Meta-QTLs, Ortho-MetaQTLs and Candidate Genes for Grain yield and Associated Traits in Wheat (*Triticum aestivum* L.)

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Abstract

The present study involved meta-QTL analysis based on 8,998 QTLs, including 2,852 major QTLs for grain yield (GY) and its following ten component/related traits: (i) grain weight (GWei), (ii) grain morphology related traits (GMRTs), (iii) grain number (GN), (iv) spikes related traits (SRTs), (v) plant height (PH), (vi) tiller number (TN), (vii) harvest index (HI), (viii) biomass yield (BY), (ix) days to heading/flowering and maturity (DTH/F/M) and (x) grain filling duration (GFD). The QTLs used for this study were retrieved from 230 reports involving 190 mapping populations (1999–2020), which also included 19 studies involving durum wheat. As many as 141 meta-QTLs were obtained with an average confidence interval of 1.37 cM (reduced 8.87 fold), the average interval in the original QTL being > 12.15 cM. As many as 63 MQTLs, each based on at least 10 original QTLs were considered to be the most stable and robust with thirteen identified as breeder's meta-QTL. Meta-QTLs (MQTLs) were also utilized for identification of as many as 1,202 candidate genes (CGs), which also included 18 known genes. Based on a comparative genomics strategy, a total of 50 wheat homologues of 35 rice, barley and maize yield-related genes were also detected in these MQTL regions. Moreover, taking the advantage of synteny, a total of 24 ortho-MQTLs were detected at co-linear regions between wheat with barley, rice and maize. The present study is the most comprehensive till date, and first of its kind in providing stable and robust MQTLs and ortho-MQTLs, thus providing useful information for future basic studies and for marker-assisted breeding for yield and its component traits in wheat.

Introduction

Wheat provides ~20% of protein and calories in human diets worldwide. Due to continuous efforts of plant breeders, the global annual production of wheat has been increasing continuously during the last five decades and reached 765 million metric tons in the year 2020. It has also been estimated that the annual production of wheat should increase by 50% by the year 2050 (<https://www.openaccessgovernment.org/demand-for-wheat/83189/>) to meet the demand of the growing population, which is expected to reach 9 to 10 billion in the year 2050. However, the rate of global annual wheat production declined in recent years to 0.9% from ~3% in the early years of the two post-green revolutions (Shiferaw et al. 2013; Yadav et al. 2019). Therefore, further improvement in yield potential is needed to improve and sustain the required annual growth rate of ~2%. This will be possible only through a further detailed understanding of the genetic architecture of grain yield associated with the use of molecular approaches with conventional wheat breeding (Gupta et al. 2020).

Grain yield is widely known to be a complex quantitative trait, which is controlled by a large number of QTLs/genes involved in plant growth and development, contributing towards yield either directly or indirectly. Yield is also known to be influenced by the environment, thus making its visual selection rather difficult. Major yield contributing traits include grain number, grain weight, grain morphology-related traits, tiller number, spike-related traits, harvest index, plant height, heading date, etc. (Gupta et al. 2020; Hu et al. 2020). Therefore, these traits are continuously targeted in wheat breeding programmes for developing novel high-yielding varieties (Zhou et al. 2007). Since these yield-related traits are each controlled by a

number of quantitative trait loci (QTLs), the markers associated with these QTLs can be exploited in molecular breeding using marker-assisted selection (MAS).

During the last two decades, a large number of QTLs for grain yield and its component traits have been identified (Table S1). However, the practical use of these QTLs seems to be minimal in actual wheat breeding. In order to make use of these QTLs in wheat breeding, and in basic research, a detailed analysis of these loci needs to be undertaken. Meta-analysis of the QTLs is an approach that has been shown to provide more robust and reliable QTLs (**Goffinet and Gerber, 2000; Salvi and Tuberosa, 2015**). Since, Meta-QTL analysis also allows identification of “QTL hotspots” (if any), we undertook the task of finding such regions for use by the wheat breeders.

Efforts have also been made to improve algorithms used for meta-QTL analysis (**Arcade et al. 2004; de Oliveira et al. 2014; Veyrieras et al. 2007**). Most of these algorithms are available in the software ‘Biomercator’ (Sosnowski et al. 2012). Using the maximum likelihood method, these algorithms test the number of possible meta-loci (MQTLs), which result from the projection of initial/original QTLs (taken from different studies) on a consensus genetic map. Criteria are also available to find out the best model for confirming the actual number of these MQTLs (**Goffinet and Gerber, 2000; Sosnowski et al. 2012**).

Wheat MQTLs have already been identified for several traits including the following: ear emergence (**Hanocq et al. 2007**), (ii) pre-harvest sprouting tolerance (**Tyagi and Gupta, 2012**), (iii) Fusarium head blight resistance (**Venske et al. 2019**), (iv) heat stress tolerance (**Acuña-Galindo et al. 2015; Kumar et al. 2020**) and (v) yield and quality-related traits (**Liu et al. 2020; Quraishi et al. 2017; Soriano et al. 2017; Zhang et al. 2010**). However, new QTLs are being regularly added to the database for QTLs. Most of these new QTLs have been identified using SNP arrays that have recently become available (**Hu et al. 2020; Kuang et al. 2020; Lin et al. 2020; Xin et al. 2020; Yu et al. 2020**). Keeping this in view, during the present study, meta-QTL analysis was conducted on grain yield (GY) and a number of its contributing traits listed above, using the QTL data from 230 studies published during 1999 to 2020 utilizing 190 different mapping populations (**Table S1**).

The MQTLs identified during the present study were also used to identify candidate genes (CGs). Ortho-MQTLs across gramineae family were also detected using synteny among cereals (Mayer et al. 2011; Hirsch et al. 2014; Kumar et al. 2009). Genomic regions associated with MQTLs that are homologous to known genes for yield in other cereals (rice, barley, and maize) were also identified. We believe that this work should prove useful not only for genomic selection based molecular breeding, but also for basic research on structural genes and regulatory elements involved in grain yield and associated traits not only in wheat, but also in other cereals.

Materials And Methods

Collection of QTL Data for Yield and Associated Traits in Wheat

The literature related to QTL mapping of grain yield and its component traits was collected from PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>) and Google Scholar (<https://scholar.google.com/>) using appropriate keywords. A total of 8,998 QTLs were available from 230 studies, which involved 190 mapping populations. The size of the mapping populations ranged from 32 to 547 DH/RIL lines; these mapping populations also included 26 F₂/BC populations. As many as 19 studies involved durum wheat, mainly published during 2015-2020. A summary of these QTLs studies is available in Table S1. For each QTL, the following data was retrieved: (1) QTL name, wherever available, (2) flanking markers or closely linked marker, (3) peak position and confidence interval, (4) type and size of the mapping population, (5) LOD score, and (6) phenotypic variance explained (PVE) or R² value. **Wherever, information about peak position was missing, mid-point between the two flanking markers was treated as the peak. Secondly, where LOD score was not available, the same was calculated using** the available test statistic. In case, when actual LOD score for an individual QTL was not available, a threshold LOD score of 3.0 was chosen for the study.

If names of QTLs were not available, names were assigned following the standard nomenclature (letter “Q” followed by abbreviated name of the trait, the institute involved and the chromosome). Different QTLs on the same chromosome were distinguished by using numerical identifiers following the chromosome. All QTLs were accommodated in the following traits: (i) ‘grain weight’ (GWei), recorded as thousand-grain weight, 50-grains weight, mean grain weight, hundred-grain weight, single grain weight, grain weight per plant, and test weight, (ii) ‘grain number’ (GN) recorded as average grain number per spike, grain number per spike, grain number per square meter, grain number per spikelet, grains per spikelet, and grains per fertile spikelet, etc; (iii) ‘grain morphology related traits’ (GMRTs) recorded as grain length, grain width, grain length-width ratio, grain thickness, grain thickness-length ratio, grain area, and grain diameter, grain volume weight, etc.; (iv) ‘spike related traits’ (SRTs) recorded as spike length, spikes per plant, spikes per square meter, spike compactness, spike formation rate, spike layer uniformity, basal sterile spikelet number, top sterile spikelet number, fertile floret per spike, and spikelets per spike, etc. (v) ‘biomass yield’ (BY) recorded as total biomass, tiller biomass, and plant biomass; (vi) ‘tiller number’ (TN) recorded as effective tiller number, tiller number per plant, and tiller number per square meter. Other remaining traits were treated individually by the available name of the trait (e.g., heading, days to flowering, days to maturity, grain filling duration, earliness per se, and plant height).

Construction of Consensus Map

A consensus map (described as Wheat_Consensus_2021) was developed using the following integrated genetic maps: (1) the ‘Wheat_Composite_2004’ map with 4403 marker loci, available at **GrainGenes database** (<http://wheat.pw.usda.gov>); (2) the ‘Wheat, Consensus SSR, 2004’ with 1235 marker loci (**Somer et al. 2004**); (3) an integrated map for durum wheat with 3669 markers (Marone et al. 2013); (4) four SNP maps developed using different SNP arrays as follows: ‘Illumina 9K iSelect Beadchip Array’ (**Cavanagh et al. 2013**) and ‘Illumina iSelect 90K SNP Array’ (**Wang et al. 2014**), ‘Wheat 55K SNP array’ (**Winfield et al. 2016**), the ‘AxiomR, Wheat 660K SNP array’ (**Cui et al. 2017**). Marker information or maps from several

other independent studies were also included for developing the consensus map. The R package LPMerge was employed for the construction of the consensus map (Endelman and Plomion, 2014).

QTL Projection and Meta-QTL analysis

Only 7,275 QTLs from 8,998 available QTLs had the information required for QTL projection. Although, from these 7,275 QTLs, only 2,852 major QTLs (explaining ≥ 10 percent of phenotypic variance for the target trait), each with the required information (estimated CIs, peak positions, original LOD scores, and R^2 or PVE value) could be used for projection on the consensus map using BioMercator V4.2 (Sosnowski et al. 2012) (Table S1).

To ensure consistency in different studies, the confidence interval (95%) was estimated for each locus, through different population-specific equations: for RILs: $CI = 163 / (\text{population size} \times R^2)$; for F_2 and backcross populations: $CI = 530 / (\text{population size} \times R^2)$; and for DH: $CI = 287 / (\text{population size} \times R^2)$ (Darvasi and Soller, 1997; Venske et al. 2019). Following projection, meta-analysis was performed, for each chromosome individually, via the Veyrieras two-step algorithm available in the software. The Akaike (AIC) statistics were used to find the best QTL model for ascertaining the actual number of MQTLs on each wheat chromosome. The statistical procedures and algorithms furnished in this software have been well-described elsewhere (Sosnowski et al. 2012).

Candidate Gene mining within MQTLs and Expression Analysis

For identification of CGs, the sequences for flanking markers of individual MQTLs were retrieved from GrainGenes (<https://wheat.pw.usda.gov/GG3>) and CerealsDB (<https://www.cerealsdb.uk.net/cerealgenomics/CerealsDB/indexNEW.php>) and used for BLASTN searches against wheat reference genome sequence available in the EnsemblPlants (<http://plants.ensembl.org/index.html>). Physical positions of the GBS-SNPs were directly obtained from URGI database (<https://wheat-urgi.versailles.inra.fr/>). Among the MQTLs obtained, those with a CI of ≤ 2 Mb were directly used for identification of the candidate genes (CGs). In the remaining cases with longer CI, a 2 Mb genomic region (including 1 MB region on either side of the MQTL peak) was examined for possible candidate genes. Gene models present within the original or estimated physical regions were retrieved using 'BioMart' of EnsemblPlant database. The function annotations of the identified gene models were explored to find the best candidate genes within each MQTL.

For the in-silico transcriptional analysis, the identified putative candidate genes (CGs) were analyzed via the 'Wheat Expression Browser-expVIP' (expression Visualization and Integration Platform) (<http://www.wheat-expression.com>) (Ramírez-González et al. 2018). Gene expression datasets relevant to the present study were utilized for this purpose, including 'Developmental time-course of chinese spring' (Choulet et al. 2014) and synthetic hexaploid' (Li et al. 2014); 'Grain tissue specific developmental time-course' (Gillies et al. 2012; Pearce et al. 2015; Pfeifer et al. 2014); 'Chinese spring leaves and roots at both seedling (Clavijo et al. 2017) and seven leaf stages' (Ramírez-González et al. 2018), and 'Gene expression during a time-course of flag leaf senescence' (Borrill et al. 2019). Following the criteria proposed by

Wagner and co-workers (2013), only CGs showing at least 2 transcripts per million (TPM) expression were considered in this study. Heat maps for expression data were constructed using the same online resource 'expVIP'.

CGs were further examined using information from cloned, and characterized wheat genes for the traits of interest. Nucleotide sequences of these collected genes were obtained from the NCBI database (<https://www.ncbi.nlm.nih.gov/>) using accession IDs given in the respective published studies and then BLASTN searches were carried out against the genomic database (available in EnsemblPlants) of wheat to find the physical positions of these genes in the genome.

MQTL Regions homologous to known genes in other cereals

Information on rice, barley, and maize genes associated with grain yield and related traits was collected from the literature and used for retrieval of the corresponding protein sequences for the identification of homologous MQTL genomic regions. Amino acid sequences for relevant genes were retrieved from the NCBI (<https://www.ncbi.nlm.nih.gov/>) and used for BLASTP search to identify the wheat protein (available in EnsemblPlants) at an E-value of $<10^{-10}$, with 60% coverage, and $>60\%$ identity. Physical positions of the corresponding genes and wheat MQTLs were then compared to detect the MQTL regions homologous to known genes in other cereals.

Results

QTLs Associated with Grain Yield and Related Traits in Wheat

The trait-wise distribution of total QTLs, along with QTLs having information required for meta QTL analysis and major QTLs associated with different yield traits is presented in Table 1. The distribution of these QTLs on different wheat sub-genomes is shown in Fig. 1. Among the three sub-genomes, the sub-genome A carried 3,457 (38.42%) QTLs, sub-genome B carried 3,566 (39.63%) QTLs and the sub-genome D carried only 1,975 (21.94%) QTLs.

Construction Of The Consensus Map

The integrated consensus map contained 2,33,856 markers, which included a variety of markers including the following types: SNPs, DArT, SSR, AFLP, RAPD, STS, EST-SSR, SRAP, ISSR and KASP markers. Following important genes are also included on this consensus maps: *Vrn*, *Ppd*, *Rht*, and *Glu* loci (Table S2). The total length of the consensus map is 11,638.76 cM; the length of individual chromosome ranged from 281.26 cM (4D) to 763.08 cM (4A). The average number of markers carried by a single chromosome was 11,136 (Table S3). The marker densities for individual linkage groups ranged from 12.76 to 48.27 markers per cM for A and B sub-genomes, and 7.74 to 18.13 markers for D sub-genome.

Ortho-mqtls In Barley, Rice And Maize

The next question, that is natural outcome of MQTL study is what will be the status of other crops, will they be harbouring similar MQTLs in their genomic regions. The study was further advanced to search

such orthologues in Gramineae family. For identification of ortho-MQTLs, 27 stable and robust wheat MQTLs were selected, each, based on > 20 QTLs. As many as 24 corresponding MQTLs (so called ortho-MQTLs) of these wheat MQTLs were identified in rice, barley and maize genomes; ortho-MQTLs for three wheat MQTLs (MQTL1A.5, MQTL2A.2, and MQTL3A.4) were not identified on any syntenic chromosome of the studied species; the details are as follows: (i) five ortho-MQTLs mainly associated with traits GY, GWei, and PH in wheat and maize, (ii) ortho-MQTLs of 11 wheat MQTLs in syntenic regions of rice and maize, and (iii) two ortho-MQTLs (ortho-MQTL2D.5 and ortho-MQTL5A.3) in syntenic regions of maize and barley. Among these, 6 ortho-MQTLs (ortho-MQTL2B.3, ortho-MQTL4A.3; ortho-MQTL4B.1; ortho-MQTL4B.5, ortho-MQTL7A.3, and ortho-MQTL7B.1) involved MQTLs in all the four crops (Table 3).

Conclusively, ortho-MQTLs were detected on five barley chromosomes 2H, 4H, 5H, and 7H; each of which comprised only one previously detected MQTLs. In rice, ortho-MQTLs were identified on all the chromosomes except chromosomes 1, 9, and 10, and underlying MQTLs ranged from 1 (on chromosome 2) to 8 (on chromosome 4) MQTLs. In maize, ortho-MQTLs were detected on all the ten chromosomes, number of MQTLs within the ortho-MQTL regions ranged from 1 to 16 MQTLs. The remaining information about ortho-MQTLs identified between wheat with barley, rice, and maize are given in Table 3 and the traits associated with these ortho-MQTLs and underlying orthologous genes along with their functional descriptions are presented in Table S5.

Candidate Genes For Wheat Mqtl

Gene mining in genomic regions carrying individual MQTL allowed the identification of 2,953 gene models; this number was reduced to 2,298, when following classes were removed: (i) duplicated genes from overlapping MQTLs; (ii) genes with no information available regarding molecular function and gene ontology (GO) terms. The *in-silico* expression analysis of the above gene models (except the gene models underlying three MQTLs) allowed the identification of 1,202 gene models, each showing at least 2 transcripts per million (TPM) expression (highlighted with yellow in Table S6). The gene models showed spatio-temporal gene expression, expressing in different plant tissues such as grains, spikes, leaves, shoots, and roots, etc. at specific times during development (for instance, see Fig. 3). Detailed information regarding these gene models, hereafter, termed as 'putative CGs' detected in different MQTL regions is provided in Table S6. These 1,202 CGs mainly belonged to the five major gene classes, including, (i) transcription factors, (ii) genes involved in metabolism and/or signalling of growth regulators- gibberellins, cytokinins and brassinosteroids, (iii) genes regulating cell division and proliferation (iv) floral regulators, and (v) genes involved in regulation of carbohydrate metabolism (Table S7).

Several known yield related genes were also mapped within the MQTLs regions (Table S8); 18 such genes were available, which included the following: *TaSnRK2.3-1B* (MQTL1B.7), *TaCwi-A1* (MQTL2A.2), *TaCYP78A5-2D* (MQTL2D.8), *FRIZZY PANICLE* (MQTL2D.5), *Btr1-A* (MQTL3A.3), *TaPSTOL* and *TaSnRK2.9-5A* (MQTL5A.3), *DEP1-5A* (MQTL5A.4), *TaCWI5D* (MQTL5D.4), *DEP1-5D* (MQTL5D.5),

TaSPL21-6A, *TaGW2-6A*, *TaPRR1-6A*, and *TaBT1-6A* (MQTL6A.2), *TaBT1-6B*, *TaPRR1-6B*, and *TaSPL21-6B* (MQTL6B.10), and *TaGS3* (MQTL7A.1).

Wheat MQTLs with Homology to Known Genes from Other Cereals

Known genes for yield and its components from other cereals including rice, barley, and maize were also used for the identification of putative wheat CGs in MQTL regions; this allowed identification of 24 putative wheat CGs of the 48 available rice genes, 3 of the 7 available barley genes and 8 of the available 13 maize genes. Of these 24 rice genes, as many as 12 genes (viz., *D2*, *DEP1*, *An-1*, *GW2*, *GIF1*, *qGL3*, *SMG1*, *OsLG3*, *OsALMT7*, *GS9*, *OsPK2*, and *FZP*) showed more than one homologues, while, remaining twelve genes showed only one homologue each in wheat MQTL regions (Table 4 and S10). No wheat homologues in MQTL regions were available for four barley genes (*Ert-m*, *HvAPETALA2*, *HvLUX1*, and *INT-C*), while, two barley genes (*vrs4* and *COM1*) each gave more than one wheat homologues and one gene showed a single homologue (Table 4 and S10). For 8 maize genes (*FASCIATED EAR2*, *ramosa2*, *ZmFrk1*, *bs1*, *BIF1*, *ZmGS3*, *KNR6* and *vt2*), 12 wheat homologues were available in different MQTL regions. In some cases, more than one homologues were available within the same MQTL regions, for instance, homologues of rice genes *An-1*, *GIF4*, *GW2*, and *OsPK2* were detected in the MQTL2A.2 region, homologues of rice genes *D11*, *GIF1*, *OsPK2*, and *FZP* rice genes were available in MQTL2D.8 region and homologues of *Vrs4* (barley), *ramosa2*, *vt2* (maize) were available in MQTL3A.3 region (Table 4).

Overall, 33 MQTL regions contained 50 wheat homologues involving 35 alien yield genes from other three cereals (rice, barley, and maize). To our knowledge, homologues of only 8 of these 34 alien genes (*GW2*, *GIF1*, *GS3*, *DEP1*, *CKX2*, *OsSPL14*, *FZP*, and *ZmVT2*) have already been cloned and characterized in wheat; following are the details of these wheat homologues: *TaGW2* (Su et al. 2011), *TaCwi-A1* (Ma et al. 2012), *TaGS-D1* (Zhang et al. 2014), *DEP1* (Vavilova et al. 2017), *TaCKX* family genes (Ogonowska et al. 2019), *TaSPL14* (Cao et al. 2021), *FRIZZY PANICLE (FZP)* (Dobrovolskaya et al. 2015), and *TaTAR2.1* (Shao et al. 2017).

Discussion

During the past two decades, starting with the first QTL studies on yield-related traits published by Araki et al. (1999) and Kato et al. (1999), a large number of studies have been conducted on QTL mapping for grain yield and its component traits in wheat (Table S1). The studies involving development of MQTLs were largely motivated by the fact that only a small fraction of QTLs identified by interval mapping are major QTLs, and majority of QTLs are each associated with a large confidence interval, with flanking markers often located away from the QTLs, thus making these QTLs not very useful for plant breeding. Also, QTLs identified using one bi-parental population may not be effective for a breeding programme involving other parents, without prior validation, unless the markers are functional markers located within the QTLs. These problems can be largely overcome through development of MQTLs, which are robust with a reduced confidence interval, thus increasing the utility of these MQTLs not only in crop

improvement programmes, but also for basic studies involving cloning and characterizing QTLs/genes for the trait of interest.

Meta-QTL analysis has been conducted for a variety of traits in all major crops. In wheat, meta-QTL analysis has been conducted for a number of traits including yield, but the information on MQTLs soon becomes out-of-date. This is largely because, a large number of studies on QTL analysis for yield traits in wheat are regularly conducted, thus creating a need for conducting further studies on MQTLs periodically to obtain improved MQTLs. The present study is one such attempt, conducted to improve upon MQTLs reported so far for grain yield and associated traits in wheat (Bilgrami et al. 2020; Gegas et al. 2010; Griffiths et al. 2009; Griffiths et al. 2012; Liu et al. 2020; Quraishi et al. 2017; Zhang et al. 2010). The maximum number of QTLs used for these earlier meta-QTL studies on yield traits in wheat was 381 for hexaploid wheat (including the QTLs detected under heat and drought stress conditions) and 1,162 (including the QTLs for disease resistance, grain yellow pigment content, grain quality traits, and root architecture-related traits) for durum wheat leading to identification of a maximum of 55 MQTLs for hexaploid wheats (Liu et al. 2020; Zhang et al. 2010) and 71 for durum wheats (Maccaferri et al. 2019). In contrast to this, the number of available QTLs that we listed were 8,998, of which 2,852 major QTLs were used for identification of as many as 141 MQTLs suggesting that the present study is so far the most comprehensive study for identification of MQTLs in wheat.

With the availability of improved algorithms, software, and recently available resources such as high quality genomic and transcriptomic data (Appels et al. 2018; Borrill et al. 2019; Choulet et al. 2014; Clavijo et al. 2017; Pearce et al. 2015; Ramírez-González et al. 2018) the study was more demanding but effective in identification of better MQTLs. Hopefully, some of the MQTLs identified during the present study will be relatively more robust, since the number of initial QTLs per MQTL could be as high as 71 (MQTL5A.2). As many as 24 MQTLs identified during the present study had their genetic positions almost overlapping those occupied by MQTLs reported in two recent studies (Bilgrami et al. 2020; Liu et al. 2020), so that these MQTLs can be used in future studies with a higher level of confidence (Table S4). On a critical evaluation of these 24 MQTLs, we selected 15 MQTLs each involving atleast 10 initial QTLs, which should be tried in molecular breeding and future studies for cloning and characterization of QTLs/genes (Table S4).

Breeder's Mqtl's

Following the criteria laid down by Löffler et al. (2009), from a total of 141 MQTLs identified during the present study, we selected thirteen most promising MQTLs, and described these MQTLs as "Breeder's MQTLs", each of which had a CI of < 2cM. Also, these MQTLs explained a significant proportion of phenotypic variance (ranging from 20.73 to 49.16 %) associated with high LOD values (ranging from 14.05 to 62.67) (Table 2). For example, one MQTL having high PVE (49.16%) can be called a mega breeder MQTL located on 3D.1 for traits GWei, GMRTs and PH. Therefore, these MQTLs have the potential to serve as most efficient targets for their direct use in MAS for wheat improvement or can be treated as major genes. Another important feature of the present study is the availability of clusters of MQTLs,

which included one cluster each on seven different chromosomes (Fig. 2). These clusters of MQTLs may be treated as hotspots and should be utilized for breeding and for future basic research with high level of confidence.

Ortho-mqtl's For Cereals

For the present analysis, we took a step ahead for identification of Ortho-MQTLs, since these are conserved and may be recommended for use in all cereals. Conserved nature of these orthoMQTLs also suggest that these may represent some regulatory genes (Jin et al. 2015; Khahani et al. 2020; Quraishi et al. 2011). Keeping this in view, we selected a total of twenty-seven most promising wheat MQTLs to investigate their evolutionary conserved syntenic regions (or so called ortho-MQTLs) reported in similar meta-QTL analysis studies on the yield-related traits in maize, barley, and rice (Table 3). Consequently, 24 ortho-MQTLs were identified for yield and associated traits conserved at orthologous positions in the barley, rice and maize. As many as six of these 24 ortho-MQTLs identified in the present study were cross-species in all the four crops, revealing the high level of conservation of wheat with barley, maize and rice. Of the CGs underlying these ortho-MQTLs, precise orthologous gene sets can be considered as direct potential candidates for further homology-based cloning, functional validation or at least as a source of accurate molecular markers such as conserved orthologous set (COS) markers for use in cereal breeding programs.

Among earlier studies on ortho-MQTLs in wheat, conducted using the above cross-genome map based strategy, an ortho-MQTL associated with nitrogen use efficiency was earlier discovered. This ortho-MQTL was common for all cereals including wheat, maize, sorghum, and rice, which enabled characterization of a structurally and functionally important conserved gene 'glutamate synthase' (*GoGAT*) at orthologous positions in a number of species (Quraishi et al. 2011). In another study, ortho-MQTLs associated with grain iron and zinc were identified using rice MQTL. Further dissection of these ortho-MQTL regions led to the identification of two maize genes of rice, namely *GRMZM2G178190*, and *GRMZM2G366919*. These genes were characterized as natural resistance-associated macrophage protein genes and considered to be the best candidate genes associated with grain iron and zinc in maize (Jin et al. 2015). The ortho-MQTLs identified during the present study can also be subjected to similar studies leading to identification of orthologs.

Candidate Genes For Mqtl's

The QTLome for grain yield and its component traits is also believed to have a significant correlation with gene density in the wheat genome (Maccaferri et al. 2019). In the present study, gene mining was performed in all MQTL regions (in $\leq$ the 2Mb region) and a total of 2298 gene models were identified. Of these, 703 gene models/putative CGs produced 2 to 5 TPM expressions (highlighted with yellow in Table S6), whereas, as many as 489 gene models showed more than 5 TPM expression (highlighted with blue in Table S6) in different plant tissues at different times (spatio-temporal gene expression). As mentioned earlier, these putative CGs mainly belonged to five major categories of the genes which are known to be

involved in controlling the grain yield and associated traits in cereals (Daba et al. 2020; Nadolska-Orczyk et al. 2017) (Table S7).

MQTLs with genes/gene families involved in grain yield and its component traits has also been shown in several studies (Daba et al. 2020; Gautam et al. 2019; Gunupuru et al. 2018; Jia et al. 2020; Li and Wei, 2020; Ma et al. 2017; Nadolska-Orczyk et al. 2017; Niño-González et al. 2019; Sakuma et al. 2018). In the present study, several such genes/gene families with similar functions were detected repeatedly in different MQTL regions, including 114 genes for leucine-rich repeat proteins, 63 genes for serine/threonine-protein kinases, 33 genes for cytochrome P450 proteins and 14 genes each for WD40/YVTN repeat-like containing proteins, UDP-glucuronosyl/UDP-glucosyltransferases, FAD/NAD(P) binding proteins, and E3 ubiquitin ligases, etc (Table S6). Moreover, some genes encoding unpredicted or uncharacterized proteins also showed significant expression in different plant tissues (Table S6). These genes deserve further attention, to explore their possible roles in the regulation of yield and its component traits in wheat.

For many MQTL regions, it was also possible to identify several F-box-like domain superfamily, UDP-glucuronosyl/UDP-glucosyltransferase, etc. (Table S6). These gene clusters are quite common in plant genomes and are known to encode proteins involved in many enzymatic pathways in plants (Medema et al. 2015; Yi et al. 2007). It has also been shown in these studies that members of a gene cluster can be located in close proximity (only a few thousand base pairs far from each other) in a small genomic region, and also encoding similar products/proteins, thus together sharing a generalized function.

We selected as many as 162 promising putative CGs which had more than 5 TPM expression in different tissues (Table 5). An extensive survey of available literature also shows association of these selected genes with the traits of interest in different plant species. These CGs may be cloned and further characterized and then can be exploited through biotechnological approaches such as transgenesis and gene editing. In a more recent study, it was observed that over-expression of the expansin gene in developing seeds minimizes the trade-off between grain number and grain weight, and ultimately improves the grain yield. Transgenic plants with enhanced expression of the Expansin gene yielded 12.3 % higher grain weight compared to the control, which finally translated into an 11.3% increase in grain yield under field conditions (Calderini et al. 2020). In the present study, we also identified many putative CGs, including genes for Expansin proteins in some MQTL regions (Table 5, Table S6). In future, the targeted transgenic approach using these potential CGs may allow improvement for grain yield in wheat. However, in some cases, where gene clusters regulate the expression of target trait, the transgenic method using a single gene may not be as effective as MAS, where flanking markers can target a much larger region encompassing all the genes of a cluster.

MQTL regions were also examined for genes already known to be associated with yield and its component traits; as many as 18 such wheat genes were identified. These genes encode a variety of proteins including the following: cell wall invertase, sucrose non-fermenting 1-related protein kinase, squamosa promoter binding protein-like protein, E3 ubiquitin ligase, APETALA2/AP2/ERF transcription

factor, cytochrome P450 protein, phosphatidylethanolamine binding protein, and transmembrane protein, etc. Similar proteins/products are also encoded by many other CGs, identified in the present study. Therefore, these CGs can be used for further functional analysis. Some of the MQTLs also had flanking markers associated with known genes including *Vrn*, *Ppd*, and *Rht* genes, *that are widely known to regulate plant phenology, ultimately influencing the grain yield and other component traits in wheat* (Gupta et al. 2020; Kamran et al. 2014).

Wheat homologues of rice, barley and maize genes

During the present study, within the wheat MQTL regions, we also identified several wheat homologues of genes that are known to control grain yield and related traits in rice, barley, and maize genes; many of these genes have not yet been cloned and functionally characterized in wheat; these genes include the following: (i) rice genes: *An-1*, *Bsg1*, *D11*, *D2*, *LP*, *PGL1*, *qGL3*, *SMG1*, *OsOTUB1*, *OsLG3*, *OsDHH1*, *OsY37*, *qWS8*, *OsALMT7*, *GS9*, *GSN1*, *OsPS1-F*, and *OsPK2*; (ii) barley genes: *vrs4* and *COM1* and (iii) maize genes: *FASCIATED EAR2*, *ramosa2*, *ZmFrk1*, *bs1*, *KNR6*, and *BIF1* (Table 4, Table S9). Using comparative genomics, orthologs of these genes can be characterized in wheat and their functional markers can be developed and validated. For instance, in a study conducted in 2018, a meta-analysis of QTLs associated with grain weight in tetraploid wheat resulted in the identification of one important locus, mQTL-GW-6A on chromosome 6A. Further analysis identified and characterized a wheat homolog of the rice gene, *OsGRF4* within this MQTL region (Avni et al. 2018). This suggests that integrating an MQTL study with a well-annotated genome can rapidly lead to the detection of CGs underlying traits of interest.

This was an *in-silico* approach for improvement of our understanding of the genetic architecture of grain yield and its component traits in wheat through identification of MQTLs, orthoMQTLs, and candidate genes. The study involved an integration of the available information about QTLs that were identified in earlier studies along with genomic and transcriptomic resources of the wheat. As many as 141 MQTLs, each associated with a narrow confidence interval and 1,202 putative CGs were identified. Thirteen of these 141 MQTLs regions given as breeder's QTL, we recommend for use in MAS for grain yield improvement in wheat. Based on a comparative genomic approach, several wheat homologs of rice, barley, and maize yield-related genes were also detected in the MQTL regions. The ortho-MQTL analysis demonstrated that MQTLs of yield-related traits appear to be transferable to other cereal crops that that may assist breeding programs in cereals. As many as 162 of 1,202 putative CGs are also recommended for future basic studies including cloning and functional characterization. However, after any *in-silico* analysis of this type, the *in-vivo* confirmation and/or validation of any of these loci, specifically the CGs identified, is needed, which can be accomplished via further approaches, such as gene cloning, reverse genetic approaches, gene silencing followed by transcriptomics, proteomics, and metabolomics. We hope that the results of the present study will help in developing a better insight into the genetic architecture and molecular mechanisms underlying grain yield and its component traits in wheat and other cereals. The information on the molecular markers linked with the MQTLs and CGs occupying the MQTL region may also prove useful in breeding for grain yield improvement in wheat.

Key Message:

The study used 8998 QTLs reported in earlier studies in wheat and identified 141 MQTLs, 162 putative CGs and thirteen breeder's QTL, for grain yield improvement.

Declarations

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Authors' contribution

D.K.S., P.S. and P.K.G. conceived and designed the project; P.K.G. and P.S. supervised the study; D.K.S. and N.P. conducted the analysis; D.K.S. wrote the paper and P.K.G. and P.S. corrected the final draft. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest: The authors declare that they have no competing interests.

Availability of data and material

Data generated or analysed during this study are included in this published article (and its **Supplementary material 1**). Datasets are also available from the corresponding author on reasonable request.

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Tables

Table 1 The trait wise distribution of total QTLs, along with QTLs having information required for analysis and major QTLs associated with studied traits

	Trait categories	Total reported QTLs				QTLs with information required for analysis				Major QTLs (selected for analysis)			
		Sub-genomes				Sub-genomes				Sub-genomes			
Sr. no.		A	B	D	Total	A	B	D	Total	A	B	D	Total
1.	GY	176	230	111	517	137	186	89	412	68	83	54	205
2.	GWei	592	622	337	1551	474	497	273	1244	191	203	93	487
3.	GN	361	312	128	801	314	264	108	686	132	115	37	284
4.	GMRTs	604	680	386	1670	484	557	314	1355	184	196	107	487
5.	SRTs	1055	963	598	2616	843	792	462	2097	306	259	189	754
6.	BY and HI	71	86	36	193	63	80	30	173	26	48	19	93
7.	DTH/F/M, GFD, EPS	288	371	196	855	215	274	133	622	84	108	72	264
8.	PH	259	272	157	688	235	226	134	595	69	90	69	228
9.	TN	51	30	26	107	44	24	23	91	25	12	13	50
	Total	3,457	3,566	1,975	8,998	2,809	2,900	1,566	7,275	1,085	1,114	653	2,852

Table 2 Yield-related MQTLs identified in the present study

Sr. no.	MQTL name (CI, in cM)	Flanking markers	^b Initial QTLs (avg. LOD score)	Traits (avg. PVE)
1.	MQTL1A.1 (21.58-22.51)	AX-110506772/AX-109884241	4 (8.41)	GWei, GY, and SRTs (12.37)
2.	MQTL1A.2 (30.39-31.33)	IWB45602/AX-111475421	10 (6.76)	SRTs, GMRTs, and TW (14.54)
3.	MQTL1A.3 (39.14-40.2)	AX-109896396/AX-95156759	11 (7.03)	GMRTs, GN, SRTs, GWei, and GY (22.75)
4.	MQTL1A.4 (45.62-46.48)	AX-109272204/AX-94547512	2 (9.15)	SRTs (21.30)
5.	MQTL1A.5 (48.7-49)	AX-110597220/AX-111596418	23 (6.53)	SRTs, PH, GWei, GN, TN, GMRTs, DTF, and HI (17.92)
6.	MQTL1A.6 (49.31-50.2)	IWB64888/Xcfe26.5	2 (9.17)	GN (22.73)
7.	MQTL1A.7 (51.91-52.5)	AX-95129506/AX-94383313	2 (4.54)	SRTs and GMRTs (11.85)
8.	MQTL1A.8 (58.82-58.95)	IWA4240/AX-94492795	23 (5.47)	GMRTs, GN, BY, SRTs, GY, GWei, and TN (16.27)
9.	MQTL1B.1 (11.97-12.18)	IWB54702.1/IWB28576	8 (8.25)	SRTs and DTF (18.74)
10.	MQTL1B.2 (48.18-50.07)	AX-94888336/AX-95186655	4 (8.70)	GMRTs and GWei (16.69)
11.	MQTL1B.3 (77.2877.9)	IWB57219/AX-95223114	7 (7.52)	SRTs, and GMRTs (16.20)
12.	^a MQTL1B.4 (88.96-89.64)	IWB43001/IWB12258	6 (38.62)	TN, SRTs, GWei, and GMRTs (26.60)
13.	MQTL1B.5 (93.01-93.2)	IWB61919/IWB11925.1	45 (5.10)	GMRTs, SRTs, DTM, DTF, HI, GWei, GY, GN, TN, BY, GFD, and PH (14.52)
14.	MQTL1B.6 (95.73-96.06)	IWB47571/IWB8902	25 (7.12)	GN, DTH, SRTs, BY, GMRTs, DTF, and GWei (15.57)
15.	MQTL1B.7 (103.4-104.59)	IWB8913/Ku_c20478_390	19 (5.86)	GWei, DTF, HI, SRTs, GMRTs, EPS, GY, GN (17.29)
16.	MQTL1B.8 (114.34-114.52)	IWB35083/Xutv1391b	14 (4.51)	GWei, SRTs, GMRTs, EPS, DTM, TN, GY and PH (12.72)
17.	MQTL1D.1 (15.75-25.05)	AX-95104817/XGli1	3 (6.78)	SRTs, TN, and DTF (16.18)
18.	MQTL1D.2 (70.42-70.93)	IWA6621/IWB35174	6 (7.34)	GMRTs, SRTs, and GWei (12.74)
19.	MQTL1D.3 (76.32-83.79)	IWB60500.2/AX-94653386	3 (6.61)	GY, GWei, and PH (14.82)
20.	MQTL1D.4 (95.78-96.28)	P32/M59-2/1DS_1914495_3816	7 (5.06)	DTH, DTM, GWei and GN (15.00)
21.	MQTL1D.5 (106.49-113.89)	XksuE18a/AX-94555171	3 (5.34)	SRTs, GWei, and PH (14.06)
22.	MQTL1D.6 (118.51-122.11)	Xwmc63.1/IWB23920	3 (3.52)	GMRT and GWei (14.18)
23.	MQTL2A.1 (122.34-123.24)	BS00021739_51/GENE-1031_48	19 (9.95)	SRTs, GMRTs GN, PH, GY, DTM, DTH, and GWei (17.77)
24.	MQTL2A.2 (142.74-143.76)	IAAV1587/IWB14868	26 (10.67)	GMRTs GN, GWei, SRTs, HI, BY, PH, and DTH (15.19)
25.	MQTL2A.3 (151.07-153.05)	AX-95140204/AX-109425280	12 (5.58)	SRTs, GWei, GN, and GMRTs (14.70)
26.	MQTL2A.4 (158.76-159.04)	Xwmc630b/AX-108741878	4 (9.26)	SRTs, GN, and GWei (13.04)
27.	^a MQTL2A.5	AX-110428539/IWB43373	4 (39.33)	GWei, and GMRTs (34.67)

	(162.13-162.23)			
28.	MQTL2A.6 (162.64-163.12)	IWB43373/tPt-9405	20 (6.38)	GY, GN, DTH, DTM, SRTs, GMRTs and GWei (20.41)
29.	MQTL2A.7 (187.13-187.29)	Ppd-A1/Xgpw2204	7 (4.18)	SRTs, GWei, TN, and GMRTs (13.38)
30.	MQTL2B.1 (72.48-73.36)	IWB40903/IWB17530	10 (7.29)	SRTs, GN, GMRTs GY, and GWei (12.66)
31.	MQTL2B.2 (83.24-84.5)	IWB65267.1/IWB41081	6 (6.63)	SRTs, GMRTs and GWei (14.44)
32.	MQTL2B.3 (102.57-103.78)	IWB65370.2/IWB45990	31 (7.07)	SRTs, DTM, GN, GMRTs, GY, HI, GWei, DTH, DTF, and PH (15.92)
33.	MQTL2B.4 (114.43-114.98)	IWB35771/IWB30649	16 (10.55)	HI, DTH, GN, GMRTs, SRTs, PH, and DTF (16.21)
34.	MQTL2B.5 (118.09-118.26)	IWB64873/IWB28040	31 (7.05)	GMRTs, GWei, GN, GY, BY, SRTs, PH, DTH, and HI (17.29)
35.	MQTL2B.6 (126.62-127.31)	IWB26439/wPt-0746	35 (9.50)	SRTs, GMRTs, DTF, GY, DTH, DTM, GN, GWei, HI, TN, and PH (17.64)
36.	MQTL2B.7 (170.03-170.04)	AX-94911223/Xwmc617.1	7 (7.02)	GN, PH, GY, SRTs, and GWei (15.37)
37.	MQTL2D.1 (0.1-0.65)	Xbarc114/AX-94611751	9 (8.70)	GY, SRTs, HI, DTH, DTM, and DTF (19.75)
38.	MQTL2D.2 (6.8-7.36)	3033925 F 0/3029203 F 0	16 (8.40)	GWei, GMRTs, GY, PH, SRTs, and DTH (17.59)
39.	MQTL2D.3 (35.55-48.99)	PPD-D1/AX-110595669	3 (41.13)	DTH and SRTs (32.13)
40.	MQTL2D.4 (59.46-61.31)	AX-110668803/2DS_5365757_8955	9 (6.22)	SRTs, GWei, GY, GMRTs, PH, HI, and GN (14.92)
41.	MQTL2D.5 (67.72-68.15)	AX-94750495/wPt-0330	35 (7.62)	GWei, GN, GY, GMRTs, SRTs, HI, PH, DTH, and DTM (15.93)
42.	MQTL2D.6 (76.43-76.84)	2DS_5390826_7647/Estssr-143	38 (8.96)	GMRTs, DTM, DTH, GWei, SRTs, PH, BY, GY, and GN (18.07)
43.	MQTL2D.7 (89.87-90.61)	Xfba400/AX-94743556	36 (9.07)	SRTs, GWei, GMRTs PH, DTH, GY, and DTM (19.11)
44.	MQTL2D.8 (100.1-100.15)	AX-110939188/JD_c63957_1176	11 (11.31)	GMRTs, TN, GN, GWei, GY, PH, and SRTs (14.73)
45.	MQTL3A.1 (40.14-40.52)	IWB73673/Xgpw7080	11 (6.09)	SRTs, PH, GMRTs, GWei, DTM, and GN (12.96)
46.	MQTL3A.2 (45.02-45.38)	IWB13817/3960111	12 (4.65)	GN, GY, PH, and GWei (16.24)
47.	MQTL3A.3 (52.56-54.93)	XPacgMctg13/Xwmc532	7 (4.37)	GN, SRTs, DTH, PH, and GMRTs (15.26)
48.	MQTL3A.4 (68.17-68.73)	AX-111488679/Xbcd372	21 (5.53)	SRTs, GWei, GMRTs, PH, GY, GN, HI, DTM and DTH (17.73)
49.	MQTL3A.5 (71.86-72.41)	wPt-440/wPt-731120	29 (5.38)	DTH, GY, GMRTs, PH, DTF, SRTs, GWei, GN, and HI (17.88)
50.	MQTL3A.6 (78.1-79.66)	Xfba167.1/P41/M41-4	18 (4.92)	GMRTs, HI, PH, SRTs, GY, GN, DTH, and GWei (16.98)
51.	MQTL3A.7 (89.7-90.45)	AX-110954980/Xmwg22	24 (5.83)	GWei, SRTs, GN, DTM, GY, DTH, and GMRTs (17.87)
52.	MQTL3A.8 (115.44-115.65)	D-4261525/IWB34397	8 (7.61)	GN, SRTs, and PH (16.16)
53.	MQTL3B.1 (82.91-83.3)	IWB65330/IWB23552	11 (6.69)	GWei, GMRTs, GN, SRTs, and PH (11.71)
54.	MQTL3B.2 (90.02-91.06)	AX-95189982/AX-94802037	3 (5.96)	SRTs, HI, and GWei (12.01)
55.	MQTL3B.3 (96.31-98.38)	XPaccMcga6/IWB5714	42 (5.81)	GN, GMRTs, SRTs, GY, BY, PH, GN, GWei, DTF, DTH, and TN (17.10)

56.	MQTL3B.4 (105.69-106.47)	S-1090569/D-3946304	14 (7.47)	PH, GN, GWei, SRTs, GMRTs, BY, DTF, and GY (15.74)
57.	MQTL3B.5 (115.05-115.25)	D-3941476/D-3532755	8 (5.44)	BY, GMRTs, GY, GN, and GWei (15.79)
58.	MQTL3B.6 (119.94-123.07)	D-4329780/AX-94925740	4 (5.91)	GY, SRTs, and GMRTs (12.99)
59.	MQTL3B.7 (148.23-148.57)	D-1370637/D-1216223	6 (6.76)	GWei, GY, TN, DTH, and SRTs (14.07)
60.	^a MQTL3D.1 (1.29-2.23)	IWB17932/wPt-1336	5 (62.67)	GWei, GMRTs and PH (49.16)
61.	MQTL3D.2 (17.05-22.9)	AX-109300980/Xwmc11	4 (4.02)	GWei, DTH, and GN (13.94)
62.	MQTL3D.3 (35.65-37.62)	Xcfd4.1/Xgwm1243	2 (4.11)	SRTs and GN (12.71)
63.	MQTL3D.4 (50.89-51.79)	AX-110430652/AX-109688927	2 (5.17)	SRTs and TN (14.55)
64.	MQTL3D.5 (54.43-54.72)	AX-110430652/AX-109688927	5 (4.82)	GWei, GN, and SRTs (23.01)
65.	MQTL3D.6 (58.69-59.45)	AX-111337684/Xwmc529	2 (7.04)	PH and SRTs (11.62)
66.	MQTL3D.7 (68.35-69.39)	TaCKX6a02-D1/CKX3D/AX-109337862	4 (4.07)	SRTs, GN, PH and HI (10.89)
67.	MQTL3D.8 (81.61-83.75)	IWB54462/IWB65811	4 (11.40)	TN, SRTs, and GN (14.13)
68.	MQTL3D.9 (117.71-119.57)	IWB66928/IWB30266	8 (3.07)	DTF, GY, GFD, SRTs, and TN (14.08)
69.	MQTL4A.1 (73.68-74.49)	Xbcd1975b/XPaggMcgt9	18 (12.85)	GN, GMRTs, SRTs, DTH, GWei, and DTM (13.58)
70.	^a MQTL4A.2 (138..6-138.91)	IWB73976/IWB39336	6 (15.25)	SRTs and GWei (24.89)
71.	MQTL4A.3 (201.97-202.22)	Xcdo414/D-1229623	10 (5.96)	SRTs, GWei, GMRTs, PH and GY (16.77)
72.	MQTL4A.4 (208.54-209.3)	D-3948044/D-4329293	34 (4.76)	GWei, SRTs, BY, PH, DTH, GN, GY, HI, DTM, GMRTs and TN (18.00)
73.	MQTL4A.5 (221.6-221.66)	BobWhite_c11327_185/Xfcp532	23 (5.14)	GWei, GN, SRTs, GY, BY, PH, GMRTs and TN (14.81)
74.	MQTL4B.1 (23.15-23.54)	1123959 F 0/ACT.CTC7	45 (15.15)	PH, GMRTs, GWei, DTM, SRTs, and GY (18.21)
75.	^a MQTL4B.2 (34.44-35.16)	IWB12274/D-2325366	8 (19.18)	GMRTs GWei, PH, and DTM (23.36)
76.	MQTL4B.3 (37.75-39.02)	IWB73905/IWB55598	3 (12.55)	GWei (19.49)
77.	^a MQTL4B.4 (47.12-48.28)	IWA7266/D-1385625	3 (32.60)	SRTs and PH (25.60)
78.	^a MQTL4B.5 (51.41-51.53)	wPt-9393/wPt-7365	22 (17.65)	GWei, SRTs, PH, GN, and DTH (22.60)
79.	MQTL4B.6 (56.37-56.62)	Xksm0154/IWB63894	44 (7.70)	HI, GY, SRTs, GMRTs, GWei, GN, PH, and DTH (19.79)
80.	MQTL4B.7 (59.28-59.63)	Xmag983/D-4002948	27 (11.51)	GWei, GN, GY, PH, and SRTs (25.02)
81.	MQTL4B.8 (74.47-74.52)	AX-111195232/AX-111625130	8 (6.78)	GMRTs, SRTs, GWei and PH (16.03)
82.	MQTL4D.1 (7.89-10.06)	AX-109230716/Xbcd1889	3 (6.93)	PH (13.65)
83.	^a MQTL4D.2 (27.64-28.96)	Xbarc359/Xwmc574	16 (24.40)	GMRTs, DTM, and PH (36.83)

84.	MQTL4D.3 (36.82-39.39)	IWB19937/IWB49180	9 (22.09)	GWei, PH, and SRTs (24.94)
85.	MQTL4D.4 (56.92-60.54)	IWB15470/IWB18250	4 (6.07)	SRTs, PH, GWei and GN (14.73)
86.	^a MQTL4D.5 (73.15-74.29)	Xsrap11a/AX-108975045	9 (20.92)	PH, GWei, SRTs, HI, GN, and GY (29.98)
87.	MQTL4D.6 (84.17-84.51)	AX-109726515/Xsrap11b	8 (10.42)	GY, BY, GMRTs, PH, GN, and HI (23.65)
88.	MQTL4D.7 (92.37-93.06)	AX-110418361/AX-95116773	5 (16.32)	GY, BY, GN, PH and GMRTs (21.24)
89.	^a MQTL4D.8 (94.83-96.12)	AX-95116773/IWB53820	20 (18.84)	GWei, PH, SRTs, TN, DTH, GY, TN, and GN (23.90)
90.	MQTL4D.9 (102.9-104.25)	AX-110005953/Xsrap6a	15 (4.54)	SRTs, GMRTs, PH, GY, BY, GN, and GWei (20.24)
91.	MQTL4D.10 (125.98-126.4)	IWB2197/IWA6784	5 (4.83)	GY, BY, and SRTs (15.73)
92.	MQTL5A.1 (61.41-62.08)	IWB586/IWB25701.2	19 (12.32)	SRTs, GMRTs, GWei, GY, and PH (15.84)
93.	MQTL5A.2 (110.97-111.43)	AX-109887759/5AS_1513496_11975	71 (7.73)	GMRTs, SRTs, TN, PH, GN, DTH, GWei, GY, DTM, and DTF (18.35)
94.	^a MQTL5A.3 (135.05-135.84)	Xgpcw2249a/D-1150907	23 (17.65)	PH, DTH, SRTs, HI, GY, GMRTs, DTF, and TN (21.24)
95.	MQTL5A.4 (175.47-176.15)	D-1109368/S-988173	9 (10.71)	GWei, SRTs, DTH, GMRTs and PH (24.88)
96.	MQTL5B.1 (34.55-36.61)	Kasp_5B6/Xmag4281	12 (8.87)	SRTs, DTH, GMRTs GWei, GY, GN, and TN (14.41)
97.	MQTL5B.2 (82.1-82.48)	AX-95249061/Xcdo665b	10 (8.52)	SRTs, GWei, DTF, GMRTs, PH, and GN (17.64)
98.	^a MQTL5B.3 (87.1-87.86)	Xfcp428/AX-110503909	4 (22.72)	SRTs, DTH and DTM (21.43)
99.	MQTL5B.4 (93.73-93.92)	Xapr1.5.4/AX-95259005	4 (7.55)	GMRTs, SRTs, HI and GN (13.12)
100.	MQTL5B.5 (97.88-98.45)	XPacgMcgg12/AX-94972602	18 (6.82)	GMRTs, GY, GWei, BY, PH, and SRTs (13.27)
101.	MQTL5B.6 (100.64-103.25)	CTCG.CAT7/D-1100080	5 (14.25)	DTH, GMRTs, GWei and SRTs (14.39)
102.	MQTL5B.7 (106.5-107.32)	wPt-3439c/S-1076657	22 (7.75)	GWei, GMRTs, DTH, TN, DTF, SRTs, and GY (15.89)
103.	MQTL5B.8 (134.04-134.31)	Xfba232a/IWB56889	5 (8.53)	GMRTs, SRTs, BY, and GY (16.45)
104.	MQTL5D.1 (48.72-49.95)	S-1045585/AX-109826869	7 (4.92)	GWei, TN, SRTs, and GY (12.79)
105.	MQTL5D.2 (76.31-79.54)	D-1237279/AX-108840042	3 (11.48)	DTH, GMRTs and GWei (14.76)
106.	MQTL5D.3 (93.16-95.14)	AX-111733701/IWB29163	11 (6.25)	PH, SRTs, GWei, GMRTs and DTH (20.41)
107.	MQTL5D.4 (104.66-105.21)	AX-109314990/AX-111075490	16 (5.85)	GY, DTF, TN, SRTs, GWei and GN (15.83)
108.	MQTL5D.5 (115.2-118.51)	AX-111758247/AX-94469027	5 (6.16)	SRTs and GWei (14.46)
109.	MQTL6A.1 (98.34-98.8)	D-3936250/GENE-4011_91	39 (7.39)	GN, SRTs, TN, GWei, GMRTs, PH, GY, and DTH (14.77)
110.	MQTL6A.2 (108.95-109.74)	P78/M87.7/wPt-3191a	27 (6.44)	GWei, PH, SRTs, GMRTs, GN, HI, GY, and DTH (17.21)
111.	MQTL6A.3 (150.19-151.48)	D-1124675/D-1076799	5 (6.96)	GN, SRTs, GMRTs and DTH (14.45)
112.	MQTL6B.1 (45.07-47.28)	XPagMctg3/AGC.TGC3	4 (4.81)	GWei, DTH, DTM, and SRTs (14.25)

113.	MQTL6B.2 (99.38-100.75)	ACT.CAT2/P8966.1	10 (4.46)	DTF, GMRTs, SRTs, GY, DTH, DTF and GWei (20.73)
114.	MQTL6B.3 (105.2-107.05)	P8444.1/Xksm45	4 (6.40)	GMRTs, GWei, and PH (12.12)
115.	MQTL6B.4 (112.61-115.42)	D-379317/AGG.CAG5	8 (5.61)	GY, GMRTs, DTH, GWei, HI, and SRTs (13.67)
116.	MQTL6B.5 (116.45-116.99)	AGG.CAG5/APaagMcgc1	2 (12.97)	SRTs (27.48)
117.	MQTL6B.6 (118.99-119.39)	AGG.CAG5/APaagMcgc1	2 (15.51)	GWei and PH (14.41)
118.	MQTL6B.7 (121.38-121.71)	AGG.CAG5/IWB67309.2	3 (8.80)	GMRTs, SRTs and GWei (16.73)
119.	MQTL6B.8 (123.2-123.74)	IWB67309.2/AX-94465053	13 (6.44)	GMRTs, SRTs, TN, GWei, PH, and DTM (14.69)
120.	MQTL6B.9 (128.28-128.56)	Xgdm136/IWA860	14 (12.26)	GMRTs, GN, GY, GWei, SRTs, and DTH (19.03)
121.	MQTL6B.10 (151.56-202.28)	IWB60027/XPaggMcat5	2 (5.45)	SRTs and GMRTs (11.05)
122.	MQTL6D.1 (0- 2.78)	IWB59376.2/IWB36391	2 (5.29)	GWei and SRTs (11.00)
123.	MQTL6D.2 (8.62-11.11)	S-3953435/1127306 F 0	3 (5.03)	SRTs (15.90)
124.	MQTL6D.3 (13.58-14.37)	AX-111501437/6DL_3297209_3422	2 (3.04)	SRTs (12.13)
125.	MQTL6D.4 (31.81-35.57)	AX-94493103/IWA1967.2	8 (4.02)	BY, GY, PH, GN, SRTs, and TN (14.58)
126.	^a MQTL6D.5 (42.88-43.58)	IWA6361/AX-110007215	3 (14.05)	GWei and GY (20.73)
127.	MQTL6D.6 (62.74-63.7)	Xwmc773/AX-109007320	4 (5.90)	GY, GWei, SRTs and PH (12.78)
128.	MQTL7A.1 (108.08-109.57)	IWB7950/XgbxG564a	39 (5.98)	DTH, GWei, DTF, DTM, TN, SRTs, GMRTs, GN, and HI (14.52)
129.	MQTL7A.2 (125.78-126.93)	7AS_4114596_204/7AS_4045514_1450	18 (10.63)	HI, GY, DTH, SRTs, GMRTs, GWei, TN, GN, and PH (19.45)
130.	MQTL7A.3 (155.23-155.25)	IWB207/7AS_4183259_787	31 (7.21)	DTF, TN, SRTs, GY, BY, GN, GWei, GMRTs and PH (19.32)
131.	MQTL7B.1 (38.69-40.06)	CTCG.CAT2/AGT.CAGT6	24 (7.42)	DTH, DTM, GY, GWei, PH, SRTs, GN, HI and BY (19.33)
132.	MQTL7B.2 (57.37-58.16)	AX-108740562/S13M23.195	32 (4.02)	SRTs, DTM, BY, GWei, DTH, GMRTs, DTF, BGY, PH, GN and HI (16.13)
133.	MQTL7B.3 (68.78-69.63)	S-1130473/wPt-4673	8 (6.58)	DTF, HI, GN, GY and DTF (19.86)
134.	MQTL7B.4 (76.76-77.69)	D-3021954/Xpsr687	7 (7.59)	GN, DTM, GMRTs, GY, and SRTs (16.75)
135.	MQTL7B.5 (106.11-107.89)	Xwmc707/Xfbb258	8 (5.84)	GMRTs, SRTs, GWei, and TN (18.73)
136.	MQTL7B.6 (236.54-236.79)	IWB68803/XPaagMcgc11	2 (5.39)	GY and BY (10.68)
137.	MQTL7D.1 (7.29-11.22)	IWB517/Xgwm735b	4 (4.38)	GFD, PH, GY, and GWei (15.19)
138.	MQTL7D.2 (75.17-76.77)	Xswes940.3/IWB17494	15 (8.85)	SRTs, GY, BY, HI, DTM, DTF, GMRTs, GWei, and PH (19.49)
139.	MQTL7D.3 (82.59-85.56)	IWB50283/IWB12642.2	13 (9.00)	GMRTs, SRTs, GN, GY, and DTM (21.32)
140.	MQTL7D.4 (96.65-100.15)	D-2247427/Xwmc42	8 (4.58)	GMRTs and SRTs (44.55)
141.	MQTL7D.5	Xpsp3123/Xswes558.1	6	GMRTs and DTM (20.70)

	(139.15-143.76)		(3.77)	
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^a‘Breeder’s MQTLs’ selected based on the criteria given by Löffler et al. (2009).

^bNo. of initial QTLs involved in MQTL, Avg. Average.

Table 3 Ortho-MQTLs in barley, rice and maize based on the syntenic region with wheat MQTLs

Sr. no.	Ortho-MQTL	Wheat MQTL (genomic position in Mb)	Original MQTL name (chr., genomic position in Mb)	Reference
1.	ortho-MQTL1A.8	MQTL1A.8 (12.11-54.01)	Barley: Nil Rice: MQTL-GW17 (5, 0.94-1.29); MQTL-HD12 (5, 21.14-27.80) Maize: MQTL17 (3, 95.27-107.57); MQTL36 (3, 90.04-118.17); MQTL-17 (3, 7.67-10.08); MQTL-39 (6, 0.5~21.9)	Chen et al. (2017); Khahani et al. (2020); Wang et al. (2013, 2016);
2.	ortho-MQTL1B.5	MQTL1B.5 (17.34-17.38)	Barley: Nil Rice: Nil Maize: MQTL65 (6, 36.55-89.17); MQTL-41 (6, 36.56-89.15); MQTL45 (8, 73.70-95.02); MQTL84 (8, 73.22-95.76)	Chen et al. (2017); Wang et al. (2013, 2016);
3.	ortho-MQTL1B.6	MQTL1B.6 (12.81-13.24)	Barley: Nil Rice: Nil Maize: MQTL37 (3, 125.71-136.45); MQTL-20 (3, 86.75-136.09)	Chen et al. (2017); Wang et al. (2016)
4.	ortho-MQTL2B.3	MQTL2B.3 (28.37-29.99)	Barley: MQTL2H.1 (2H, 28.25-41.95) Rice: MQTL-HD9 (4, 2.08-6.98) Maize: MQTL12 (2, 154.64-174.69); MQTL24 (2, 152.70-175.81); MQTL-11 (2, 154.53-177.65); MQTL13 (2, 192.59-201.8); MQTL26 (4, 198.38-225.80); MQTL51 (4, 198.68-234.16); MQTL54 (5, 1.54-2.02); MQTL29 (5, 14.11-29.39); MQTL57 (10, 14.86-77.02); mQTL10-2 (5, 16.15-31.71); MQTL107 (10, 42.26-87.32); MQTL108 (10, 95.27-109.08); MQTL-70 (10, 85.27-102.52)	Chen et al. (2017); Khahani et al. (2019, 2020); Wang et al. (2013, 2016); Zhao et al. (2018)
5.	ortho-MQTL2B.5	MQTL2B.5 (7.11-30.49)	Barley: Nil Rice: MQTL-GW14 (4, 15.74-18.44); MQTL-PH15 (4, 20.56-23.90); MQTL-PH20 (7, 12.78-14.95); MQTL-HD15 (7, 12.78-14.95) Maize: MQTL11 (2, 43.63-100.18); mQTL2-2 (2, 21.78-61.80); MQTL18 (4, 9.54-14.47); mQTL5-2 (5, 135.81-168.13)	Khahani et al. (2020); Wang et al. (2013); Zhao et al. (2018)
6.	ortho-MQTL2B.6	MQTL2B.6 (7.77-11.08)	Barley: Nil Rice: MQTL-HD9 (4, 2.08-6.98); MQTL-PH16 (4, 30.63-33.12) Maize: MQTL27 (2, 202.93-210.5); MQTL-14 (2, 209.83-211.52); MQTL26 (4, 198.37-225.80); MQTL51 (4, 198.68-234.17); MQTL-37 (5, 188.65-193.45); mQTL10-2 (10, 14.86-77.02)	Chen et al. (2017); Khahani et al. (2020); Wang et al. (2013, 2016); Zhao et al. (2018)
7.	ortho-MQTL2D.5	MQTL2D.5 (14.36-88.35)	Barley: MQTL2H.1 2H (2H, 28.25-41.95) Rice: Nil Maize: MQTL21 (2, 14.79-20.08); MQTL13 (2, 192.59-201.8); MQTL-13 (2, 199.17-205.84); MQTL46 (4, 42.17-75.57); MQTL-27 (4, 39.32-144.04); MQTL-69 (10, 13.06-24.61); mQTL10-2 (10, 14.86-77.02); MQTL107 (10, 42.26-87.32)	Chen et al. (2017); Khahani et al. (2019); Wang et al. (2013, 2016); Zhao et al. (2018)
8.	ortho-MQTL2D.6	MQTL2D.6 (14.90-21.06)	Barley: Nil Rice: MQTL-HD9 (4, 2.08-6.98); MQTL-GW15 (4, 23.43-24.49) Maize: MQTL11 (2, 43.63-100.17); MQTL23 (2, 70.33-149.74); MQTL-10 (2, 62.92-149.11); MQTL47 (4, 146.39-154.56); MQTL22 (4, 157.61-166.91); mQTL4-2 (4, 153.69-171.70); MQTL26 (4, 198.37-225.80); MQTL51 (4, 198.68-234.17); MQTL60 (5, 159.12-168.29); MQTL-36 (5, 162.84-167.47); mQTL5-2 (5, 135.81-168.13); MQTL62 (5, 202.86-207.78); MQTL-38 (5, 205.44-207.73); mQTL5-4 (5, 205.44-217.01); MQTL108 (10, 95.27-109.08); MQTL-70 (10, 85.27-102.52)	Chen et al. (2017); Khahani et al. (2020); Wang et al. (2013, 2016); Zhao et al. (2018)
9.	ortho-MQTL2D.7	MQTL2D.7	Barley: Nil Rice: MQTL-HD9 (4, 2.08-6.98)	Chen et al. (2017);

		(23.42-25.04)	Maize: MQTL11 (2, 43.63-100.18); MQTL23 (2, 70.33-149.75); MQTL-10 (2, 62.92-149.11); MQTL-27 (4, 39.32-144.04); MQTL59 (5, 76.25-137.57)	Khahani et al. (2020); Wang et al. (2013, 2016)
10.	ortho-MQTL3A.5	MQTL3A.5 (21.22-30.56)	Barley: Nil Rice: Nil Maize: MQTL16 (3, 11.67-29.84); MQTL83 (8, 10.85-20.83)	Wang et al. (2013, 2016)
11.	ortho-MQTL3A.7	MQTL3A.7 (17.6-19.6)	Barley: Nil Rice: Nil Maize: MQTL16 (3, 11.67-29.84); MQTL83 (8, 10.85-20.83)	Wang et al. (2013, 2016)
12.	ortho-MQTL4A.3	MQTL4A.3 (709.90-713.52)	Barley: MQTL4H.6 (4H, 632.20-641.09) Rice: MQTL-HD5 (3, 1.03-1.66); MQTL-TN4 (3, 7.23-9.31); MQTL-GW10 (3, 9.49-11.30); MQTL-YLD8 (3, 9.24-10.39); MQTL-GW32 (11, 5.37-8.10); MQTL-GW10 (3, 9.49-11.30); MQTL-YLD8 (3, 9.24-10.39); MQTL-GW32 (11, 5.37-8.10) Maize: MQTL3 (1, 34.78-44.14); MQTL6 (1, 37.47-40.20); mQTL1-3 (1, 14.79-43.06); mQTL5-2 (5, 135.81-168.13); MQTL59 (5, 76.25-137.57); MQTL-35 (5, 78.36-123.21); MQTL-66 (9, 120.2-133.6); mQTL9-3 (9, 120.65-135.91)	Chen et al. (2017); Khahani et al. (2019, 2020); Wang et al. (2013, 2016); Zhao et al. (2018)
13.	ortho-MQTL4B.1	MQTL4B.1 (0.62-7.04)	Barley: MQTL4H.1 (4H, 2.26-8.72) Rice: MQTL-TN4 (3, 7.23-9.31); MQTL-YLD19 (11, 9.06-14.95) Maize: MQTL1-3 (1, 14.79-43.06); mQTL1-4 (1, 148.62-191.47); mQTL1-7 (1, 258.87-290.14); MQTL29 (5, 14.11-29.39); MQTL57 (5, 16.15-31.71); mQTL1-4 (1, 148.62-191.47); mQTL1-7 (1, 258.87-290.14); MQTL29 (5, 14.11-29.39); MQTL57 (5, 16.15-31.71)	Khahani et al. (2019, 2020); Wang et al. (2013, 2016); Zhao et al. (2018)
14.	ortho-MQTL4B.5	MQTL4B.5 (13.05-14.90)	Barley: MQTL4H.1 (4H, 2.26-8.72) Rice: MQTL-GW13 (3, 30.10-30.38) Maize: MQTL16 (1, 214.97-224.20); mQTL1-5 (1, 209.51-, 233.37); MQTL8 (1, 256.34-262.95); mQTL1-6 (1, 257.38-269.96); MQTL29 (5, 14.11-29.39)	Khahani et al. (2019, 2020); Wang et al. (2013, 2016); Zhao et al. (2018)
15.	ortho-MQTL4B.7	MQTL4B.7 (605.16-619.07)	Barley: Nil Rice: MQTL-PH11 (3, 1.66-2.48); MQTL-YLD19 (11, 9.06-14.95) Maize: MQTL6 (1, 80.18-93.0); MQTL62 (5, 202.86-207.78)	Khahani et al. (2020); Wang et al. (2013, 2016)
16.	ortho-MQTL5A.2	MQTL5A.2 (10.84-17.53)	Barley: Nil Rice: MQTL-PH28 (12, 22.45-23.06) Maize: MQTL26 (4, 198.37-225.80); MQTL51 (4, 198.68-234.17)	Khahani et al. (2020); Wang et al. (2013, 2016)
17.	ortho-MQTL5A.3	MQTL5A.3 (11.05-403.72)	Barley: MQTL5H.1 (5H, 178.37-248.57) Rice: Nil Maize: MQTL20 (4, 31.32-42.02); MQTL-27 (4, 39.32-144.04); mQTL4-1 (4, 32.24-46.45); MQTL22 (4, 157.61-166.91); MQTL48 (4, 162.92-174.12); mQTL4-2 (4, 153.69-171.70)	Chen et al. (2017); Khahani et al. (2019); Wang et al. (2013); Zhao et al. (2018)
18.	ortho-MQTL5B.7	MQTL5B.7 (13.72-15.05)	Barley: Nil Rice: MQTL-PH28 (12, 22.45-23.06) Maize: MQTL19 (4, 17.42-20.51)	Khahani et al. (2019, 2020); Wang et al. (2013)
19.	ortho-MQTL6A.1	MQTL6A.1 (555.67-563.51)	Barley: Nil Rice: Nil Maize: MQTL12 (2, 154.64-174.69); MQTL24 (2, 152.70-175.81); MQTL-11 (2, 154.53-177.65); MQTL23 (4, 173.32-181.39); MQTL49 (4, 179.77-182.35); mQTL5-4 (5, 205.44-217.01)	Chen et al. (2017); Wang et al. (2013, 2016); Zhao et al. (2018)
20.	ortho-MQTL6A.2	MQTL6A.2 (25.63-55.57)	Barley: Nil Rice: MQTL-GW6 (2, 9.56-11.75) Maize: MQTL51 (4, 198.68-234.17)	Khahani et al. (2020);

				Wang et al. (2016)
21.	ortho-MQTL7A.1	MQTL7A.1 (3.21-8.26)	Barley: Nil Rice: MQTL-PH23 (8, 6.03-8.68); MQTL-GW25 (8, 5.80-8.15); MQTL-YLD16 (8, 11.58-17.51) Maize: MQTL48 (9, 26.82-28.44); mQTL9-2 (9, 26.96-105.50)	Khahani et al. (2020); Wang et al. (2013); Zhao et al. (2018)
22.	ortho-MQTL7A.3	MQTL7A.3 (44.45-47.03)	Barley: MQTL7H.2 (7H, 21.73-24.48) Rice: MQTL-HD13 (6, 1.64-2.36) Maize: MQTL92 (9, 5.79-9.59); MQTL47 (9, 16.66-22.11); MQTL93 (9, 17.75-23.89); MQTL-64 (9, 19.2-22.68); MQTL95 (9, 43.84-87.99); mQTL9-2 (9, 26.96-105.50)	Chen et al. (2017); Khahani et al. (2020); Wang et al. (2013, 2016); Zhao et al. (2018)
23.	ortho-MQTL7B.1	MQTL7B.1 (3.70-6.37)	Barley: MQTL7H.3 (7H, 34.08-38.12) Rice: MQTL-HD19 (8, 4.17-5.42) Maize: MQTL47 (9, 16.66-22.11); MQTL93 (9, 17.75-23.89); mQTL9-1 (9, 16.24-19.09)	Khahani et al. (2019, 2020); Wang et al. (2013, 2016); Zhao et al. (2018)
24.	ortho-MQTL7B.2	MQTL7B.2 (18.10-44.62)	Barley: Nil Rice: MQTL-YLD14 (6, 27.37-29.62) Maize: MQTL46 (9, 14.14-18.04)	Khahani et al. (2020); Wang et al. (2013)

Table 4 Wheat homologues of rice, barley and maize yield-related genes in MQTL regions

Sr. no.	Gene (associated trait)	Gene product	Wheat homologues (corresponding MQTL)	References
Rice				
1.	^a <i>An-1</i> (GS, GN)	helix-loop-helix DNA binding domain protein	TraesCS2A02G275600 (MQTL2A.2), TraesCS2D02G274600 (MQTL2D.8)	Luo et al. (2013)
2.	^a <i>Bsg1</i> (PH, FD, GY)	protein of unknown function (DUF640 domain containing protein)	TraesCS6D02G361900 (MQTL6D.1)	Yan et al. (2013)
3.	^a <i>D11</i> (GL)	cytochrome P450	TraesCS2D02G331100 (MQTL2D.8)	Tanabe et al. (2005)
4.	^a <i>D2</i> (GL)	cytochrome P450	TraesCS3A02G103800 (MQTL3A.3), TraesCS3D02G106100 (MQTL3D.6)	Hong et al. (2003)
5.	<i>DEP1</i> (PA, PE)	phosphatidylethanolamine-binding protein (PEBP) like domain protein	DEP1-5A (MQTL5A.4), DEP1-5D (MQTL5D.5)	Sun et al. (2014)
6.	<i>GIF1</i> (GF)	cell-wall invertase	TaCwi-A1 (MQTL2A.2)	Wang et al. (2008)
7.	<i>GS3</i> (GS)	protein having 3 domains viz., transmembrane region, a TNFR/NGFR family cysteine-rich domain and a von Willebrand factor type C	TaGS-D1, TraesCS7A02G017700 (MQTL7A.1)	Mao et al. (2010)
8.	<i>GW2</i> (GW, GWei)	RING-type protein with E3 ubiquitin ligase	TaGW-A2 (MQTL6A.2), TraesCS6B02G215300 (MQTL6B.10)	Song et al. (2007)
9.	<i>OsSPL14</i> (PB)	squamosa promoter-binding-like transcription activator	TraesCS5D02G273900 (MQTL5D.3, MQTL5D.5)	Miura et al. (2010)
10.	^a <i>LP</i> (PL)	remorin, C-terminal region domain containing protein	TraesCS5D02G244300 (MQTL5D.3, MQTL5D.5)	Liu et al. (2016)
11.	^a <i>PGL1</i> (GL, GWei)	similar to DNA-binding protein like, helix-loop-helix (bHLH) proteins	TraesCS4B02G287900 (MQTL4B.8)	Heang et al. (2012)
12.	^a <i>qGL3</i> (GS)	similar to serine/threonine protein phosphatase	TraesCS5A02G030300 (MQTL5A.1), TraesCS5B02G029100 (MQTL5B.8)	Qi et al. (2012)
13.	^a <i>SMG1</i> (GS)	mitogen-activated protein kinase kinase 4,	TraesCS6B02G379500 (MQTL6B.10), TraesCS6D02G328800 (MQTL6D.1, MQTL6D.2, MQTL6D.3)	Duan et al. (2014)
14.	^a <i>OsOTUB1</i> (TN, GN, GWei)	squamosa promoter-binding-like protein 14	TraesCS5D02G273900 (MQTL5D.3, MQTL5D.5)	Wang et al. (2017)
15.	^a <i>OsLG3</i> (GL)	APETALA2/ethylene-responsive element binding protein 125	TraesCS6A02G097500 (MQTL6A.2), TraesCS6B02G375400 (MQTL6B.10)	Yu et al. (2017)
16.	^a <i>OsDHHC1</i> (TN)	Zinc finger, DHHC-type domain containing protein	TraesCS6D02G379300 (MQTL6D.1)	Zhou et al. (2017)
17.	^a <i>OsY37</i> (DTH)	protein similar to GRAB2	TraesCS7D02G452500 (MQTL7D.5)	Mannai et al. (2017)
18.	^a <i>qWS8</i> (PBN)	SBP-domain transcription factor	TraesCS5D02G273900 (MQTL5D.3, MQTL5D.5)	Zhang et al. (2017)
19.	^a <i>OsALMT7</i> (PD)	aluminum-activated malate transporter 10	TraesCS6A02G255200 (MQTL6A.2), TraesCS6B02G270300 (MQTL6B.10)	Heng et al. (2018)
20.	^a <i>GS9</i> (GS)	uncharacterized protein	TraesCS5A02G233400 (MQTL5A.4), TraesCS5D02G240300 (MQTL5D.3, MQTL5D.5)	Zhao et al. (2018)

21.	^a <i>GSN1</i> (GS, GN)	mitogen-activated protein kinase phosphatase	TraesCS1A02G045300 (MQTL1A.2)	Guo et al. (2018)
22.	^a <i>OsPS1-F</i> (PH, TN)	<i>Oryza sativa</i> PHOTOSYSTEM 1-F subunit	TraesCS5D02G422800 (MQTL5D.1, MQTL5D.3)	Ramamoorthy et al. (2018)
23.	^a <i>OsPK2</i> (SD, GF)	protein similar to pyruvate kinase	TraesCS2A02G240200 (MQTL2A.2), TraesCS2D02G237900 (MQTL2D.8)	Cai et al. (2018)
24.	<i>FZP</i> (GS)	ethylene-responsive transcription factor FZP-like	TraesCS2A02G116900 (MQTL2A.1), TraesCS2D02G118200 (MQTL2D.5, MQTL2D.8)	Ren et al. (2018)
Barley				
25.	<i>HvCKX2</i> (YA)	cytokinin oxidase/dehydrogenase	TraesCS1D02G237200 (MQTL1D.4)	Galuszka et al. (2004)
26.	^a <i>Vrs4</i> (IA)	LOB domain TF HvRA2	TraesCS3A02G093200 (MQTL3A.3), TraesCS3D02G093500 (MQTL3D.6)	Koppolu et al. (2013)
27.	^a <i>COM1</i> (IA)	AP2/ERF transcription factor	TraesCS5A02G207300 (MQTL5A.4), TraesCS5D02G213400 (MQTL5D.3)	Poursarebani et al. (2020)
Maize				
28.	^a <i>FASCIATED EAR2</i> (KRN)	leucine-rich repeat receptor-like protein	TraesCS6A02G214600 (MQTL6A.2), TraesCS6B02G244700 (MQTL6B.10)	Bommert et al. (2013)
29.	^a <i>ramosa2</i> (IA)	LOB Domain Protein	TraesCS3A02G093200 (MQTL3A.3), TraesCS3D02G093500 (MQTL3D.6)	Bortiri et al. (2006)
30.	^a <i>ZmFrk1</i> (GD)	fructokinase	TraesCS5D02G293800 (MQTL5D.3)	Zhang et al. (2003)
31.	^a <i>bs1</i> (IA)	a putative ERF transcription factor	TraesCS2A02G116900 (MQTL2A.1), TraesCS2D02G118200 (MQTL2D.8)	Chuck et al. (2002)
32.	^a <i>BIF1</i> (IA)	AUXIN/INDOLE-3-ACETIC ACID (Aux/IAA) protein	TraesCS5A02G058600 (MQTL5A.3)	Galli et al. (2015)
33.	<i>ZmGS3</i> (SD)	protein with 198 amino acids	TraesCS7A02G017700 (MQTL7A.1), TraesCS6B02G136400 (MQTL6B.10)	Li et al. (2010)
34.	<i>ZmVT2</i> (IA)	grass-specific tryptophan aminotransferase	TraesCS3A02G093000 (MQTL3A.3)	Phillips et al. (2011)
35.	^a <i>KNR6</i> (KRN)	a serine/threonine protein kinase	TraesCS7D02G451300 (MQTL7D.5)	Jia et al. (2020)

GN grain number, GS grain size, PH plant height, FD floral development, GY grain yield, GL grain length, PA panicle architecture, PE panicle erectness, GF grain filling, GWei Grain weight, GW grain width, PB panicle branching, PL panicle length, TN tiller number, DTH days to heading, PBN primary branch number, PD panicle development, SD seed development, YA yield attributes, IA inflorescence architecture, and KRN kernel row number

^aOrthologs of these genes have not yet been functionally characterized in wheat.

Table 5 Putative candidate genes (only those genes which had >5 TPM expression) of MQTLs

MQTL name	Putative Gene ID	Gene Function Description
MQTL1A.2	TraesCS1A02G043600	RNA polymerase II transcription factor SIII
	TraesCS1A02G044200	WD40/YVTN repeat-like-containing protein
MQTL1A.3	TraesCS1A02G040600	Phosphoglucose isomerase
	TraesCS1A02G041300	Proteinase inhibitor I13
MQTL1A.4	TraesCS1A02G042700	SANT/Myb protein
MQTL1A.6	TraesCS1A02G060700	Ribosomal biogenesis regulatory protein
MQTL1A.7	TraesCS1A02G046500	E3 UFM1-protein ligase 1
	TraesCS1A02G047000	HAD-like superfamily
MQTL1A.8	TraesCS1A02G050400	SWEET sugar transporter
	TraesCS1A02G050800	Defensin
MQTL1B.1	TraesCS1B02G006500	Serine/threonine-protein kinase
	TraesCS1B02G008000	RNA-binding domain superfamily
MQTL1B.2	TraesCS1B02G068200	HSP20-like chaperone
MQTL1B.3	TraesCS1B02G020700	Serine/threonine-protein kinase
MQTL1B.5	TraesCS1B02G036500	Calcium-dependent channel
MQTL1B.4	TraesCS1B02G026500	Leucine-rich repeat protein
MQTL1B.7	TraesCS1B02G223600	Putative NADH dehydrogenase
	TraesCS1B02G224300	Trehalose-phosphatase
MQTL1B.8	TraesCS1B02G261700	GDSL lipase/esterase
	TraesCS1B02G262000	Oxoglutarate/iron-dependent dioxygenase
MQTL1D.1	TraesCS1D02G003900	Ribosomal protein L28/L24
MQTL1D.6	TraesCS1D02G037900	Chalcone isomerase
MQTL2A.2	TraesCS2A02G245900	Ribosomal protein S19
MQTL2A.3	TraesCS2A02G089300	Heat shock transcription factor family
	TraesCS2A02G090000	P-loop containing nucleoside triphosphate hydrolase
MQTL2A.4	TraesCS2A02G064300	Zinc finger protein
MQTL2A.5	TraesCS2A02G065100	Protein-tyrosine phosphatase
	TraesCS2A02G065700	Major intrinsic protein
MQTL2A.6	TraesCS2A02G071500	Flavin monooxygenase
MQTL2A.7	TraesCS2A02G086400	P-loop containing nucleoside triphosphate hydrolase
MQTL2B.1	TraesCS2B02G027000	Protein kinase-like domain superfamily
	TraesCS2B02G030700	Zinc finger protein
MQTL2B.2	TraesCS2B02G053200	Glycoside hydrolase
MQTL2B.3	TraesCS2B02G059500	Flowering-promoting factor 1
MQTL2B.4	TraesCS2B02G063500	P-loop containing nucleoside triphosphate hydrolase
MQTL2B.6	TraesCS2B02G020400	Polycomb protein
	TraesCS2B02G021500	Protein kinase-like domain superfamily
MQTL2B.7	TraesCS2B02G090300	RmlC-like cupin protein
MQTL2D.1	TraesCS2D02G006500	Cytochrome P450 protein
MQTL2D.2	TraesCS2D02G020900	Photosystem II PsbI
	TraesCS2D02G021500	Cytochrome P450 protein
	TraesCS2D02G022700	Chalcone/stilbene synthase
MQTL2D.3	TraesCS2D02G057000	Glycoside hydrolase
	TraesCS2D02G055000	UDP-glycosyltransferase
MQTL2D.5	TraesCS2D02G099400	Ethylene insensitive 3-like protein
	TraesCS2D02G100300	Zinc finger protein
MQTL2D.6	TraesCS2D02G047800	Defensin
	TraesCS2D02G049500	Chaperonin containing TCP-1
MQTL2D.8	TraesCS2D02G250300	P-loop containing nucleoside triphosphate hydrolase
	TraesCS2D02G251000	RNA-binding protein
MQTL3A.1	TraesCS3A02G008700	Aquaporin transporter
	TraesCS3A02G011100	Expansin
MQTL3A.2	TraesCS3A02G003800	Thiolase-like
MQTL3A.3	TraesCS3A02G097100	Sugar phosphate transporter
	TraesCS3A02G099200	AP2/ERF
MQTL3A.4	TraesCS3A02G041800	Tryptophan synthase
MQTL3A.5	TraesCS3A02G049600	Serine/threonine-protein kinase
MQTL3A.6	TraesCS3A02G044800	Mannose-6-phosphate isomerase
MQTL3A.7	TraesCS3A02G033900	HSP20-like chaperone
MQTL3A.8	TraesCS3A02G490300	Flavoprotein-like protein
	TraesCS3A02G489700	Helix-loop-helix DNA-binding protein
MQTL3B.1	TraesCS3B02G045700	Glycoside hydrolase family 10
	TraesCS3B02G047300	Sugar/inositol transporter
MQTL3B.2	TraesCS3B02G050500	Mitochondrial carriers
	TraesCS3B02G052600	Serine/threonine-protein kinase
MQTL3B.4	TraesCS3B02G061700	Photosystem I Psal
MQTL3B.6	TraesCS3B02G048900	Short-chain dehydrogenase/reductase

MQTL3B.7	TraesCS3B02G517100	RNA-binding protein
MQTL3D.1	TraesCS3D02G037600	Ribosomal protein S10
MQTL3D.2	TraesCS3D02G024500	Glycosyltransferase 61
	TraesCS3D02G024700	Cytochrome P450 protein
MQTL3D.3	TraesCS3D02G046700	HSP20-like chaperone
MQTL3D.4, & 5	TraesCS3D02G063100	Serine/threonine-protein kinase
MQTL3D.6	TraesCS3D02G099900	Golgi to ER traffic protein 4
MQTL3D.7	TraesCS3D02G126500	UDP-glucuronosyl/UDP-glucosyltransferase
MQTL3D.9	TraesCS3D02G446700	C2 domain superfamily
MQTL4A.1	TraesCS4A02G00740	Thiolase-like
	TraesCS4A02G011300	Protein of unknown function DUF538
MQTL4A.2	TraesCS4A02G035400	AP2/ERF
MQTL4A.3, 4 & 5	TraesCS4A02G442900	Peroxisomal biogenesis factor 11
MQTL4B.1	TraesCS4B02G005900	Cytochrome P450 protein
MQTL4B.2	TraesCS4B02G011500	HPT domain superfamily
MQTL4B.3	TraesCS4B02G015100	Replication factor A protein-like
MQTL4B.4	TraesCS4B02G017500	RmlC-like cupin
MQTL4B.5	TraesCS4B02G020300	RNA-binding protein
MQTL4B.7	TraesCS4B02G321200	Fasciclin-like arabinogalactan protein
	TraesCS4B02G321300	Glycosyl transferase
MQTL4B.8	TraesCS4B02G266700	GRAS TF
MQTL4D.1	TraesCS4D02G014100	WRKY TF
	TraesCS4D02G018100	Zinc finger protein
MQTL4D.2	TraesCS4D02G012100	Short-chain dehydrogenase/reductase
MQTL4D.3	TraesCS4D02G008700	Signal transduction histidine kinase
MQTL4D.4	TraesCS4D02G006100	Glycoside hydrolase
	TraesCS4D02G006900	Ubiquitin-like protein
MQTL4D.5	TraesCS4D02G003100	Major facilitator superfamily
MQTL4D.8	TraesCS4D02G021100	MADS-box TF
	TraesCS4D02G022600	Homeobox-like domain superfamily
	TraesCS4D02G064400	WD40/YVTN repeat-like-containing protein
	TraesCS4D02G065300	MFS transporter superfamily
MQTL4D.10	TraesCS4D02G065600	Glycoside hydrolase family 9
	TraesCS4D02G065600	Glycoside hydrolase family 9
MQTL5A.1	TraesCS5A02G025900	YABBY protein
MQTL5A.2	TraesCS5A02G019200	Fatty acid hydroxylase
MQTL5A.3	TraesCS5A02G110200	Pentatricopeptide repeat
MQTL5A.4	TraesCS5A02G196400	Ubiquitin-like domain superfamily
	TraesCS5A02G197000	Protein kinase-like domain superfamily
MQTL5B.1	TraesCS5B02G080200	Ubiquitin-like domain superfamily
MQTL5B.3	TraesCS5B02G007100	Cytochrome P450 protein
	TraesCS5B02G007500	Ankyrin repeat-containing protein
MQTL5B.4	TraesCS5B02G010500	Thiolase-like
	TraesCS5B02G011700	Glycoside hydrolase
MQTL5B.5 & 6	TraesCS5B02G013200	RNA recognition motif domain
	TraesCS5B02G014400	Small GTPase
MQTL5B.7	TraesCS5B02G015000	ATP synthase
MQTL5B.8	TraesCS5B02G028300	Short-chain dehydrogenase/reductase
	TraesCS5B02G029000	Regulator of K ⁺ conductance
MQTL5D.1	TraesCS5D02G431400	Armadillo-like helical
	TraesCS5D02G430000	Clathrin adaptor complex
MQTL5D.2	TraesCS5D02G044100	Subtilisin-like protease
MQTL5D.4	TraesCS5D02G536500	Nucleotide-diphospho-sugar transferase
	TraesCS5D02G536100	Mitochondrial carrier
	TraesCS5D02G535400	Cytochrome P450 protein
MQTL5D.5	TraesCS5D02G211200	TIFY/JAZ family
	TraesCS5D02G211900	Ubiquitin-like domain superfamily
	TraesCS5D02G211900	Ubiquitin-like domain superfamily
MQTL6A.1	TraesCS6A02G325400	Oxoglutarate/iron-dependent dioxygenase
	TraesCS6A02G325100	Transcription elongation factor Spt5
	TraesCS6A02G325300	Glycoside hydrolase
MQTL6A.2	TraesCS6A02G196800	RmlC-like jelly roll fold
MQTL6A.3	TraesCS6A02G196600	Glycosyltransferase
MQTL6B.1	TraesCS6B02G313100	WD40/YVTN repeat-like-containing protein
	TraesCS6B02G313400	GPI-anchored protein LORELEI-like
MQTL6B.2 & 3	TraesCS6B02G012100	GroEL-like apical domain superfamily
MQTL6B.7	TraesCS6B02G017700	RNA-binding protein
MQTL6B.10	TraesCS6B02G224800	Translation elongation factor EFTu-like
MQTL6D.1	TraesCS6D02G392100	Glycoside hydrolase

	TraesCS6D02G392600	Serine/threonine-protein kinase
MQTL6D.2	TraesCS6D02G331400	Amino acid transporter
	TraesCS6D02G330800	Diacylglycerol kinase
MQTL6D.3	TraesCS6D02G334000	Glycosyl transferase
	TraesCS6D02G332900	Dehydrin
MQTL6D.4	TraesCS6D02G375700	Serine/threonine-protein kinase
MQTL6D.5	TraesCS6D02G399500	Leucine-rich repeat protein
	TraesCS6D02G397800	Gibberellin regulated protein
MQTL7A.1	TraesCS7A02G014100	Ribosomal protein L9
	TraesCS7A02G015300	Serine-threonine/tyrosine-protein kinase
MQTL7A.2	TraesCS7A02G009400	Glycoside hydrolase
	TraesCS7A02G009900	WD40/YVTN repeat-like-containing protein
MQTL7A.3	TraesCS7A02G082000	Ribosomal protein L5
MQTL7B.1	TraesCS7B02G008400	F-box-like domain superfamily
	TraesCS7B02G009200	Mitogen-activated protein kinase
MQTL7B.2	TraesCS7B02G031400	Casparian strip membrane protein
MQTL7B.5	TraesCS7B02G304500	Glycoside hydrolase
MQTL7B.6	TraesCS7B02G450100	Senescence/spartin-associated
	TraesCS7B02G451200	SWEET sugar transporter
MQTL7D.1	TraesCS7D02G036600	Sucrose synthase
	TraesCS7D02G036900	Cytochrome P450 protein
MQTL7D.2	TraesCS7D02G106400	Mitogen-activated protein kinase
	TraesCS7D02G108900	GDSL lipase/esterase
MQTL7D.3	TraesCS7D02G398900	Glycoside hydrolase
MQTL7D.5	TraesCS7D02G455900	Small auxin-up RNA
	TraesCS7D02G456600	Ribosomal protein S13
	TraesCS7D02G457400	SANT/Myb protein
	TraesCS7D02G458200	Papain-like cysteine peptidase

Figures

Figure 1

Distribution of collected QTLs for grain yield and associated traits on A, B and D sub-genomes of wheat.

Figure 2

Diagrammatic representation of MQTL clusters detected on chromosomes 1A, 1B, 2B, 4B, 5B, 6B and 6D; Only desired parts of the chromosomes are shown for better visualization; different colours correspond to different MQTLs on each chromosome.

Figure 3

Heatmaps showing differential expression of important candidate genes underlying some selected Breeder's MQTLs. The scale drawn on the lower left of each heatmap represents the range of TPM values.

Supplementary Files

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- [Supplementarymaterial1.xls](#)