have harnessed domestication knowledge to enhance crop improvement through neo-domestication utilizing CRISPR-based breeding techniques. Two pioneering studies employed CRISPR-Cas tools in wild tomato (*Solanum pimpinellifolium*), to enhance fruit quality and yield while retaining disease resistance and salt tolerance traits (Li et al. 2018; Zsögön et al. 2018). To optimize these plants for high density planting and urban agriculture, key domestication genes associated with compact plant architecture, fruit size, and nutrient content were targeted (Li et al. 2018; Zsögön et al. 2018). These studies involved editing coding sequences, cis-regulatory regions, and upstream open reading frames of genes such as *SELF-PRUNING 5G* (for floral induction), *FASCIATED*, *CLAVATA3*, *WUSCHEL* and *FRUIT WEIGHT 2.2* (for fruit size), *SELF-PRUNING* (for determinate growth habit), *OVATE* (for fruit shape), *MULTIFLORA* (for fruit number), *LYCOPENE BETA CYCLASE* (for lycopene content), and *GDP-L-GALACTOSE PHOSPHORYLASE* (for vitamin C content) (Li et al. 2018; Zsögön et al. 2018). The resulting mutants exhibited improved yield, fruit traits, and plant architecture in a single generation through a single transformation event. Similarly, Rodríguez-Leal et al. (2017) targeted the *CLAVATA-WUSCHEL* signaling pathway in promoter regions and generated lines with varying gene expression levels to enhance fruit size and number. Transformation efficiency varied significantly across genotypes, with success rates ranging from approximately 10–40% in *Agrobacterium*-mediated transformation and often lower in direct protoplast editing approaches due to regeneration challenges. Gene-editing success determined by Sanger sequencing, amplicon deep sequencing, or PCR-RE assays, demonstrated a mutagenesis efficiency of 50–90%, with biallelic or homozygous edits observed at frequencies above 30% in regenerated lines. Notably, off-target effects were minimized through the use of highly specific gRNAs and bioinformatics predictions, but genetic mosaicism in early regenerants posed limitations, requiring multiple cycles of screening to identify stable homozygous edits. Key challenges encountered included low transformation efficiency in certain accessions, unintended phenotypic trade-offs, and genetic compensation effects that influenced the predictability of phenotypic outcomes. Future improvements necessitate optimizing transformation protocols tailored to wild germplasm, refining multiplex editing strategies to achieve precise allelic variations, and integrating novel base editing or prime editing technologies to enhance efficiency and specificity.

In parallel, CRISPR-Cas has been applied to African-cultivated rice (*Oryza glaberrima*), particularly the landrace Kabre, which is known for its environmental stress tolerance but suffers from lower yield and susceptibility to lodging. Targeting domestication loci such as *HIGH TILLER DWARF 1 (HTD1)* for plant height and *GRAIN SIZE (GS3)*, *GRAIN WIDTH (GW2)*, and *GRAIN NUMBER (Gn1a)* for grain quality resulted in considerable improvements in grain yield and reduced lodging (Lacchini et al. 2020). Moreover, targeting *HTD1*, *Gn1a*, *GS3*, and *GW2* via *Agrobacterium*-mediated rice transformation in 13 screened accessions, 61.5% (8/13) regenerated plantlets under optimized hormone conditions with Kabre prioritized for its vigor. Multiplex editing generated 76 T_0 mutants lines with variable editing efficiency, including 3 *gn1a* single, 19 *gs3* single, 38 *gn1a/gs3* double, and 16 *gn1a/gs3/gw2* triple mutants, though *GW2* efficiency was low (6.25% homozygosity) (Lacchini et al. 2020). Expanding this approach to polyploid systems, which offer advantages like genome buffering and environmental resilience, studies in the perennial allotetraploid wild rice *O. alta* (CCDD genome) targeted six domestication-related traits, including seed shattering (*OsqSH1)*, awn length *(OsAN-1)*, plant height *(OsSD1),* seed size *(OsGS3)* and long heading date (*OsDTH7* and *OsGhd7*). Edited lines exhibited reduced shattering, shorter awns, earlier flowering, reduced plant height, and higher yield (Yu et al. 2021). These studies demonstrate a potential path forward for creating stress-resistant rice by combining genomics knowledge of cultivated crops and rapid genetic change via genome editing (Yu et al. 2021). Despite these advances, both studies highlight persistent bottlenecks such as off-target effects, variable transformation and multiplex efficiency, and genetic heterogeneity emphasizing the need for scalable protocols for non-regenerating landraces and field validation to translate CRISPR gains into sustainable agricultural outcomes.

Similarly, orphan crop groundcherry (*Physalis pruinosa*), CRISPR was used to overcome undesirable traits such as sprawling growth habits and small fruits, leading to enhanced fruit density and improved plant architecture (Lemmon et al. 2018). In potato, knocking out the self-incompatibility gene S-RNase allowed the neo-domestication of potato into an inbred-line-based diploid crop, presenting a promising alternative to traditional clonal propagation of tetraploid potato (Ye et al. 2018). Major technical challenges included tissue culture recalcitrance in Physalis, low regeneration rates, unintended pleiotropic effects on plant morphology, and genetic mosaicism in early-generation mutants, necessitating multiple propagation cycles to obtain stable lines. Additionally, in potato, overcoming linkage drag associated with deleterious alleles remained a key limitation, requiring further genomic selection and backcrossing strategies. Future improvements should focus on optimizing regeneration protocols, enhancing multiplex editing for polygenic trait modification, and integrating base or prime editing to minimize off-target effects and maximize precise allele replacement. These studies highlight CRISPR's transformative potential for neo-domestication via precisely targeting for loss of functions or modifying specific gene expression in wild pigmented rice, which enables the rapid development of varieties with enhanced traits, contributing to food security and sustainability.

CRISPR editing toolbox

Genome-editing tools like CRISPR-Cas are invaluable for generating allelic variations in crops mimicking natural genetic diversity and enabling targeted trait improvement (Ahmad et al. 2021; Ali et al. 2020; Butt et al. 2020a; Doudna and Charpentier 2014). These tools use specific nucleases to create double-strand breaks (DSBs) in the DNA at precise genomic locations. These breaks are repaired via homology-directed repair (HDR), which requires a donor template, or through the error-prone non-homologous end-joining (NHEJ) pathway (Sedeek et al. 2019; Zafar et al. 2020). Traditional nucleases like zinc-finger nucleases, transcription activator-like effector nucleases (TALENs), and mega-nucleases have been used in plant gene editing but are limited by their complex protein engineering requirements, reducing their versatility and applicability for gene engineering (Mahfouz and Li 2011). In contrast, CRISPR-Cas has emerged as the leading genome-editing tool due to its simplicity, high efficiency, versatility, and cost-effectiveness. It is capable of targeting a wide range of genomic sites, enabling precise editing with a high degree of accuracy in domesticating wild relatives of crops (Chen et al. 2021a; Fernie and Gutierrez-Marcos 2019; Gasparini et al. 2021; Khan et al. 2019; Zsögön et al. 2018). Furthermore, efficient Cas nucleases like Cas9, Cas12a, Cas12b, and Cas12f, along with advanced CRISPR variants such as base, prime, and twin prime editors, facilitate precise gene insertion, deletion, or base substitution, offering powerful tools for neo-domestication of wild pigmented rice (Fig. 3) (Hua et al. 2019; Veillet et al. 2019).

Utilizing efficient CRISPR-Cas nucleases for trait improvement in wild pigmented rice

CRISPR-Cas9 nuclease is primarily and widely adopted for generating targeted loss-of-function mutations by deleting regulatory regions that suppress desirable traits, thereby improving crop performance (Sedeek et al. 2019). Cas9 mainly generates double-stranded breaks (DSBs) at specific genomic locations having G-rich PAM sequence (NGG) and repaired through non-homologous end joining (NHEJ) pathway (Fig. 3a). Moreover, Cas9 nucleases are a remarkably efficient wide-range of crops traits improvement but having certain limitation such as dependency on G-rich PAM sequences (NGG) and its relatively large size (~4.2 kb) poses challenges for delivery into plant cells (Sedeek et al. 2019). Additionally, while NHEJ efficiently facilitates knockouts, the homologous-directed repair (HDR) pathway, necessary for precise DNA integrations, remains inefficient in plants, restricting its broader applicability in genome editing. The advancement in Class 2 systems Cas12 family of nucleases, such as Cas12a, Cas12b, and Cas12f, address these limitations along with more efficient and flexible genome editing (Fig. 3b). Unlike Cas9 which requires NGG PAM sequences, Cas12a and Cas12b target T-rich PAM sequences, significantly expanding the range of editable genomic sites (Garcia-Doval and Jinek 2017; Tang and Fu 2018) (Fig. 3b). Cas12a generates staggered DSBs, which enhance the efficiency of NHEJ-based knock-in strategies, while its shorter guide RNA (~43 bp) facilitates simpler delivery compared to Cas9's sgRNA (~100 bp) (Moon et al. 2019). Cas12a-mediated genome editing has been successfully utilized in rice and soybean (Xu et al. 2017). Furthermore, Cas12b is smaller in size compared to Cas9 and Cas12a, making it a promising CRISPR system for genome editing in crops. In rice, Cas12b recognizes VTTV PAMs, with a preference for ATTV and GTTG PAMs, additionally, Cas12b has been used in *Arabidopsis thaliana* to induce mutations, including creating large deletions at multiple loci without observed off-target effects (Wu et al. 2020). Unlike Cas12 a and b, Cas12f works as an RNA-guided DNA nuclease, specifically cleaving single-stranded DNA (ssDNA) in a target-specific manner (Fig. 3b) (Harrington et al. 2018; Khan et al. 2019). Unlike other Class 2 systems, Cas12f does not require a specific PAM sequence to target and cleave ssDNA. Instead, factors such as seed region, secondary structure, thermodynamic stability, and cofactors help recognize the target sequence (Harrington et al. 2018). Cas12f is the smallest functional CRISPR system known, at only one-third the size of Cas9. The CRISPR-Cas12f system shows promising applications in crop defense against ssDNA viruses and mobile genetic elements. It has been successfully utilized to confer field resistance against ssDNA viruses, such as those from the *Geminiviridae* and *Nanoviridae* families (Khan et al. 2019), significantly expanding the application of the CRISPR system in crop genomes. In summary, the

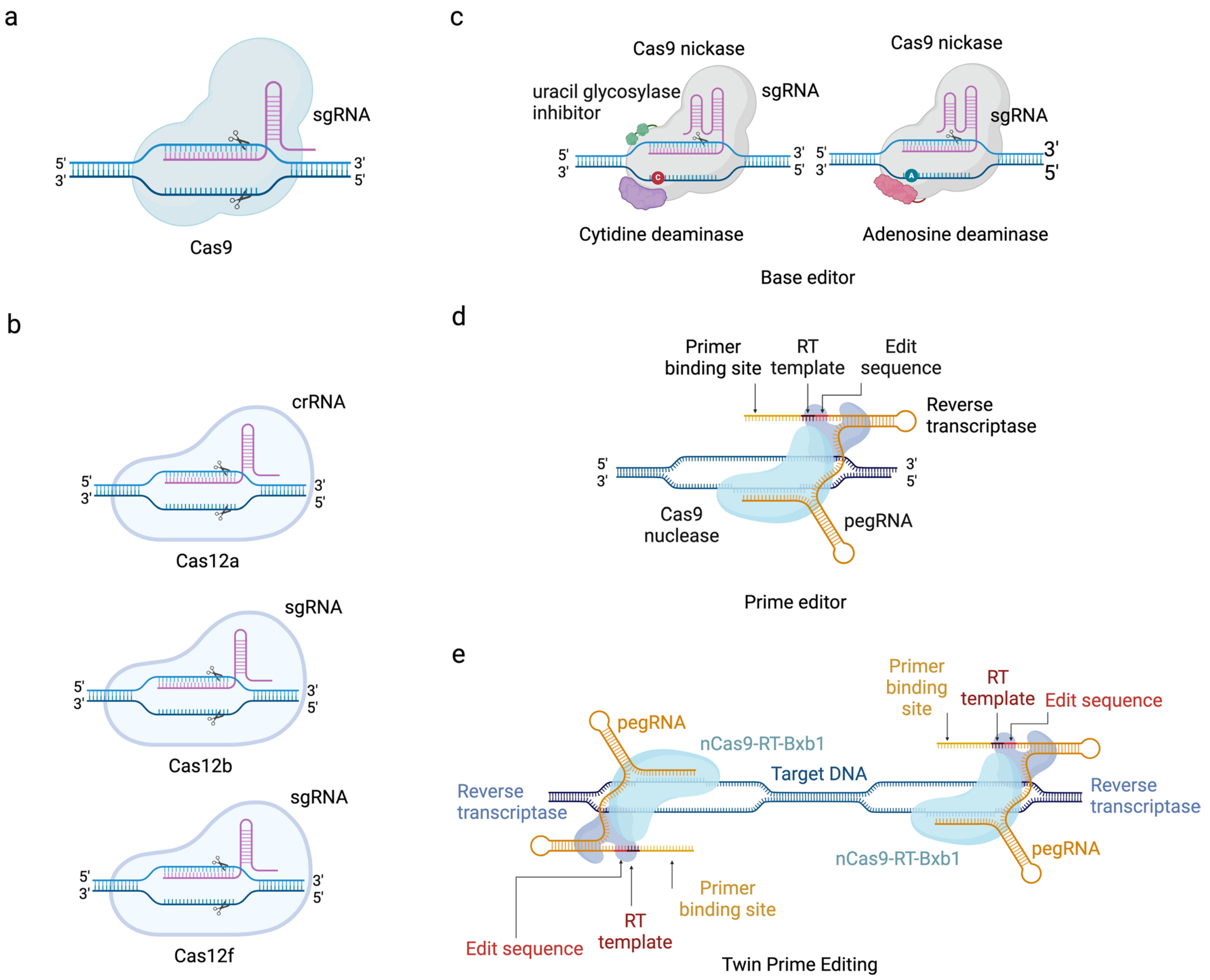


Fig. 3 Different genome editing tools for neo-domestication of pigmented rice. **a**. Guided by single-guide RNA (sgRNA), the CRISPR-Cas9 system can generate site-specific double-strand breaks. **b** Other than Cas9, Cas nucleases such as Cas12a, Cas12b, and Cas12f have been harnessed for RNA-guided genome editing. Cas12a: works like Cas9 but allows editing of additional genomic regions having AT-rich PAM sites. Cas12b works like Cas9 but allows editing of additional genomic regions having AT-rich PAM sites and a smaller size than Cas12a, which is a Class 2 Type V-B nuclease. Cas12f is a highly compact Class 2 Type V nuclease that functions as an RNA-guided DNA nuclease and specifically cleaves single-stranded DNA in a target-specific manner. **c** The base editor method enables precise base conversions without double-strand breaks by fusing Cas9 nickase with cytidine deaminase or adenosine deaminase. Cytosine base editors (CBEs) and adenine base editors (ABEs) can convert C:G to T:A or A:T to G:C, respectively. **d** The prime editor method uses engineered reverse transcriptase with a Cas9 H840 nickase and a prime editing guide RNA (pegRNA). The 5′ overhang is cleaved by exonucleases and 3′ sequences are ligated to the DNA strand. **e** The prime editor method for useful for larger genomic rearrangements, such as inserting entire genes or removing large genomic segments with high precision

Cas12 family of nucleases provides a robust toolkit for the neo-domestication of pigmented rice, e.g., Os*SPL14* can be targeted to enhance yield and drought tolerance by modulating tillering and grain size (Miura et al. 2010), while *IPA1* can be edited to optimize plant architecture and increase grain production (Liu et al. 2019). Genes involved in anthocyanin biosynthesis, such as Os*MYB2* and Os*DFR*, can be modified to enhance pigmentation and antioxidant properties, improving nutritional value (Nie et al. 2024; Yang et al. 2021) in the neo-domestication of wild pigmented rice.

Applications of base, prime, and twin prime editing and other emerging technologies for trait improvement in wild pigmented rice

Base editing, prime editing, and twin prime editing represent advanced CRISPR-based techniques that offer precise and efficient methods for domain knock-in or knockout in genetic research (Fig. 3c–e). These tools are invaluable for the neo-domestication of wild pigmented rice, primarily focusing on crop improvement.

Base editors are ideal for introducing precise point mutations to enhance or knockout gene function. They enable the conversion of one base pair into another without creating double-strand breaks, making them useful for precise point mutations to correct or introduce single nucleotide polymorphisms (Fig. 3c) (Komor et al. 2016). Base editing has been used to introduce point mutations in the ALS gene, resulting in herbicide-resistant plants without off-target effects, ensuring stable trait modifications without double-strand breaks (Shimatani et al. 2017). Prime editing can introduce more complex genetic changes, such as correcting loss-of-function mutations or inserting beneficial alleles. Prime editors offer greater precision by allowing targeted insertions, deletions, and all 12 possible base-to-base conversions without needing double-strand breaks (Fig. 3d). This system uses a reverse transcriptase to copy an RNA template directly into the DNA (Anzalone et al. 2019). Butt et al. (2020b) successfully edited 3 genes using prime editing in rice for herbicide tolerance and increase in yield they targeted *ACETOLACTATE SYNTHASE* (*OsALS*), *IDEAL PLANT ARCHITECTURE 1* (*OsIPA*) and *TEOSINTE BRANCHED* 1 (*OsTB1*). Twin prime editing builds on the prime editing principle and is useful for larger genomic rearrangements, such as larger insertions, deletion of genomic region, and introduction of new biosynthetic pathways with high precision (Fig. 3e) (Anzalone et al. 2022). Although its application in plants remains underexplored, twin prime editing could revolutionize the neo-domestication of wild rice by allowing the precise integration of beneficial alleles while preserving genetic diversity. By leveraging the precision and versatility of base editing, prime editing, and twin prime editing, researchers can introduce beneficial traits, improve yield, and enhance stress resistance in pigmented rice varieties.

Harnessing emerging technologies for the neo-domestication of pigmented rice extends beyond advanced CRISPR-Cas systems to include innovative platforms like Retron Library Recombineering (RLR) and the Cas-CLOVER system. This platform allows for the simultaneous introduction of numerous genomic variants, creating pooled and barcoded variant libraries that can be analyzed via targeted deep sequencing, thus surpassing the scale and specificity of traditional CRISPR-Cas methodologies (Orozco-Arias et al. 2022). Successful applications in crops such as Musa spp. demonstrate its potential (Thomson et al. 2019; Tripathi et al. 2023). Moreover, Cas-CLOVER can facilitate the development of transgene-free genome-edited crops through the piggyBac transposon system, which introduces targeted double-strand breaks and excises T-DNA without altering the insertion site, thereby maintaining genome integrity (Madison et al. 2022). Furthermore, recent advancements in epigenome editing and synthetic biology approaches can be harnessed to improve traits in pigmented rice varieties. Epigenome editing, using tools like CRISPR/dCas9 fused with epigenetic modifiers, allows for precise and reversible regulation of gene expression by modifying DNA or histone marks without altering the genetic code which can further harness for upregulate beneficial genes, such as those involved in stress response and nutrient biosynthesis, thereby enhancing crop resilience and nutritional content (Ghoshal et al. 2021; Goell and Hilton 2021). Additionally, synthetic biology techniques like gene drives offer a powerful method for rapidly spreading desirable traits, such as disease resistance, through rice populations, accelerating the neo-domestication process (Berr et al. 2015; Bewick et al. 2017). These innovations represent a significant leap forward in the genetic improvement of rice, particularly in adapting to environmental challenges and meeting nutritional needs.

Balancing coding vs non-coding DNA editing for neo-domestication of wild pigmented rice

When contemplating the neo-domestication of wild-pigmented rice, both coding and non-coding DNA editing offer substantial and unique advantages. Coding DNA editing directly manipulates genes, altering their function or expression to excise negative regulators impacting yield, nutrition, stress tolerance, and other agronomically desirable traits. This method has proven efficacious in engendering significant phenotypic transformations, notwithstanding the occasional pleiotropic effects that may arise (Chen et al. 2019b; Zhang et al. 2020). Coding DNA editing through CRISPR/Cas9-mediated loss of function mutation has shown significant potential in improving key agronomic and quality traits in *Oryza sativa*, providing a foundation for the neo-domestication of wild pigmented rice through targeted gene modifications. For example, knocking out of *GS3*, a positive regulator of grain weight and size, has resulted in elevated grain length, enhancing yield potential (Wang et al. 2018; Yuyu et al. 2020). Modifications in Amino Acid Permease 6 (*AAP*6) and *AAP*10, which regulate grain growth and production, have improved eating and cooking quality, making rice more appealing to consumers (Wang et al. 2020). Additionally, loss-of-function mutations in *BADH*2, which plays a role in synthesizing aromatic compounds like 2-acetyl-1-pyrroline, have produced aromatic rice variants, significantly increasing market value (Ashokkumar et al. 2020). So, this knowledge of gene functions, along with rational multiplexing of 4–6 pivotal genes for various traits, can help in fastening the process of neo-domestication of pigmented wild rice.

In contrast, non-coding DNA editing focuses on natural sequence variations within promoter regions, 3’ and 5’

UTRs, enhancers, silencers, and transposable elements, allowing for the fine-tuning of gene expression without altering protein-coding sequences. Various studies show that non-coding DNA editing has remarkable potential for improving rice traits through targeted modifications in diverse genomic regions. For example, editing the promoter of the xa13 gene enhanced bacterial blight resistance without compromising fertility, as partial promoter deletions suppressed pathogen-induced gene expression while maintaining normal yield (Li et al. 2020). Modifications in the 3' UTR of TAWAWA1, particularly within conserved non-coding sequences downstream of the gene, increased panicle branching and improved yield traits, illustrating the role of UTRs in fine-tuning gene expression (Lv et al. 2023; Yoshida et al. 2013). Enhancer editing, such as the insertion of the nDart1 transposon upstream of miR156d, produced the gain-of-function mutant *Bushy dwarf tiller 1*, characterized by increased tillering and dwarfism, highlighting the importance of enhancers in trait development (Hayashi-Tsugane et al. 2015; Nishimura et al. 2019). Similarly, studies on the Ac transposon demonstrated its utility in insertional mutagenesis for identifying silencer elements that regulate gene expression in rice (Castanera et al. 2023; Greco et al. 2003). These advancements in non-coding DNA editing provide a powerful framework for fine-tuning gene expression and optimizing agronomic traits in rice. By harnessing these insights, researchers can precisely modify regulatory elements in wild pigmented rice, enabling its neo-domestication while preserving its genetic diversity and enhancing its nutritional, environmental, and economic value. By judiciously choosing coding and non-coding editing approaches, the advantages of genetic editing can be maximized, augmenting desirable traits while maintaining genetic diversity and stability.

Domestication genes amenable to CRISPR breeding in wild pigmented rice

The genus *Oryza sativa* presents a rich genetic pool, and insights gleaned from domestication-associated genes can pave the way for the neo-domestication of wild pigmented rice. During the domestication of today's cultivated rice, a series of changes were marked in their morphological traits, physiological characteristics, and ecological adaptability. These changes mainly occurred through either altered or loss-of-function mutations in specific traits governing genes (Meyer and Purugganan 2013). These changes include genes for seed shattering, seed dormancy, awn length, plant height, tiller and panicle numbers, heading date, grain number, size, and weight (Fig. 4). Here we summarized a plethora of candidate genes that played a major role in rice domestication and some newly identified gene which can further harness for neo-domestication of pigmented wild rice through CRISPR.

Seed dispersal loss due to shattering has played a crucial role in the domestication process of major cereal crops (Fig. 4) The occurrence of seed shattering in rice is governed by two primary QTLs: *shattering4* (*SH4*)/*Shattering1* (*SHA1*) and *Seed shattering in chromosome 1* (*qSH1*). A SNP positioned 12 kb upstream of *qSH1* significantly impacts its expression at the separation layer, leading to the loss of seed shattering (Konishi et al. 2006). The loss of seed shattering during the domestication of Asian and African rice can be attributed to two independent causative SNPs located in the coding region of *SH4* (Li et al. 2006; Lin et al. 2007). Further research has unveiled complex gene regulatory network beyond SH4 and qSH1 involved in seed shattering, such as *SH5*, *SHAT1*, *SSH1*, *SH1*, *OSH15*, *CPL1*, *GRF4*, and *NPC1* (Qin et al. 2010; Subudhi et al. 2013). These loci are linked to regulatory pathways like auxin signaling, cytokinin levels, and certain transcription factors that fine-tune abscission zone (AZ) development and seed dispersal. Through a detailed understanding of the AZ regulatory network with precisely edited genes like *SH4, qSH1,* and other related genes using CRISPR it is possible to enhance non-shattering traits in wild pigmented rice while preserving desirable characteristics like nutrition and stress tolerance. Furthermore, these facilitate easier harvesting and increase the commercial viability of wild pigmented rice for supporting sustainable agriculture. Furthermore, the reduction of seed dormancy played a major role in cereal crop domestication. Wild and African-cultivated rice varieties exhibit more dormancy than Asian-cultivated rice (Sarla and Swamy 2005; Vaughan et al. 2008). Rice seed dormancy is primarily regulated by two genes, *SEED DORMANCY 4* (*Sdr4*) and qSD7-1/Rc during rice domestication (Sugimoto et al. 2010; Wang et al. 2018). *Sdr4* is regulated by the *OsVP1* transcription factor, and *qSD7-1* encodes basic helix-loop-helix (bHLH) transcription factors, both integrated ABA signaling and biosynthesis pathways; transcriptomic analysis of knockout mutants revealed they regulate multiple metabolic, hormonal pathways and regulatory network (Chen et al. 2023; Sugimoto et al. 2010). By leveraging this knowledge and precisely targeting these genes could fine-tune seed dormancy in pigmented rice, promoting synchronized germination. Similarly, reduction or elimination of awns has been pivotal in rice domestication (Fig. 4). Three genes associated with the transition from long awns to short or no awns have been successfully cloned and characterized: *Awn-1* (*An-1*), *Awn-2* (*An-2*)/*LONG AND BARBED AWN1* (*LABA1*), and *GRAIN NUMBER, GRAIN LENGTH AND AWN DEVELOPMENT* (*GAD1*)/*REGULATOR OF AWN ELONGATION 2* (*RAE2*). *An-1* and *An-2* show additive effects on awn length, with An-1 promoting awn formation and An-2 enhancing awn elongation (Bessho-Uehara et al. 2023; Gu et al. 2015;

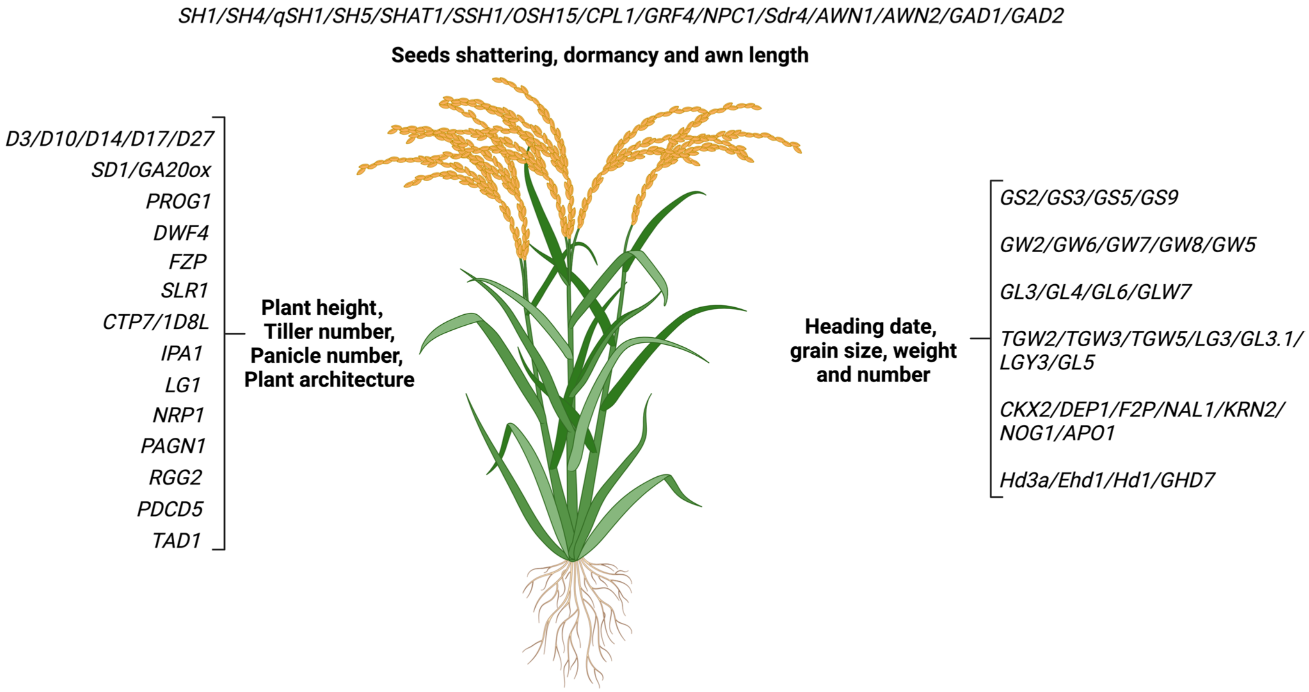


Fig. 4 Knowledge of the genetic pool to determine which domesticated genes and genes are associated with the improvement of traits is of utmost importance. This illustration depicts the important genes involved in domestication and improvement of traits in pigmented rice, including seed shattering, dormancy, awn structure, flowering time, grain characteristics, plant height and architecture, and tiller number. These genes have great potential both to rapidly facilitate the domestication and further improvement of pigmented rice and to enhance its cultivation

Jin et al. 2016; Luo et al. 2013). Recently, an intricate regulatory network governing awn length revealed that hormonal pathways including auxin and gibberellin signaling are critical for determining awn length and overall spikelet architecture (Yuan et al. 2020). For example, *GAD2*/*EPFL2* encodes small peptides belonging to the EPIDERMAL PATTERNING FACTOR-LIKE (EPFL) peptide family and modulates awn growth through receptor-like kinases, and this gene undergoes positive selection during rice domestication (Xiong et al. 2022). Understanding these networks provides a foundation for fine-tuning awn traits using CRISPR in wild pigmented rice.

Rice plant architecture has been a prime target for domestication because shorter plants with more tillers produce more grain and resist lodging (Fig. 4). Foremost, a gene is *PROSTRATE GROWTH 1* (*PROG1*), which encodes a Cys2/His2-type zinc-finger transcription factor shown transition from prostrate to erect growth in rice, enhancing lodging resistance (Jin et al. 2008; Tan et al. 2008; Wu et al. 2018). Similarly, *IDEAL PLANT ARCHITECTURE 1* (*IPA1*), which regulates plant height and tiller number, altering IPA1 expression can lead to an ideal plant architecture with fewer tillers and sturdier stems, enhancing yield and resistance to lodging (Jiao et al. 2010). PROG1 and IPA1 encode transcription factors that act as central hubs in regulatory circuits modulating growth patterns and plant morphology. Recent studies have shown that IPA1 is regulated post-transcriptionally by miR156 and miR529, which modulate its expression to balance tiller number and stem robustness, optimizing yield and lodging resistance. This highlights IPA1 as a master regulator integrating hormonal and environmental signals into developmental programs (Miura et al. 2010). *LIGULELESS1* (*LG1*), encoding a SQUAMOSA promoter-binding transcription factor, regulates panicle architecture, targeting an SNP located 11 kb upstream of *LG1* affects its expression, resulting in compact panicles (Ishii et al. 2013; Zhu et al. 2013). Gene expression network analysis suggests that LG1 modulates auxin signaling pathways by influencing the expression of auxin transporters and biosynthetic genes, further integrating hormonal regulation into panicle morphology. Another gene, *FRIZZY PANICLE* (*FZP*), increases the number of secondary branches per panicle and enhances grain yield during rice domestication (Huang et al. 2018). Transcriptional repression of FZP by TAWAWA1 (TAW1) forms a feedback loop limiting excessive branching, ensuring optimal panicle architecture. The semi-dwarfing allele sd-1, found at the SD-1 locus, has a major role in gibberellic acid (GA). This gene became a major contributor to the green revolution (Ashikari et al. 2005), SD-1 loss functions resulting in rice plants with shorter, thicker culms associated with increased harvest index, lodging resistance, and improved response to nitrogen fertilizer (Ashikari et al. 2005; Hedden 2003; Monna et al. 2002; Spielmeyer et al. 2002). *SD1* also regulates downstream genes in the GA signaling pathway, interacting with DELLA proteins such as *SLENDER RICE 1 (SLR1),* which mediate growth responses. *SLR1*, regulated by the F-box protein *GIBBERELLIN INSENSITIVE DWARF2 (GID2),* is essential for GA signaling, and mutations result in a dwarf plant phenotype (Ikeda et al. 2001; Sasaki et al. 2003). *DWARF4* (*DWF4*) has a role in the BR homeostasis loss function of these genes, resulting in a more erect leaf phenotype and a higher yield compared to wild-type plants (Sakamoto and Matsuoka 2006). Strigolactones (SLs), a class of phytohormones derived from carotenoids, are also essential for plant architecture. SLs repress branching, and their function is highly conserved in monocots (Gomez-Roldan et al. 2008). In rice, genes like *DWARF3* (*D3*), *D10*, *D14*, *D17* (*HTD1*), and *D27* are involved in SL biosynthesis or signaling. Loss of function of these genes results in a SL-insensitive dwarf phenotype and an increased number of tillers (Arite et al. 2007, 2009; Ishikawa et al. 2005; Lin et al. 2009; Zhou et al. 2013). Additionally, some transcription factor genes like *NEGATIVE REGULATOR OF PHOTOSYNTHESIS 1* (*NRP1*) negatively regulate the overall height, yield, and biomass. knockout of these genes shows increased plant height, panicle number, and biomass compared to wild-type plants (Chen et al. 2021b). CRISPR-Cas9 knockout of *PLANT ARCHITECTURE AND GRAIN NUMBER 1* (*PAGN1*) results in plants with increased height, tiller number, and grains per panicle (Yan et al. 2022). *RICE G-PROTEIN Γ SUBUNIT 2* (*RGG2*), encoding a type B heterotrimeric G-protein, negatively impacts plant height (Miao et al. 2019). Genes that influence senescence, such as *PROGRAMMED CELL DEATH 5* (*PDCD5*), also negatively regulate plant height and grain yield (Dong et al. 2021). The tiller number and tillering pattern determine the panicle number. Genes like *TILLERING AND DWARF 1* (*TAD1*), encoding an anaphase-promoting complex (APC/C) subunit of E3 ligase, affect the tiller number, mutant of tad1 plants exhibit decreased height but increased tillers, resulting in higher yield (Xu et al. 2012). These genes are part of broader transcriptional and hormonal networks integrating environmental and developmental signals, with significant implications for neo-domestication. Furthermore, these analyses facilitate the identification of previously uncharacterized regulatory elements, such as non-coding RNAs and cis-regulatory regions, which can provide additional layers of control for trait refinement through CRISPR technology.

Generally, domesticated rice varieties have larger and heavier grains compared to wild rice species (Fig. 4). Numerous QTLs associated with natural variations in grain characteristics have been functionally characterized. These include *GRAIN SIZE 2* (*GS2*), *GS3*, *GS5*, *GS9*, *GRAIN WIDTH 2* (*GW2*), *GW5*, *GW6*, *GW7/GRAIN LENGTH 7* (*GL7*), *GW8*, *GL4*, *GL6*, *GRAIN LENGTH AND WIDTH 7* (GLW7), *THOUSAND-GRAIN WEIGHT 2* (*TGW2*), *TGW3*, *TGW6*, *LARGE GRAIN* (*LG3*), *GL3.1*, *GRAIN YIELD QTL* (*qLGY3*), and *LARGE GRAIN QTL* (*qGL5*) (Fan et al. 2006; Hu et al. 2015; Ishimaru et al. 2013; Li et al. 2011; Liu et al. 2018; Qi et al. 2012; Qiao et al. 2021; Ruan et al. 2020; Shi et al. 2020; Song et al. 2007; Wang et al. 2019, 2015a, 2012; Weng et al. 2008; Ying et al. 2018; Yu et al. 2017; Zeng et al. 2013). Many of these genes encode proteins involved in regulatory signaling pathways such as the ubiquitin–proteasome pathway, G-protein signaling, phytohormone signaling, and transcriptional regulation. For instance, *GW2* encodes a predicted RING-type protein with E3 ubiquitin ligase activity, promoting cell proliferation and increasing the size of the spikelet hull through the ubiquitin–proteasome pathway (Song et al. 2007). *GS3* regulates grain length and weight through G-protein signaling (Fan et al. 2006). *TGW6* has indole-3-acetic acid (IAA)-glucose hydrolase activity that positively regulates grain yield by acting on the source organs such as starch (Ishimaru et al. 2013). *TGW3* interacts with *AUXIN RESPONSE FACTOR 4* (*ARF4*) to regulate grain length and weight (Hu et al. 2018), and *GL3.1/qGL3* controls grain length and yield through interactions with *GSK3* that modulate BR signaling (Qi et al. 2012). *GW5* is a positive regulator of BR signaling and enhances grain yield in rice (Li et al. 2011). *GS9* interacts with *OFP14* and *OFP8* to regulate grain morphology and is a regulatory target of *GSK2* kinase (Liu et al. 2018). *GW6* encodes a GA-regulated GAST family protein that positively influences grain width (Shi et al. 2020), and *GW8* encodes the *SPL16* transcription factor, which controls grain width via transcriptional regulation of GW7 (Wang et al. 2015b, 2012). Similarly, *GLW7*, *GS2*, and *GL6* are all transcriptional regulators contributing to grain size determination (Hu et al. 2015; Wang et al. 2019). The QTL *qLGY3* affects rice grain yield and encodes the transcription factor *MADS1*, which contains the MADS domain and is a crucial effector downstream of the G-protein βγ dimer. The variable splicing protein of *MADS1* leads to longer grains and improves the quality and yield of rice grains (Liu et al. 2018). *LG3* is a transcription factor in the ERF family and positively regulates rice grain length without affecting grain quality (Yu et al. 2017). Loss of function of the QTL *qGL5* (*AUX3*) results in more significant grain length and weight (Qiao et al. 2021). The transcription factor *ARF6* binds directly to the auxin response elements of the *AUX3* promoter and regulates grain length by altering longitudinal expansion and auxin distribution and content in glume cells (Qiao et al. 2021). These studies suggest that all these qTL are interconnected through regulatory hubs and co-expression modules that integrate hormonal signaling (e.g., auxins, brassinosteroids, and gibberellins) and epigenetic regulation and provide actionable insights for precise genetic interventions using CRISPR to enhance grain yield and quality in rice.

Several genes regulating grain number in cultivated rice include *Gnla/CKX2*, *DEP1*, *FZP*, *NAL1*, *KRN2*, *NOG1*, and *APO1* (Fig. 4). Among these, *CKX2*, encoding a cytokinin oxidase/dehydrogenase, has been identified as a major QTL for grain number (Ashikari et al. 2005). Natural variations in *CKX2* result in reduced expression or loss of function, elevating the cytokinin level and increasing grain number and secondary panicle branching (Rashid et al. 2024). Use of *DENSE AND ERECT PANICLE 1* (*DEP1*) that encodes G protein γ subunit, which regulates the architecture of dense and erect panicles (Huang et al. 2009). *FRIZZY PANICLE* (*FZP*), encoding an AP2/ERF domain transcription factor, and natural variations in the regulatory region of *FZP* lead to decreased expression and consequently elevated grain number (Komatsu et al. 2003; Xu and Sun 2021). Similarly, natural variations in *NARROW LEAF 1* (*NAL1*) influence grain number (Ren et al. 2021). Knocking out *KERNEL ROW NUMBER* (*KRN2)* encodes WD40 proteins and increases grain number and secondary branching, which results in increased grain yield by ~ 8%, without any observable trade-offs in other agronomic traits (Chen et al. 2022). *NUMBER OF GRAINS 1* (*NOG1*) encodes an enoyl-CoA hydratase/isomerase, and the insertion of 12 base pairs into the promoter region of *NOG1* elevates its expression, subsequently increasing grain number (Huo et al. 2017). *ABERRANT PANICLE ORGANIZATION 1* (*APO1*), which plays a role in the transition from rachis branch meristem to spikelet meristem and positively regulates the grain number per panicle (Yin et al. 2021). Gene expression network analysis reveals that these genes are part of interconnected pathways involving cytokinin signaling, transcription factor activity, and metabolic regulation. Integrating such insights with tools like CRISPR allows precise manipulation of key nodes, to optimize grain number without compromising other agronomic traits.

Day length affects flowering time for many plants, and this restricts where plants can be grown to specific latitudes. It has an important role in rice domestication in different geological places around the globe. In-depth investigations of the core genes involved in the regulation of flowering pathways have established a strong correlation between the expression of *Heading Date 3a* (*Hd3a*) and flowering time in 64 cultivated rice varieties collected from various regions worldwide (Takahashi et al. 2009). The observed variations in *Hd3a* expression can be partly attributed to the allelic diversity in *Heading Date 1* (*Hd1)* as well as to the expression levels of *Early Heading Date 1* (*Ehd1)*. Additionally, polymorphisms in *GRAIN NUMBER, PLANT HEIGHT, and HEADING DATE 7* (*Ghd7)* have been associated with flowering time and the geographical distribution of rice cultivation in China (Fig. 4) (Xue et al. 2008). These genes form a complex regulatory network integrating photoperiodic signals with developmental pathways. Gene expression network analyses have revealed that interactions between *Hd1*, *Ehd1*, *Hd3a*, and *Ghd7* are modulated by environmental cues like day length and temperature, as well as epigenetic factors such as histone modifications and DNA methylation. Understanding these networks provides insights into the molecular mechanisms of photoperiodic adaptation and enables the targeted manipulation of flowering time using tools like CRISPR. Such interventions could enhance the adaptability of rice to changing climates and expand its cultivation to new geographic regions.

Understanding traditional knowledge, genetic resources, and biotechnological potential of wild pigmented rice

Identification of pigmented rice varieties exhibiting superior potential

The starting materials are crucial for neo-domestication, and the first step is to select elite materials that exhibit superior potential for further improvement (Cang et al. 2016; Goralogia et al. 2021). The ideal germplasm for neo-domestication will have: (1) disease resistance, (2) tolerance to abiotic stress, (3) adaptive growth habit, (4) genetic diversity, (5) ease of breeding and genetic transformation, (6) nutritionally rich, (7) cultural acceptance, and (8) easy regulatory compliance.

Furthermore, efficient use of germplasm resources via integrating knowledge from genetics, genomics, genetic engineering, and computational biology, will also facilitate the selection of superior wild pigmented rice varieties for neo-domestication (Huang et al. 2022; Sedeek et al. 2023; Zhang et al. 2023a). Germplasm offers a reservoir of genetic diversity that is essential for selecting elite pigmented rice varieties (Huang et al. 2022). In addition, genomics plays a pivotal role in understanding the genetic basis underlying desirable pigmented rice traits. Whole-genome sequencing enables the identification of key genes associated with ideal traits and the molecular mechanisms governing these traits (Zhang et al. 2023b). Molecular markers such as single nucleotide polymorphisms (SNPs) and simple-sequence repeats (SSRs) allow the precise delineation of genomic regions linked to desirable traits, facilitating marker-assisted selection that can expedite breeding efforts (Kurniasih et al. 2019; Singh et al. 2020). Population genomics offers valuable insights into the evolutionary dynamics that have shaped pigmented rice diversity by elucidating genetic diversity patterns and population structures (Huang et al. 2022). Association mapping studies leverage genomic data to discover correlations between genetic markers and phenotypic traits, thereby pinpointing candidate genes responsible for yield, and nutritional properties. Genetic studies, including analysis of quantitative trait loci (QTLs) and trait mapping, contribute to understanding the genetic architecture of pigmented rice traits, guiding the selection of parental lines harboring favorable alleles for trait improvement (Mbanjo et al. 2023). Furthermore, phylogeny-driven pharmacological screening holds considerable promise in refining the selection criteria for the creation of elite pigmented rice varieties, while offering deeper insights into their translational applications (Bartlett et al. 2023). Translating foundational knowledge from extensively studied related species can offer valuable insights into developing newly domesticated plant varieties. Additionally, indigenous knowledge systems play a significant role in selecting elite pigmented rice for neo-domestication, as ethnobotanical records offer valuable insights into cultural significance, traditional uses, and ecological significance (Ramirez-Villegas et al. 2022). Hence, indigenous and scientific knowledge must be integrated to select appropriate starting materials for the neo-domestication of pigmented rice.

Multi-omics resources for wild and cultivated pigmented rice to unveil key gene regulatory network and complex biological processes

Genomic resources for wild and cultivated pigmented rice remain limited but are essential for uncovering the genetic basis of pigmentation, yield, and nutritional quality. Although various japonica and indica rice varieties have been sequenced, however, high-quality reference genomes for pigmented varieties remain scarce. Expanding these resources is crucial for identifying key genes and pathways that can enhance precision breeding in pigmented rice (Qin et al. 2021; Shang et al. 2022). Recent efforts have aimed to bridge this gap by constructing comprehensive genomic datasets. For instance, rice pan-genome encompassing 251 accessions of cultivated and wild Asian and African rice species has been aimed to identify novel haplotypes to improve crop potential (Shang et al. 2022). Additionally, Qin et al. (2021) assembled 31 high-quality genomes from a diverse rice collection, providing valuable insights into genetic diversity. More specifically, Sedeek et al. (2023) generated genome assemblies of five pigmented rice varieties, evaluating genetic variation in 51 varieties by resequencing 46 additional ones revealed significant genetic variation. Furthermore, Xie et al. (2023) analyzed approx. 5 k rice accessions globally, including 2,794 with red or black pericarps, shedding light on the evolutionary trajectory of red landraces originating from wild rice. These studies collectively enhance our understanding of the genetic foundation of pigmented rice and provide essential resources for its precision breeding.

Building on these genomic resources, multi-omics approaches offer a deeper understanding of trait development and genetic regulation in pigmented rice, which is crucial for its neo-domestication. Multi-omics data, including genomes, transcriptomes, metabolomes, proteomes, and epigenomes, are crucial for understanding complex traits in crops. Modern crops, show higher gene expression levels and alternative splicing than their wild ancestors,, reprogramming the transcriptome during adaptation (Chen et al. 2018; Liu et al. 2015). However, multi-omics also reveals a consistent reduction in allelic diversity across domesticated crops, with major crops containing only a fraction of the genetic diversity found in wild gene pools (Fernie et al. 2006). For example, RNA sequencing (RNA-seq) data from six rice varieties identified genes associated with grain pigmentation, nutrition, and aromatic properties (Zainal-Abidin and Mohamed-Hussein 2020). Additionally, epigenomics studies provides insights into partial heritability in domestication, revealing differential DNA methylation patterns in promoter regions of key transcription factors such as MYB and bHLH shows without selective sweeps, and the causal relationship between genetic variation and resultant phenotypes, offering valuable perspectives on the molecular mechanisms underlying crop domestication (Meyer and Purugganan 2013; Razifard et al. 2020; Schmitz et al. 2013).

To translate these insights into actionable breeding strategies, advanced data integration approaches are essential for accelerating the neo-domestication of wild pigmented rice. Co-expression network analysis methods such as weighted gene co-expression network analysis (WGCNA) facilitate the identification of hub genes that regulate complex traits, including those involved in anthocyanin biosynthesis and stress adaptation (Langfelder and Horvath 2008). Furthermore, combining quantitative trait loci (QTL) mapping with genome-wide association studies (GWAS) has proven effective in identifying genomic regions controlling flavonoid biosynthesis and nutritional properties in pigmented rice. For instance, the QTL GS3.1 has been identified as a regulator of grain size by influencing the metabolic flux between flavonoid and lignin biosynthesis pathways (Zhang et al. 2021). This QTL encodes a MATE transporter that directs p-coumaric acid toward flavonoid biosynthesis, affecting grain size without compromising stress tolerance (Zhang et al. 2021). Furthermore, multi-layered regulatory network analysis incorporating transcription factor binding sites, chromatin accessibility, and metabolomic profiling can delineate key regulatory nodes governing secondary metabolism (Liu et al. 2023; Zhu et al. 2023). Machine learning-driven integration of transcriptomics and metabolomics data has further improved the identification of biomarkers for precision breeding, enabling the selection of pigmented rice with enhanced antioxidant profiles (Zhang et al. 2023a).

Metabolomics, used in QTL studies, investigates genetic determinants of quality traits, although studies explicitly on pigmented rice are limited. Nonetheless, recent efforts have begun addressing this gap. Recently, in pigmented rice, the multi-omic resources disseminated by Sedeek et al. (2023) have furnished an all-encompassing array of genomic, metabolomic, and nutrient data for pigmented rice. A similar metabolomics study was carried out by Zhang et al. (2023b) and Tiozon et al. (2023b) shows how black and red rice have high levels of the flavonoids anthocyanin and proanthocyanidin. Additionally, Chen et al. (2019a) conducted a study to comprehensively characterize the intricate molecular mechanisms operating in the biosynthetic pathway of flavonoids in red, white, and black rice cultivars. Using RNA sequencing of caryopses and isobaric tags for relative and absolute quantitation (iTRAQ) analysis, they performed a detailed analysis of mRNA content and expressed proteins in various colored rice varieties. Specifically, for the red, white, and black rice cultivars, 3417, 329, and 227 distinct genes were discovered, respectively (Chen et al. 2019b). Moreover, proteomic analysis has further strengthened our understanding of these metabolic pathways. Proteomic analysis of these colored rice varieties revealed the presence of 13,996 distinct peptides corresponding to 3,916 proteins. Notably, a total of 32 genes that play a role in the biosynthesis pathway of flavonoids were identified. These findings underscore the importance of integrating high-throughput multi-omics approaches, particularly through gene regulatory network modeling and predictive analytics, to advance precision breeding strategies for pigmented rice.

To enhance the integration of multi-omics datasets, bioinformatics pipelines serve as pivotal tools for constructing gene regulatory networks (GRNs) that elucidate the interactions between genes, metabolites, and regulatory elements. These networks are developed by correlating genomic, transcriptomic, and metabolomic datasets using advanced computational approaches, including weighted gene co-expression network analysis (WGCNA), machine learning algorithms, and Bayesian inference techniques. For instance, metabolite–gene correlation networks have been instrumental in linking flavonoid biosynthesis genes with anthocyanin accumulation, a critical trait in pigmented rice. For example, Zhang and Wong (2022) demonstrated that these networks can identify key enzymes, such as glycosyltransferases, that modulate pigment modification, presenting viable genetic targets for precision breeding strategies. Similarly, integrating transcriptomic and proteomic data derived from RNA-seq and iTRAQ analyses (Chen et al. 2019a) with QTL mapping has unveiled epistatic interactions and regulatory nodes that govern pigmentation mechanisms. These insights are essential for guiding the selection and modification of wild rice germplasm to develop improved pigmented rice varieties with enhanced nutritional and agronomic traits. Beyond identifying regulatory elements, multi-omics approaches also facilitate the functional validation of key pigmentation-related genes. Transcriptome-wide association studies (TWAS) and chromatin immunoprecipitation sequencing (ChIP-seq) have been pivotal in identifying regulatory elements involved in anthocyanin biosynthesis in pigmented rice. These studies have highlighted the central role of the MYB-bHLH-WD40 (MBW) complex in pigment accumulation. Within this complex WD40 repeat gene OsTTG1 has been identified as a crucial component directly influencing anthocyanin production in rice (Yang et al. 2021). Experimental validation using CRISPR-Cas9 knockout lines of OsTTG1 demonstrated that disrupting these genes reduced flavonoid accumulation and simultaneously altered responses to oxidative stress, revealing functional redundancy and compensatory pathways that could be leveraged for neo-domestication (Yang et al. 2021). Beyond pigmentation, research also indicates that transcription factors such as NAC and DREB play significant roles in abiotic stress responses in rice. For instance, overexpression of the NAC transcription factor gene OsNAC022 has been shown to enhance drought and salt tolerance in rice plants (Hong et al. 2016). Similarly, DREB transcription factors have been associated with improved stress tolerance, with studies demonstrating that overexpression of DREB1B in tobacco confers enhanced resistance to various abiotic stresses (Gutha and Reddy 2008). While direct interactions between the MBW complex and stress-responsive transcription factors like NAC and DREB in rice remain to be fully elucidated, the involvement of these factors in both anthocyanin biosynthesis and stress responses suggests potential regulatory crosstalk. To further refine neo-domestications strategies, pathway enrichment analyses, such as Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG), augment multi-omics data integration by identifying metabolic and biosynthetic pathways associated with pigmentation and nutritional enhancement. Additionally, multi-omics-based genome-wide association studies (GWAS) have further revealed co-localization of anthocyanin biosynthesis loci with yield-related traits, such as grain size and starch metabolism, where key regulators like OsC1 and OsDFR influence both flavonoid accumulation and agronomic performance demonstrating the feasibility of breeding strategies that optimize both pigmentation and crop productivity (Zheng et al. 2019). Further aiding in neo-domestication, visualization platforms like Cytoscape enable the exploration of GRNs, facilitating the identification of hub genes responsible for phenotypic variation in pigmented rice. Studies show that linked the upregulation of key enzymes, including phenylalanine ammonia-lyase and chalcone synthase, to increased flavonoid biosynthesis in colored rice cultivars (Zhang et al. 2023b). Integrating these findings into neo-domestication strategies highlights the potential of multiplex genome editing and precision breeding to optimize pigmentation, stress tolerance, and yield-related traits in wild rice germplasm, ultimately accelerating the development of nutritionally enriched and climate-resilient rice cultivars.

Moreover, along with the high-quality reference genome and multi-omics resources, population genetic analyses should be expanded to include more accessions of pigmented rice to better understand their evolutionary dynamics and identify beneficial alleles. Furthermore, integrating indigenous knowledge systems and scientific research will enrich the selection criteria for elite pigmented rice varieties, considering cultural significance, traditional uses, and ecological importance (Ramirez-Villegas et al. 2022). By leveraging these integrative multi-omics data and generating additional ones, researchers can more precisely identify key regulatory genes and pathways for neo-domestication of wild pigmented rice via keeping its genetic diversity and nutritional values intact.

Amenability of wild pigmented rice varieties to tissue culture, transformation, and regeneration

Tissue culture techniques, including callus induction, somatic embryogenesis, and organogenesis, have been successfully applied to wild rice species, albeit with varying degrees of efficiency. Recent studies showed that a few wild rice and some of cultivated pigmented rice varieties possess the inherent ability to regenerate from explants, a critical trait for genetic transformation and subsequent plant development (Sedeek et al. 2023; Wang et al. 2019).

Transformation efficiency in wild pigmented rice can be enhanced through the optimization of *Agrobacterium*-mediated transformation protocols. Advances in vector design, such as the use of binary vectors with strong promoters and selectable marker genes, have improved the integration and expression of cisgenes in pigmented rice (Molina-Risco et al. 2021; Sedeek et al. 2023; Susanto et al. 2020). Additionally, the application of biolistic methods, although less common, has shown promise in delivering transgenes into recalcitrant genotypes (Gantait et al. 2022; Kausch et al. 2019). Regeneration of transgenic plants from transformed tissues is a critical step in developing genetically modified varieties. Wild pigmented rice varieties, such as Chaling common wild rice (*Oryza rufipogon*), have shown efficient regeneration capabilities, producing fertile plants capable of setting seeds and passing on introduced traits to subsequent generations. Additionally, optimized A*grobacterium*-mediated transformation protocols, specifically utilizing scutellum tissue of embryos from mature seeds, these wild rice varieties can achieve high transformation and regeneration efficiencies. For example, the regeneration system developed for Chaling common wild rice resulted in transformation efficiencies between 87–94%, with subsequent regeneration of fertile plants that could reproduce and retain introduced traits across generations (Xiang et al. 2022). The regeneration efficiency of rice varieties, including wild pigmented types, can be significantly enhanced by optimizing the composition of the regeneration medium. Key factors influencing regeneration rates include the concentration and type of growth hormones (such as auxins and cytokinins) and the choice of gelling agents. For example, specific combinations of kinetin, naphthalene acetic acid, and agarose have been shown to improve the regeneration frequency in various rice cultivars (Susanto et al. 2020; Xiang et al. 2022). Overall, the amenability of wild pigmented rice varieties to tissue culture, transformation, and regeneration is promising, making them suitable candidates for genetic improvement through biotechnological approaches. Continued refinement of these techniques and further exploration of genotype-specific responses will enhance the efficiency of producing improved pigmented rice varieties with desirable traits.

Additionally, recent advancements in genetic transformation technologies, including *Agrobacterium*-mediated transformation, have seen significant improvements through the overexpression of morphogenic factors such as *BBM*, *WUS2*, and *GRF4*/*GIF1*, which enhance somatic embryogenesis and regeneration processes (Debernardi et al. 2020; Lowe et al. 2016). These advancements have been successfully applied in crops like *Zea mays*, *Sorghum bicolor*, and *Oryza sativa L.*, showing enhanced transformation efficiency (Debernardi et al. 2020; Lowe et al. 2016). Additionally, novel systems such as the ternary vector system with type III secretion to repress host defenses have further increased transformation success rates (Raman et al. 2022). Direct transformation methods, including biolistic delivery, nanotubes, virus transfection, and PEG-Ca^{2+} mediated methods, bypass the need for DNA insertion by delivering Cas protein and sgRNA as RNP complexes, facilitating precise genetic modifications without chromosomal integration (Chen et al. 2022; Doyle et al. 2023).

Moreover, innovative techniques like the cut-dip-budding delivery method for tuberous and woody species, and RNA virus-mediated delivery into the apical meristem, present efficient alternatives for genetic transformation (Cao et al. 2023; Ellison et al. 2020). The integration of nanotechnology with CRISPR technologies is also being explored, offering transgene-free genome transformation capabilities by leveraging the unique properties of nanoparticles for precise cargo delivery (Demirer et al. 2019). This recent advancement can be further utilized to speed up the process of neo-domestication of pigmented rice.

Promotion and application of neo-domestication of wild pigmented rice

Addressing nutritional needs in low-income areas is essential due to the pressing challenges of food security, hidden hunger, and the growing population. According to the FAO 2022 report on "The State of Food Security and Nutrition in the World 2022," over 820 million people worldwide suffer from hunger, and malnutrition remains a significant issue in many low-income countries ((FAO, 2022). Hidden hunger, which refers to micronutrient deficiencies that occur even when caloric intake is sufficient, affects over 2 billion people globally, particularly in many parts of Africa and Asia (Muthayya et al. 2013). With the global population projected to reach 9.7 billion by 2050, increasing the demand for nutritious and sustainable food sources is imperative (United Nations, 2019).

Recent studies highlight the potential health benefits of pigmented rice (Chen et al. 2017; Sedeek et al. 2023). Increasing the availability and affordability of pigmented rice can thus provide a valuable dietary supplement to populations suffering from hidden hunger. By integrating pigmented rice into the diets of these populations, multiple nutritional deficiencies can be addressed simultaneously. The economic impact of promoting pigmented rice cultivation and consumption extends beyond nutritional benefits. For producers, particularly smallholder farmers, pigmented rice varieties offer an opportunity to diversify crops and increase income. These varieties often fetch higher market prices due to their perceived health benefits and unique culinary qualities (Gunaratne et al. 2013; Sompong et al. 2011). Additionally, it fosters cultural pride, reduces healthcare burdens by alleviating diet-related diseases, and empowers marginalized groups through targeted training and market access programs (Goswami et al. 2023; Horgan et al. 2018). These multifaceted benefits contribute to enhanced livelihoods, environmental sustainability, and inclusive development. Consequently, promoting pigmented rice can enhance the livelihoods of farmers and stimulate local economics. For example, in Thailand, initiatives to cultivate black rice (*hom nil*) have improved farmers' incomes and enhanced local food security by providing a nutritious alternative to conventional rice (Boonjung and Fukai 1996; Suwannaporn and Linnemann 2008). In China, the long-standing cultivation of black rice has been further boosted by recent government initiatives. Farmers in regions like Guangxi and Yunnan have benefited from higher incomes due to the increased demand for black rice, known for its high antioxidant content and health benefits (Hu et al. 2003; Liu et al. 2022; Wang et al. 2024). In Indonesia, black rice cultivation is gaining popularity, particularly in regions like Bali and Java. The Indonesian government has implemented programs to support farmers through financial aid and agricultural extension services, helping them improve their cultivation practices, leading to higher yields and better-quality rice (Sitaresmi et al. 2023). In India, integrating red rice into public food distribution systems has helped mitigate iron deficiency anemia among vulnerable populations and shown the dual benefits of health improvement and economic support (Nandeep et al. 2024). In India, a study by Goswami et al. (2023) revealed that the return on investment for black rice cultivation is significantly higher compared to conventional rice, with one rupee invested in black rice yielding a return of 2.15 rupees. This shift not only improves the economic status of the farmers but also contributes to better health outcomes in the region.

Overall, making pigmented rice available and affordable is essential to provide significant health benefits and solve local problems for those in low-income areas. By addressing both nutritional deficiencies and economic challenges, promoting pigmented rice cultivation and consumption stands to benefit producers and consumers alike. This integration contributes to sustainable agricultural practices and enhanced food security, addressing the urgent need to support vulnerable populations.

Conclusions and perspectives

The neo-domestication of wild-pigmented rice offers a transformative opportunity to enhance human health and food security. A multipronged approach is imperative for the successful neo-domestication of wild pigmented rice. This approach requires the integration of insights from previous rice domestication studies, the identification and deployment of efficient CRISPR tools and target genes for precise genome editing, the application of advanced knowledge systems for the selection of elite germplasm, the development and utilization of comprehensive genomic resources, the identification of genotypes amenable to tissue culture and genetic transformation, and the implementation of effective breeding strategies. This comprehensive strategy enhances the agronomic performance and promotes pigmented rice for sustainable agriculture that ultimately results in eradicating hunger and malnutrition.

Despite its immense potential for neo-domestication, pigmented rice still has several crucial questions and challenges that must be addressed. One such question revolves around the efficient introduction of desired genes associated with domestication while preserving the genetic diversity of pigmented rice. Additionally, the identification of optimal combinations of genes and traits to focus on wild pigmented rice is essential for enhancing its nutritional value, yield, and ability to withstand environmental stressors. Furthermore,

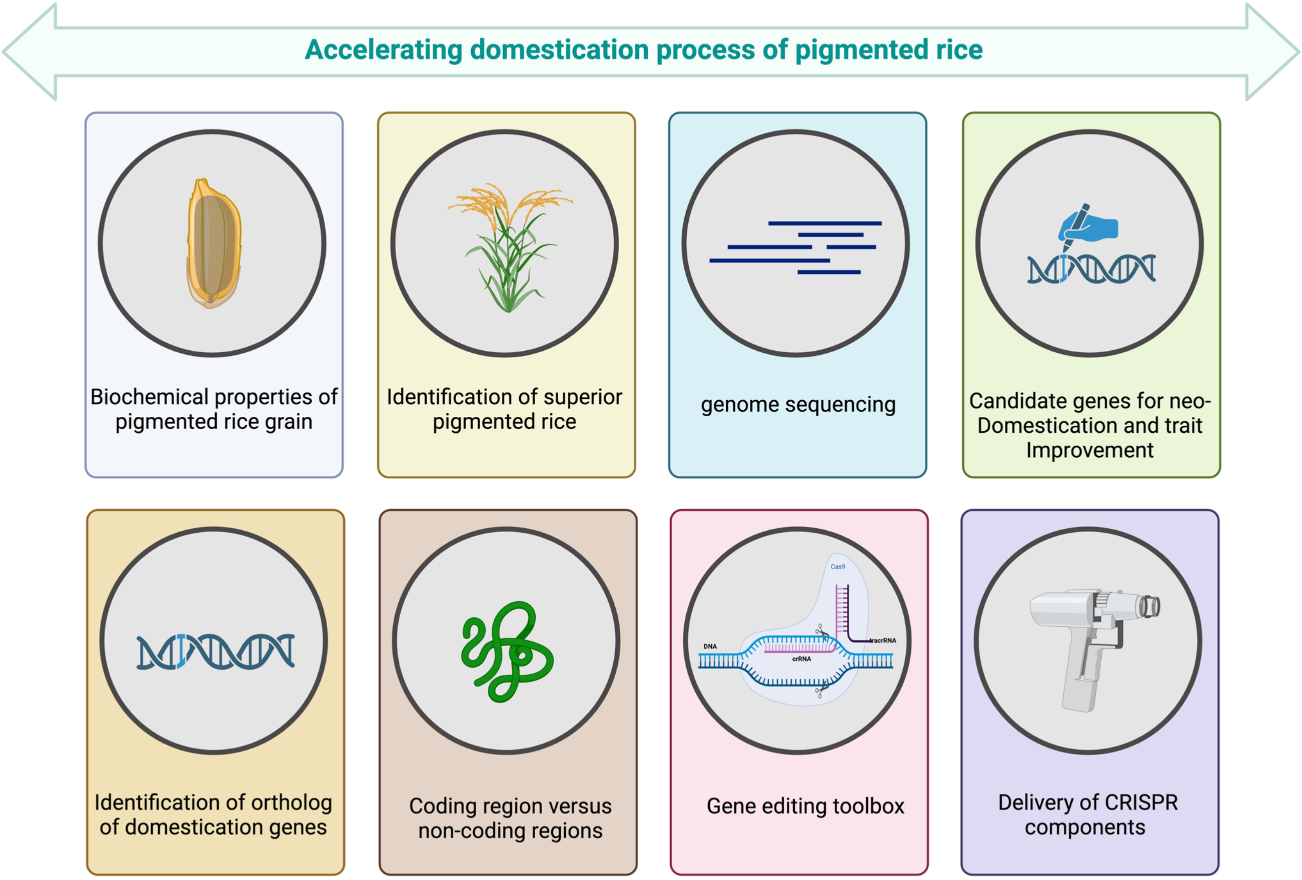


Fig. 5 An overview of the strategic plan outlining the essential measures necessary for the efficient advancement of the entire procedure of neo-domestication pertaining to wild pigmented rice

determining how genome editing tools should be utilized for coding versus non-coding genome sequences in pigmented rice is of utmost importance. Identifying the most efficient genome editing tools and techniques for precise and targeted modifications in pigmented rice and determining the most effective methods for delivering editing components into pigmented rice cells to achieve the desired trait modifications are crucial aspects. Furthermore, extensive educational and communication efforts outside the scientific community are necessary to clarify distinctions between genome editing and traditional genetic modification, address regulatory uncertainties, and promote societal acceptance of neo-domestication approaches in pigmented rice.

Future directions should focus on specific goals for the next decade regarding research, policy, and implementation. Research efforts should aim to expand genomic resources for pigmented rice, facilitating comprehensive trait improvement. Policy initiatives should support the integration of advanced biotechnological tools in breeding programs and ensure regulatory frameworks that enable the rapid adoption of neo-domesticated varieties. Strategies should promote the cultivation and consumption of pigmented rice in low-income areas, leveraging its nutritional benefits to address hidden hunger and improve public health outcomes. By pursuing these goals, the neo-domestication of wild pigmented rice can make a substantial contribution to sustainable agriculture and global food security. In summary (Fig. 5 roadmap for neo-domestication), genome editing and other emerging technologies provide formidable tools in the endeavor to speed up neo-domestication of pigmented rice and to develop novel crop varieties that can withstand the challenges posed by climate change. By embracing these advancements, we can envision a future in which agriculture assumes a pivotal role in promoting human health, environmental sustainability, and food security for future generations.

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Declarations

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