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ORIGINAL ARTICLE

Unravelling consensus genomic regions associated with quality traits in wheat using meta-analysis of quantitative trait loci

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Abstract

Main conclusion **Meta-analysis in wheat for three major quality traits identified 110 meta-QTL (MQTL) with reduced confidence interval (CI). Five GWAS validated MQTL (viz., 1A.1, 1B.2, 3B.4, 5B.2, and 6B.2), each involving more than 20 initial QTL and reduced CI (95%) (< 2 cM), were selected for quality breeding programmes. Functional characterization including candidate gene mining and expression analysis discovered 44 high confidence candidate genes associated with quality traits.**

Abstract A meta-analysis of quantitative trait loci (QTL) associated with dough rheology properties, nutritional traits, and processing quality traits was conducted in wheat. For this purpose, as many as 2458 QTL were collected from 50 interval mapping studies published during 2013–2020. Of the total QTL, 1126 QTL were projected onto the consensus map saturated with 249,603 markers which led to the identification of 110 meta-QTL (MQTL). These MQTL exhibited an 18.84-fold reduction in the average CI compared to the average CI of the initial QTL (ranging from 14.87 to 95.55 cM with an average of 40.35 cM). Of the 110, 108 MQTL were physically anchored to the wheat reference genome, including 51 MQTL verified with marker-trait associations (MTAs) reported from earlier genome-wide association studies. Candidate gene (CG) mining allowed the identification of 2533 unique gene models from the MQTL regions. In-silico expression analysis discovered 439 differentially expressed gene models with > 2 transcripts per million expressions in grains and related tissues, which also included 44 high-confidence CGs involved in the various cellular and biochemical processes related to quality traits. Nine functionally characterized wheat genes associated with grain protein content, high-molecular-weight glutenin, and starch synthase enzymes were also found to be co-localized with some of the MQTL. Synteny analysis between wheat and rice MQTL regions identified 23 wheat MQTL syntenic to 16 rice MQTL associated with quality traits. Furthermore, 64 wheat orthologues of 30 known rice genes were detected in 44 MQTL regions. Markers flanking the MQTL identified in the present study can be used for marker-assisted breeding and as fixed effects in the genomic selection models for improving the prediction accuracy during quality breeding. Wheat orthologues of rice genes and other CGs available from MQTLs can be promising targets for further functional validation and to better understand the molecular mechanism underlying the quality traits in wheat.

Keywords Candidate genes · Differentially expressed genes · GWAS · Meta-QTL · Orthologous · Synteny

Abbreviations

CG	Candidate gene
CI	Confidence interval
DEGs	Differentially expressed genes
GPC	Grain protein content
GWAS	Genome-wide association studies
MQTL	Meta-QTL
MTA	Marker-trait association
PPO	Poly phenol oxidase
TPM	Transcripts per million

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Introduction

Wheat is a globally grown cereal crop and is a significant contributor of calories and protein to the human diet (Pal et al. 2022b). Currently, wheat is widely consumed and processed into bread, noodles, cakes, pasta, beer, and other products. Developing high-yielding varieties with enhanced quality characters has become the foremost concern of the wheat breeders (Nuttall et al. 2017). Improving end-use qualities is a difficult task because firstly, it is challenging to measure the seed quality and rheological properties such as grain protein content (GPC), sedimentation rate (SDS), hectolitre weight, 1000-grain weight, wet gluten content, dry gluten content, flour–water absorption, dough development time, dough stability time, mixing tolerance index, breakdown time, and kernel hardness as they are labour intensive and also require a large quantity of seeds for analysis. Secondly, quality characters are complex traits governed by various gene networks primarily influenced by several environmental conditions (Quraishi et al. 2017).

The linkage-based QTL mapping has emerged as a powerful approach for dissecting complex traits into component loci and studying the relative effects of the loci on the target trait (Doerge 2002). Since the first report on QTL mapping for wheat quality traits (Blanco et al. 1996), several QTL studies have been conducted using different mapping populations, which have led to the identification of hundreds of QTL for different quality traits, including GPC (e.g., Fatiukha et al. 2020), processing and baking qualities (e.g., Goel et al. 2019), SDS (e.g., Goel et al. 2019), falling number (Börner et al. 2018; Guo et al. 2020), and starch pasting properties (Goel et al. 2019). The QTL mapping results are strongly influenced by the experimental conditions, type and size of the mapping population, density of genetic markers, and statistical methods employed (Swamy et al. 2011). Thus, the practical implication of these QTL for quality improvement via positional cloning of QTL and marker-assisted selection (MAS) has largely been limited (Quraishi et al. 2017; Saini et al. 2020). Therefore, it becomes imperative to identify QTL that significantly affects the target phenotype and are stable across multiple genetic backgrounds and environments. Further, genome-wide association studies (GWAS) have been effectively used in identifying the marker-trait associations (MTAs) for different quality traits in wheat (Saini et al. 2022a). In addition, several GWAS-identified MTAs were confirmed by interval mapping studies (Chen et al. 2019; Wu et al. 2021), which indicates that the combination of interval mapping and GWAS can be effective in the identification of promising genomic regions for functional analysis and breeding programmes.

Meta-analysis of QTLs identifies consensus and robust QTL or MQTL regions most frequently associated with trait variations from multiple studies and reduces their confidence interval (CI) (Goffinet and Gerber 2000; Veyrieras et al. 2007). Different software, such as Meta-QTL and BioMercator facilitate meta-analysis of QTL derived from independent studies by formulating and embedding specific sets of algorithms for exact evaluation and recalculation of the genetic position for the given set of QTL (Wang et al. 2014). In wheat, MQTL analysis has already been conducted for different traits, including ear emergence (Griffiths et al. 2009), fusarium head blight resistance (Liu et al. 2009; Venske et al. 2019; Zheng et al. 2021), tan spot resistance (Liu et al. 2020), multiple disease resistance (Saini et al. 2021a; Pal et al. 2022a), pre-harvest sprouting tolerance (Tyagi and Gupta 2012), abiotic stress tolerance (Acuña-Galindo et al. 2015; Darzi-Ramandi et al. 2017; Kumar et al. 2020), yield and related traits (Tyagi et al. 2015; Quraishi et al. 2017; Yang et al. 2021), nitrogen use efficiency (NUE) (Saini et al. 2021b), baking-quality and GPC (Quraishi et al. 2017). Quraishi et al. (2017) identified six and eight MQTL for GPC and baking quality traits, respectively, using 155 initial QTL collected from only eight interval mapping studies published in or before the year 2013. Hundreds of QTL associated with different quality traits have been reported after the year 2013. Therefore, the present study was carried out (based on interval mapping studies published during 2013–2020) to identify the novel MQTL and candidate genes (CGs) associated with quality traits. Further, the meta-analysis results were integrated with GWAS and transcriptomics studies to identify promising genomic regions and CGs affecting wheat quality traits. Further, by utilizing the synteny and collinearity of wheat with other cereals (Sorrells et al. 2003), ortho-MQTL analysis was also conducted to see if the generated information could be transferred to other cereals such as rice. The findings from this study may help identify diagnostic markers and aid marker-assisted breeding (MAB) or genomic selection (GS) to improve quality traits in wheat.

Materials and methods

Bibliographic search and QTL data collection

A comprehensive bibliographic survey was conducted for interval mapping studies reporting QTL associated with quality traits published during 2013–2020. From each of the collected studies, following information was retrieved: (i) QTL name (wherever available), (ii) flanking or closely linked markers, (iii) peak position and CI, (iv) LOD scores, (v) phenotypic variation explained (PVE) by individual QTL, and (vi) type and size of the mapping

population (Tables S1 and S2). When there was no information given on the peak positions of QTL, these were estimated as the midpoint of the genetic positions of given flanking markers. Whenever the LOD score for individual QTL was not available from source studies, a LOD score of 3.0 was assumed for the purpose of analysis.

All the quality traits were grouped into the following three major trait categories: (i) *Dough rheology properties (DRP)* recorded as dough colour, polyphenol oxidase activity (PPO), mixolab, mixograph, mixogram, alveograph, farinograph, dough mixing, pasting properties, etc.; (ii) *Nutritional traits (NT)* recorded as lipoxygenase activity, yellow pigment, iron (Fe), zinc (Zn), β-glucan, protein, starch content, etc.; and (iii) *Processing quality traits (PQT)* recorded as milling, baking qualities, sedimentation volume, water solvent retention capacity (SRC), alkaline SRC, sucrose SRC, sucrose softness equivalent SRC, water-extractable, water-unextractable arabinoxylan content (Ax), etc. (Table S3).

Construction of consensus map

An R package LPmerge (Endelman and Plomion 2014) was used to construct the consensus map by merging the marker data from the following linkage maps: "Wheat_Composite_2004" (http://wheat.pw.usda.gov), "Wheat_Consensus_SSR_2004" (Somers et al. 2004); "Durum wheat integrated map" (Marone et al. 2013), and four single nucleotide polymorphism (SNP) array-based maps including "Illumina 9K iSelect Beadchip Array" (Cavanagh et al. 2013), "Illumina iSelect 90K SNP Array" (Wang et al. 2014), "Wheat 55K SNP array" (Winfield et al. 2016), and "AxiomR, Wheat 660K SNP array" (Cui et al. 2017). Markers flanking the initial QTL identified from individual mapping studies were also used to develop the consensus map (Fig. 1).

QTL projection and MQTL analysis

QTL projection and MQTL analysis were performed with the BioMercator V4.2 (Sosnowski et al. 2012). This software

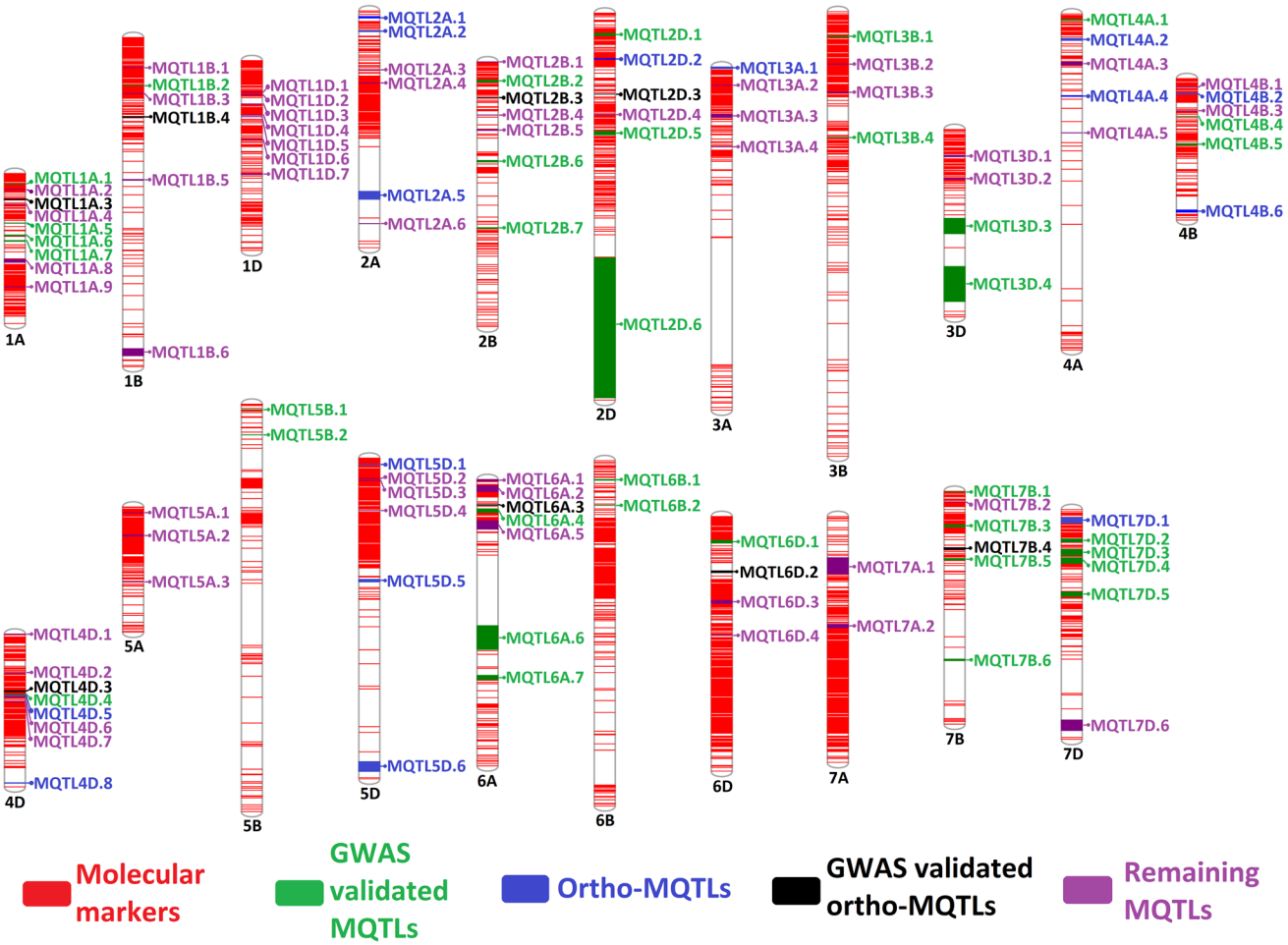

Fig. 1 Distribution of different MQTL on wheat chromosomes. The explanation for different colours utilized to represent the MQTL is given at the bottom of the figure

requires a minimal set of descriptors characterizing each collected QTL: the QTL position, its CI and its individual R^2 value, the trait associated with QTL, and the size of the mapping population utilized for identification of the QTL. For the QTL with no CI available, CI (95%) was calculated by using the following population-specific equations (Darvasi and Soller 1997; Guo et al. 2006).

For RIL populations, CI (95%) $=163/(R^2 \times N)$

For DH populations, CI (95%) $= 287/(R^2 \times N)$

The input mapping studies are supposed to be independent of each other, according to the statistical method used in the software. QTL mapping experiments that were repeated in time and space frequently identified redundant QTLs for the same trait. In that situation, we only kept the QTL with the highest effect (R^2) to avoid giving that QTL too much weight in the meta-analysis. QTLProj command available in the software allowed the homothetic projection of the positions and the CIs of the individual QTL onto the consensus map. It is based on a scaling rule between the flanking markers of QTLs on their original maps and their positions on the consensus map.

Meta-analysis was performed for the individual chromosomes separately, using the Veyrieras two-step algorithm available in the software. In the first step, the best meta-QTL model was chosen when the lowest values of the selection criteria were obtained in at least three models; the selection criteria used for this purpose are as follows: Akaike information criterion (AIC), AIC correction (AICc), AIC model 3 (AIC3), Bayesian information criterion (BIC), and Average weight of evidence (AWE). In the second step, the selected best model was utilized to ascertain the following: (i) the number of MQTL on each chromosome (based on the number of input QTL on the standard genetic map); (ii) their consensus positions (based on the variance of input QTL positions); and (iii) 95% CI (based on the variance of input QTL intervals) (Sosnowski et al. 2012).

Delineating the physical positions of the MQTL and gene mining

Nucleotide sequences of the markers flanking the MQTL were retrieved from either of the following databases/websites: (i) the GrainGenes (https://wheat.pw.usda.gov/GG3), (ii) Diversity array technology (https://www.diversityarrays.com), and (iii) CerealsDB (https://www.cerealsdb.uk.net). These sequences were used to obtain the physical positions of markers by Basic Local Alignment Search Tool (BLAST) searches against the wheat reference genome (Chinese Spring RefSeq v1.0) (IWGSC et al. 2018) available in the Ensembl Plants database (http://plants.ensembl.org/index.html). Physical positions of some of the SNP markers were directly obtained from the JBrowseWHEAT URGI database (https://urgi.versailles.inra.fr/jbrowseiwgsc/). Peak physical positions of the MQTL were calculated by using the following formula:

$$\text{Peak position (bp)} = \text{start position (bp)} + \frac{[\text{end position (bp)} - \text{start position (bp)}]}{[\text{end position (cM)} - \text{start position (cM)}]} \times \frac{\text{CI (95\%)}}{2}$$

Gene models available in 2 Mb genomic region, i.e., 1 Mb region on either side of the MQTL peak position, were retrieved using the 'BioMart' tool (https://plants.ensembl.org/biomart/) available in the Ensembl Plants database. Function descriptions for available gene models were retrieved from the InterPro database (https://www.ebi.ac.uk/interpro/).

Further, a search was also made for known wheat genes for the quality traits in question. Protein sequences of these genes were retrieved from the NCBI database (https://www.ncbi.nlm.nih.gov/). Protein BLAST searches were conducted against the wheat reference genome available in Ensembl Plants to find the physical positions of the corresponding genes. The physical positions of these genes were compared with the physical coordinates of the MQTL to ascertain their co-localization.

Expression analysis of gene models identified from the MQTL regions

Gene models available from the MQTL regions were further subjected to expression analysis using an 'Expression Visualization and Integration Platform' (expVIP) (http://www.wheat-expression.com/) (Ramírez-González et al. 2018). Following gene expression datasets were utilized for the expression analysis: (i) a grain tissue-specific developmental time course (Gillies et al. 2012; Li et al. 2013; Pfeifer et al. 2014); (ii) a grain tissue-specific expression at 12 days post-anthesis (Pearce et al. 2015); and (iii) a grain developmental time course with 4A dormancy QTL (Barrero et al. 2015). Details of these studies, including tissues analysed, are provided on expVIP. In accordance with Wagner et al. (2013), gene models with ≥ 2 transcripts per million (TPM) expressions were considered significantly expressed in different grain tissues.

Validating MQTL with GWAS

Information on the most stable and significant SNPs associated with the quality traits was collected from the 11 independent GWAS to validate the MQTL detected in the present study. These GWAS involved one durum wheat population (with a population size of 194), four spring wheat populations (with population sizes ranging from 189 to 2038), three

winter wheat populations (with population sizes ranging from 267 to 1325), and three mixed populations of spring and winter wheat (with population sizes ranging from 163 to 4095). Physical positions of SNPs were obtained either from the source papers or from the JBrowse-WHEAT URGI database (https://wheat-urgi.versailles.inra.fr/Tools/JBrowse). Finally, the physical positions of these significant SNPs or marker-trait associations (MTAs) were compared with the physical coordinates of the MQTL; any MQTL co-localizing with at least one MTA was considered as a GWAS-validated/verified MQTL.

Ortho-MQTL analysis

Information on MQTL identified in the present study and quality-related MQTL previously detected in rice (Youlin et al. 2021) were utilized to investigate the conserved regions (or ortho-MQTL) for quality characters between wheat and rice. This analysis involved the following steps: (i) genes models present in the wheat MQTL regions were used for BLAST searches against the rice genome database available in Ensembl Plants to identify the rice orthologues, (ii) the rice orthologues of wheat genes were extracted with their physical positions, (iii) physical positions of the rice orthologues were compared with the rice MQTL regions (Youlin et al. 2021), and (iv) rice MQTL harbouring at least four corresponding genes were considered as ortho-MQTL.

MQTL characterization using cloned genes from rice

Functionally validated rice genes associated with different quality traits (involving starch and protein metabolism, embryo and endosperm development, sugar transportation, grain development, etc.) were collected from the available literature, and their protein sequences were retrieved from the Rice Annotation Project Database (rap-dB) (https://rapdb.dna.affrc.go.jp/index.html). The protein sequences of the collected rice genes were then used for protein BLAST searches against the wheat reference genome available in the Ensembl Plants database to obtain the corresponding genes in the MQTL regions.

Results

Characterization of QTL studies involving quality traits

As many as 50 interval mapping studies involving 63 biparental populations reporting QTL for different quality traits were collected (some studies utilized more than one mapping population). Among these 63 populations, five were durum wheat populations (with population sizes ranging from 83 to 208), 22 were spring wheat populations (with population sizes ranging from 100 to 286), 35 were winter wheat populations (with population sizes ranging from 94 to 290), and one was a mixed population of spring and winter wheat (with a population size of 240). As many as 2458 QTL associated with quality traits were collected from these studies. These QTL were unequally distributed on different wheat chromosomes and among the three sub-genomes (Fig. S1a). Sub-genome B carried the maximum number of QTL (995), while sub-genome D carried the minimum (607).

There were 45 sets (including one $F_{2:3}$) of RIL populations (with population sizes ranging from 83 to 290) and 18 sets of DH populations (with population sizes ranging from 94 to 192) (Fig. S1b, c; Tables S1, S2). The number of studies involving different types of populations, molecular markers, and mapping methods are presented in Fig. S1c, d, and e. Most mapping studies used simple sequence repeats (SSR) as the markers and composite interval mapping as a method for QTL mapping, respectively (Fig. S1d, e). The maximum number of QTL were associated with DRP (1004), while the minimum number of QTL were associated with nutritional traits (NT; 514). Phenotypic variation explained (PVE) values of individual QTL ranged from 2.03% to 95.24%, with an average of 10.77%, whereas more than 50% QTL showed LOD score less than 5 (Fig. S1f, g, h; Table S2).

Construction of consensus genetic map

The consensus map, "Wheat_Reference_GeneticMap-2022" showed significant variation for the genetic lengths of the individual linkage groups/chromosomes (ranging from 165 cM for 5A to 577.9 cM for 3B, with a mean of 353.53 cM) and for the number of markers positioned on each chromosome (ranging from 2212 on 4D to 21,242 on 3B with an average of 11,885.86 markers per chromosome) (Fig. 1). The total length of the consensus map was 7424.07 cM, which included 249,603 markers. Since different genetic maps with varying numbers and types of markers were used to construct the consensus map, the distribution of markers at the two ends varied significantly with higher marker density at one end of the chromosomes (Table S4). The marker density on individual chromosomes ranged from 10.51 markers/cM on 4D to 84.88 markers/cM on 1A, with a mean of 33.62 markers/cM on the whole genome.

Projected QTL and MQTL for quality traits in wheat

After careful examination and evaluation of 2458 QTL for the availability of information on the genetic positions and PVE values, 1986 QTL were selected and utilized for the projection onto the consensus map. The remaining 472 QTL lacked the necessary information; hence, they were not

considered for projection. Of the total 1986 QTL with complete information available for analysis, only 1128 (56.79%) could be projected onto the consensus map. Of the 1128 projected QTL, 1121 QTL were grouped into 110 MQTL, while seven QTL remained singletons (Table 1; Figs. 1, 2 and Fig. S2). Eight hundred and fifty-eight (858) QTL were not projected onto the consensus map owing to either of the following reasons: (i) unavailability of common markers between the consensus and initial linkage maps and (ii) large CI of initial QTL.

Further, based on the source of initial QTL included in the MQTL, the identified MQTL were grouped into (i) spring type (S-type, 16 MQTL), (ii) winter type (W-type, 9 MQTL), (iii) spring-winter type (SW type, 65 MQTL), (iv) winter-durum type (WD type, 3 MQTL), and (v) spring-winter-durum type (SWD type, 17 MQTL) (Table S5). The S-type MQTL involved the QTL identified mainly from spring wheat populations; similarly, W-type MQTL integrated the QTL identified mainly from winter wheat populations and so on.

MQTL on individual chromosomes ranged from two on chromosomes 5B, 6B, and 7A to a maximum of 9 MQTL on chromosome 1A (Fig. S2a; Table S5). Among the 110 MQTL, 91, 81, and 103 MQTL contained QTL for DRP, NT, and PQT, respectively (Fig. S2b, Table S5). The average CI of MQTL (5.56 cM) was 18.84-fold less than that of the initial QTL (40.35 cM), and there were significant differences among different wheat chromosomes (Fig. S2c). The number of clustered QTL per MQTL ranged from 2 (in several MQTL) to 85 (in MQTL1B.1), with 11 MQTL involving at least 20 initial QTL from different mapping populations (Fig. S2d; Table S5). Of these 11 MQTL, four were located on chromosome 1B, and the remaining seven MQTL were each located on different chromosomes. Further, as many as 11 MQTL were exclusively associated with a single quality trait (either DRP, NT, or PQT), whereas 40 and 59 MQTL were associated with two and all three quality traits, respectively (Fig. S2e, Table 1).

Gene models available in MQTL regions and their expression analysis

A total of 108 MQTL were anchored to the physical map of the wheat reference genome. Physical positions of two MQTL (viz., MQTL6D.3 and MQTL6D.4) could not be deduced, as nucleotide sequences of the markers flanking these MQTL were not available. Gene mining from 108 MQTL regions led to the identification of 2533 gene models. The maximum number of gene models (276) was identified for the MQTL located on chromosome 2A. In contrast, the minimum number of gene models (6) was available from the MQTL located on chromosome 6B (Tables S6, S8). Several previously characterized wheat genes associated with GPC (e.g., *GPC-B1*/*NAM-B1*), high molecular weight glutenin (e.g., *Glu-B1-1b*, *Glu-1D-1d*, *1Dx2t*, and *Glu-1By9*), and starch synthase enzymes (e.g., *TaSSI*, *TaSSIIa*, *TaGBSSIa*, and *TaSSIVb*) were found to be co-localized with 12 MQTL regions (Table S9).

Expression analysis of 2533 gene models allowed the identification of 556 gene models with > 2 TPM expressions, which included 94 gene models with > 5 TPM and six gene models with > 10 TPM expressions in grains and their component tissues such as seed coat, starchy endosperm, whole endosperm, aleurone layer, and grain transfer cells (Fig. 2; Table S7). Of these 556 gene models, 117 showed constitutive expressions in all the tissues studied. In contrast, the remaining 439 gene models showed tissue-specific expressions. These 439 differentially expressed genes (DEGs) included 44 high-confidence CGs with known functions previously reported to be important for quality traits in different crops, including cereals (Fig. S3, Table 2). These genes were mainly associated with metal ion binding, Zn-transporter and zinc-binding site, small hydrophilic seed protein, amino acid transporter, and seed storage helical domain, sweet-sugar transporters, UDP-glucuronosyl/UDP-glucosyltransferase and sugar/inositol transporter, cupin 1, etc. (Table 2 and Table S7). Further, all the six CGs, *TraesCS3D02G095700*, *TraesCS3D02G096000*, *TraesCS4B02G017500*, *TraesCS4D02G016000*, *TraesCS4D02G016100*, and *TraesCS6D02G000200* with > 10 TPM expressions have been shown to be involved in improving the seed quality through nutrient reservoir activity (Table 2).

MQTL validated with GWAS

The physical coordinates of the MQTL identified in the present study were compared with MTAs reported in earlier GWAS (Table S10). Among the 108 MQTL, as many as 43 MQTL (39.81%) were co-localized with at least one MTA (Fig. 1; Table S10). Some MQTL co-localized with MTAs available from more than one GWAS; for instance, MQTL6A.7 co-localized with MTAs identified in seven different GWAS. Each of the five MQTL (viz., 1A.1, 1B.2, 3B.4, 5B.2, and 6B.2) involving at least 20 initial QTL were co-localized with multiple MTAs reported from different GWAS. Further, five CGs, *TraesCS1A02G040600*, *TraesCS2D02G531100*, *TraesCS3B02G449200*, *TraesCS3D02G095700*, and *TraesCS3D02G096000* reported from earlier GWAS (Yang et al. 2020) were overlapped with four MQTL identified in the present study. Among them, the first three genes were co-localized with MQTL1A.1, MQTL2D.6, and MQTL3B.1, respectively, whereas the last two genes were co-localized with MQTL3D.3.

Table 1 Summary of wheat MQTL associated with different quality traits

MQTL	Genetic position (cM)	Flanking markers	No. of QTL projected	Trait
MQTL1A.1	14.7–15.1	*IWB72800–D_1377838*	24	NT, DRP, and PQT
MQTL1A.2	22.3–22.7	*3980487_1al_11151–IWB35066*	20	NT, DRP, and PQT
MQTL1A.3	36.1–36.4	*BobWhite_c5793_372–3955448_1al_1513*	10	DRP and PQT
MQTL1A.4	42.6–43.1	*3881592_1al_184–wPt2311*	14	DRP and PQT
MQTL1A.5	68.6–69.1	*AX_109031595–wPt8172*	6	PQT
MQTL1A.6	85.5–87.8	*Tdurum_contig47183_205–Xwpt3698*	2	DRP and PQT
MQTL1A.7	92.9–94.8	*Xbarc174–wPt1906*	15	NT, DRP, and PQT
MQTL1A.8	118.4–123.1	*snp2584–wPt7030*	10	NT, DRP, and PQT
MQTL1A.9	156.6–156.9	*D_3022884–Xcfe0242b*	12	NT, DRP, and PQT
MQTL1B.1	41.2–41.4	*AX_95133874–Xwmc44*	85	NT, DRP, and PQT
MQTL1B.2	66.3–66.8	*IWB65744–AX_94462160*	21	NT, DRP, and PQT
MQTL1B.3	77–77.6	*IWB13393–IWA7298*	27	NT, DRP, and PQT
MQTL1B.4	110–111.7	*Ku_c241_460–IWB6906*	12	NT, DRP, and PQT
MQTL1B.5	195.5–197.3	*wPt1973–wPt_2315*	21	NT, DRP, and PQT
MQTL1B.6	428.3–439.3	*Kukri_rep_c111991_498–XPaggMcgg6*	9	NT, DRP, and PQT
MQTL1D.1	43.6–43.9	*Xbarc229.2–cfd92*	21	NT, DRP, and PQT
MQTL1D.2	47.2–47.6	*2257978_1dl_15913–2281626_1dl_570*	11	NT, DRP, and PQT
MQTL1D.3	60.1–60.7	*D_1073588–D_1234123*	14	NT, DRP, and PQT
MQTL1D.4	76–76	*TA004476_0719–Glu_D1*	2	DRP and PQT
MQTL1D.5	77–77	*TA004476_0719–Glu_D1*	16	NT, DRP, and PQT
MQTL1D.6	109.4–110.6	*AX_95218664–AX_94769043*	10	NT, DRP, and PQT
MQTL1D.7	156.9–158.3	*IWB9092–IWB56444*	12	PQT
MQTL2A.1	8.1–11.9	*Xgwm328_2A–GBS_210*	11	NT, DRP, and PQT
MQTL2A.2	28.4–28.6	*Kukri_c36139_292–BS00063632_51*	15	DRP and PQT
MQTL2A.3	81.2–82.3	*RAC875_c17787_274–TA004602_1630*	14	NT, DRP, and PQT
MQTL2A.4	99.5–100.3	*wPt_8049–IWB23030*	9	NT, DRP, and PQT
MQTL2A.5	248.2–260.8	*BS00082084_51–RAC875_c54668_102*	2	PQT
MQTL2A.6	292.9–292.9	*RAC875_c54668_102–wsnp_Ku_c1292_2572110*	10	NT, DRP, and PQT
MQTL2B.1	0.7–0.9	*M35745–D_1162944*	12	DRP and PQT
MQTL2B.2	25.3–29.2	*Xwmc435–IWA897*	6	DRP and PQT
MQTL2B.3	49.9–50.3	*Ex_c55735_1012–Xwpt8004*	11	NT, DRP, and PQT
MQTL2B.4	73.2–75	*Xgwm55b–Excalibur_c33221_681*	6	DRP and PQT
MQTL2B.5	93.9–95.2	*CAP7_6910_523–8086989_2bl_2189*	9	NT, DRP, and PQT
MQTL2B.6	136.7–139.7	*8074934_2bl_7628–Kukri_c9507_495*	12	DRP and PQT
MQTL2B.7	228.7–230	*Xgwm1273–U296*	8	DRP and PQT
MQTL2D.1	28.8–32.1	*2DS_5366150_1491–AX_95093513*	6	NT, DRP, and PQT
MQTL2D.2	63.7–65.8	*AX_110230565–Xctg05205*	14	NT, DRP, and PQT
MQTL2D.3	112.5–113.6	*Kukri_c44769_750–BS00011109_51*	5	NT and PQT
MQTL2D.4	140–140.1	*IWB64805–IWB34403*	2	NT
MQTL2D.5	163.8–169.7	*IWB29964–IWB32041*	2	DRP and PQT
MQTL2D.6	337.3–530.5	*IWB44461–GENE_4086_115*	3	NT and PQT
MQTL3A.1	0–3.5	*Excalibur_c12875_1573–4397491_3al_1806*	3	NT and PQT
MQTL3A.2	25.5–25.6	*AX_109316906–P41/M41_4*	19	NT, DRP, and PQT
MQTL3A.3	65.7–70.5	*IWB54878.1–KUKRI_REP_C69970_717*	4	NT, DRP, and PQT
MQTL3A.4	110.5–111	*XPaggMcgg1–Excalibur_c5416_846*	9	NT, DRP, and PQT
MQTL3B.1	34–36.7	*XPaggMctg16–wPt7502*	10	NT, DRP, and PQT
MQTL3B.2	72.4–73.7	*IWB6207–D_4329487*	6	NT, DRP, and PQT
MQTL3B.3	111.5–113.6	*AX_109869742–AX_109842601*	11	NT, DRP, and PQT
MQTL3B.4	173.9–174.4	*ACA.CTGA12–Xctgacg317*	21	NT, DRP, and PQT

Table 1 (continued)

MQTL	Genetic position (cM)	Flanking markers	No. of QTL projected	Trait
MQTL3D.1	36.2–39.2	*AX_95218150–AX_110037813*	6	NT, DRP, and PQT
MQTL3D.2	67.2–69.2	*IWB40541–IWB19457*	8	DRP and PQT
MQTL3D.3	122.3–144.9	*wPt669255–RFL_Contig5276_1756*	4	DRP and PQT
MQTL3D.4	189.1–238.9	*RFL_Contig5276_1756–BS00066932_51*	3	PQT
MQTL4A.1	8.9–10.8	*Kukri_c17417_797–Xgwm113*	11	NT, DRP, and PQT
MQTL4A.2	34.7–38.8	*wPt7924–wPt0538*	6	DRP and NT
MQTL4A.3	66.7–71.5	*wPt0105–snp1066*	3	NT and PQT
MQTL4A.4	113.2–115.3	*IAAV5818–SSRabg390.DI*	30	NT, DRP, and PQT
MQTL4A.5	164.7–165	*RAC875_c78248_115–BS00067074_51*	19	NT, DRP, and PQT
MQTL4B.1	12.3–12.5	*Xfbb255a–D_3939025*	15	DRP and PQT
MQTL4B.2	20.9–21.4	*Xmag983–S_3025233*	6	NT, DRP, and PQT
MQTL4B.3	44.9–45.2	*AX_110396575–BS00076259_51*	11	NT, DRP, and PQT
MQTL4B.4	52.3–52.8	*wPt_3908–Xgwm538*	16	NT, DRP, and PQT
MQTL4B.5	89.3–92.3	*IWB73486–IWB15523*	11	NT, DRP, and PQT
MQTL4B.6	181.8–185.4	*Xgwm637b–wsnp_CAP12_c1101_569783*	10	NT and PQT
MQTL4D.1	0.7–1.6	*Xwmc617–AX_110527441*	10	DRP and PQT
MQTL4D.2	53.6–53.9	*IWB16077–Xsrap16*	5	DRP and PQT
MQTL4D.3	78.7–80.4	*Xgdm129–wPt2379*	2	DRP and PQT
MQTL4D.4	83.3–83.9	*AX_94881415–AX_94383842*	8	NT, DRP, and PQT
MQTL4D.5	86–86.7	*Xsrap11b–IWB62209*	2	DRP and NT
MQTL4D.6	87.9–88.5	*AX_110418361–Xgdm125*	4	DRP and NT
MQTL4D.7	93.9–94.5	*Xbarc1183–AX_94403999*	8	NT, DRP, and PQT
MQTL4D.8	205.4–206	*Xscss30.2.2–Kukri_c40437_66*	3	NT and PQT
MQTL5A.1	8.8–9.5	*Xgwm0304b–AX_95186387*	10	NT, DRP, and PQT
MQTL5A.2	39–42	*D_1206650–XACG.GAC1.2*	10	NT, DRP, and PQT
MQTL5A.3	103.5–103.8	*Xgwm410.3–IWB61598*	24	NT, DRP, and PQT
MQTL5B.1	8.6–8.8	*Xbarc133–GBS_257*	3	DRP and PQT
MQTL5B.2	42.7–44	*wPt5168–IWB36196*	26	NT, DRP, and PQT
MQTL5D.1	9.7–10.9	*D_4329273–S_1046500*	16	DRP and PQT
MQTL5D.2	28.1–28.3	*S_982589–S_1052739*	5	DRP
MQTL5D.3	31.6–31.7	*D_4329207–D_1116418*	4	NT, DRP, and PQT
MQTL5D.4	72.2–72.3	*IWB58798–Xswes342a*	7	NT, DRP, and PQT
MQTL5D.5	168.3–173	*wPt1197–5DL_4588938_1981*	12	NT and PQT
MQTL5D.6	418.1–432.6	*Jagger_c550_91–JD_c4438_839*	6	DRP and PQT
MQTL6A.1	0–3.3	*AX_94788664–D_3952327*	3	NT and PQT
MQTL6A.2	9.4–18.2	*IWB44292–D_2278273*	2	PQT
MQTL6A.3	35.3–35.9	*Tdurum_contig46828_1430–S_1116215*	9	NT, DRP, and PQT
MQTL6A.4	40.4–46.3	*S_1116215–IWB23460.2*	3	NT, DRP, and PQT
MQTL6A.5	57.6–70.3	*IWA504–wPt4791*	4	NT, DRP, and PQT
MQTL6A.6	202–235.7	*104.172–Xcdo1090a*	2	PQT
MQTL6A.7	270.9–277.3	*XPaggMctg18–Xbarc146b*	5	NT and PQT
MQTL6B.1	27–28.7	*S_1054930–GTG.CTT1*	6	DRP and PQT
MQTL6B.2	62.7–62.9	*Xdupw16–wPt745074*	24	NT, DRP, and PQT
MQTL6D.1	33.7–38.2	*AX_86177993–cfd13c*	15	NT, DRP, and PQT
MQTL6D.2	75.8–78.7	*BobWhite_c13435_700–wPt666008*	8	NT, DRP, and PQT
MQTL6D.3	116.5–121.7	*Xfbb9b–AX_94381525*	5	NT and PQT
MQTL6D.4	165–165.1	*IWB4527–IWB58414*	4	DRP
MQTL7A.1	57.1–80.6	*M103823–GBS_539*	2	NT
MQTL7A.2	148.1–154.4	*tarc0748–gwm332*	3	NT and PQT

Table 1 (continued)

MQTL	Genetic position (cM)	Flanking markers	No. of QTL projected	Trait
MQTL7B.1	1.1–1.3	*Excalibur_c22830_2010–Excalibur_c16580_388*	6	NT and PQT
MQTL7B.2	14.7–15	*Kukri_c16416_647–Xgwm1250*	6	NT, DRP, and PQT
MQTL7B.3	46.8–50.4	*wPt_0789–snp2273*	16	NT, DRP, and PQT
MQTL7B.4	78.1–81.8	*wPt_2592–D_3938216*	6	NT, DRP, and PQT
MQTL7B.5	92.3–95.8	*wPt_732048–wPt7368*	3	NT and PQT
MQTL7B.6	231.3–234.5	*Xgwm0037–RFL_Contig4686_700*	5	NT, DRP, and PQT
MQTL7D.1	12.7–20.2	*Xgwm350–Xgwm974*	7	NT, DRP, and PQT
MQTL7D.2	40.1–45.8	*AX_110940110–wPt664368*	4	DRP and NT
MQTL7D.3	55.3–64.2	*IWB6964–S_1162003*	2	DRP
MQTL7D.4	66.8–75.1	*Xgwm0437–D_1135134*	17	NT, DRP, and PQT
MQTL7D.5	114.9–121.2	*AX_110579501–Excalibur_rep_c83019_155*	7	NT and PQT
MQTL7D.6	290.6–305.4	*CAP8_rep_c9420_186–Excalibur_rep_c85891_96*	10	DRP and PQT

NT nutritional traits; *DRP* dough rheology properties; *PQT* processing quality traits

Ortho-MQTL for quality traits

Extensive investigation of gene models underlying the wheat MQTL and rice MQTL showed the synteny of 23 wheat MQTL with 16 rice MQTL (Fig. 1, Fig. S4; Table S11). In some cases, more than one wheat MQTL was syntenic to single rice MQTL; for instance, three wheat MQTL (viz., 2B.3, 2D.2, and 2D.3) were found to be syntenic to single rice MQTL (i.e., MQTL4.5) (Fig. 2, Fig. S5). Conversely, a single wheat MQTL was found to be syntenic to more than one rice MQTL; for instance, wheat MQTL4A.4 was syntenic to two rice MQTL located on chromosome 8 (viz., MQTL8.6 and MQTL8.8), and MQTL4B.6 was syntenic to two rice MQTL located on chromosome 3 (MQTL3.3 and MQTL3.4).

The number of gene models conserved between wheat and rice MQTL ranged from four (in MQTL1A.3) to a maximum of 19 (in MQTL2D.2). Five promising ortho-MQTL (viz., 2A.1, 2D.2, 4D.8, 5D.1, and 7D.1), each involving more than ten conserved gene models at corresponding positions between wheat and rice MQTL are presented in Fig. S5.

Wheat homologues of known rice genes in MQTL regions

Information on 34 rice genes associated with different quality traits was collected. These genes encode proteins belonging to the following families: starch synthase, glycosyltransferase, aldehyde dehydrogenase, SWEET sugar transporter, alpha-amylase, glycoside hydrolase, glycogen debranching, protein kinase, peptidase, legumain, and seed storage proteins. Sixty-four wheat homologues of 30 rice genes were detected in the 44 wheat MQTL regions (Table S12) (wheat homologues for the remaining four rice genes could not be identified in any MQTL region). Some MQTL regions included homologues of more than one rice gene; for instance, MQTL4A.2 included wheat homologues of three rice genes (*wx1*, *OsACS6*, and *GBSSII*) (Table S12). Wheat homologues for nine rice genes were identified on multiple wheat chromosomes, for instance, wheat homologues for the rice gene *Wx1* were detected on chromosomes 4A and 7A.

Discussion

The discovery of molecular markers and advancements in QTL mapping strategies have facilitated the identification of a large number of QTL associated with quality traits in wheat (Tables S1, S2). Most of these QTL are minor QTL [with low phenotypic variation explained (PVE) value] and have larger CI, making them unsuitable for marker-assisted breeding (MAB; Saini et al. 2022b). It has been observed that QTL identified from one population may not be effective for a breeding programme involving another population (Yang et al. 2021). The downsides of these QTL promoted us to reanalyse all these loci together, to integrate this huge amount of data so that breeders and researchers could make greater use of these already identified QTL. Meta-analysis of QTLs has been proved as one of the most promising methods for integration of QTLs which better tackles the between-study heterogeneity (Saini et al. 2022b).

Meta-analysis has the great capability to compile the information from multiple QTL mapping studies involving diverse environments with different genetic backgrounds to identify stable and reliable MQTL with reduced CI (Welcker et al. 2011). The MQTL analysis has already been conducted for the major crops, including rice, wheat,

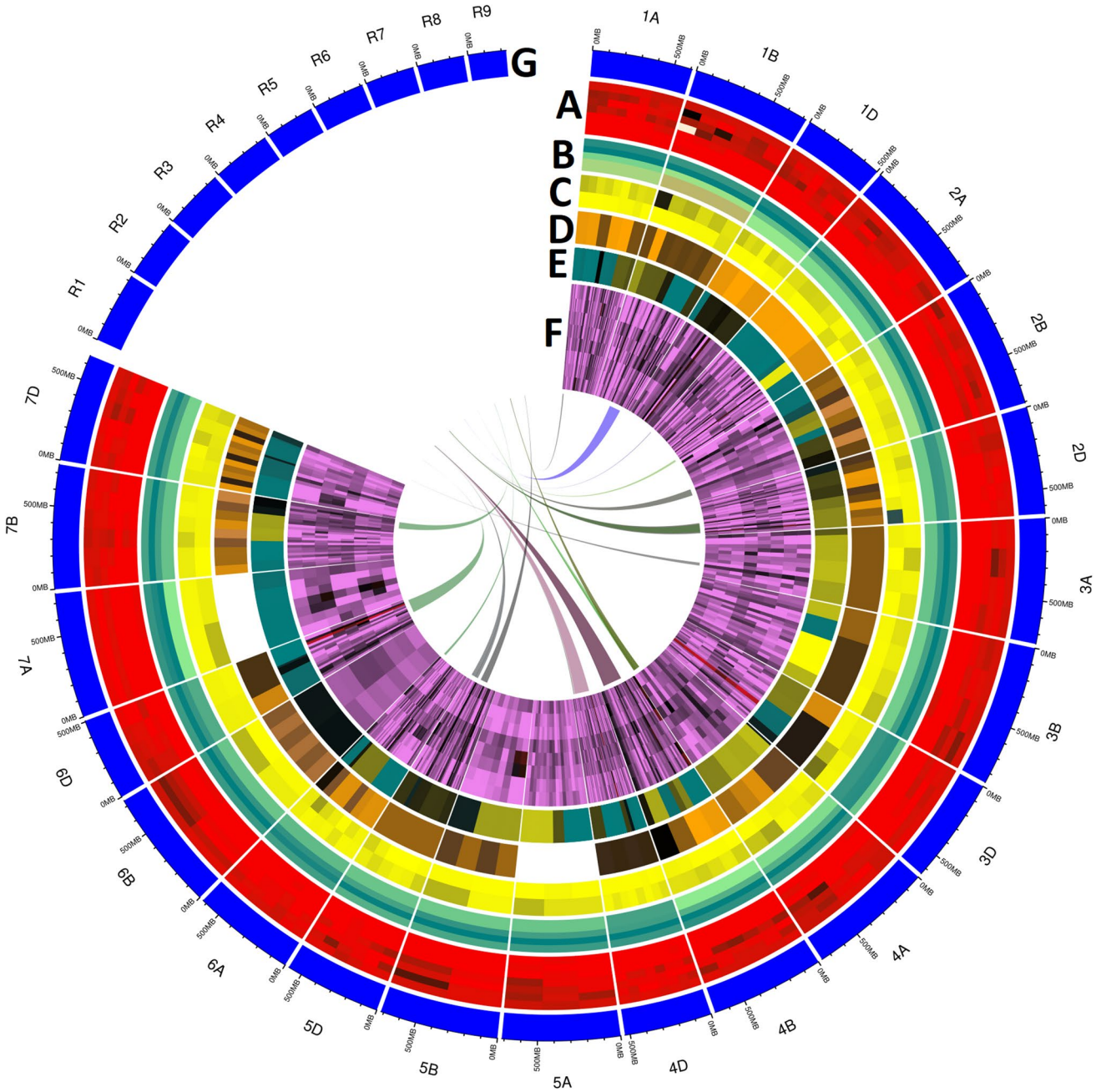

Fig. 2 Circular diagram showing the different features of QTL and MQTL. Circle **A** Number of QTL for each trait in each MQTL (i.e., dough rheology properties, nutritional traits, processing quality traits) and the number of traits in each MQTL. **B** Chromosome wise distribution of the initial number of QTL, projected QTL, average confidence interval (CI) of MQTL and average CI of initial QTL. **C** Number of initial QTL projected on each of the MQTL. **D** MQTL co-localized with known wheat genes, GWAS-MTAs and functionally characterized rice genes. **E** Gene density distribution in the MQTL regions. **F** Expression pattern of CG models with > 2 TPM in the eight different tissues (i.e., whole grain, whole endosperm, starchy endosperm, aleurone layer, seed coat, starchy endosperm + seed coat, transfer cells, and aleurone layer + starchy endosperm). **G** Syntenic region between wheat and rice MQTL. The outer circle represents wheat (1A–7D) and rice chromosomes (R1–R9)

maize, etc. (Li et al. 2013; Quraishi et al. 2017; Sandhu et al. 2021b; Yang et al. 2021). Previously, an MQTL analysis for quality traits in wheat identified the six MQTL for GPC and eight MQTL for baking quality using a total of only 155 QTL (Quraishi et al. 2017). However, the results of the MQTL analysis are significantly and positively correlated with the initial number of QTL used (Quraishi et al. 2017; Yang et al. 2021). Furthermore, as molecular

Table 2 High-confidence CGs (each with > 2 TPM expression and known to be associated with quality traits in different crops) identified in the present study

MQTL	Gene ID	Gene position (bp)	GO term name	Function description	Expression (TPM)	Trait
MQTL1A.2	*TraesCS1A02G060100*	41,357,284–41,362,423	Peptidase activity	Peptidase C13, legumain	> 2	NT, DRP, and PQT
MQTL1A.5	*TraesCS1A02G224000*	394,325,250–394,328,538	–	Peptidase M24	> 5	PQT
MQTL1A.5	*TraesCS1A02G224200*	394,482,047–394,482,797	Cytosol	Small hydrophilic plant seed protein	> 5	PQT
MQTL1A.5	*TraesCS1A02G224600*	394,587,930–394,588,284	Cytosol	Small hydrophilic plant seed protein	> 5	PQT
MQTL1A.7	*TraesCS1A02G062500*	42,670,658–42,671,830	–	seed storage helical domain superfamily	> 5	NT, DRP, and PQT
MQTL1A.7	*TraesCS1A02G062700*	42,695,416–42,698,084	–	seed storage helical domain superfamily	> 5	NT, DRP, and PQT
MQTL1A.7	*TraesCS1A02G062900*	42,721,261–42,721,834	–	seed storage helical domain superfamily	> 5	NT, DRP, and PQT
MQTL1B.1	*TraesCS1B02G407800*	634,934,360–634,934,858	–	seed storage helical domain	> 2	NT, DRP, and PQT
MQTL1B.6	*TraesCS1B02G274300*	481,540,499–481,542,564	Nucleus	NAC domain	> 2	NT, DRP, and PQT
MQTL1D.2	*TraesCS1D02G346100*	433,899,291–433,905,345	Metal ion binding	Peptidase M16, zinc-binding site	> 2	NT, DRP, and PQT
MQTL1D.4	*TraesCS1D02G317300*	412,223,432–412,224,112	IgE binding	seed storage helical domain	> 5	DRP and PQT
MQTL2A.1	*TraesCS2A02G028400*	12,990,103–12,992,210	Transferase activity, transferring hexosyl groups	UDP-glucuronosyl/UDP-glucosyltransferase	> 2	NT, DRP, and PQT
MQTL2A.1	*TraesCS2A02G028500*	13,002,991–13,004,793	Transferase activity, transferring hexosyl groups	UDP-glucuronosyl/UDP-glucosyltransferase	> 5	NT, DRP, and PQT
MQTL2A.6	*TraesCS2A02G081100*	36,700,022–36,701,587	Transferase activity, transferring hexosyl groups	UDP-glucuronosyl/UDP-glucosyltransferase	> 2	NT, DRP, and PQT
MQTL2B.3	*TraesCS2B02G430900*	619,754,863–619,757,940	Serine-type carboxypeptidase activity	Peptidase S10, serine carboxypeptidase	> 2	NT, DRP, and PQT
MQTL2D.4	*TraesCS2D02G382400*	486,390,272–486,392,935	Peptidase activity	Peptidase C13, legumain	> 5	NT
MQTL3A.3	*TraesCS3A02G446200*	686,762,258–686,767,701	Serine-type carboxypeptidase activity	Peptidase S10, serine carboxypeptidase	> 2	NT, DRP, and PQT
MQTL3A.4	*TraesCS3A02G408200*	653,303,151–653,306,203	An integral component of membrane	SWEET sugar transporter	> 2	NT, DRP, and PQT
MQTL3B.2	*TraesCS3B02G059300*	31,058,376–31,059,986	Hydrolase activity	Peptidase C26	> 2	NT, DRP, and PQT
MQTL3B.2	*TraesCS3B02G059500*	31,066,580–31,068,297	Hydrolase activity	Peptidase C26	> 2	NT, DRP, and PQT
MQTL3D.1	*TraesCS3D02G514700*	598,160,861–598,163,274	Transferase activity, transferring hexosyl groups	UDP-glucuronosyl/UDP-glucosyltransferase	> 2	NT, DRP, and PQT
MQTL3D.3	*TraesCS3D02G095700*	48,543,331–48,543,795	Serine-type endopeptidase inhibitor activity	Cereal seed allergen/trypsin and alpha-amylase inhibitor	> 10	DRP and PQT
MQTL3D.3	*TraesCS3D02G096000*	48,732,052–48,732,516	Serine-type endopeptidase inhibitor activity	Cereal seed allergen/trypsin and alpha-amylase inhibitor	> 10	DRP and PQT

Table 2 (continued)

MQTL	Gene ID	Gene position (bp)	GO term name	Function description	Expression (TPM)	Trait
MQTL3D.3	*TraesCS3D02G096500*	48,836,328–48,842,240	An integral component of membrane	Amino acid/polyamine transporter I	> 2	DRP and PQT
MQTL4B.1	*TraesCS4B02G017500*	13,052,500–13,054,709	Nutrient reservoir activity	Cupin 1	> 10	DRP and PQT
MQTL4B.1	*TraesCS4B02G017600*	13,077,784–13,080,425	Nutrient reservoir activity	Cupin 1	> 5	DRP and PQT
MQTL4B.1	*TraesCS4B02G020000*	14,117,806–14,125,905	Zinc ion binding	Peptidase M1, alanine aminopeptidase	> 2	DRP and PQT
MQTL4B.6	*TraesCS4B02G196600*	423,357,718–423,362,900	–	Alpha/beta hydrolase fold-1	> 2	NT and PQT
MQTL4D.2	*TraesCS4D02G051100*	26,933,336–26,934,958	–	Alpha/beta hydrolase fold-1	> 2	DRP and PQT
MQTL4D.5	*TraesCS4D02G336100*	494,050,540–494,057,878	An integral component of membrane	Sugar/inositol transporter	> 2	DRP and NT
MQTL4D.5	*TraesCS4D02G337300*	494,829,139–494,833,871	Serine-type carboxypeptidase activity	Peptidase S10, serine carboxypeptidase	> 2	DRP and NT
MQTL4D.6	*TraesCS4D02G016000*	7,182,216–7,204,066	Nutrient reservoir activity	Cupin 1	> 10	DRP and NT
MQTL4D.6	*TraesCS4D02G016100*	7,203,800–7,206,343	–	Cupin 1	> 10	DRP and NT
MQTL4D.6	*TraesCS4D02G017700*	7,826,751–7,834,962	Zinc ion binding	Peptidase M1, alanine aminopeptidase	> 2	DRP and NT
MQTL4D.8	*TraesCS4D02G350300*	502,576,795–502,579,734	An integral component of membrane	Peptidase S54, rhomboid	> 2	NT and PQT
MQTL4D.8	*TraesCS4D02G350700*	502,747,671–502,751,833	–	Alpha/beta hydrolase fold-1	> 2	NT and PQT
MQTL5D.4	*TraesCS5D02G381000*	451,173,705–451,179,099	–	Peptidase S1, PA clan	> 2	NT, DRP, and PQT
MQTL5D.4	*TraesCS5D02G381200*	451,542,024–451,547,417	–	Peptidase S1, PA clan	> 2	NT, DRP, and PQT
MQTL6A.4	*TraesCS6A02G370300*	595,182,823–595,186,561	Hydrolase activity, acting on carbon–nitrogen bonds	Acetamidase/Formamidase	> 5	NT, DRP, and PQT
MQTL6D.1	*TraesCS6D02G091300*	57,107,880–57,116,429	Serine-type endopeptidase activity	Peptidase S9, prolyl oligopeptidase	> 2	NT, DRP, and PQT
MQTL6D.4	*TraesCS6D02G000200*	52,444–52,899	Serine-type endopeptidase inhibitor activity	Cereal seed allergen/trypsin and alpha-amylase inhibitor	> 10	DRP
MQTL7B.5	*TraesCS7B02G193800*	332,923,582–332,926,431	An integral component of membrane	Diacylglycerol acyltransferase	> 2	NT and PQT
MQTL7D.2	*TraesCS7D02G121200*	75,330,927–75,337,847	Serine-type peptidase activity	Peptidase S9, prolyl oligopeptidase, catalytic domain	> 2	DRP and NT
MQTL7D.2	*TraesCS7D02G121900*	75,930,917–75,945,541	Serine-type endopeptidase activity	Peptidase S8/S53 domain	> 2	DRP and NT

CGs candidate genes; *TPM* transcript per million; *MQTL* meta-QTL; *bp* base pair; *GO* gene ontology; *NT* nutritional traits; *DRP* dough rheology properties; *PQT* processing quality traits

genetics and QTL mapping methodologies are advancing, novel QTL are regularly being identified and published; therefore, we must keep up with this pace to integrate new QTL into more stable and reliable MQTL. Therefore, in the present study, we conducted a meta-analysis using 1,986 initial QTL reported during 2013–20 and identified 110 MQTL for three major quality traits. In addition to Zn, Fe, GPC, and baking quality traits previously studied

by Quraishi et al. (2017), the present study also considered the other important quality parameters such as starch, PPO, Ax content, bread making properties, etc.

The present study assigned the identified MQTL to different wheat types (e.g., winter wheat, spring wheat, and durum wheat) based on the source of QTL involved in MQTL. Winter wheat is harder than spring wheat and has a higher protein level, making it ideal for preparing pasta and bread. Spring wheat is utilised in products like tender pastries and cakes that do not require high-protein content. Although, bread wheat and durum wheat have similar nutritional profiles, but, slight differences in genetic makeup influence the elasticity, extensibility, and fermentability of their doughs, making durum wheat best suitable for pasta (Ciudad-Mulero et al. 2020). The quality aspects of these wheat types may either be governed by their specific genomic regions as revealed by S and W-type MQTL or conserved genomic regions across the different wheat types as indicated by the detection of SW, WD and SWD-type MQTL. However, no durum wheat specific or D-type MQTL were identified in the current study, which may be owing to (i) the involvement of a small number of durum wheat QTL in the meta-analysis (QTL retrieved from only five studies); (ii) genomic regions associated with quality traits are conserved among durum, spring, and winter wheat types (as indicated by the detection of SWD-type MQTL). However, it is possible to identify the D-type MQTL by incorporating a large number of QTL from multiple durum wheat populations in future studies.

From the breeding perspective, it is noteworthy to identify the most stable and reliable MQTL involving the large number of initial QTL identified across the different populations and environments. Eleven such MQTL involving more than 20 initial QTL were detected in the present study. One MQTL located on chromosome 1B (MQTL1B.1) included as many as 85 initial QTL, which is much higher than the reports of earlier meta-analysis (Quraishi et al. 2017). The present study aggregated vast information on QTL from multiple genetic backgrounds. It efficiently reduced the CI of the QTL, thereby improving the accuracy of CG identification from the important MQTL regions. The average CI of MQTL was 18.84-fold less than that of the average CI of the initial QTL used for the analysis.

Some of the MQTL with reduced CI identified in the present study may lay the foundation for molecular cloning and functional characterization of genes associated with quality traits in wheat. Further, this may offer the possibilities for marker-assisted gene transfer across the populations and contribute to wheat quality improvement. Flanking markers of the MQTL can also be used as fixed effects in the genomic selection (GS) models, which may help to improve the prediction accuracy of GS for quality traits. GS has been used for predicting various complex traits in wheat, especially grain yield (Sandhu et al. 2022). However, only a few GS studies for quality traits are available in wheat (Sandhu et al. 2021a).

CGs available from MQTL regions associated with quality traits

MQTL are considered potential targets for mining CGs associated with the traits in question. Further, MQTL regions have been shown to have a high correlation with gene density in the genome, as revealed by earlier reports on MQTL studies (Swamy et al. 2011; Quraishi et al. 2017; Yang et al. 2021). In wheat, previous studies have reported 15,772 gene models for yield, baking quality, and grain protein content (Quraishi et al. 2017), 324 gene models for fusarium head blight resistance (Venske et al. 2019), 228 gene models for drought (Kumar et al. 2020), and 237 gene models (Yang et al. 2021) for yield-related traits. In the present study, gene mining within 108 MQTL identified 2533 gene models; at least some of them should be associated with quality traits in wheat.

Gene expression analysis is the study of how genes are transcribed to produce functional gene products, such as RNA or protein. In silico expression analysis identified 556 gene models with > 2 TPM expressions. Among 556 genes, 439 genes showed differential expressions in different grain tissues. Out of 439 DEGs, 44 high-confidence CGs were selected and recommended for future studies. Functional characterization of these genes and survey of available literature revealed their involvement in transcriptional and translational regulation of various genes, signalling mechanism, metabolism, cellular development, transfer, etc. These genes were mainly associated with metal ion binding (maybe related to PPO), Zn-transporter and zinc-binding site (Zn and Fe content), small hydrophilic plant seed protein, amino acid transporter, and seed storage helical domain (seed storage protein), sweet-sugar transporters, UDP-glucuronosyl/UDP-glucosyltransferase, sugar/inositol transporter (starch content), cupin 1 (seed allergy), etc. These genes may be cloned and functionally characterized to be associated with quality traits. In addition, SNPs may also be identified within the coding sequences of promising CGs identified in the present study. Favourable allelic variants associated with quality traits may be explored and used in haplotype-based breeding programmes (Bhat et al. 2021).

Recently, gene expression analysis of hexaploid wheat and its diploid progenitors through RNA-seq and the GeneChip®Wheat Genome array identified numerous DEGs related to starch biosynthesis, nutrient reservoir activity, carbohydrate metabolism, and seed storage protein synthesis (Kaushik et al. 2020). Seven DEGs identified in above study were co-localized with MQTL (located on 1A, 2A,

2B, 4A, 6A, 7A, and 7B) identified in the present study. Of these seven genes, six were downregulated, and one gene was up-regulated. Among the downregulated genes, two genes, *TraesCS1A02G041100* and *TraesCS2A02G042500*, were mapped to MQTL1A.1 and MQTL2A.2, respectively, which encode NB-ARC domain-containing proteins, and one gene, *TraesCS4A02G316100*, located on MQTL4A.5, encodes an F-box domain. In contrast, the functions of the three downregulated genes, *TraesCS2B02G430500*, *TraesCS6A02G365500*, and *TraesCS7A02G078900*, available from MQTL2B.3, MQTL6A.3, and MQTL7A.2, respectively, have not been characterized yet. The up-regulated gene, *TraesCS7B02G194000*, available from MQTL7B.5 encodes the alpha/beta hydrolase enzyme, which is known to take part in many biochemical processes including bioluminescence, fatty acid, and polyketide biosynthesis and metabolism (Holmquist 2000).

Comparing MQTL with known genes for quality traits in wheat may further help to better understand the genetic architecture underlying complex traits, including those related to end-use quality. Therefore, an association of MQTL with known quality-related genes was also examined during the current study. This analysis reported the occurrence of nine functionally characterized important wheat genes including *GPC-B1/NAM-B1*, *Glu-B1-1b*, *Glu-1D-1d*, *1Dx2t*, *Glu-1By9*, *TaSSI*, *TaSSIIa*, *TaGBSSIa*, and *TaSSIVb* in different MQTL regions. Genes co-localized with MQTL6B.1 and MQTL6B.2 are known to be associated with GPC, which may also take part in the nutrient remobilization from leaves to developing grains (Distelfeld et al. 2014). Genomic regions underlying the five wheat MQTL (viz., 1B.2, 1B.3, 1B.4, 1D.4, and 1D.5) carried some known genes viz., *Glu-B1-1b*, *Glu-1D-1d*, *1Dx2t*, and *Glu-1By9* which are the precursors of HMW glutenin, a prime deciding factor for determining the dough elasticity and bread-making quality in wheat (Anjum et al. 2007). Genes for the starch synthase enzyme available from MQTL1D.2, 7D.2, 7D.3, 7D.4, and 7D.5 regions are responsible for the amylopectin biosynthesis via α-1,4-glycosidic linkages. Amylopectin-A is the unique chemical compound present in wheat that triggers the low-density lipoproteins, which take part in the transportation and delivery of fatty acids, triacylglycerol, and cholesterol in many plant organs (Horstmann et al. 2017).

Checking the efficacy of MQTL with GWAS

GWAS is a powerful tool that allows the investigation of complex characters by exploiting the recent and historical recombination events present in the association panel and permits high-resolution mapping (Bush and Moore 2012). High-throughput and low-cost sequencing technologies have facilitated the identification of MTAs for many quality traits utilizing genome-wide variants (Godoy et al. 2018; Suliman et al. 2021). In the present study, around 40% (43/108) of the identified MQTL were verified with MTAs for quality traits. It is apparent from previous studies (Yang et al. 2021; Saini et al. 2021a, b, 2022b; Kumar et al. 2021; Pal et al. 2021) and the present study that the GWAS-MTAs could verify only a part of the MQTL which may be owing to the following reasons: (i) none of the approaches, whether MQTL analysis (relying on interval mapping studies involving bi-parental populations) or GWAS approach (involving sets of diverse genotypes), included all the genetic variation present in the crop species. (ii) Genetic materials used in the two approaches were largely different from each other. (iii) Further, GWAS are designed to identify only common (or frequent) variants (with a minor allele frequency > 5%). In contrast, linkage-based interval mapping studies can efficiently detect rarely occurring alleles that have a large effect on the phenotype.

The MQTL could be considered more stable and consistent if validated with MTAs identified in more than one GWAS and included many QTL from different interval mapping studies. Five such MQTL (1A.1, 1B.2, 3B.4, 5B.2, and 6B2) with more than 20 initial QTL and reduced genetic CI (95%) (< 2 cM) were verified with multiple MTAs derived from different GWAS. These MQTL are considered the promising MQTL and they may be utilized in marker-assisted breeding (MAB) programmes to improve the quality traits in wheat. More interestingly, five genes identified in a wheat multi-locus GWAS (Yang et al. 2021) were co-localized with four MQTL detected in the present study. These genes are known to participate in the various biological processes to improve the grain quality in wheat. For instance, the gene *TraesCS1A02G040600* encodes a cupin superfamily protein, i.e., phospho-glucose isomerase, which takes part in the non-enzymatic protein storage in seeds (Dunwell and Gane 1998). Genes *TraesCS3D02G095700* and *TraesCS3D02G096000*, encode for two different wheat allergens (viz., trypsin and alpha-amylase inhibitor, respectively). Wheat allergens such as seed storage proteins causing celiac disease may reduce the nutritional value of wheat seeds. Creating the null mutants for such genes through RNAi or CRISPR/Cas9 may reduce the percentage of such allergic compounds in the seeds (Zhang et al. 2014). Alpha-amylase inhibitors prevent the hydrolysis of storage starch granules present in the endosperm, thereby maintaining starch integrity in the seeds (Ali and Elozeiri 2017).

Ortho-MQTL mining: revealing conserved genomic regions between wheat and rice

Identification of ortho-MQTL between wheat and rice genomes is another interesting feature of the present study. Ortho-MQTL analysis has been sparingly conducted in

wheat, with only a few such recent studies available for different traits, including nitrogen use efficiency (NUE; Quraishi et al. 2017; Saini et al. 2021b), salinity stress tolerance (Pal et al. 2021), grain yield and associated traits (Saini et al. 2022b), and thermotolerance (Kumar et al. 2020). However, to our knowledge, no study has reported the ortho-MQTL associated with quality traits in wheat and other cereals so far. This is the first report where we identified as many as 23 MQTL associated with quality traits conserved between wheat and rice.

Several conserved genes underlying the ortho-MQTL have already been characterized for their association with different quality-related traits. For instance, *TraesCS1B02G248000* underlying wheat MQTL1B.4 and its corresponding gene (*BGIOSGA019745*) in rice MQTL5.6 encode a NAC transcription factor that regulates the grain size in rice (Mathew et al. 2016). Similarly, *TraesCS2B02G430300* underlying the wheat MQTL2B.3 and its corresponding gene (*BGIOSGA016898*) in rice MQTL4.5 belong to the hydrophobic seed protein domain, which accumulates hydrophobic proteins on the seed surface (Gijzen et al. 1999).

Overall, using synteny and collinearity information, the ortho-MQTL analysis revealed conserved genomic regions between wheat and rice; these regions contain many uncharacterized and characterized genes that are believed to be associated with the quality traits. The ortho-MQTL identified in the present study could be beneficial in future research for discovering conserved genes and generating conserved orthologous set markers for cereal breeding programmes. At least two previous studies have demonstrated the effectiveness of this approach. One of which involved the discovery of the conserved gene 'glutamate synthase' (GoGAT) linked to an ortho-MQTL for NUE (Quraishi et al. 2011). The other study includes the discovery of two genes (*GRMZM2G178190* and *GRMZM2G366919*) linked to grain Fe/Zn ortho-MQTL. These genes were identified as naturally existing resistance-associated macrophage protein genes and were considered as the best CGs for grain Fe and Zn content in maize (Jin et al. 2015).

Wheat homologues of known rice genes in MQTL regions

Comparative genomics study of wheat with model grasses such as rice has revolutionized molecular genetics and contributed to wheat improvement by identifying the linkage blocks, gene rearrangements, and conserved regions in wheat (Sorrells et al. 2003). Functionally characterized rice genes have a similar function in wheat (Hanif et al. 2016), and their homologues have been identified as co-located with MQTL for the various traits (Saini et al. 2022b). For instance, three wheat homologues of one rice gene (*OsSWEET4*) were identified in different MQTL located on homoeologous group 2 chromosomes; these wheat homologues may be engaged in the embryo nourishment by supplying a sufficient amount of nutrients to the developing embryo in the wheat (Yang et al. 2018).

Using comparative genomics, homologues of these genes in wheat can be characterized, and functional markers for these genes can be developed and validated. A meta-analysis of QTL associated with grain weight in tetraploid wheat, for instance, resulted in the identification of one important locus, mQTL-GW-6A, on chromosome 6A (Avni et al. 2018). Within this MQTL region, authors discovered and characterized a wheat homologue of the rice gene, *OsGRF4* (Avni et al. 2018). This suggests that combining an MQTL study with a well-annotated genome can rapidly identify CGs underlying traits of interest. However, this approach is not suitable for identifying unknown functional genes; ortho-MQTL analysis may prove quite useful in such cases (as discussed above). Manipulation and integration of these genes in the breeding programme may contribute to the enhanced wheat quality.

Conclusion

In the present study, a meta-analysis of QTL and comparative genomic approaches were used to dissect the complex genetic architecture underlying various quality traits such as GPC, total starch, Zn, Fe, PPO, baking, and bread-making properties in the wheat. Identified MQTL and corresponding high-confidence CGs may prove useful for marker-assisted quality improvement in wheat. Molecular cloning and functional characterization of these CGs may further improve the understanding of complex genetics underlying the quality traits. In addition, flanking markers of MQTL identified in our study can be used as fixed effects in the GS models for improving prediction accuracy. Ortho-MQTL identified in the present study may help in understanding the common evolutionary pathways underlying the quality traits between wheat and rice. Breeders may use the most promising MQTL (viz., 1A.1, 1B.2, 3B.4, 5B.2, and 6B.2) and CGs associated with multiple quality traits identified in our study to improve the quality-related traits in wheat.

Author contribution statement AS, SG, and DKS conceived and planned this study. SG, PH, PK, MS, and MJT performed the literature search, retrieved data, developed a consensus map and conducted the meta-analysis. GS, DKS, and SS helped SG in the analysis and interpretation of results and writing of the first draft of the manuscript. AS, DKS, and GS critically revised and edited the manuscript.

All authors have read and agreed to the final version of the manuscript.

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Declarations

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