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Yield QTLome distribution correlates with gene density in maize

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1 **Yield QTLome distribution correlates with gene density in maize**

2

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14

15 **ABSTRACT**

16

17 The genetic control of yield and related traits in maize has been addressed by many quantitative  
18 trait locus (QTL) studies, which have produced a wealth of QTL information, also known as  
19 QTLome. In this study, we assembled a yield QTLome database and carried out QTL meta-analysis  
20 based on 44 published studies, representing 32 independent mapping populations and 49 parental  
21 lines. A total of 808 unique QTLs were condensed to 84 meta-QTLs and were projected on the 10  
22 maize chromosomes. Seventy-four percent of QTLs showed a proportion of phenotypic variance  
23 explained (PVE) smaller than 10% confirming the high genetic complexity of grain yield. Yield  
24 QTLome projection on the genetic map suggested pericentromeric enrichment of QTLs. Conversely,  
25 pericentromeric depletion of QTLs was observed when the physical map was considered, suggesting  
26 gene density as the main driver of yield QTL distribution on chromosomes. Dominant and  
27 overdominant yield QTLs did not cluster differently from additive effect QTLs.

28

29 **Keywords**

30 Heterosis; Meta-analysis; QTL; QTLome; yield; *Zea mays*

31

32

33 **1. Introduction**

34

35 Progress in molecular biology and genomics platform allows us to identify the quantitative trait  
36 loci (QTL) that govern the expression of yield and other important agronomic traits, hence providing  
37 unprecedented opportunities to enhance the effectiveness of selection targeting the key loci via  
38 genomics-assisted breeding [1-4]. The number of mapped QTLs for a given trait and species,  
39 collectively known as QTLome [5] is growing at an impressive pace, prompting increased efforts in  
40 the synthesis and interpretation of QTL information.

41 In maize, grain yield is the most important and genetically complex trait and is generally modelled  
42 as controlled by a large number of small effect QTLs, in the contexts of both phenotypic and marker-  
43 assisted selection [6,7,8]. While breeding has certainly succeeded in improving grain yield in maize  
44 during the last century, maintaining the same rate of improvement will be increasingly more difficult  
45 due to more extreme climatic conditions and the need to adopt new cropping systems requiring  
46 reduced inputs [9]. For these reasons, a better understanding of the grain yield QTLome (in terms of  
47 number of QTLs, their map position, size and type of genetic effects and interactions) remains a  
48 priority in maize breeding.

49 One way to synthesize QTL information is by QTL meta-analysis [10,11] which allows one to  
50 identify the regions of the genome that more frequently govern trait variation and to narrow down the  
51 confidence intervals of QTLs by leveraging existing information. In maize, MetaQTLs (MQTLs)  
52 were described for flowering time [12,13], leaf architecture [14], grain moisture [15] and ear rot  
53 resistance [16]. Hao et al. [17] used meta-analysis to identify candidate genes potentially involved in  
54 drought tolerance networks. Meta-analysis was also applied to yield and yield components QTLs  
55 [18,19,20]. By collecting QTL [21,22] and transcriptomic [23] data from multiple studies, a  
56 predominant centromeric location of heterotic QTLs was observed.

57 This study reports the results of the largest MQTL analysis so far conducted for yield and yield  
58 components in maize. QTLs were projected on the genetic and physical maps and utilized to compute  
59 MQTLs. Our main objectives were to produce an informed repository of yield QTL information in  
60 maize and to search for patterns of QTL distribution on chromosomes, with particular attention to  
61 QTLs involved in yield heterosis.

62

## 63 **2. Materials and Methods**

64

### 65 *2.1 Bibliographic collection and construction of a maize yield QTLome database*

66

67 Literature was retrieved from Web of Science (Thomson Reuters™)  
68 (<http://apps.webofknowledge.com>) using the keywords ‘maize yield QTL’ which eventually  
69 identified 44 manuscripts published from 1992 to 2014. While papers presented QTL data for multiple  
70 traits, we only considered yield and yield components traits which were classified in eight main  
71 categories (Table 1). A summary of the QTL studies is reported in Table 2.

72 The yield QTLome database included information on: parents of the cross, type of cross, number  
73 of progenies, name of QTLs, trait, LOD score, proportion of phenotypic variance explained (PVE)  
74 by each QTL, QTL position on the authors’ linkage map in terms of LOD peak and QTL supporting  
75 or confidence interval (CI) (Supplementary Material 1). In studies reporting multi-environment  
76 results, only QTLs from the overall analysis were considered; alternatively, if two QTLs for the same  
77 trait were reported in two experiments (eg. two different water regimes) in the same study (ie. in the  
78 same publication), and their map positions corresponded, they were considered as the same QTL and  
79 were included in our QTL database as one.

80

81 For each QTL, flanking molecular markers with their genetic position in the original map and  
82 with the highly saturated maize map ‘Genetic’ used as a reference map and available at

83 [http://www.maizegdb.org/complete\\_map?id=1203637](http://www.maizegdb.org/complete_map?id=1203637), were searched and recorded. In order to avoid  
84 heterogeneity in definition of *CI* across studies, 95% *CI* values were estimated using the approach  
85 described by [66] and extended by [67] according to the population type:  $CI = 163/(N \cdot R^2)$  for  
86 recombinant inbred line (RIL) progenies, and  $CI = 530/(N \cdot R^2)$  for the rest of non-RIL progenies (i.e.  
87 F<sub>2</sub>, BC, TC), where *N* is the size of the population and *R*<sup>2</sup> is the proportion of variance explained by  
88 the QTLs. Estimated *CI* values were utilized for QTL projection (Supplementary Material 1).

89 When available, the degree of dominance (often indicated as gene action) for each QTL was  
90 recorded as provided by the authors. More specifically, QTLs were declared as heterotic QTLs (HQ)  
91 when gene action was reported as dominant (D, with dominant effect/additive effect > 0.8) or  
92 overdominant (OD, with  $d/a > 1$ ). QTL were declared as additive (AQ) when gene action was reported  
93 as additive or partially dominant ( $0 < d/a < 0.8$ ). When not available, the degree of dominance was  
94 attributed on the basis of the type of experimental population, as follows: QTLs identified in RIL  
95 populations were considered as AQ; QTLs identified in mapping populations evaluated as testcrosses  
96 were classified as potentially heterotic QTLs (PHQ).

97

## 98 2.2. QTL projection and meta-analysis

99

100 QTLs were projected onto the ‘Genetic’ maize reference map available at  
101 [http://www.maizegdb.org/complete\\_map?id=1203637](http://www.maizegdb.org/complete_map?id=1203637) (see also [68]), using the software  
102 Biomercator v4.1 (<http://moulon.inra.fr>) [11,69]. The frequency (probability) of identification of  
103 QTL for every cM position in the ‘Genetic’ map was estimated following the approach described as  
104 ‘QTL-overview index’ [12]. Meta-analysis was carried out using BioMercator v. 4.1. The input file  
105 for BioMercator is provided as Supplementary Material 2.

106 For *n* individual QTLs, BioMercator tests the most likely assumption between 1, 2, 3, 4 and *n*  
107 underlying QTLs. Decision rules are based on an Akaike-type criterion (AIC) and the one with the  
108 lowest AIC value was considered the best fit. Consensus QTL from the optimum model is regarded  
109 as meta-QTL (MQTL). In order to study the QTL distribution based on physical distances QTLs were  
110 projected onto the B73 RefGen\_v2 reference genome [70] (<http://www.maizegdb.org/>). Additionally,  
111 variation of QTL density across the maize genome was studied by counting QTLs on each 20-cM bin  
112 (roughly equivalent to 1/100 of the genetic map) and on each 25-Mb bin (again roughly equivalent to  
113 1/100 of maize physical map), starting from the centromeric region of each chromosome (ie. the  
114 middle point of a centromere interval was considered as position 0). A QTL was assigned to a bin  
115 based on its LOD peak as reported in original studies. Centromeres positions were obtained from the  
116 <http://www.maizegdb.org/> and from [71, 72]. Gene density distribution was determined from the

117 maize genome sequence B73RefGen\_v2 available at <http://www.maizgedb.org/>. QTLs, MQTLs and  
118 overview index were visually represented using CIRCOS [73].

119

### 120 **3. Results**

121

#### 122 *3.1. Main features of QTL mapping experiments in maize*

123

124 Our survey covered 44 studies which reported QTLs for yield and yield components in maize,  
125 based on biparental populations and published from 1992 to 2014 (Table 2). The studies covered 32  
126 different experimental crosses, which utilized 47 inbred lines as parents, the most popular being B73  
127 and Mo17 (six and five crosses, respectively). The most common cross types were F<sub>2:3</sub> or F<sub>2:4</sub>  
128 evaluated *per se*, RIL *per se* and F<sub>2:3</sub> or F<sub>2:4</sub> evaluated as testcross/backcross (14, eight and seven  
129 populations, respectively; Table 2).

130 Although in many cases the original papers reported on QTLs for multiple morpho-physiological  
131 traits, we focused our survey on QTLs for grain yield (GY) and seven additional grain yield  
132 components of common interest in maize breeding (Table 1). The QTL database eventually included  
133 808 unique QTLs. The number of QTLs per trait ranged from 23 to 253 (Ear Number and GY,  
134 respectively; Supplementary Material 3). The average number of QTL per study was 7.2 for GY,  
135 while it ranged between 4.6 and 7.5 for component traits (for Ear Number and Kernel Weight,  
136 respectively; Supplementary Material 3).

137 The frequency distribution for the proportion of phenotypic variance explained (PVE) by single  
138 QTLs followed a truncated (on minor values) L-shape with the majority of the QTLs showing low  
139 PVE values (74% of the QTLs with PVE < 0.1. Supplementary Material 4). The shape of the  
140 distribution did not differ between GY and GY components (Supplementary Material 4) and/or  
141 between heterotic and additive QTLs (not shown).

142 The number of GY (and other traits) QTLs per study did not correlate with population dimension  
143 (Supplementary Material 5).

144

#### 145 *3.2. QTL distribution on chromosomes*

146

147 As evidenced in Figs. 1A-B, yield QTLs were evenly distributed among the ten chromosomes as  
148 also confirmed by the very high correlation ( $r = 0.94$ ;  $P < 0.01$ ) between number of QTLs and  
149 chromosome length. For example, chrs. 6 and 1, the shortest and the longest, respectively, carried the  
150 lowest and the highest number of QTLs (61 and 144, respectively).

151 The projection of all QTLs on the maize genetic reference map showed a statistically significant  
152 clustering of QTLs at centromeric and pericentromeric regions (Fig. 1A, Fig. 2A). A 20-cM interval  
153 spanning from -10 to +10 cM from the centromere and representing approx. 10% of an average  
154 chromosome included 18% of all QTLs (Fig. 2A.). Mid-chromosome arm bins such as those around  
155 -60 and +60 cM from centromeres included significantly fewer QTLs (8 and 12% QTLs.  $P < 0.01$ ,  $\chi^2$   
156 distribution), and increasingly so at subtelomeric bins (Fig. 2A). No difference in distribution was  
157 observed when the full 808 QTL set was subdivided in QTLs for GY and QTLs for GY component  
158 traits (not shown).

159 A different distribution pattern was observed when QTLs were projected on the maize reference  
160 physical map (Fig. 1B, Fig. 2B). On the physical map (Fig. 1B), QTLs appeared as almost evenly  
161 distributed with no sign of centromeric clustering (with the exception of chr. 9). When QTL  
162 distribution was tested by assigning QTLs to chromosome regions based on the map position of their  
163 QTL peaks, all the centromeric and pericentromeric 25-Mb bins were depleted of QTLs. For example,  
164 the 25-Mb bins spanning the centromeres had on average just 7% of the QTLs while telomeric bins  
165 at -75 or at +75 Mb distance from centromere each gathered approx. 18% of the QTLs each ( $P < 0.01$ ,  
166  $\chi^2$  distribution. Fig. 2B).

167 Prompted by the above-described QTL distribution on chromosomes, we tested the correlation  
168 between yield QTL density and gene density per 25-Mb bin starting from the centromere. QTL and  
169 gene densities showed a highly significant correlation (Pearson  $r = 0.41$ ,  $P < 0.01$ ).

170 Based on QTL-overview index the chromosome bins with the highest frequency of QTLs were  
171 1.06, 2.04, 5.05, 8.05, 9.03 and 10.06. Conversely, bins 3.07-09 and 5.07-08 appeared depleted in  
172 QTLs based on both genetic and physical projections. Small regions with strikingly low QTL density  
173 were observed both on the genetic and physical projections at bins 1.04 (approx. 50 Mb), 1.09  
174 (approx. 255 Mb), 4.03 (approx.. 20 Mb) and 6.06 (approx.. 140 Mb). It should be noted that  
175 subtelomeric bins were not considered in these comparisons since these chromosome portions were  
176 likely underrepresented in the original linkage maps, especially in the earlier QTL mapping studies.

177 Finally we found no difference in the average QTL PVE values computed considering all QTLs  
178 mapping within each 20-cM bin from centromeres to telomeres (Supplementary Material 6).

179

### 180 *3.3 Distribution patterns of heterotic QTLs*

181

182 Based on population types and QTL gene action as reported on original studies, our collection  
183 included 206 (26%) heterotic QTLs, 136 (17%) potentially heterotic QTLs and 466 (58%) additive  
184 QTLs. The highest proportions (67, 69 and 73%) of heterotic QTLs over the total number of QTLs



185 were observed for GY, Ear Length and Kernel Number, respectively, whereas the lowest proportion  
186 (24%) was observed for Ear Row Number (Supplementary Material 3).

187 Heterotic QTLs mapped unevenly on all chromosomes. Chrs. 1, 8 and 9 showed 35, 32 and 33%  
188 of heterotic QTLs, respectively, while chrs. 5, 4 and 7 showed 16, 18 and 19%, respectively. Like the  
189 global set of QTLs, heterotic and potentially heterotic QTLs clustered at pericentromeric regions  
190 when projected on the genetic map (Fig. 2C) whereas an opposite pattern of higher density at  
191 subtelomeric regions was apparent when physical distance was considered (Fig. 2D). In order to  
192 reduce the bias and noise potentially present in the latter two distributions, GY-only (ie. without grain  
193 yield components) heterotic and additive QTLs were extracted and their distributions compared (Fig.  
194 2E-F). Again, no significant difference between heterotic and additive QTLs was observed in terms  
195 of distribution pattern along genetic maps ( $\chi^2 = 7.97$ ,  $df = 8$ ,  $P > 0.1$ ). While the two distributions on  
196 physical maps differed ( $\chi^2 = 22.7$ ,  $df = 8$ ,  $P < 0.05$ ), the patterns revealed no obvious trend (eg.  
197 higher concentration of HQ vs. AQ at subtelomeric or at pericentromeric regions).

198

### 199 *3.4. Meta-QTL analysis*

200

201 Among 808 GY and grain yield-related traits QTLs projected onto the reference ‘Genetic’ map,  
202 610 QTLs were grouped into 84 meta-QTLs (MQTLs) (Supplementary Material 7). The remaining  
203 198 QTLs were not assigned to any MQTL. Confidence intervals (CI) of the MQTLs were narrower  
204 than the mean of the respective original QTL CIs, on average up to 7 fold. MQTLs CI ranged from  
205 0.1 (Seven MQTL with  $CI < 1$  cM) to 8.78 cM, with an average of 3.1 cM. MQTLs mapped on all  
206 ten chromosomes, and like single QTLs, suffered from an enlarged CI when mapped at peri-  
207 centromeric regions (Figs. 1A-B). MQTL positions reported in this study were compared with those  
208 reported in Wang et al. [20] (Supplementary Material 8). MQTLs were also tentatively compared  
209 with those reported in Semagn et al [19], although in this case a different map was used for MQTL  
210 projection. Based on overlapping MQTL CIs, 19 MQTLs are common with those reported by Wang  
211 et al. [20] ranging from one MQTL on chr. 3 and 5 to six MQTLs on chr. 4 (Supplementary Material  
212 8). Twenty-six MQTLs are putatively shared with those reported by Semagn et al. [19] involving  
213 yield and related traits and ranging from one MQTL on chrs. 1 and 10 to five on chr. 9 (data not  
214 shown).

215

## 216 **4. Discussion**

217

### 218 *4.1. Gene density appears as the main driver of QTL density*

219

220         Based on current knowledge, QTLs result from the genetic segregation of sequence  
221 polymorphisms at functional elements, such as regulatory sequences upstream of genes and/or coding  
222 sequences [74,5]. Therefore, it is expected that QTL density on a genetic map is driven by gene  
223 density, polymorphism rate at functional sites in genic regions and by frequency of recombination.  
224 Our results showed for the first time that the distribution pattern of QTLs on chromosomes differs  
225 strongly between genetic and physical maps. While QTLs appeared to more densely map near  
226 centromeres on genetic maps, they showed higher density at subtelomeric regions on physical maps.  
227 In maize and other species, gene density is higher at subtelomeric regions and lower at  
228 pericentromeric regions [75]. A similar distribution pattern was shown in this study for QTL density,  
229 which correlated well ( $r = 0.41$ ) with gene density. Interestingly, a recent investigation on crossover  
230 density distribution in maize [76] reported a tight correlation between crossover distribution, gene  
231 density and cytosine methylation. Additionally, the authors showed that recombination is strongly  
232 suppressed in  $\sim 100$  Mb interval encompassing the centromere [76], which corresponds well to the  
233 low QTL-density region observed in our study (Fig. 2B).

234         Testing for the presence of correlation between QTL density and sequence polymorphism rate  
235 appears less straightforward. In maize, sequence polymorphism rate expressed as nucleotide diversity  
236 ( $\pi$ ) drops significantly in the proximity (approx.  $\pm 10$  Mb) of centromere regions only, and levels off  
237 in the rest of the chromosomes length [77]. Estimates of molecular polymorphism (e.g. SNP) are  
238 available across the maize genome for coding, coding-enriched or low-complexity regions only [72,  
239 79], however they are expected to be gene-density driven and not expected to represent well  
240 regulatory sequence polymorphism (e.g. allelic difference at promoters or enhancers) often  
241 interspersed with transposons, which have been shown to underpin many QTLs [80]. Finally, given  
242 that recombination is a main factor in enabling purifying selection [81], regions with reduced  
243 recombination are expected to show a higher rate of deleterious variants (as shown in [76]), which  
244 should translate into higher rates of functionally different QTL alleles, and eventually higher QTL  
245 density. However, this is exactly the opposite of what we observed. One possible explanation is that  
246 the reduced gene density in low recombination regions completely overturns the impact of higher  
247 rates of deleterious variants on QTL density. Following the observations above, we have not  
248 attempted to correlate QTLs and sequence polymorphism densities as we felt it to be too speculative.  
249 Taken all these observations together, and accounting for the cline of recombination rate along  
250 chromosomes, gene density appears to be a strong driver of QTL density on chromosomes.

251

252 *4.2. Distribution pattern for heterotic QTLs*

253

254 Our study included 206 heterotic QTLs for GY and grain yield components. For GY, the  
255 majority of QTLs (67%) showed dominant or overdominant types of gene action, accordingly with  
256 previous observations [21,22]. The same two former reports [21,22] found a higher-than-expected  
257 clustering of heterotic QTLs at low-recombining pericentromeric regions. Thiemann et al. [23]  
258 complemented the results of Schon et al. [22] by showing that pericentromeric regions are enriched  
259 in genes with an expression pattern correlated with grain yield heterosis. These results appear to  
260 support the dominance hypothesis for heterosis, in this case driven by the low recombination rate at  
261 pericentromeric regions which should maintain higher allelic diversity at different heterotic loci  
262 linked in the repulsion phase [22,82,83]. Our results confirmed the clustering of heterotic QTLs at  
263 centromeres on the genetic map. Additionally, we found little or no evidence for a distribution pattern  
264 difference between heterotic and additive QTLs, in line with what was reported by Larièpe et al. [22]  
265 based on a smaller set of QTLs. Indeed, the low recombination rate at pericentromeric regions can  
266 favour the fixation of both repulsion-phase and coupling-phase allelic combinations between  
267 breeding pools, potentially leading to large effect QTLs, both ‘heterotic’ and ‘additive’ [22,82]. In  
268 contrast with this last hypothesis, however, our data also showed that the average QTL PVE values  
269 did not significantly change across chromosome regions (Supplementary Material 6). In conclusions,  
270 additional investigations are required to test these hypotheses by also considering the higher  
271 frequency of deleterious variants expected at centromeres (see previous paragraph).

272

#### 273 *4.3. Additional observations on QTL distribution pattern*

274

275 Some less obvious features were observed in the QTL projections on genetic and physical maps  
276 (Figs. 1A-B). Of the six chromosome bins (1.06, 2.04, 5.05, 8.05, 9.03 and 10.06) characterized by  
277 high QTL density peaks, four were located at pericentromeric regions, leaving little room for  
278 speculation on correspondence with genes. However, two peaks (at bins 8.05, and 10.06) were not in  
279 proximity of centromeres. The peak at bin 8.05 corresponds well with the *Vgt1/Vgt2* region [84, 85]  
280 and bin 10.06 peak corresponds with a previously reported flowering time MQTL [12]. Meta-analysis  
281 identified MQTLs in the same positions (MQTL62-63 and MQTL78-79) (Table 3). These QTLs are  
282 among the strongest and most frequently found flowering time QTLs in maize and this  
283 correspondence suggests that their alleles have remarkable effects on grain yield.

284 It is tempting to link regions with reduced QTL density with chromosome regions which have  
285 undergone selective sweep. Unfortunately, the generally low precision of QTL maps, as compared to  
286 the kb- to Mb-range typical of selective sweep studies (e.g. [86,87]) and the remarkably low linkage

287 disequilibrium in maize precluded meaningful comparisons. However, two chromosome regions  
288 identified in our study with a strikingly low level of QTL density (on chr. 1, at approx. 50 Mb and on  
289 chr. 6, at approx. 130 Mb) may correspond to regions characterized by high identity-by-descent of  
290 the parental lines and by a relatively high recombination rate, as identified in the maize HapMap2  
291 study (Supp. Fig. 9 in [77]).

292

#### 293 4.4. Meta-analysis and breeding implications

294

295 Meta-analysis allowed for a remarkable simplification of the yield QTLome since the initial  
296 number of QTLs was reduced by 65% of the initial number of QTLs and the average QTL confidence  
297 interval was reduced 7-fold. However, no clear trend of MQTL distribution on chromosomes was  
298 evidenced. MQTL positions reported in this study have some congruency with other results recently  
299 published. Nineteen MQTLs are shared with [20] using the same reference map for QTL projection  
300 (Supplementary Material 7). In three of these MQTLs (MQTL7, MQTL10 and MQTL36) maize  
301 orthologs of rice yield genes were identified [20]. Additionally, 27 MQTLs are putatively shared with  
302 [19]. In this case, we can only speculate on relative map positions since the map developed by [19]  
303 was based on SNPs and shares no markers with the reference map 'Genetic' used in the present study.  
304 On chromosome 4, our MQTL31 corresponds to the position where Bommert et al. [88] found a QTL  
305 for Ear Row Number containing the candidate gene *FASCIATED2* (*FEA2*).

306 It should be noted that QTL meta-analysis could gain power and precision if raw genotypic and  
307 phenotypic data from published QTL experiments were made available [5].

308 In a breeding perspective, accordingly to Löffler et al. [89], three criteria must be taken into  
309 consideration when deploying MQTL information: i) MQTLs should have small supporting intervals,  
310 ii) a MQTL should include a high number of initial QTLs and iii) the initial QTLs should be  
311 characterized by high PVE. The identification of MQTL-linked markers will help to prioritize  
312 QTL/loci for marker-assisted breeding programs and for QTL cloning [90], thus possibly positively  
313 influencing the improvement of crop models [91].

314

315

## 316 5. Conclusions

317

318 The analysis of a large set of QTL data enables to verify emerging properties typically precluded  
319 by smaller datasets. In this study, we verified for the first time whether yield QTLs, on a large scale,  
320 are characterized by specific mapping patterns on maize chromosomes. When QTLs were projected

321 on the genetic map, clustering at pericentromeric regions was identified as a consequence of the much  
322 lower recombination frequency at the same regions. Conversely, when QTLs were projected on the  
323 physical maps and QTL peaks rather than confidence interval were considered, low QTL density was  
324 observed at centromeric regions and high QTL density at subtelomeric regions. QTL density was  
325 found to be significantly associated with gene density. Despite previous preliminary indications, our  
326 study did not evidence difference in density pattern of heterotic and additive effect QTLs across  
327 chromosomes. However, the inherent statistical noise of QTL data may have precluded us from  
328 revealing the existence of distinguished mapping pattern of heterotic QTLs.

329 Although our study represents the largest meta- analysis so far carried out in maize, it only  
330 includes a small fraction of all QTL information published in maize. Further extension of the maize  
331 yield QTLome information through the inclusion of QTLs from genome-wide association studies will  
332 improve our understanding of the molecular and evolutionary basis of this key quantitative trait, an  
333 important prerequisite for enhancing the effectiveness of maize breeding.

334

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336

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338

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**Table 1**

List of trait categories utilized in this study.

Trait	Acronym	Traits included <sup>1</sup>
Grain Yield <sup>2</sup>	GY	Grain yield
Kernel Weight	KW	Hundred Kernel Weight Kernel Weight Kernel Weight per Ear Thousand Kernel Weight
Ear Row Number	ERN	Ear row number
Kernel Number	KN	Kernel Number Kernel Number per Ear Kernel Number per Plant Kernel Number per Row
Ear Length	EL	Ear Length
Ear Diameter	ED	Ear Diameter
Ear Number	EN	Ear Number Ear Number per Plant
Ear Weight	EW	Ear Weight

<sup>1</sup> Traits as defined from original papers which were included in the same category in our study.

<sup>2</sup> Grain Yield trait category strictly included QTL data for overall grain production per unit of area, with the exception of QTL information from studies [18] and [37], where Ear weight per plant and Grain weight per plant were provided and utilized, respectively.

**Table 2**

Summary of QTL studies included in QTL meta-analysis for grain yield and grain yield related traits.

Reference	Cross	Population type <sup>a</sup>	Size	Exp. (no.) <sup>b</sup>	Traits <sup>c</sup>	Notes	QTLs (no.)
Ajmone Marsan et al. [24]	B73 x A7	F3 as TC	232	1	GY, TW	Testers: A1, Mo17	11
Almeida et al. [25]	CML444xSC-Malawi (234)	RIL as TC	781	2	GY	WW and WS; Testers:CM312,	17
	CML444xCML441 (300)	F2:3 as TC				CML395	
	CML440xCML504 (247)	F2:3 as TC					
Barriere et al. [26]	F838 x F826	RIL as TC	240	1	GY	Tester: F353	8
Bohn et al. [27]	D06 x D408	F3	230	1	GY		6
Cai et al. [28]	Ye478 x Wu312	RIL	218	3	EL, GY, KN, KW	LN, LP, normal N and P	47
Cañas et al. [29]	Io x F2	RIL	100	1	EN, EL		2
Coque & Gallais [30]	Io x F2	RIL as TC	99	2	GY, KW, KN	HN and LN; Tester: F252	23
Frascaroli et al. [31]	B73 x H99	RIL as BC/TC	142	1	GY, KN, KW	Testers: B73, H99, their F1	46
Guo et al. [32]	Zheng58 x Chang7-2	F2:3	231	2	EW, KW, EL, ERN, KN, ED	Low density, High density	37
Huang et al. [33]	F2 x F252	F3:4 and IF3 as TC	300, 322	1	GY	Tester: MBS847	16
Jansen et al. [34]	B73 x Mo17	RIL (IBMSyn4)	206	1	GY, KW		9
Lariepe et al. [22]	IoxF252 (144); F2xF252 (113); F2xIo (145)	RIL as BC/TC	402	1	GY	Testers: F2, F252, Io	10
Li et al. [35]	Huangzao 4 x Ye 107	F3	184	2	GY	WW and WS	9
Li et al. [36]	Dan232 x N04	F2:3	259	1	KW, EL, ED, ERN, KN		16
Li et al. [37]	8984 x GY220	F2:3	284	1	GY, KW, EL, ED, ERN, KN		18
	8622 x GY220	F2:3	265	1	GY, KW, EL, ED, ERN, KN		14
Li et al. [18]	Dan232 x N04	RIL	258	5	GY, EW, KW, EL, ERN, KN, ED		58
Liu et al. [38]	Huangzao4 x Mo17	RIL	239	2	KW	HN and LN	4
Liu et al. [39]	Huangzao4 x Mo17	RIL	239	2	GY	HN and LN	6
Liu et al. [40]	Huangzao4 x Mo17	RIL	239	2	EW	HN and LN	2
Liu et al. [41]	Huangzao4 x Mo17	RIL	239	2	ERN, KN	HN and LN	8
Liu et al. [42]	Huangzao4 x Mo17	RIL	239	2	KN	HN and LN	7
Liu et al. [43]	Ye478 x Wu312	RIL	218	2	GY		5
		BC4F3	187	2	GY		5

Liu et al. [44]	Mc x V671	F2:3	270	1	KW		9
Lu et al. [45]	LH200 x LH216	F2syn as BC	351	1	GY	Testers: LH200, LH216	29
Lu et al. [46]	Zong 3 x 87-1	RIL	221	2	GY, EL, KN, KW	WW and WS	26
Lu et al. [47]	Ye478 x Dan340	F2:3	397	1	ERN		13
Marino et al. [48]	B73 x H99	RIL	142	1	EL, EW, KW, KN		22
Melchinger et al. [49]	KW1265 x D146	F3 as TC	451	1	GY, KW	Testers: KW4115, KW5361	20
Messmer et al. [50]	CML444 x SC-Malawi	RIL	236	2	GY, KW, KN	WW and WS	20
Moreau et al. [51]	F2 x F252	F3:4 as TC	300	1	GY, KW, KN	Tester: MBS847	13
Ribaut et al. [52]	Ac7643S5 x Ac7729/TZSRWS5	F3	234	4	GY, EN, KN	WW, IS, WS and IS+WS	30
Ribaut et al. [53]	Ac7643S5 x Ac7729/TZSRWS5	F3	240	2	GY, KN, KW, EN	HN and LN	21
Stuber et al. [54]	B73 x Mo17	F3 as BC	264	1	GY	Recurrent parents: B73, Mo17	11
Tang et al. [55]	Zong3 x 87-1	IF2	294	1	GY, EL, ERN, KW		8
Tian et al. [56]	Y1648 x Y2348	F2:3, F2:4	180	1	ERN		9
Tuberosa et al. [57]	Lo964 x Lo1016	F3	171	2	GY	WW and WS	13
Veldboom et al. [58]	Mo17 x H99	F2:3	150	1	GY, KW, EN, EL, ED, ERN		21
Wassom et al. [59]	((IHO90 x B73) x B73) S1)	BC1S1 as TC	150	1	GY	Tester: Mo17	3
Xiao et al. [60]	B73 x X178	F2:3	234	2	KW, EN, EW, GY, KN	WW and WS	26
Yan et al. [61]	Zong3 x 87-1	F2:3	266	1	GY, KN, ERN, KW		20
Yang et al. [62]	8984 x GY220	RIL	282	1	GY, EW, KN, KW, EL, ED, ERN		48
	8622 x GY220	RIL	263	1	GY, EW, KN, KW, EL, ED, ERN		40
Zhang et al. [63]	Huangzao4 x Mo17	RIL	239	2	EL, ED	HN and LN	5
Zhang et al. [64]	Huang C x Xu178	IF2	243	1	KW		6
Zheng et al. [65]	Qi-319 x Mo17	F2:3	166	1	GY, ED, KW		11

<sup>a</sup> RIL: recombinant inbred line; TC: testcross, BC: backcross; IF2: immortalized F2;

<sup>b</sup> Number of experiments

<sup>c</sup> GY: grain yield, KW: kernel weight, KN: kernel number, ER: ear number, ERN: ear row number, EW: ear weight, EL: ear length, ED: ear diameter.

WS: water stress, WW: well watered, IS: intermediate stress, HN: high nitrogen, LN: low nitrogen, LP: low phosphorus.



**Table 3**

Summary of MQTL information for grain yield and grain yield-related traits.

Chromosome	MQTL	Position <sup>a</sup>	CI <sup>b</sup> (cM)	QTLs <sup>c</sup> (no.)	Traits
1	1	40.69	2.48	33	ED, EL, EN, ERN, GY, KN, KW
	2	75.2	2.09	7	EL, KN, KW
	3	100.31	1.08	12	ED, EW, GY, KN, KW
	4	112.72	2.74	7	EL, GY, KW
	5	132.52	3.24	6	ED, GY, KN, KW
	6	139.7	0.1	3	GY, KW
	7	162.37	2.48	19	ED, EL, ERN, GY, KN, KW
	8	191.91	3.11	6	ED, GY
	9	243.49	0.65	16	EL, EN, ERN, EW, GY, KN, KW
2	10	10.57	3.06	6	ED, EL, EW, KN, KW
	11	33.13	6.29	3	ERN, GY, KW
	12	49.27	8.31	1	KW
	13	61.1	0.2	4	GY, KW
	14	71.72	3.96	7	EN, GY, KW
	15	85.48	4.75	5	GY, KN, KW
	16	96.58	3.99	7	ERN, GY, KW
	17	112.5	1.91	6	ED, EL, ERN, GY, KN
	18	124.66	3.74	2	GY, KW
3	19	152.75	0.78	9	ED, EL, EW, GY, KW
	20	8.06	3.72	11	ED, EL, ERN, GY, KN, KW
	21	34.43	3.27	11	ERN, EW, GY, KN, KW
	22	47.13	3.58	11	ED, EL, EW, GY, KN, KW
	23	68.08	4.42	8	EL, ERN, EW, KN, KW
	24	90.73	4.75	6	EW, GY, KN
	25	105.94	5.28	5	EN, ERN, GY, KN
	26	139.01	2.97	6	ERN, GY, KN, KW
	27	172.73	0.7	7	ED, EL, ERN, KW
4	28	13.38	2.07	12	ED, EL, ERN, EW, GY, KN, KW
	29	46.55	3.14	5	ERN, EW, GY
	30	65.37	3.9	4	EL, GY, KN
	31	76.04	4.35	8	ED, ERN, GY, KN
	32	96.08	3.08	4	EL, ERN, KW
	33	104.55	1.08	5	ED, ERN, KW
	34	127.13	2.55	6	ED, ERN, GY, KN, KW
	35	135.72	3.75	4	ERN, GY
	36	146.46	3.7	8	ED, ERN, GY, KN
5	37	170.18	0.28	9	ED, EL, ERN, GY, KN, KW
	38	3.91	3.13	3	EL, GY, KN
	39	31.44	3.64	9	EL, ERN, KN, KW
	40	47.22	2.28	10	EL, ERN, EW, KW
	41	63.54	2.73	14	EL, EW, GY, KN, KW
	42	84.21	1.96	16	ED, ERN, GY, KN, KW
	43	108.62	4.97	5	EL, ERN, GY, KW
	44	117.36	3.62	2	ED, KW
	45	135.36	0.33	12	EL, GY, KN, KW
6	46	25.54	2.18	23	EL, EW, GY, KN, KW
	47	48	3.17	8	GY, KN, KW
	48	62.75	8.78	2	ERN, KW
	49	94.59	2.22	8	ED, EL, EN, GY, KN, KW

	50	114.5	2.1	6	ED, ERN, GY, KW
	51	131.34	1.24	5	EL, GY, KN, KW
7	52	31.85	2.39	16	ED, ERN, GY, KN, KW
	53	64.69	1.71	10	ED, EL, GY, KN, KW
	54	76.52	3.47	8	EW, GY, KW
	55	88.08	1.81	7	ERN, GY, KW
	56	113.52	1.57	9	EL, ERN, GY, KN, KW
	57	144.95	1.49	4	EL, GY, KN
8	58	25.03	4.57	4	GY, KN, KW
	59	49.18	2.28	8	ERN, GY, KN, KW
	60	57.09	2.8	6	ERN, GY, KN, KW
	61	67.4	6.16	4	GY, KN
	62	87.89	4.45	6	ERN, GY, KW
	63	92.81	1.27	7	EL, EW, GY, KW
	64	105.3	3.6	8	ED, EL, EN, ERN, GY, KN
	65	121.99	2.63	8	EL, EN, GY, KN, KW
	66	142.49	2.03	2	EL, KN
9	67	6.05	1.8	2	KW
	68	27.95	3.95	6	EW, GY, KN, KW
	69	50.82	3.18	7	ED, EN, ERN, GY, KN, KW
	70	62.14	3.31	6	ED, EN, GY, KN, KW
	71	66.26	2.21	5	ERN, EW, GY
	72	76.29	5.32	4	EL, ERN, GY, KN
	73	85.61	6.33	2	EW, KN
	74	96.54	5.16	3	GY, KW
	75	107.66	4.06	5	EN, ERN, GY, KN, KW
	76	147.25	1.94	4	EL, ERN, GY, KW
10	77	27.39	7.37	6	EL, GY, KN
	78	56.63	3.26	7	EL, ERN, EW, GY
	79	67.08	3.64	8	EL, GY, KN, KW
	80	80.63	4.27	4	EL, GY, KN, KW
	81	89.02	2.68	10	ED, EL, ERN, EW, GY, KW
	82	101.17	1.28	7	ERN, EW, GY, KN, KW
	83	119.72	3.79	4	ERN, GY, KW
	84	132.09	1.09	1	KW

<sup>a</sup> Most probable position on the consensus map in cM.

<sup>b</sup> Length of the 95% confidence interval (CI) centered on the most probable position in cM

<sup>c</sup> Number of QTLs corresponding to the same MQTL

## Figure legends

**Figure 1.** Concentric circles showing yield QTL distribution on: A) maize reference map ‘Genetic’ and B) B73 RefGen\_v2 reference genome. 1) Reference chromosomes with positions of bins as alternating gray and white bands. Approximate centromere positions are indicated by black bands. 2) QTL positions represented by confidence interval. Red bars correspond to QTLs with heterotic effect (HQ) and black bars correspond to all other QTLs. 3) Frequency of QTLs computed as QTL-overview index (Chardon et al., 2004). 4) MQTLs position with a CI of 95%.

**Figure 2.** Distribution of QTLs on chromosomes expressed as QTL frequency (%) per bin distance (20 cM- or 25 Mb-bin) from centromere. Histograms report mean QTL frequency values of ten chromosomes, with the following exceptions: -60 cM, mean value of six chrs; -40 cM, nine chrs; +100 cM, eight chrs; -75 Mb, five chrs; +125 Mb, 6 chrs. A and B) Distribution of all QTLs (total no.: 808). C and D) Distribution of 342 QTL with heterotic and potentially heterotic effects (PHQ). E and F) Distribution of 91 additive grain yield QTLs (GY AQ) and 96 heterotic grain yield QTLs (GY HQ). See Materials and Methods for definition of AQ, HQ and PHQ QTLs.

## Supplementary Materials

**Supp Mat 1.** Grain yield and grain yield components QTLome database.

**Supp Mat 2.** Database of QTLs projected onto the maize ‘Genetic’ map and ready to use as input file for BioMercator.

**Supp Mat 3.** Number of QTLs per trait and per study and frequency of heterotic QTLs.

**Supp Mat 4.** Frequency distribution of the number of QTLs based on proportion of phenotypic variance explained (PVE).

**Supp Mat 5.** Relationship between number of detected QTLs and population size (expressed as number of progenies) for GY (solid circles) and grain yield component traits (empty circles).

**Supp Mat 6.** Mean values of Proportion of Variance Explained (PVE) of QTLs computed per chromosome intervals of 20 cM.

**Supp Mat 7.** Detailed results of MQTL analysis.

**Supp Mat 8.** Comparison of common MQTL positions detected in the present study and those from Wang et al. [20].