doi:10.20944/preprints202208.0154.v1

Article.

Integrated genetic and omics approaches for the regulation of nutritional activities in rice (*Oryza sativa* L.)

Muhammad Junaid Zaghum[1,2,4], Kashir Ali [3] and Sheng Teng[1,4*]

[1]Laboratory of Photosynthesis and Environmental Biology, CAS Center for Excellence in Molecular Plant Sciences, Institute of Plant Physiology and Ecology, Chinese Academy of Sciences, 200032 Shanghai, China
[2]Seed physiology Laboratory, Department of Agronomy, University of Agriculture Faisalabad, 38000, Pakistan
[3]Institute of soil and environmental sciences, University of Agriculture Faisalabad, 38000, Pakistan
[4]University of Chinese Academy of Sciences, 100049 Beijing, China
* Correspondence: Sheng Teng, Email: steng@cemps.ac.cn

Abstract: The primary considerations while producing rice (*Oryza sativa* L.) include improving its nutritional quality and production. To tackle widespread hunger globally, better nutritional, high-yielding rice cultivars need to be developed. The conventional ways are to increase the production of rice and add balanced nutrients in the daily diet to fulfill the need of yield and nutrient quality. This article focuses on nutritional strategies for rice and illustrates the availability of omics technologies. Current advancements providing many methodologies and approaches for exploring genetic resources and for understanding the molecular mechanisms involved in trait formation have been highlighted. Studying the genetic influences of various characteristics has been proven to expedite crop breeding processes. In this perspective, genome-wide association research, genome selection (GS), and QTL mapping are all genetic analysis that helps in increasing the nutritional content of rice. Implementation of several omic techniques are effective approaches to enhance and regulate the nutritional quality of rice cultivars. Advancements in different types of omics including genomics and pangenomics, transcriptomics, metabolomics, nutrigenomics, and proteomics are also relevant to rice development initiatives. This review article compiles genes, locus, mutants and all omic approaches for rice enhancement. This knowledge will be very useful for now and for the future regarding rice studies.

Keywords: Genome selection; Rice breeding; Genetic analysis; Omics assisted markers; Nutritional quality; Genomics and Pangenomics; Biofortification

1. Introduction

Rice is the most edible and nutritional globally staple food. It is mostly used as a staple food in Asia and has nutritional importance in cereal families [1]. Rice is farmed on about 162 million hectares of land in tropical and subtropical zones with different temperatures (25ºC to 35ºC) and climatic conditions and globally produces 755 million tonnes of rice in a year (FAOSTAT) (http://www.fao.org/faostat/en/#data/QC/visualize). Rice contains a variety of complex carbohydrates, amino acids, minerals, nutritional fiber, and vitamins. Due to use as a staple food in numerous impoverished nations, it offers around 27% of calories, 20% of protein, and 715 kcal/day in the diet. Global population growth has necessitated a double increase in agricultural output and quality to fulfill the rising demand. Approximately 100 million additional tonnes of rice are estimated to be needed to feed the world population growth of one billion people. Together with quantity, rice quality and nutritional value are critical components of food security [2]. The World Health Organization (WHO) establishes standards for rice basic composition and structural quality characteristics depending on the amino acids, mineral, flavonoid content, proteins, carbohydrate, and essential vitamins that are present in rice grain [3]. Pure rice has acceptable levels of inorganic and organic unwanted matter and free from toxic heavy metals such as mercury (Hg), arsenic (As), lead (Pb), and cadmium (Cd) are considered to be of edible quality [4]. Rice is a good source of nutrients, including iron (Fe), calcium (Ca), essential vitamins, phosphorus (P), potassium (K) and sodium (Na) [5]. Several methods are adopted to reduce the Cd accumulation intake in rice by altering the cropping pattern, phytoremediation, breeding Cd tolerant varieties, and maintaining the pH in rice fields [6]. Brown rice is high in iron, proteins, and phosphorus are usually regarded as the more nutritious variety of rice. The most famous basmati rice includes lipid 6-gram, 19 g of protein, and 364 kcal of energy, and jasmine rice has 356 kcal of energy, approximately 6.67 g of protein, and some amount of lipids [5].

FAO estimated over two billion people globally suffer from hidden hunger. Developing and impoverished nations are trying for several years to improve productivity and fulfill the need of some staple crops that provide the majority of nutritional benefits and required calories. This type of usage and evaluation of nutritional quality are missing in other micronutrients, vitamins, and mineral-containing crops [7]. Rice biofortification is one of the most successful strategies in this direction. Rice can be biofortified by agronomic techniques, traditional breeding, or genetic modification. Conventional plant breeding refers to the process of selecting and crossing desirable characteristics in crops over several generations. Modern biofortification technologies, such as genetically engineered, offer ways for altering genetic sequences to confer desired characteristics [8]. According to the WHO, the most essential challenge is to fortify rice to eliminate malnutrition among a big population worldwide suffering from folic acid, iron, and vitamin A deficiencies [3]. Biofortification by genetic advancement is a reliable and cost-effective method of increasing access to fortified food for economically deprived groups of the population [8].

The traditional breeding approaches aren’t much complicated because it is not only dependent on the basic gene pool that is the only genetic resource and makes significant contributions to rice production and development. In addition, the utilization of transgenic approaches helps in the identification of genetic materials from multiple living organisms that enable the engineering of desired features in plants [9]. Golden Rice is one of the most noticeable achievements of the transgenic method, especially in terms of nutritional quality improvement. Transgenic Golden Rice is a low-cost solution for vitamin A deficiency. Golden Rice has been biofortified with β-carotene, which the human body transforms to vitamin A. Vitamin A is essential for boosting immunity and preventing night blindness. UNICEF estimates that around 125 million children worldwide are vitamin A deficient. Because rice is eaten globally, it was considered as a source of vitamin A and a transporter for β-carotene. Golden rice has encountered difficulties associated with the correct management of Genetically Modified Organisms (GMOs) and opposition to GM technology [10]. The issues slowed the progress of several additional transgenic varieties and many other crop initiatives and ultimately cause the researchers to abandon transgenic technologies. Several of these technologies, collectively referred to as genome editing technologies, have demonstrated enormous value and lower sociocultural stigma than GMOs. Gene editing techniques are drawn from mechanisms found in living species, including DNA repair and the defensive mechanisms adopted by bacteria against infections and do not need the insertion of foreign genes into the desired genome. Effective research of genomic technologies is contributing to overcoming the normal barriers to the commercialization of genetically engineered crops [11]. Omics assisted breeding of rice has the potential of genetic enhancement and largely considered as a sustainable, suitable, safe, unbiased, and significant method for the betterment of rice crops. The advanced omics techniques encompass variety of technologies including proteomics, transcriptomics, nutrigenomics, ionomics, metabolomics, and genomics, that facilitate scientists to predict, recognize, and analyze a wide variety of reproductive molecules present in a living organism, including RNA, protein, ions, DNA and metabolites [12]. Due to advancements in sequencing techniques during the last decade, a large amount of data of transcriptome, sequence, and whole genome have been created for major crops. We have discussed the efforts taken in this article to increase the nutritional content of rice, the problems and challenges facing rice breeders, and the existing omics resources and techniques for boosting rice improvement initiatives.

2. Nutritional quality enhancement by QTL mapping in rice

Over the last few decades, tremendous progress has been made in increasing food output and affordability for resource-poor populations. Milled rice is composed of starch, that is, a complex carbohydrate. Rice has a slightly low protein content than wheat, maize, and pulses, protein is the 2nd most essential component of cereal crops, even though little effort has been made to increase [13]. Therefore, fortification of rice with antioxidants, vitamins, modified starch, and dietary fibres are desirable characteristics to make rice a better complete staple meal at a reasonable price [8]. Genetic enhancement of such characteristics needs a thorough study of the genetic control of the trait, the genetics and molecular pathways underlying trait regulation, as well as environmental influences. The majority of these characteristics are complicated and are regulated by a large number of moderate impact genes. The self-pollinated nature of rice enables the establishment of a variety of mapping populations, which includes F2 population, doubled haploid (DH), backcross inbred lines (BILs) and recombinant inbred line (RIL) [14]. Some newly formed innovative mapping populations such as NAM (nested association mapping) [15] and MAGIC (multiparent advanced generation intercross) populations and used to map complex traits [16].

Mapping of quantitative trait loci investigated to determine the genetic region controlling rice nutritional quality characteristics. The rice mutants with high Fe and Zn concentrations showed Zn concentrations ranging from 15.36 to 28.95 mg/kg and Fe concentrations ranging from 0.91 to 28.10 mg/kg [17]. The complexities of nutrition quality-related characteristics vary significantly; for example, certain variables, such as folate content, have a limited number of significant QTLs, While others, such as protein content, have a large number of minor effect QTLs. Considerable effort is being made to identify quantitative trait loci for protein content of rice grains that are mainly located on rice chromosomes segment 3 and 5 [18]. Numerous characteristics associated with nutritional quality are linked, and their QTLs typically co-localize. For example, on rice chromosome 6, retrogradation, peak viscosity, QTLs for gel consistency, amylose concentration, breakdown viscosity, final viscosity, setback viscosity and trough viscosity were identified [19]. Consequently, many improved nutritional traits are adversely controlled, making simultaneous improvement difficult. For example, grain iron content is inversely linked to grain production per plant. Similarly, the phytic acid concentration of rice affects mineral bioavailability [17].

Increase in QTL span and uncertainty in localization that occurs in the complication of QTL mapping applicability to the breeding program. Consensus QTLs are selected for meta-QTL analysis, and a couple of previously completed researches are used to improve the locations of the aforementioned QTLs. Additionally, metaQTLs are specified at the 95% confidence level [20]. In this perspective, the MetaQTL method offers an ideal chance to combine published QTL mapping information from several researches to determine more exact statistically significant levels and phenotypic changes in rice, as well as accurately characterize the QTL span. On chromosome five, one such example involves a shared QTL for phosphate and phytate [21]. Further study attempts found three MetaQTLs associated with higher Zn and Fe concentrations in rice. A similar MetaQTL study was done to discover potential genes for salt tolerance, rice root shape and grain size [22]. Although research on the combined or antagonistic impact of multiple QTLs for enhanced nutritional characteristics has been done, further studies are necessary to explore the combined or antagonistic impacts of multiple QTLs for enhancing nutritional contents [17].

Table 1. Some Rice genes that control regulation of nutritional quality traits.

Gene	Function	Locus	References
glu4a	Gene involves in storage proteins of seed	Os01g55690	[23]
lpa1	Metabolize the phytic acid	Os02g57400	[24]
OsbZIP58, OsSMF1	Helps in accumulating the storage protein	Os07g08420	[25]
OsNAS3	Improve the fortification of iron in rice seed	Os07g48980	[26]
OsVIT2	Involve in translocation of iron	Os09g23300	[27]
OsYSL2	Transportation of manganese and iron at long distance	Os02g43370	[28]
RAG2	Functioning in yield and grain quality	Os07g11380	[29]
XS-lpa2-1	Involve with phytic acid accumulation	Os03g04920	[30]

3. GWAS analysis improves rice nutritional quality traits

While the effectiveness in identifying segments of chromosome linked to characteristic QTL mapping has two significant downfalls. The QTL mapping resolution is very limited and is only used to study segregated alleles from parent line [31]. These drawbacks of QTL mapping are eliminated by using the GWAS techniques [32]. GWAS is a technique for rapidly scanning markers throughout the whole set of DNA to identify genetic changes linked to a certain trait of several species. Following the finding of novel genetic interactions, efficient breeding methods can be used to enhance the yields of rice and other crops [33]. Additionally, the GWAS technique has numerous drawbacks, including the increasing of genotype markers, diverse resources of big germplasm collection, allele data, such as the presence of minor alleles in at least 5% of the germplasm pool [32]. For unique alleles found in a small number of genotypes, QTL mapping is generally the best method. Recognizing the limits of both methods, it is recommended that they be used in conjunction to identify QTL [34]. The rice seed-related characteristics are analyzed by the usage of QTL mapping and GWAS analysis in combination. The concentrations of Zn, Mo, As, and Cu in 300 brown rice varieties were determined by using GWAS mapping [35]. These elements show variations in grain composition that are linked to the number of candidate genes and SNPs, and the main reason of variation is environmental circumstances [36]. Mappings of GWAS and QTL are performed in combination to investigate traits such as Al accumulates, although combined research on grain nutrient content is rare [37]. In comparison to QTL mapping, fewer efforts are undertaken to characterize nutritional quality traits using GWAS.

4. Efficacy and capability of nutrient-rich rice breeding through genome selection (GS)

Molecular marker-assisted breeding is an effective strategy for incorporating desirable characteristics from a pool of high-yielding cultivars, which can only be done with previous information on specific gene loci, associated markers, and repeated backcrossing of large segregating progenies [13]. Additionally, the recently introduced trait might not always improve as predicted because its belong to a diverse genetic background and the undesired attachment leads to a significant issues of marker-supported breeding [38]. Meuwissen et al. (2001) proposed genomic selection (GS) to overcome these constraints by estimating the potential of breeding lines of rice that are based on high density markers and phenotypic values. Genome selection is a genetic analysis that is done by using marker selection in which the genetic markers of whole genome are applied to ensure the linkage of QTL with at least one marker [40]. Genome selection is being reconsidered in light of current genotyping technologies like genotyping of the next generation. The efficacy of genome selection analysis is enhanced and cost-effective by innovative genotyping methods [41]. Despite the availability of several genotyping technologies and whole-genome sequenced genotypes, the genome selection method relatively takes some extra effort for rice [42]. Genome selection is more likely to utilize in the addition of NGS (next generation selection) genotyping technologies in many breeding processes. GS genotyping technique is cost effective and it increases the efficacy of genome selection technology many times. There are many genotyping methods that are publicly introduced such as whole genome sequences but the usage of genome selection method for rice genotyping done with minimum efforts [43]. The efficacy of genome selection was studied in rice for the first time by using inbred lines to improve grain or seed quality characteristics such as height of the plant, total yield, grain yield, and blooming duration [42]. The combination of GS and GWAS discovered that genomic forecast models outperformed pedigree-based prediction in predicting the phenotype [44]. This study shows that the expense of genotyping technology has increased the value of GS, when coupled with GS and GWAS data on genetic layout and population size also boost rice breeding efficiency [45]. In comparison to yield-related features, the majority of quality-related traits may be predicted accurately. Because quality characteristics have a greater heritability, implementing of GS becomes easier [41]. The GEBV (genomic estimated breeding values) computed using the GS technique demonstrated a broad range of reliability for characteristics within the rice plant like flowering time, plant height, grain yield, and panicle weight. To understand the impact of population structure and marker density on the reliability of genomic prediction, researchers may also look at the structure of characteristics, as well as the reliability of prediction based on genotype [46]. In 2014, a novel approach termed genomic hybrid breeding for prediction model was suggested with the combination of epistasis and dominance [47]. Combination of phonological modeling and genome prediction to enhance the phenotypic prediction of complex traits among various settings for rice genomic hybrid breeding [48]. While genome selection is increasingly utilized to examine rice quality features, the investigation into its efficacy in evaluating nutritional aspects remains lagged.

5. Mutation mapping and mutagenesis techniques: Triggers the nutritional quality of rice

Mutations contribute to heredity and genetic diversity and utilized to investigate the functioning of several genes. Conventional hybridization utilizes known genetic changes and new mutations are occasionally added to acquire unique characteristics. Mutations can occur spontaneously or be caused by chemical and physical agents. Chemical agents such as ethyl methanesulfonate, diepoxybutane, physical agents such as gamma rays, fast neutrons, thermal neutrons, UV light, X rays, beta and alpha particles, intercalating agents such as ethidium bromide, and alkylating agents such as ethylmethanesulfonate [49].

The combination of hybridization and gamma rays have been utilized to produce novel varieties of aromatic rice that increase the level of iron content, indicating that hybridization methods can be used to generate new cultivars with much better characteristics. Numerous mutant rice lines have been produced, including the Thai jasmine rice in which the anthocyanin concentration was enhanced to give blue color by the bombardment of ion-beam [50]. BKOS jasmine rice variety extracts from the mutant strain that enhanced the antioxidant activity and had high phenol content [51]. The mutant lines of low phytic acid (LPA) were produced by using physical and chemical mutagenesis from the Japonica rice and Indica rice species because phytic acid is usually recognized as an antinutritional factor [52].

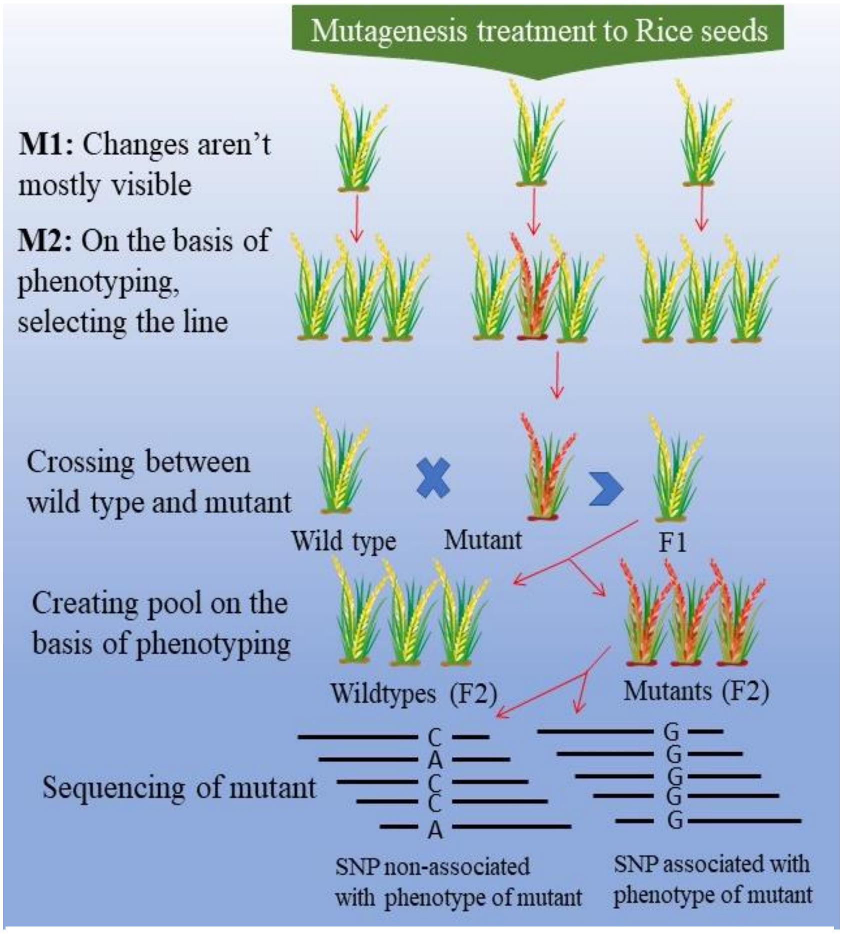

Figure 1. The process of MutMap approach.

While inducing mutations significantly taking less effort and easier, identifying, the future use of mutation for the breeding process requires more considerable work. Many approaches for mutation mapping are established with the introduction of next-generation sequencing technique (NGS) [53]. Such as MutMap is a new technique used for identifying primary mutation mapping and mutant loci through the use of sequencing variation in segregated mutant lines. In this technique, the plants have acquired most of their mutations through mutagenesis treatment, and as a result, there are no obvious differences to be seen. Line segregation and homozygosity of the plant for the demonstration of mutant phenotypic variations in the following generation (M2). Produce the F1 population by crossing the wild type variety with the mutant phenotype and further F1 populations are crossed to produce the next generation (F2). Next-generation sequencing (NGS) is then used to analyse the sequencing data from individuals with a wild-type and a mutant phenotype to identify mutations that are linked to the mutant phenotype. It characterizes the mutation by evaluating SNP frequency in the wild-type DNA and mutant offspring of the M3 generation acquired just after self-pollination of the M2 heterozygous lines as shown in Figure 1. The technique was initially applied on rice by Abe et al. (2012). When coupled with MutMap, a similar approach called MutMap-GAP facilitates the recognition of the specific gene from gaps within the specific reference genome. MutMap has been used to determine regions that may have the desired mutation. The de novo assembling is carried out after determining the targeted region that preceded by alignment and detected the mutation from different regions [55]. Not only the mutation and mutagenesis methods allowed us to discover genetic regions associated with the desired characteristics, but they have also contributed to the expansion of diversity and the development of mutant rice varieties with improved agronomic quality.

6. Integrative omics technologies for enhancement of rice nutritional quality traits

Extensive understanding of agronomically relevant characteristics is which facilitated by integrating effective studies that incorporate relevant information from proteomics, metabolomics, genomes, nutrigenomics, and transcriptomics. Meanwhile, many advancements in advanced technology are made in sequencing methods and data analysis, as well as the availability of the entire rice genome sequences, have accelerated attempts to enhance significant the characteristics of crops nutritionally and agronomically [12]. Along with identifying genes involved in agronomic characteristics, an integrated omics-based research method attempts to unravel biochemical mechanisms and connections between biomolecular regulation and activities. Although the whole rice genome was sequenced a long time ago, several specific proteome, transcriptome, ionome, and metabolome research have been conducted to improve the nutrient content of grains by using genomic data. However, still, there are large embedded omics initiatives that have not been used to their full capacity [56].

Effective gene information exploration requires a thorough knowledge of genetic control, molecular mechanisms, and complicated genes environment and gene-with--with-gene interactions. omics technologies enable the collection of comprehensive data necessary for product development [57]. Numerous genes of rice influencing nutrient quality-related characteristics are being actively researched in new ongoing studies. The knowledge on these genes is growing due to various omics tools and being effectively investigated using molecular breeding, transgenic approaches, and even comparatively new technologies such as genome editing [58].

Among the several combined omics studies providing a large amount of data includes research in which researchers found 3000 metabolites by using metabolomics from ten cooked rice varieties. Functional genomics are utilized to explore the genetic differences that result in metabolite diversity. It also allowed researchers to investigate the gene variety of phenolic chemicals and identify SNPs in their UTRs which control gene expression [12]. An investigation was done to examine the genetic and metabolic differences between traditional and enhanced waxy rice cultivars. This study determined nutritional and yield variations between three varieties of rice [59]. There is the scarcity of such integrated omics initiatives aimed at deducing connections between and extensively studying rice crops nutritionally and agronomically significant characteristics.

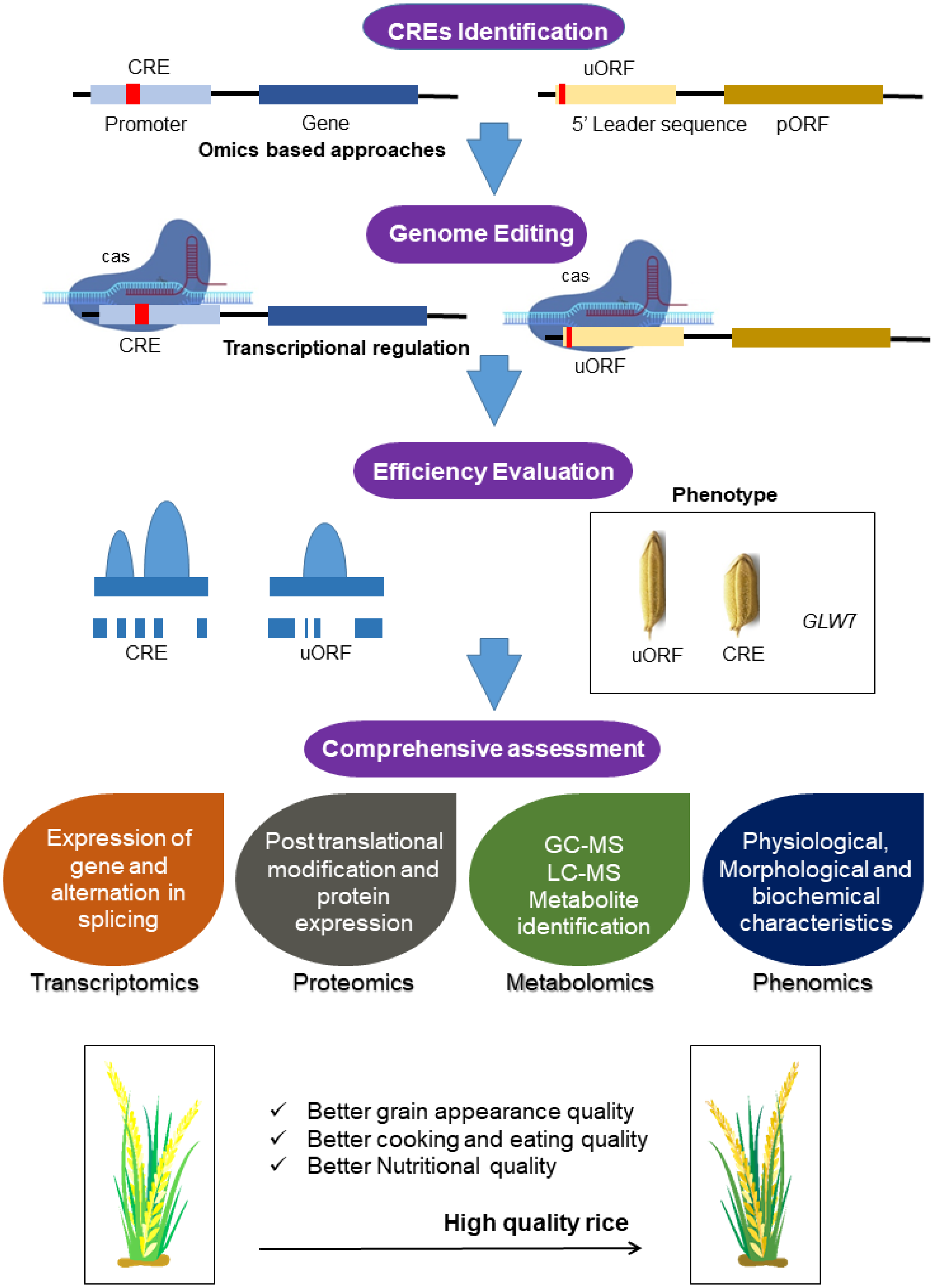

Figure 2: Flowchart demonstrating the use of genome editing techniques to produce high-quality rice grains.

6.1. Genomics and pan-genomics analysis

Several rice genomes have been constructed to diverse levels of quality during the last two decades, ranging from draft genome to relatively close high reference sequencing, using a variety of sequence and construction methodologies [54]. Using single molecule real-time sequencing (PacBio), and high-throughput short-read sequencing (Illumina), several additional rice genome sequences have been created since the availability of the nip reference sequence from the International Rice Genome Sequencing Project in 2005 [60] based on bacterial artificial chromosome Sanger sequencing. BioNano genome mapping (BioNano Genomics, San Diego, CA, USA), Single-molecule sequencing, and high-throughput chromosomal conformation capture (Hi-C) sequencing are some of the latest genome assembling methods that take use of the enhanced read length and/or base precision of single-molecule sequencing. Combining these techniques, as well as the development of novel assembly tools, has resulted in a significant improvement in assembly quality, allowing for the generation of highly consistent chromosome-level assemblages at a low cost. PacBio's introduction of HiFi sequencing in 2019 constitutes a technological milestone [61]. Since the introduction of R498, several rising rice genomes have been constructed, such as 12 genomes with an average gap count of 18 per genome and an average completeness of up to 98.75 percent [62] and 31 genomes with an average contig N50 of 12.89 Mb and a gap count of 63 [63]. Through precise gene mapping and genome-wide association studies (GWAS) [64], these genomes have aided in the analysis of population diversification and gene characterization.

The BB genome of *Oryza punctata* [65], the KKLL genome of *Oryza coarctata* [66], and six AA genomes have been constructed in the past decade using different methodologies. All wild rice genomes are able to be arranged with the conjunction of SMRT, PacBio sequence analysis, BioNano genome mapping, and Hi-C sequence analysis, as demonstrated by the last several arrangements of a rising chromosome-scale AA genome (contig N50, 13.2 Mb) from an extremely heterozygous *Oryza rufipogon* accession [67] and of the heterozygous allotetraploid *Oryza alta* CCDD genome (contig N50, 18.2 Mb) with comprehensiveness similar to that of the cultivated rice genome.

Numerous sequences and genes that are not included in the nip reference genome have been found via pan-genomic investigations, as well as genes that are not present across all genomes. It was found that 1300 novel genes (missing from nip) and 3144 dispensable genes, including several genes involved with disease resistance, were found in the draught genomes of Xian IR64 and aus DJ123 when compared to the reference genome. It was found that 268 mb of novel sequences, 12,465 complete new genes, and 19,721 nonessential genes were discovered in a study of the 3010 rice genomes [68]. Researchers discovered 10,872 novel genes that were at least largely absent in nip and 16,208 expendable genes using de novo assembly drafted genomes of 66 typical cultivated and wild A-genome rice accessions [69]. For agronomic variables such as grain length, grain breadth, and bacterial blight resistant rice, pangenomic studies have helped improve gene mapping by GWAS and offered fresh information on rice's evolution and domestication [68,69]. Technology advancements in genomics and synthetic biology have the potential to speed up agricultural improvement [70]. It is possible to create rice cultivars with high yield, excellent quality, and resistance to stressors by precise breeding of numerous favourable alleles [71]. Many genes in Asian rice have been altered to increase quality, resilience, or yield, in contrast to the de novo adoption of *Oryza alta* [72]. Using these technologies on a wide scale for rice development demands an in-depth awareness of the agronomic characteristics' complicated genetic architecture. As it is, the bulk of genetic variation in rice is not covered by existing rice pan-genomes, which include just AA genomes from a few Oryza species. For this reason, it is imperative to build Oryza pangenomes to incorporate different cultivated and wild rice genomes, so that the entire Oryza genus may be studied.

6.2. Transcriptomics: Rice nutritional quality enhancement through RNA sequences

Transcriptomics is an analysis of RNA expression patterns that considers both coding and noncoding sequences of RNA present in cells at any particular point. Different methods have been established to characterize the pattern of gene expression of rice plants, including the sequences of RNA and microarrays. Many RNA sequence samples are uploaded in the NCBI SRA database and this database increases day by day with RNA sequences [73]. Likewise, using the RNA sequence data, the gene expression omnibus (GEO), has been openly available for the usage of collected data of transcriptome profiling by using microarrays (GEO) (https://www.ncbi.nlm.nih.gov/geo/). The first attempt was taken in the 1990s to identify the whole transcriptome. The transcription patterns of the whole genomes of rice species (*O. sativa* indica and japonica) were acquired by RNA-sequencing [74]. Researchers found that the analysis of RNA-seq on large-scale improved the coding of the rice genome by identifying 101 novel loci and 1584 unique peptides that are matched with new peptides. Additionally, different splicing has been examined concerning the regulation of mineral nutrient equilibrium in rice [75]. Transcriptomic and microarray investigations have been undertaken to better understand the antagonistic relationships between micronutrients [73]. Zheng et al. (2009) used microarray data to determine the antagonistic relationship between P and Fe in rice plants. Microarray analysis of rice roots was used to characterize based on molecular genetics for adjustment of macronutrient (nitrogen, phosphorus, potassium) deficiencies.

Transcriptomics permits the investigation of changes in gene expression, the explanation of previously unknown genes, and the control of genes. Large-scale genome-wide association studies (GWAS) and transcriptome studies have assisted in the prediction of genes that affect the glycaemic index (GI) of rice and less glycaemic index in nutritional quantity is critical for Type II diabetes patients and some dietary diseases including hypertension and diabetes [77]. To generate a cell-type transcriptome database, laser microdissection was employed as well as microarray profiling [78]. The majority of rice transcriptome profiling research has focused on stress tolerance with comparatively few efforts are required for nutritional quality traits.

6.3. Proteomics: Rice nutritional quality enhancement through protein

Proteomics is the study of a large number of proteins in an organism, their location, quantity, and posttranslational alterations. Proteomics supports genomics and transcriptomics to enhance our understanding of molecular structure and function. Numerous advanced techniques, including gel-free techniques such as MALDI-TOF, tandem mass spectrometry (MS), liquid chromatography mass spectrometry (LCMS-MS), and gel-assisted techniques. Researchers have used combinations of these technologies to develop large amounts of proteomics information [79]. Proteomics is concerned with the pattern of translation of biochemical and physiological activities in rice plants. Several studies demonstrate the understanding of different levels of expression of bioactive chemical compounds providing a more in-depth examination of rice's nutritional quality under a variety of circumstances. The rice KDML105 and Mali Daeng (MD) comparison revealed variations in the expression trends of antioxidant activity, anthocyanins, phenolic compounds, and during germination. The research reveals that red rice MD had more antioxidant activity, anthocyanin, and phenolic compounds when compared to KDML105 white rice [80]. Proteomics techniques appear to be promising for assessing the potential influence of transgenic on the nutritional content of food or any expression of genes followed by translation functions [79].

Many Investigations focusing on seed rice storage protein expression levels and their relationship with nutritional quality have been conducted to better understand protein regulation. Proteomic techniques were utilized to characterize 302 candidate proteins for their biochemical functions such as catalytic and hydrophilic activities, as well as binding affinity in metabolic pathways [81]. Proteome and glycomic analysis of rice chalky grains exposed to high environmental stresses showed the breakdown of starch rather than the synthesis of starch that is responsible for rice chalkiness. Proteome analysis was performed on 25 genes that are related to metals in rice and includes zinc and iron concentration in seed which are beneficial for biofortification reasons. The finding focuses on the chemical process through which metal is transported from flag leaves to seeds [82]. The cultivar-specific two high-yielding rice cultivars were analyzed to determine the phenolic content and antioxidants when exposed to varied ozone concentrations. The study observed alterations in the antioxidant defense pathways and proteome of the leaf, as well as a decline in grain quality and production [83]. Thus, proteome study is integrated with genetics to aid in understanding the changing protein content in plants and their genes involved in the efficient protein concentration in grains.

6.4. Metabolomics: Rice nutritional quality improvement through metabolic regulation

Metabolomics is the qualitative and quantitative analysis, systematic identification, and quantification of small molecules in biological organisms. Many such analytical methods for the analysis of plant metabolomes are including mass spectrometry (MS) techniques such as liquid chromatography (LC-MS), gas chromatography (GC-MS), capillary electrophoresis (CE), nuclear magnetic resonance (NMR), metabolic fingerprinting using ion cyclotron spatial mass spectrometry (FT-MS) and Raman spectroscopy (microscopy) [84]. Metabolomic studies found variations in bioactive chemicals between uncooked and cooked rice varieties. The research identified thousands of chemical compounds and gene SNPs controlling nutritionally significant metabolism. The variability in the metabolome of cooked rice was investigated, as well as the influence of SNPs on several cultivars of rice that have nutrient content such as vitamin E and phenolics concentration [85]. Metabolomics is a term that refers to the molecular phenotyping of biological activities and metabolic processes that occur inside it. The technique was applied to 68 rice accessions for metabolic phenotyping and identified 10 typical metabolites. In this research, metabolite profiling of rice is introduced and utilized to determine the genes, QTL, and modifications that are the main reason for nutrient quality in rice grains [86]. The research examined the rice metabolome genetically and identified 2,800 QTLs for 900 metabolites. This research illustrates the twenty-four candidate genes that are primarily responsible for the amount of rice phenolic chemicals [87]. Extensive researches are establishing about the usefulness of metabolomic in elucidating the biomolecular mechanisms behind various quality-related characteristics. Additionally, researchers developed a multiplatform metabolomics technique to analyze various metabolomics data sets to identify discriminating chemical compounds important to nutritional quality in rice. Metabolomics enables the rapid evaluation of a large number of metabolites and identifies several genetic architectures that are responsible for the regulation of bioactive chemical compounds on the nutritional content of rice. Metabolomics data can assist in the identification of breeding material for superior rice variety development [85].

Many studies reveal the metabolomics specified breeding is an important tool for improving the genetics of rice crop. The process of metabolite profiling is used to determine the vitamins, secondary metabolites, amino acids, and cofactors to help in enhancing the existing information that is supplied by dietary supplementation. Research has revealed that metabolic phenotype is correlated with the geographical origins of Japonica and Indica rice varieties [88]. Along with the metabolomics studies of commercial rice, comparable research has been conducted on wild rice varieties to identify and develop useful food. For example, the North American (*Zizania palustris*) and China (*Zizania latifolia*) species are varied in 357 secondary metabolites contents, mostly in catechins and anthocyanins [89]. Likewise, metabolomics analysis to determine the beneficial chemicals present in different shaped embryos (large and regular size) of rice grains and research reveal the large embryos may have maximum accumulating beneficial chemicals indicating the maximum nutritional grain quality of rice [90]. The metabolomic has permitted a thorough examination of the micro metabolites of rice plants that are intimately associated with phenotypic characteristics. The primary difficulty in metabolomics technology is the interpretation and extraction of massive amounts of data from biological systems.

6.5. Nutrigenomics approach enhances rice nutritional quality

Nutrigenomics focuses on the connection between nutritional consumption and health impacts. Its objective is to get a molecular knowledge of how dietary regimens and nutrients affect gene expression. Malnutrition is mostly caused by a persistent deficiency of vitamins and minerals. Nutrigenomics seeks to increase nutritional food quality by increasing the bioavailability of macronutrients and micronutrients in cereals and vegetables or by adding bioactive chemicals into agricultural crops [91]. Additionally, the functional characteristics and nutrigenomic impacts of germinated brown rice rich in bioactive compounds have been investigated to get a better understanding of the grain role in balanced diets. Applying gene-based markers and modern technology are helpful for breeders to accumulate alleles of genes known to influence nutritional grain quality characteristics in rice [92]. Recently, great success has been achieved in amino acid and grain protein content, glycemic index , vitamins, phytic acid, flavonoid and phenolic compounds, iron and zinc and iron content as well as linkage with QTLs but need more studies and efforts to enhance the nutritional quality of rice and curative properties [5]. Rice improvement is shown in recent studies with the introduction of high protein and zinc-rich rice cultivars and ultimately enhances the nutritional value [82]. Along with preventing potential diseases, nutrigenomics studies populations that are currently affected by a variety of disorders. The transgenic techniques are allowed to improve grain nutrition at a quicker rate. Genomic technologies have the potential to improve rice nutritional quality by working hand in hand with genetic improvement.

7. Conclusion

Rice innovation has largely concentrated on yield-related characteristics, with a lesser concentration on nutritional quality enhancement. Due to the rising population and limited resources, the use of advanced technologies and protocols will be needed to increase crop quality. In comparison to other omics branches, transcriptomics and genomics have made substantial progress, and the ensuing combination of genomics and transcriptomics has grown more common. Numerous GWAS and QTL mappings have been conducted nowadays for commercial quality-related characteristics such as elongation ratio, grain size, and fragrance yield, but these efforts are rarely to achieve the best quality of nutritional rice. The resources created for GWAS and QTL analysis may be effectively used to construct a genetic selection prediction model. Sequential use of many techniques that utilize comparable resources will be a successful approach for crop enhancement initiatives. The combination of high genotyping methods with genome selection (GS), QTL mapping, GWAS appears to be viable and cost-effective. Therefore, the publicly available omics resources for rice must be efficiently examined. Mutagenesis is one such field that has benefited from the advancement of NGS technology. The new mutation mapping techniques are more accurate, cost-effective, and rapid. Similar techniques investigating the effectiveness of diverse tools and methodologies are anticipated. Apart from making significant achievements in other omics fields, interdisciplinary research and integrated techniques have not been fully used to achieve targeted rice grain quality. In addition to conventional breeding, the omics strategy is shown more effective in improving traits. Integrating omics techniques such as proteomics, genome, ionomics, transcriptomics, and metabolomics and is critical for obtaining a full picture of rice's nutritional quality-related characteristics. The critical evaluation of rice improvement advances revealed a shortage of cheap and practical elevated phenotyping platforms capable of integrating with many other branches of omics for effective research. The implementation of omics is improving the nutritional content of rice, it can aid in the eradication of hidden hunger and helping to achieve the sustainable development goals of United Nations organization for upcoming World.

Author Contributions: M. J. Z. wrote the manuscript. S. T. designed and guided with an innovative ideas. S. T. and K. A. revised and helped in preparing the manuscript.

References

1. Dobermann, A.; Witt, C.; Dawe, D.; Abdulrachman, S.; Gines, H.C.; Nagarajan, R.; Satawathananont, S.; Son, T.T.; Tan, P.S.; Wang, G.H.; et al. Site-specific nutrient management for intensive rice cropping systems in Asia. *Field Crops Research* **2002**, *74*, 37–66, doi:10.1016/S0378-4290(01)00197-6.
2. Yankah, N.; Intiful, F.D.; Tette, E.M.A. Comparative study of the nutritional composition of local brown rice, maize (obaatanpa), and millet—A baseline research for varietal complementary feeding. *Food Science and Nutrition* **2020**, *8*, 2692–2698, doi:10.1002/fsn3.1556.
3. World health organization. Fortification of rice with vitamins and minerals as a public health strategy. **2014**. https://www.who.int/publications/i/item/9789241550291 [accessed June 15, 2021].
4. Zakaria, Z.; Zulkafflee, N.S.; Mohd Redzuan, N.A.; Selamat, J.; Ismail, M.R.; Praveena, S.M.; Tóth, G.; Abdull Razis, A.F. Understanding potential heavy metal contamination, absorption, translocation and accumulation in rice and human health risks. *Plants* **2021**, *10*, 1–29, doi:10.3390/plants10061070.
5. Ye, J.; Hu, X.; Luo, S.; McClements, D.J.; Liang, L.; Liu, C. Effect of endogenous proteins and lipids on starch digestibility in rice flour. *Food Research International* **2018**, *106*, 404–409, doi:10.1016/j.foodres.2018.01.008.
6. Liu, T.; Sun, L.; Meng, Q.; Yu, J.; Weng, L.; Li, J.; Deng, L.; Zhu, Q.; Gu, X.; Chen, C.; et al. Phenotypic and genetic dissection of cadmium accumulation in roots, nodes and grains of rice hybrids. *Plant and Soil* **2021**, *463*, 39–53, doi:10.1007/s11104-021-04877-1.
7. Food and agriculture organization. A regional rice strategy for Sustainable food security in Asia and the pacific. **2014**. http://www.fao.org/3/i3643e/i3643e00.htm [accessed June 15, 2021].
8. Simkin, A.J. Genetic engineering for global food security: Photosynthesis and biofortification. *Plants* **2019**, *8*, 1–29, doi:10.3390/plants8120586.
9. Liu, Q.; Yang, X.; Tzin, V.; Peng, Y.; Romeis, J.; Li, Y. Plant breeding involving genetic engineering does not result in unacceptable unintended effects in rice relative to conventional cross-breeding. *Plant Journal* **2020**, *103*, 2236–2249, doi:10.1111/tpj.14895.
10. Paine, J.A.; Shipton, C.A.; Chaggar, S.; Howells, R.M.; Kennedy, M.J.; Vernon, G.; Wright, S.Y.; Hinchliffe, E.; Adams, J.L.; Silverstone, A.L.; et al. Improving the nutritional value of Golden Rice through increased pro-vitamin A content. *Nature Biotechnology* **2005**, *23*, 482–487, doi:10.1038/nbt1082.
11. Chen, H.; Lin, Y. Promise and issues of genetically modified crops. *Current Opinion in Plant Biology* **2013**, *16*, 255–260, doi:10.1016/j.pbi.2013.03.007.
12. Baxter, I. Ionomics: studying the social network of mineral nutrients. *Current Opinion in Plant Biology* **2009**, *12*, 381–386, doi:10.1016/j.pbi.2009.05.002.
13. Phing Lau, W.C.; Latif, M.A.; Y. Rafii, M.; Ismail, M.R.; Puteh, A. Advances to improve the eating and cooking qualities of rice by marker-assisted breeding. *Critical Reviews in Biotechnology* **2016**, *36*, 87–98, doi:10.3109/07388551.2014.923987.
14. Chen, J.; Lu, L.; Robb, S.M.C.; Collin, M.; Okumoto, Y.; Stajich, J.E.; Wessler, S.R. Genomic diversity generated by a transposable element burst in a rice recombinant inbred population. *Proceedings of the National Academy of Sciences of the United States of America* **2020**, *117*, 26288–26297, doi:10.1073/pnas.2015736117.
15. Fragoso, C.A.; Moreno, M.; Wang, Z.; Heffelfinger, C.; Arbelaez, L.J.; Aguirre, J.A.; Franco, N.; Romero, L.E.; Labadie, K.; Zhao, H.; et al. Genetic architecture of a rice nested association mapping population. *G3: Genes, Genomes, Genetics* **2017**, *7*, 1913–1926, doi:10.1534/g3.117.041608.
16. Liu, S.; Zou, W.; Lu, X.; Bian, J.; He, H.; Chen, J.; Ye, G. Genome-wide association study using a multiparent advanced generation intercross (Magic) population identified qtls and candidate genes to predict shoot and grain zinc contents in rice. *Agriculture (Switzerland)* **2021**, *11*, 1–14, doi:10.3390/agriculture11010070.
17. Liu, C.; Ding, S.; Zhang, A.; Hong, K.; Jiang, H.; Yang, S.; Ruan, B.; Zhang, B.; Dong, G.; Guo, L.; et al. Development of nutritious rice with high zinc/selenium and low cadmium in grains through QTL pyramiding. *Journal of Integrative Plant Biology* **2020**, *62*, 349–359, doi:10.1111/jipb.12909.
18. Ye, G.; Liang, S.; Wan, J. QTL mapping of protein content in rice using single chromosome segment substitution lines. *Theoretical and Applied Genetics* **2010**, *121*, 741–750, doi:10.1007/s00122-010-1345-2.
19. Yan, B.; Tondi Yacouba, N.; Chen, J.; Wang, Y.; Gao, G.; Zhang, Q.; Liu, X.; He, Y. Analysis of minor quantitative trait loci for eating and cooking quality traits in rice using a recombinant inbred line population derived from two indica cultivars with similar amylose content. *Molecular Breeding* **2014**, *34*, 2151–2163, doi:10.1007/s11032-014-0170-8.
20. Raza, Q.; Riaz, A.; Sabar, M.; Atif, R.M.; Bashir, K. Meta-analysis of grain iron and zinc associated QTLs identified hotspot chromosomal regions and positional candidate genes for breeding biofortified rice. *Plant Science* **2019**, *288*, 110214, doi:10.1016/j.plantsci.2019.110214.
21. Smita, S.; Katiyar, A.; Lenka, S.K.; Dalal, M.; Kumar, A.; Mahtha, S.K.; Yadav, G.; Chinnusamy, V.; Pandey, D.M.; Bansal, K.C. Gene network modules associated with abiotic stress response in tolerant rice genotypes identified by transcriptome meta-analysis. *Functional and Integrative Genomics* **2020**, *20*, 29–49, doi:10.1007/s10142-019-00697-w.
22. Norton, G.J.; Deacon, C.M.; Xiong, L.; Huang, S.; Meharg, A.A.; Price, A.H. Genetic mapping of the rice ionome in leaves and grain: Identification of QTLs for 17 elements including arsenic, cadmium, iron and selenium. *Plant and Soil* **2010**, *329*, 139–153, doi:10.1007/s11104-009-0141-8.
23. Qu, L.Q.; Wei, X.L.; Satoh, H.; Kumamaru, T.; Ogawa, M.; Takaiwa, F. Biochemical and molecular characterization of a rice glutelin allele for the GluA-1 gene. *Theoretical and Applied Genetics* **2003**, *107*, 20–25, doi:10.1007/s00122-003-1228-x.

24. Kim, S.I.; Andaya, C.B.; Goyal, S.S.; Tai, T.H. The rice OsLpa1 gene encodes a novel protein involved in phytic acid metabolism. *Theoretical and Applied Genetics* **2008**, *117*, 769–779, doi:10.1007/s00122-008-0818-z.
25. Kawakatsu, T.; Takaiwa, F. Differences in transcriptional regulatory mechanisms functioning for free lysine content and seed storage protein accumulation in rice grain. *Plant and Cell Physiology* **2010**, *51*, 1964–1974, doi:10.1093/pcp/pcq164.
26. Lee, S.; Jeon, U.S.; Lee, S.J.; Kim, Y.K.; Persson, D.P.; Husted, S.; Schjørring, J.K.; Kakei, Y.; Masuda, H.; Nishizawa, N.K.; et al. Iron fortification of rice seeds through activation of the nicotianamine synthase gene. *Proceedings of the National Academy of Sciences of the United States of America* **2009**, *106*, 22014–22019, doi:10.1073/pnas.0910950106.
27. Zhang, Y.; Xu, Y.H.; Yi, H.Y.; Gong, J.M. Vacuolar membrane transporters OsVIT1 and OsVIT2 modulate iron translocation between flag leaves and seeds in rice. *Plant Journal* **2012**, *72*, 400–410, doi:10.1111/j.1365-313X.2012.05088.x.
28. Ishimaru, Y.; Masuda, H.; Bashir, K.; Inoue, H.; Tsukamoto, T.; Takahashi, M.; Nakanishi, H.; Aoki, N.; Hirose, T.; Ohsugi, R.; et al. Rice metal-nicotianamine transporter, OsYSL2, is required for the long-distance transport of iron and manganese. *Plant Journal* **2010**, *62*, 379–390, doi:10.1111/j.1365-313X.2010.04158.x.
29. Zhou, W.; Wang, X.; Zhou, D.; Ouyang, Y.; Yao, J. Overexpression of the 16-kDa α-amylase/trypsin inhibitor RAG2 improves grain yield and quality of rice. *Plant Biotechnology Journal* **2017**, *15*, 568–580, doi:10.1111/pbi.12654.
30. Xu, X.H.; Zhao, H.J.; Liu, Q.L.; Frank, T.; Engel, K.H.; An, G.; Shu, Q.Y. Mutations of the multi-drug resistance-associated protein ABC transporter gene 5 result in reduction of phytic acid in rice seeds. *Theoretical and Applied Genetics* **2009**, *119*, 75–83, doi:10.1007/s00122-009-1018-1.
31. Lei, L.; Zheng, H.L.; Wang, J.G.; Liu, H.L.; Sun, J.; Zhao, H.W.; Yang, L.M.; Zou, D.T. Genetic dissection of rice (Oryza sativa L.) tiller, plant height, and grain yield based on QTL mapping and metaanalysis. *Euphytica* **2018**, *214*, 1–17, doi:10.1007/s10681-018-2187-2.
32. Korte, A.; Ashley, F. The advantages and limitations of trait analysis with GWAS : a review Self-fertilisation makes Arabidopsis particularly well suited to GWAS. *Plant methods* **2013**, *9*, 29.
33. Su, J.; Xu, K.; Li, Z.; Hu, Y.; Hu, Z.; Zheng, X.; Song, S.; Tang, Z.; Li, L. Genome-wide association study and Mendelian randomization analysis provide insights for improving rice yield potential. *Scientific Reports* **2021**, *11*, 1–11, doi:10.1038/s41598-021-86389-7.
34. Ishikawa, A. A strategy for identifying quantitative trait genes using gene expression analysis and causal analysis. *Genes* **2017**, *8*, 1–15, doi:10.3390/genes8120347.
35. Norton, G.J.; Douglas, A.; Lahner, B.; Yakubova, E.; Guerinot, M. Lou; Pinson, S.R.M.; Tarpley, L.; Eizenga, G.C.; McGrath, S.P.; Zhao, F.J.; et al. Genome wide association mapping of grain arsenic, copper, molybdenum and zinc in rice (Oryza sativa L.) grown at four international field sites. *PLoS ONE* **2014**, *9*, doi:10.1371/journal.pone.0089685.
36. Eizenga, G.C.; Jackson, A.K.; Edwards, J.D. Prototype for developing SNP markers from GWAS and biparental QTL for rice panicle and grain traits. *Agricultural & Environmental Letters* **2021**, *6*, 1–8, doi:10.1002/ael2.20047.
37. Zhang, P.; Zhong, K.; Zhong, Z.; Tong, H. Mining candidate gene for rice aluminum tolerance through genome wide association study and transcriptomic analysis. *BMC Plant Biology* **2019**, *19*, 1–10, doi:10.1186/s12870-019-2036-z.
38. Liang Jiang, G. Plant Marker-Assisted Breeding and Conventional Breeding: Challenges and Perspectives. *Advances in Crop Science and Technology* **2013**, *01*, 1–3, doi:10.4172/2329-8863.1000e106.
39. Meuwissen, T.H.E.; Hayes, B.J.; Goddard, M.E. Prediction of total genetic value using genome-wide dense marker maps. *Genetics* **2001**, *157*, 1819–1829, doi:10.1093/genetics/157.4.1819.
40. Collard, B.C.Y.; Jahufer, M.Z.Z.; Brouwer, J.B.; Pang, E.C.K. An introduction to markers, quantitative trait loci (QTL) mapping and marker-assisted selection for crop improvement: The basic concepts. *Euphytica* **2005**, *142*, 169–196, doi:10.1007/s10681-005-1681-5.
41. Zhao, K.; Wright, M.; Kimball, J.; Eizenga, G.; McClung, A.; Kovach, M.; Tyagi, W.; Ali, M.L.; Tung, C.W.; Reynolds, A.; et al. Genomic diversity and introgression in O. sativa reveal the impact of domestication and breeding on the rice genome. *PLoS ONE* **2010**, *5*, doi:10.1371/journal.pone.0010780.
42. Spindel, J.; Begum, H.; Akdemir, D.; Virk, P.; Collard, B.; Redoña, E.; Atlin, G.; Jannink, J.L.; McCouch, S.R. Correction: Genomic Selection and Association Mapping in Rice (Oryza sativa): Effect of Trait Genetic Architecture, Training Population Composition, Marker Number and Statistical Model on Accuracy of Rice Genomic Selection in Elite, Tropical Rice Breeding. *PLoS Genetics* **2015**, *11*, 1–26, doi:10.1371/journal.pgen.1005350.
43. Chen, H.; He, H.; Zhou, F.; Yu, H.; Deng, X.W. Development of genomics-based genotyping platforms and their applications in rice breeding. *Current Opinion in Plant Biology* **2013**, *16*, 247–254, doi:10.1016/j.pbi.2013.04.002.
44. Li, H.; Su, G.; Jiang, L.; Bao, Z. An efficient unified model for genome-wide association studies and genomic selection. *Genetics Selection Evolution* **2017**, *49*, 1–8, doi:10.1186/s12711-017-0338-x.
45. Spindel, J.E.; Begum, H.; Akdemir, D.; Collard, B.; Redoña, E.; Jannink, J.L.; McCouch, S. Genome-wide prediction models that incorporate de novo GWAS are a powerful new tool for tropical rice improvement. *Heredity* **2016**, *116*, 395–408, doi:10.1038/hdy.2015.113.
46. Grenier, C.; Cao, T.V.; Ospina, Y.; Quintero, C.; Châtel, M.H.; Tohme, J.; Courtois, B.; Ahmadi, N. Accuracy of genomic selection in a rice synthetic population developed for recurrent selection breeding. *PLoS ONE* **2015**, *10*, 1–25, doi:10.1371/journal.pone.0136594.
47. Xu, S.; Zhu, D.; Zhang, Q. Predicting hybrid performance in rice using genomic best linear unbiased prediction. *Proceedings of the National Academy of Sciences of the United States of America* **2014**, *111*, 12456–12461, doi:10.1073/pnas.1413750111.

48. Onogi, A.; Watanabe, M.; Mochizuki, T.; Hayashi, T.; Nakagawa, H.; Hasegawa, T.; Iwata, H. Toward integration of genomic selection with crop modelling: the development of an integrated approach to predicting rice heading dates. *Theoretical and Applied Genetics* **2016**, *129*, 805–817, doi:10.1007/s00122-016-2667-5.
49. Mba, C.; Afza, R.; Bado, S.; Jain, S.M. Induced Mutagenesis in Plants using physical and chemical agents. *Plant Cell Culture: Essential methods* **2010**, *20*, 111–130.
50. Phanchaisri, B.; Chandet, R.; Yu, L.D.; Vilaithong, T.; Jamjod, S.; Anuntalabhochai, S. Low-energy ion beam-induced mutation in Thai jasmine rice (Oryza sativa L. cv. KDML 105). *Surface and Coatings Technology* **2007**, *201*, 8024–8028, doi:10.1016/j.surfcoat.2006.02.057.
51. Semsang, N.; Kawaree, R.; Cutler, R.W.; Chundet, R.; Yu, L.D.; Anuntalabhochai, S. Improved antioxidant activity of BKOS Thai jasmine rice. *Natural Product Research* **2012**, *26*, 1145–1151, doi:10.1080/14786419.2011.561207.
52. Liu, Q.L.; Xu, X.H.; Ren, X.L.; Fu, H.W.; Wu, D.X.; Shu, Q.Y. Generation and characterization of low phytic acid germplasm in rice (Oryza sativa L.). *Theoretical and Applied Genetics* **2007**, *114*, 803–814, doi:10.1007/s00122-006-0478-9.
53. Zhou, X.; Bai, X.; Xing, Y. A rice genetic improvement boom by next-generation sequencing. *Current Issues in Molecular Biology* **2018**, *27*, 109–126, doi:10.21775/CIMB.027.109.
54. Abe, A.; Kosugi, S.; Yoshida, K.; Natsume, S.; Takagi, H.; Kanzaki, H.; Matsumura, H.; Yoshida, K.; Mitsuoka, C.; Tamiru, M.; et al. Genome sequencing reveals agronomically important loci in rice using MutMap. *Nature Biotechnology* **2012**, *30*, 174–178, doi:10.1038/nbt.2095.
55. Takagi, H.; Uemura, A.; Yaegashi, H.; Tamiru, M.; Abe, A.; Mitsuoka, C.; Utsushi, H.; Natsume, S.; Kanzaki, H.; Matsumura, H.; et al. MutMap-Gap: Whole-genome resequencing of mutant F2 progeny bulk combined with de novo assembly of gap regions identifies the rice blast resistance gene Pii. *New Phytologist* **2013**, *200*, 276–283, doi:10.1111/nph.12369.
56. Peng, H.; Wang, K.; Chen, Z.; Cao, Y.; Gao, Q.; Li, Y.; Li, X.; Lu, H.; Du, H.; Lu, M.; et al. MBKbase for rice: An integrated omics knowledgebase for molecular breeding in rice. *Nucleic Acids Research* **2020**, *48*, D1085–D1092, doi:10.1093/nar/gkz921.
57. Wang, J.; Qi, M.; Liu, J.; Zhang, Y. CARMO: A comprehensive annotation platform for functional exploration of rice multi-omics data. *Plant Journal* **2015**, *83*, 359–374, doi:10.1111/tpj.12894.
58. Kumar, A.; Kumar, S.; Satish Chhapekar, S.; Sreedharan, S.; Singh, S.; Ryun Choi, S.; Ramchiary, N.; Pyo Lim, Y. Linking omics and gene editing tools for rapid improvement of traditional food plants for diversified foods and sustainable food security. *Preprints* **2021**, doi:10.20944/preprints202106.0363.v1.
59. Li, Q.; Yan, J. Sustainable agriculture in the era of omics: Knowledge-driven crop breeding. *Genome Biology* **2020**, *21*, 5–9, doi:10.1186/s13059-020-02073-5.
60. Matsumoto, T.; Wu, J.; Kanamori, H.; Katayose, Y.; Fujisawa, M.; Namiki, N.; Mizuno, H.; Yamamoto, K.; Antonio, B.A.; Baba, T.; et al. The map-based sequence of the rice genome. *Nature* **2005**, *436*, 793–800, doi:10.1038/nature03895.
61. Wenger, A.M.; Peluso, P.; Rowell, W.J.; Chang, P.C.; Hall, R.J.; Concepcion, G.T.; Ebler, J.; Fungtammasan, A.; Kolesnikov, A.; Olson, N.D.; et al. Accurate circular consensus long-read sequencing improves variant detection and assembly of a human genome. *Nature Biotechnology* **2019**, *37*, 1155–1162, doi:10.1038/s41587-019-0217-9.
62. Zhou, Y.; Chebotarov, D.; Kudrna, D.; Llaca, V.; Lee, S.; Rajasekar, S.; Mohammed, N.; Al-Bader, N.; Sobel-Sorenson, C.; Parakkal, P.; et al. A platinum standard pan-genome resource that represents the population structure of Asian rice. *Scientific Data* **2020**, *7*, 1–11, doi:10.1038/s41597-020-0438-2.
63. Yu, P.; Wang, C.H.; Xu, Q.; Feng, Y.; Yuan, X.P.; Yu, H.Y.; Wang, Y.P.; Tang, S.X.; Wei, X.H. Genome-wide copy number variations in Oryza sativa L. *BMC Genomics* **2013**, *14*, doi:10.1186/1471-2164-14-649.
64. Morrell, P.L.; Buckler, E.S.; Ross-Ibarra, J. Crop genomics: Advances and applications. *Nature Reviews Genetics* **2012**, *13*, 85–96, doi:10.1038/nrg3097.
65. Stein, J.C.; Yu, Y.; Copetti, D.; Zwickl, D.J.; Zhang, L.; Zhang, C.; Chougule, K.; Gao, D.; Iwata, A.; Goicoechea, J.L.; et al. Genomes of 13 domesticated and wild rice relatives highlight genetic conservation, turnover and innovation across the genus Oryza. *Nature Genetics* **2018**, *50*, 285–296, doi:10.1038/s41588-018-0040-0.
66. Mondal, T.K.; Rawal, H.C.; Chowrasia, S.; Varshney, D.; Panda, A.K.; Mazumdar, A.; Kaur, H.; Gaikwad, K.; Sharma, T.R.; Singh, N.K. Draft genome sequence of first monocot-halophytic species Oryza coarctata reveals stress-specific genes. *Scientific Reports* **2018**, *8*, 1–13, doi:10.1038/s41598-018-31518-y.
67. Xie, X.; Du, H.; Tang, H.; Tang, J.; Tan, X.; Liu, W.; Li, T.; Lin, Z.; Liang, C.; Liu, Y.G. A chromosome-level genome assembly of the wild rice Oryza rufipogon facilitates tracing the origins of Asian cultivated rice. *Science China Life Sciences* **2021**, *64*, 282–293, doi:10.1007/s11427-020-1738-x.
68. Wang, W.; Mauleon, R.; Hu, Z.; Chebotarov, D.; Tai, S.; Wu, Z.; Li, M.; Zheng, T.; Fuentes, R.R.; Zhang, F.; et al. Genomic variation in 3,010 diverse accessions of Asian cultivated rice. *Nature* **2018**, *557*, 43–49, doi:10.1038/s41586-018-0063-9.
69. Zhao, Q.; Feng, Q.; Lu, H.; Li, Y.; Wang, A.; Tian, Q.; Zhan, Q.; Lu, Y.; Zhang, L.; Huang, T.; et al. Pan-genome analysis highlights the extent of genomic variation in cultivated and wild rice. *Nature Genetics* **2018**, *50*, 278–284, doi:10.1038/s41588-018-0041-z.
70. Gao, C. Genome engineering for crop improvement and future agriculture. *Cell* **2021**, *184*, 1621–1635, doi:10.1016/j.cell.2021.01.005.
71. Zeng, D.; Tian, Z.; Rao, Y.; Dong, G.; Yang, Y.; Huang, L.; Leng, Y.; Xu, J.; Sun, C.; Zhang, G.; et al. Rational design of high-yield and superior-quality rice. *Nature Plants* **2017**, *3*, 4–8, doi:10.1038/nplants.2017.31.
72. Yu, H.; Lin, T.; Meng, X.; Du, H.; Zhang, J.; Liu, G.; Chen, M.; Jing, Y.; Kou, L.; Li, X.; et al. A route to de novo domestication of wild allotetraploid rice. *Cell* **2021**, *184*, 1156–1170, doi:10.1016/j.cell.2021.01.013.

73. Xia, L.; Zou, D.; Sang, J.; Xu, X.; Yin, H.; Li, M.; Wu, S.; Hu, S.; Hao, L.; Zhang, Z. Rice Expression Database (RED): An integrated RNA-Seq-derived gene expression database for rice. *Journal of Genetics and Genomics* **2017**, *44*, 235–241, doi:10.1016/j.jgg.2017.05.003.
74. Lowe, R.; Shirley, N.; Bleackley, M.; Dolan, S.; Shafee, T. Transcriptomics technologies. *PLoS Computational Biology* **2017**, *13*, 1–23, doi:10.1371/journal.pcbi.1005457.
75. Ren, Z.; Qi, D.; Pugh, N.; Li, K.; Wen, B.; Zhou, R.; Xu, S.; Liu, S.; Jones, A.R. Improvements to the rice genome annotation through large-scale analysis of RNA-seq and proteomics data sets. *Molecular and Cellular Proteomics* **2019**, *18*, 86–98, doi:10.1074/mcp.RA118.000832.
76. Zheng, L.; Huang, F.; Narsai, R.; Wu, J.; Giraud, E.; He, F.; Cheng, L.; Wang, F.; Wu, P.; Whelan, J.; et al. Physiological and transcriptome analysis of iron and phosphorus interaction in rice seedlings. *Plant Physiology* **2009**, *151*, 262–274, doi:10.1104/pp.109.141051.
77. Anacleto, R.; Badoni, S.; Parween, S.; Butardo, V.M.; Misra, G.; Cuevas, R.P.; Kuhlmann, M.; Trinidad, T.P.; Mallillin, A.C.; Acuin, C.; et al. Integrating a genome-wide association study with a large-scale transcriptome analysis to predict genetic regions influencing the glycaemic index and texture in rice. *Plant Biotechnology Journal* **2019**, *17*, 1261–1275, doi:10.1111/pbi.13051.
78. Takehisa, H.; Sato, Y.; Igarashi, M.; Abiko, T.; Antonio, B.A.; Kamatsuki, K.; Minami, H.; Namiki, N.; Inukai, Y.; Nakazono, M.; et al. Genome-wide transcriptome dissection of the rice root system: Implications for developmental and physiological functions. *Plant Journal* **2012**, *69*, 126–140, doi:10.1111/j.1365-313X.2011.04777.x.
79. Zhang, H.Y.; Lei, G.; Zhou, H.W.; He, C.; Liao, J.L.; Huang, Y.J. Quantitative iTRAQ-based proteomic analysis of rice grains to assess high night temperature stress. *Proteomics* **2017**, *17*, 1–12, doi:10.1002/pmic.201600365.
80. Maksup, S.; Pongpakpian, S.; Roytrakul, S.; Chaum, S.; Supaibulwatana, K. Comparative proteomics and protein profile related to phenolic compounds and antioxidant activity in germinated Oryza sativa KDML105 and Thai brown rice Mali Dang for better nutritional value. *Journal of the science of food and agriculture* **2018**, *28*, 303–325, doi:10.1002/j.
81. Graziano, S.; Marmiroli, N.; Gullì, M. Proteomic analysis of reserve proteins in commercial rice cultivars. *Food Science and Nutrition* **2020**, *8*, 1788–1797, doi:10.1002/fsn3.1375.
82. Sperotto, R.A.; Boff, T.; Duarte, G.L.; Santos, L.S.; Grusak, M.A.; Fett, J.P. Identification of putative target genes to manipulate Fe and Zn concentrations in rice grains. *Journal of Plant Physiology* **2010**, *167*, 1500–1506, doi:10.1016/j.jplph.2010.05.003.
83. Feng, Y.W.; Komatsu, S.; Furukawa, T.; Koshiba, T.; Kohno, Y. Proteome analysis of proteins responsive to ambient and elevated ozone in rice seedlings. *Agriculture, Ecosystems and Environment* **2008**, *125*, 255–265, doi:10.1016/j.agee.2008.01.018.
84. Ernst, M.; Silva, D.B.; Silva, R.R.; Vêncio, R.Z.N.; Lopes, N.P. Mass spectrometry in plant metabolomics strategies: From analytical platforms to data acquisition and processing. *Natural Product Reports* **2014**, *31*, 784–806, doi:10.1039/c3np70086k.
85. Heuberger, A.L.; Lewis, M.R.; Chen, M.H.; Brick, M.A.; Leach, J.E.; Ryan, E.P. Metabolomic and functional genomic analyses reveal varietal differences in bioactive compounds of cooked rice. *PLoS ONE* **2010**, *5*, 1–10, doi:10.1371/journal.pone.0012915.
86. Kusano, M.; Fukushima, A.; Kobayashi, M.; Hayashi, N.; Jonsson, P.; Moritz, T.; Ebana, K.; Saito, K. Application of a metabolomic method combining one-dimensional and two-dimensional gas chromatography-time-of-flight/mass spectrometry to metabolic phenotyping of natural variants in rice. *Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences* **2007**, *855*, 71–79, doi:10.1016/j.jchromb.2007.05.002.
87. Gong, L.; Chen, W.; Gao, Y.; Liu, X.; Zhang, H.; Xu, C.; Yu, S.; Zhang, Q.; Luo, J. Genetic analysis of the metabolome exemplified using a rice population. *Proceedings of the National Academy of Sciences of the United States of America* **2013**, *110*, 20320–20325, doi:10.1073/pnas.1319681110.
88. Hu, C.; Shi, J.; Quan, S.; Cui, B.; Kleessen, S.; Nikoloski, Z.; Tohge, T.; Alexander, D.; Guo, L.; Lin, H.; et al. Metabolic variation between japonica and indica rice cultivars as revealed by non-targeted metabolomics. *Scientific Reports* **2014**, *4*, 1–10, doi:10.1038/srep05067.
89. Yan, N.; Du, Y.; Liu, X.; Chu, M.; Shi, J.; Zhang, H.; Liu, Y.; Zhang, Z. A comparative UHPLC-QqQ-MS-based metabolomics approach for evaluating Chinese and North American wild rice. *Food Chemistry* **2019**, *275*, 618–627, doi:10.1016/j.foodchem.2018.09.153.
90. Zhao, G.C.; Zhang, Y.X.; Sun, S.Y.; Xie, M.X.; Hu, C.Y.; Shi, Y.Q.; Shi, J.X.; Li, J.Y. Identification of the biochemical characteristics of developing giant embryo rice grains using non-targeted metabolomics. *Journal of Cereal Science* **2019**, *85*, 70–76, doi:10.1016/j.jcs.2018.10.011.
91. Ravichanthiran, K.; Ma, Z.F.; Zhang, H.; Cao, Y.; Wang, C.W.; Muhammad, S.; Aglago, E.K.; Zhang, Y.; Jin, Y.; Pan, B. Phytochemical profile of brown rice and its nutrigenomic implications. *Antioxidants* **2018**, *7*, 1–16, doi:10.3390/antiox7060071.
92. Romero, C.; Lopez-Perez, P.A.; Toledo, A.K.M.; Perez-Espana, V.H.; Aparicio-Burgos, J.E.; Cuervo-Parra, J.A. Nutrigenomics and Nutrigenetics in Functional Foods. *International Journal of Bio-resource and Stress Management* **2018**, *9*, 661–672, doi:10.23910/ijbsm/2018.9.6.1922.