Advances in the Uptake and Transport Mechanisms and QTLs Mapping of Cadmium in Rice

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Abstract: Cadmium (Cd), as a heavy metal, presents substantial biological toxicity and has harmful effects on human health. To lower the ingress levels of human Cd, it is necessary for Cd content in food crops to be reduced, which is of considerable significance for ensuring food safety. This review will summarize the genetic traits of Cd accumulation in rice and examine the mechanism of Cd uptake and translocation in rice. The status of genes related to Cd stress and Cd accumulation in rice in recent years will be summarized, and the genes related to Cd accumulation in rice will be classified according to their functions. In addition, an overview of quantitative trait loci (QTLs) mapping populations in rice will be introduced, aiming to provide a theoretical reference for the breeding of rice varieties with low Cd accumulation. Finally, existing problems and prospects will be put forward.

Keywords: cadmium accumulation; absorption and transport; QTL location; mapping population; rice (Oryza sativa L.)

1. Introduction

Cadmium (Cd) is a soil contaminant and with a high mobility in living organisms, and is characterized as a toxic heavy metal [1,2]. In China, about $2.786 \times 10^9$ m$^2$ of agricultural land is contaminated by Cd [3]. Frequent applications of nitrogen fertilizer in the agricultural land of many areas of China have resulted in more acidic soil, and acidic soil means that cadmium is more easily absorbed by plants [4]. Rice (Oryza sativa L.) is the main food for more than half of the world’s population. Cd is easily transferred from soil to rice and accumulates in rice plants and grains [2,3], and is then enriched in the human body through the food chain, thereby threatening human health [5–7], and causing effects such as anemia, cancer, heart failure, hypertension, cerebral infarction, proteinuria, severe lung damage, eye cataract formation, osteoporosis, emphysema, and renal insufficiency [8,9]. It is worth mentioning that Itai-itai disease, which occurred in Japan in the 1950s, was caused by the long-term intake of cadmium-contaminated rice [10]. On average, weekly Cd accumulation was as high as 3–4 mg kg$^{-1}$ body weight in Japan at that time [11]. Between 1990 and 2015, the average dietary Cd intake of the general population more than doubled in China [12,13]. Therefore, reducing Cd uptake by crops, especially rice, is of great significance to food safety and human health.

The purpose of this review is to explore the mechanism of cadmium uptake and transport and the genetic characteristics of Cd accumulation in rice, and to summarize the research status of genes and QTLs related to cadmium stress and cadmium accumulation in rice. It has important guiding
significance for breeding high-quality rice varieties with a low accumulation of Cd in grain and the safe production of rice in mild and moderate Cd-contaminated soil.

2. Toxic Effects of Cadmium Exposure on Rice

Cd stress seriously affects rice germination and growth [2,3,14–18], and it was found that excessive Cd exposure can not only significantly decrease the rice seed germination rate [14], but also cause chlorosis and necrosis in rice plants during the vegetative stage [19,20]. Cd stress causes severe physical and physiological changes in rice plants as it causes a reduction in the length; width; and number of roots, shoots, and leaves. Furthermore, chlorophyll contents, stomatal conductance, and the water use efficiency of rice are also significantly affected [3,17,18,21–23]. Cd also affects the absorption and transport of essential nutrients in rice [15,16,18–20]. Additionally, Cd can be transported to rice grains, reducing their yield, quality, and nutrients [15,16,24–27]. In general, Cd stress inhibits rice growth [18,28–30].

Rice possesses some tolerance mechanisms to cadmium at physiological and molecular levels [31–35]. As root cell walls of the outermost layer have direct contact with the soil solution, this protects the protoplasts against Cd toxicity [36–38]. Furthermore, plants reduce Cd translocation to the shoots by immobilizing Cd in the cell walls and vacuoles of root cells, thus reducing their sensitivity and the harm of Cd to another cellular organelle [39–42]. Several adenosine triphosphate (ATP)-binding cassette (ABC) proteins have been reported to mediate vacuolar compartmentation of Cd-glutathione and/or phytochelatin (PC) conjugates in Arabidopsis thaliana [43,44]. Rice OsPDR5/ABCG43 is likely to encode ABC-type protein functions in Cd extrusion from the cytoplasm [45]. Overexpression of Cd transporter OsHMA3 located in vacuole membranes in rice roots can increase the tolerance of rice to Cd and reduce the accumulation of Cd in grains [46,47]. Exudates of roots contain metal chelators which play a role in the adjustment of the rhizosphere pH and the metal chelating process [48]. Most of the chelated toxic metals inside plants target vacuoles through metal detoxification processes [38,49]. Organic acids secreted from roots, e.g., malate, citrate, etc., are involved in metal uptake, the long-distance transport of metal, and the transport of metal into vacuoles [50,51]. It was found that chelators play a crucial role in keeping Cd in the rice roots and form a barrier in Cd translocation [52].

Cd stress can induce plants to enhance their antioxidant defense system and regulate ion homeostasis to improve their tolerance to Cd [32,53–58]. For example, Cd stress can induce plants to increase the production of glutathione (GSH), abscisic acid (ABA), salicylic acid (SA), jasmonic acid (JA), and nitric oxide (NO) [59–65]. Mitogen-activated protein kinase OsWJUMK1, OsMSRMK2, OsMSRMK3, and OsMAPK2 can affect rice root growth under Cd stress by regulating auxin signal changes [66–69]. Auxin transporter OsAUX1 has been reported to be involved in root development and the Cd stress response in rice [34]. In addition, the concentration of iron and cadmium was positively correlated during rice seedling growth [70]. It has been reported that increasing the supply of boron, iron, zinc, silicon, or magnesium can reduce the accumulation and toxicity of cadmium in rice [71–76].

In addition, some genes related to Cd stress have been reported in rice (Table 1). OsHMA9 is a copper efflux protein located in the plasma membrane, which may have a cadmium efflux function to excrete Cd from root cells and reduce Cd accumulation in rice [77]. Knock-out of the low cadmium gene (LCD) reduced the accumulation of cadmium and increased the growth of rice under the condition of an excessive cadmium supply, and LCD may be a protein related to cadmium homeostasis [78]. Overexpression of OsCDT1 can increase the growth of Arabidopsis thaliana under cadmium treatment; the cysteine-rich peptide encoded by OsCDT1 is possibly involved in rice Cd tolerance [79]. OsCLT1 probably mediates the export of γ-glutamylcysteine and glutathione from plastids to the cytoplasm, which in turn affects As and Cd detoxification in rice [80].
| Gene       | Chr. | Physical Location (bp) | Gene Name                                                                 | Function                                                      | Reference |
|------------|------|------------------------|---------------------------------------------------------------------------|---------------------------------------------------------------|-----------|
| OsCDT3     | 1    | 4066623–4067218        | Encoding a Cys-rich peptide Cd uptake inhibitor                           |                                                               | [79]      |
| Ospdr9     | 1    | 24075065–24082181      | Multidrug resistance ABC transporter Redox protection in Cd stress         |                                                               | [81]      |
| OsWJUMK1   | 1    | 29398191–29402466      | Mitogen-activated protein kinase Cd signal                                  |                                                               | [82]      |
| OsHsfA4s   | 1    | 31370413–31372729      | Heat shock transcription factor gene Cd tolerance                          |                                                               | [83]      |
| OsAUX1     | 1    | 36998334–37004685      | Auxin transport protein Root development and Cd stress response            |                                                               | [34]      |
| OsCLT1     | 1    | 42086484–42095424      | CRT-like transporter 1 Cd tolerance                                        |                                                               | [80]      |
| OsLCD      | 1    | 42162592–42166462      | Low cadmium Cd tolerance and accumulation                                   |                                                               | [78]      |
| OsZIP1     | 1    | 42905566–42907474      | Zinc- and iron-regulated transporter Cd and Zn transport                   |                                                               | [84,85]  |
| ricMT      | 1    | 43047164–43047861      | Metallothionein gene Cd tolerance                                          |                                                               | [86]      |
| OsCDT4     | 2    | 6078179–6079111        | Encoding a Cys-rich peptide Cd uptake inhibitor                            |                                                               | [79]      |
| OsNAAT1    | 2    | 11997094–12002633      | Nicotinamide aminotransferase gene Cd accumulation                         |                                                               | [87]      |
| CAL1       | 2    | 25190487–25191188      | defensin-like protein Cd accumulation in leaf                              |                                                               | [88]      |
| OsYSL2     | 2    | 26170387–26174970      | Metal-nicotinamide transporter Cd translocation                           |                                                               | [89]      |
| OsCd1      | 3    | 842577–846408          | Major facilitator superfamily Cd uptake                                    |                                                               | [90]      |
| OsNramp2   | 3    | 5655157–5659147        | Natural resistance-associated macrophage protein Cd transporter, Cd        |                                                               | [91]      |
| OsMSRMK2   | 3    | 9847700–9850473        | Mitogen-activated protein kinase Cd signal                                 |                                                               | [67]      |
| OsMTI-1b   | 3    | 9957335–9958362        | Metallothionein-like protein 1B Cd tolerance                               |                                                               | [92]      |
| PEZ1       | 3    | 20793053–20799805      | Phenol efflux protein Cd accumulation                                      |                                                               | [93]      |
| OsCDT1/OsCCX2 | 3  | 25613825–25616179     | Cation/calcium (Ca) exchanger 2 Cd tolerance and translocation            |                                                               | [79,94]  |
| OsIRT2     | 3    | 26276301–26277206      | Iron-regulated transporter Cd and Fe transporter                           |                                                               | [95]      |
| OsIRT1     | 3    | 26286156–26292023      | Iron-regulated transporter Cd and Fe transporter                           |                                                               | [95,96]  |
| Gene     | Chr | Physical Location (bp) | Gene Name                                      | Function                        | Reference |
|----------|-----|------------------------|------------------------------------------------|----------------------------------|-----------|
| OsZIP3   | 4   | 31078200–31080734      | Zinc- and iron-regulated transporter           | Cd accumulation                  | [84]      |
| OsMTP1   | 5   | 1675488–1679056        | Metal tolerance protein gene                   | Cd translocation                 | [97]      |
| OsZIP6   | 5   | 3807974–3810752        | Zinc- and iron-regulated transporter           | Cd transport                     | [98]      |
| OsCDT5   | 5   | 4665325–4667853        | Encoding a Cys-rich peptide                    | Cd uptake inhibitor              | [79]      |
| OsZIP7   | 5   | 6090801–6094068        | Zinc- and iron-regulated transporter           | Cd and Zn accumulation           | [99]      |
| OsPCS2   | 6   | 167367–174319          | Plant chelatase synthase 2                    | Cd tolerance                     | [100]     |
| OsCDT2   | 6   | 2261681–2263972        | Encoding a Cys-rich peptide                    | Cd uptake inhibitor              | [79]      |
| OsLCT1   | 6   | 22566775–22571982      | Low affinity cation transporter                | Cd transporter in phloem         | [101,102] |
| OsHMA9   | 6   | 27517100–27523604      | P-Type Heavy Metal ATPase                     | Cd efflux                        | [77]      |
| OsMSRMK3 | 6   | 29398191–29402466      | Mitogen-activated protein kinase               | Cd signal                        | [82]      |
| OsHMA2   | 6   | 29477949–29480905      | P-Type Heavy Metal ATPase                     | Cd and Zn translocation          | [103,104] |
| OsHMA3   | 7   | 7405745–7409553        | P-Type Heavy Metal ATPase                     | Sequestration of Cd in root      | [46,47,105] |
| OsNramp5 | 7   | 8871436–8878905        | Natural resistance-associated macrophage protein | Cd, Mn, and Fe transporters     | [106–110] |
| OsNramp1 | 7   | 8966025–8970882        | Natural resistance-associated macrophage protein | Cd and Fe transporters          | [111–113] |
| OsABCG43 | 7   | 20214025–20218702      | ATP-binding cassette transporter               | Cd compartmentalization          | [45]      |
| OsMAPK2  | 8   | 3307520–3310590        | Mitogen-activated protein kinase               | Cd signal                        | [68]      |
| OsHIR1   | 8   | 19011814–19015998      | Heavy metal-induced RING E3 ligase 1          | Cd uptake                        | [114]     |
| SISAP1   | 9   | 18760704–18761836      | Subspecies indica stress-associated protein gene | Cd tolerance                    | [115]     |
| OsPCR1   | 10  | 826309–824623          | Plant cadmium resistance 1                    | Cd tolerance                     | [116]     |
| rgMT     | 11  | 28827746–28828439      | Metallothionein-like protein                   | Cd tolerance                     | [117]     |
| RCS1     | 12  | 26698650–26703087      | Cytosolic cysteine synthase gene               | Cd complexation via sulfur       | [118]     |
3. Uptake and Transport Pathway of Cd in Rice

Cadmium is transported from the roots to shoots and then to grains through four steps: (i) uptake by roots; (ii) transportation to shoots through loading to the xylem; (iii) distribution and transportation through nodes; and (iv) transportation to grains through the phloem from leaf blades (Figure 1).

![Figure 1](image_url)

**Figure 1.** A schematic of cadmium transport from the soil to grains in rice. Cadmium is absorbed from the soil by the roots, and OsNramp1, OsNramp5, and OsCd1 mediate this process. OsHMA3 plays a key role in cadmium segregation to vacuoles in root cells and thus negatively regulates cadmium xylem loading. OsHMA2, OsCCX2, and CAL1 regulate cadmium transport to the xylem. OsLCT1 contributes to cadmium remobilization from leaf blades via the phloem and is likely to play a part in intervascular cadmium transfer at nodes.

3.1. Functional Analysis of Related Genes

Cd can enter rice plants through the uptake mechanism of essential elements such as Mn, Zn, and Fe, etc. [106,107,119]. Fe$^{2+}$ transporters OsIRT1 and OsIRT2 display Cd$^{2+}$ influx activity in yeast, which indicates that OsIRT1 and OsIRT2 may play a role in cadmium uptake in the root system [95,120]. Overexpression of OsIRT1 significantly increased the accumulation of Cd in roots and shoots in Murashige & Skoog (MS) medium containing excess Cd, but no obvious phenotype was observed under field conditions, suggesting that OsIRT1 may be involved in cadmium uptake in roots, but its contribution is largely affected by environmental conditions [96]. Oryza sativa Natural Resistance-Associated Macrophage Protein 5 (OsNramp5), located at the plasma membrane of root cells, was found to be the major transporter of Cd uptake in rice roots, responsible for the transport of Cd from the soil solution to the root cells [106,107]. OsNramp5 is also an Mn transporter, and the knock-out of OsNramp5 can significantly reduce the uptake and accumulation of cadmium in grains, but also lead to the decrease of growth and yield due to manganese deficiency [107–109]. Recently, Liu et al. [121] located a major QTL, qGMN7.1, according to the Mn concentration in the grains of a recombinant inbred line (RILS) crossed between 93–11 (low grain Mn) and PA64s (high grain Mn). Fine mapping delimited qGMN7.1 to a 49.3 kb region containing OsNRAMP5, and sequence variations in
the OsNRAMP5 promoter caused changes in its transcript level and in grain Mn levels. Tang et al. [110] reported that a series of new indica rice lines with low cadmium accumulation were developed by knocking out the metal transporter OsNramp5 using the CRISPR/CAS9 system. OsNRAMP1, located on the plasma membrane, also exhibits the activity of Cd transport, and participates in the uptake and transport of Cd in root cells [111,112]. OsZIP1, a zinc-regulated/iron-regulated transporter-like protein, expression in yeast can enhance its sensitivity to Cd [84], and the overexpression of OsZIP6 can increase the Cd uptake in X. laevis oocytes [98].

After root absorption, xylem-mediated Cd translocation from the roots to shoots is the main factor determining the cadmium accumulation in shoots [122]. OsHMA2 and OsHMA3 were reported to play a role in this process [46,103,123,124]. OsHMA2 participates in the transport of Cd from the roots to shoots and plays an important role in controlling the distribution of Cd through the phloem to developing tissues [103,104,123]. Compared with wild-type (WT) samples, the Cd concentration in the shoots of an oshma2 mutant was significantly lower [104]. OsHMA3 plays a role in the vacuolar sequestration of Cd in root cells, the overexpression of OsHMA3 reduces the Cd load in the xylem and Cd accumulation in shoots, and the functional deficiency of OsHMA3 results in very high root-to-shoot Cd translocation in rice [46,47,105,125]. Recent reports showed that OsCCX2, a putative cation/calcium (Ca) exchanger, was localized in the plasma membrane and plays an important role in Cd transport by impacting Cd root-to-shoot translocation and the Cd distribution in the shoot tissues, and the knock-out of OsCCX2 resulted in a significant Cd reduction in the grains [94]. Tan et al. [99] reported that OsZIP7 plays a key role in xylem-loading in roots and inter-vascular transfer in nodes to deliver Zn and Cd upward in rice.

Nodes are the central organ of Cd transport from the xylem to phloem, and play an important role in Cd transport to grains [126–128]. OsLCT1 is a Cd-efflux transporter on the plasma-membrane involved in phloem Cd transport [101]. OsLCT1 expression was higher in leaf blades and nodes during the reproductive stage, especially in node I. Compared with wild-type (WT), the Cd concentration in phloem exudates and in grains of OsLCT1 RNAi plants decreased significantly, although the Cd concentration in xylem sap did not differ. These results suggest that OsLCT1 in leaf blades functions in Cd remobilization by the phloem, and in node I, OsLCT1 is likely to play a part in intervascular Cd transfer from enlarged large vascular bundles to diffused vascular bundles, which connect to the panicle [101,102]. The positions of cloned cadmium stress-related genes in rice chromosomes are shown in Figure 2.

![Positions of cloned cadmium stress-related genes in rice chromosomes.](image-url)
3.2. Location of Related QTLs

Rice varieties show obvious genetic variation in terms of their cadmium accumulation ability, which is a valuable resource for dissecting functional alleles and genetic improvement [19,20,25]. However, only a few quantitative trait loci (QTLs) related to cadmium accumulation in rice have been reported. OsHMA3, CAL1 (Cd Accumulation in Leaf 1), and OsCd1 are the only Cd-related QTLs cloned so far. OsHMA3 encodes a cadmium transporter located in the vacuole membrane, which transports cadmium into vacuoles for sequestration [105]. Loss of OsHMA3 function significantly increased cadmium transport to rice shoots and grains [101,129]. On the other hand, the overexpression of OsHMA3 can increase the tolerance of rice to Cd and reduce Cd accumulation in grains [46,105,119]. CAL1 (cadmium accumulation in leaf 1) was identified and cloned by Luo et al. [88] as a quantitative trait locus (QTL) in rice, which explained 13% of the variation in leaf cadmium concentration in a doubled haploid population. CAL1 regulates the root-to-shoot translocation of cadmium via the xylem vessels, and knockout mutants of CAL1 significantly reduced the concentration of cadmium in rice leaves [88]. Yan et al. [90] discovered that the gene OsCd1 belongs to the major facilitator superfamily through genome-wide association studies (GWAS), which was associated with divergence in rice grain Cd accumulation. Interestingly, the natural variation OsCd1V449 in Japonica, which is associated with a reduced Cd transport ability and decreased grain Cd accumulation, shows a potential value in low-Cd rice selection [90].

A series of QTLs related to rice varieties that control the Cd concentration in rice have been reported (Table 2). Ishikawa et al. [130] obtained a mapping population consisting of 85 back-cross inbred lines (BIL) from hybridization between a low-cadmium-accumulation variety of Japonica rice (Sasanishiki) and a high-cadmium-accumulation variety of Indica rice (Habataki). Two QTLs were located on chromosomes 2 and 7, separately, with an increased cadmium concentration in grains. qGCd7 plays an important role in increasing the cadmium concentration in grains, which can explain 35.5% of phenotypic variation [130]. Kashiwagi et al. [131] identified two QTLs, known as qcd4–1 and qcd4–2, affecting the cadmium concentration in shoots. Sato et al. [132] reported two QTLs controlling the cadmium concentration in brown rice: qLCdG11 explained 9.4%–12.9% of phenotypic variation and qLCdG3 explained 8.3%–13.9% of phenotypic variation. Yan et al. [133] constructed an recombinant inbred lines (RIL) population of F7 to identify Cd accumulation and distribution. A total of five main effect QTLs (scc10 was correlated with Cd accumulation in shoots; gcc3, gcc9, and gcc11 with Cd accumulation in grains; and sgr5 with the Cd distribution ratio in shoots and roots) were detected. Among them, sgr5 had the greatest effect on the distribution of Cd in grains. Abe et al. [134] used a population consisting of 46 chromosome segment substitution lines (CSSL) to identify eight QTLs related to the grain cadmium content by single-label analysis using ANOVA. The result showed that qlGCd3 had a high F-test value. A recombinant inbred population derived from Xiang 743/Katy was grown in Cd-polluted fields and used to map the QTLs for Cd accumulation in rice grains, and two QTLs, qCd-2 and qCd-7, were identified in 2014 and 2015 [135]. Liu et al. [136] used 276 accessions with 416 K single nucleotide polymorphisms (SNPs) and performed a genome-wide association analysis of grain Cd concentrations in rice grown in heavily multi-contaminated farmlands, and 17 QTLs were found to be responsible for the grain Cd concentration.
| Stage             | Parent Sources          | Population       | Marker       | Trait                                | Chr. | QTL          | Reference |
|-------------------|-------------------------|------------------|--------------|--------------------------------------|------|--------------|-----------|
| Seedling stage    | Tainan1/Chunjiang06     | 119 DH, 3651     | RFLP         | Cd accumulation in leaves            | 2    | CAL1         | [88]      |
| Seedling stage    | Nipponbare/Anjana Dhan  | 965 F2           | SSR          | Cd concentration in shoots           | 7    | OsHMA3       | [105]     |
| Seedling stage    | SNU-SG1/Suwon490        | 91 RIL           | 124 SSR      | Cd concentration in shoots           | 10   | scc10        | [133]     |
| Seedling stage    | Koshihikari/LAC23       | 46 CSSLs         | 345 SNP      | Cd concentration in shoots           | 3    | qGCd3        | [134]     |
| Seedling stage    | Anjana Dhan/Nipponbare | 177 F2           | SSR          | Root-to-shoot Cd translocation       | 7    | qCd7         | [137]     |
| Seedling stage    | Badari Dhan/Shwe War    | 184 F2           | 141 SSR      | Cd concentration in shoots           | 2, 5, 11 | —         | [138]     |
| Seedling stage    | JX17/ZYQ8               | 127 DH           | 160 RFLP/83 SSR | Shoot/root rate of Cd concentration | 3    | qSRR3        | [139]     |
| Seedling stage    | JX17/ZYQ8               | 127 DH           | 160 RFLP/83 SSR | Cd concentration in roots and shoots | 6, 7 | qCD7, qCDR6.1, qCDR6.2 | [139]     |
| Seedling stage    | Azucena/Bala            | 79 RIL           | 164 SSR      | Cd concentration in leaves           | 1, 3, 6 | qCd1, qCd3, qCd6, | [140]     |
| B before heading  | Kasalath/Nipponbare     | 98 BILs          | RFLP and SSR | Cd concentration in leaves and culms | 4, 11 | qCd3, qCd4, qCd4-2, qCd11 | [131]     |
| Mature period     | Sasanishiki/Habataki    | 85 BIL           | SSR          | Cd accumulation in grains            | 2, 7 | qGCd7        | [130]     |
| Mature period     | Fukuhibiki/LAC23        | 126 RIL          | 454 SNP      | Cd accumulation in grains            | 3, 11 | gLCdG3, gLCdG11 | [132]     |
| Mature period     | SNU-SG1/Suwon490        | 91 RIL           | 124 SSR      | Cd accumulation in grains            | 3, 5, 9, 11 | gcc3, sgr5, gcc9, gcc11 | [133]     |
| Mature period     | Xiang 743/Katy          | 115 RIL          | SSR          | Cd accumulation in grains            | 2, 7 | qCd-2, qCd-7 | [135]     |
| Mature period     | Kasalath/Koshihikari    | 39CSSL           | 129 RFLP     | Cd accumulation in grains            | 3, 6, 8 | —         | [141]     |
| Mature period     | Koshihikari/Jarjan      | 103 BIL          | 169 SSR      | Cd accumulation in grains            | 7    | —           | [142]     |
| Mature period     | JX17/ZYQ8               | 127 DH           | 160 RFLP/83 SSR | Cd accumulation in grains           | 3, 6 | qCd3, qCd5, qCd5.2 | [143]     |
| Mature period     | 127 rice cultivars      | GWAS             | Cd accumulation in grains | 3 | OsCd1 | [90] |
| Mature period     | 378 rice cultivars      | GWAS             | Cd accumulation in grains | 3, 5 | qCd3, qCd5.1, qCd5.2 | [144]     |
4. Future Perspectives

Cadmium is a kind of heavy metal that presents extreme biological toxicity. Cd accumulated in rice can enter the food chain, thereby threatening human health [5–7]. Cadmium in rice can be reduced by agronomic practices (including soil amendments, fertilizer management, water management, and tillage management) and bioremediation (including phytoremediation and microbial remediation) [18,145–150]. In addition, understanding the mechanism of cadmium translocation and the factors affecting cadmium accumulation in rice are also important for formulating effective strategies to reduce cadmium accumulation in rice. In recent years, some genes related to cadmium transport in rice have been studied, and significant progress has been made in understanding the mechanism of cadmium uptake and transport. In order to understand the mechanism of cadmium transport in rice, it is necessary to identify more unknown transporters or other molecules.

Biotechnology offers a promising approach to reducing the Cd content in rice grains. Mutations of the OsNramp5 gene result in obvious decreases in Cd uptake in roots and Cd accumulation in rice grains [106,108,151]. Using the CRISPR/Cas9 gene editing technology to knock out OsNramp5 in both parental lines, Tang et al. [110] generated a hybrid rice cultivar that accumulated very low levels of Cd in the grain. Another target for gene editing is OsLCT1, which is involved in the phloem transport of Cd from the vegetative tissues to the grains [101]. Knockdown of this gene by RNAi reduced the grain Cd concentration by 30%–50% [101]. Overexpression of functional OsHMA3 in Nipponbare decreased Cd translocation and Cd accumulation in rice grains [46,105]. Overexpression of OsHMA3 is a highly effective method for reducing Cd accumulation in Indica rice, and rice grains produced using this approach are almost Cd-free, with little effect on the grain yield or essential micronutrient concentrations [152].

However, commercial transgenic rice is not commonly accepted by the general public and prohibited in many countries. Ishikawa et al. [151] produced three rice mutants by carbon ion-beam irradiation, where cadmium was hardly detected in mutant seeds when planted in cadmium-contaminated paddy fields and there was no significant difference between the mutant and wild-type (WT) in agronomic traits, which could be directly applied to breeding projects. Another possible strategy is marker-assisted breeding, which uses molecular markers to track the genetic composition of rice and bred rice varieties. For example, identifying a low-cadmium-related QTL and then introducing it into high-cadmium cultivars might be a viable approach [122]. However, only a few of QTLs related to cadmium accumulation in rice have been cloned [90,105], and the natural allele variation of grain cadmium accumulation differences among rice varieties has not been fully explored. Further research is necessary to clone more QTLs for controlling grain Cd accumulation, thus providing tools for the marker-assisted molecular breeding of rice cultivars with a low accumulation of Cd in grains.

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