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Research Paper

A novel genotype DATTO5 developed using the five genes exhibits the fastest heading date designed in rice

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The optimization of heading date is a key aspect for maximizing grain productivity in cereal crops including rice. The combinations of genes for heading date, a quantitative trait, are a major driver in the wide adaptability of cultivated rice worldwide. Here, we identified a novel QTL, *qDTH3* (quantitative trait locus for days-to-heading on chromosome 3), for early flowering time in the F_2 population derived from a cross between Hoshinoyume (HS) and Daichinohoshi (DH) among local rice populations with extremely early heading date. The DH allele at *qDTH3*, $qDTH3^{DH}$, headed 2.7 days earlier than the HS allele at *qDTH3*, $qDTH3^{HS}$. We sought to design a genotype for earlier heading date by pyramiding of five heading date genes. We designated this aggregate of the five genes as DATTO5. Plants with DATTO5 were selected from the F_2 population derived from a cross between DH and HShd5, which is a near-isogenic line carrying a loss-of-function of *days to heading 8* in a genetic background of HS. Plants with DATTO5 exhibited earlier heading date but reduced fitness, including shorter culm and panicle length and fewer seeds compared with HS, as a representative local rice variety with extremely early heading date.

Key Words: rice, heading date, QTLs pyramiding, DATTO5, *qDTH3*.

Introduction

Heading date in crop species is a major factor limiting species range. Variation in heading date is determined by the response to seasonal cues from changing environmental factors including day length and temperature (Blümel *et al.* 2015, Hill and Li 2016, Hu *et al.* 2019). Expanding species range is a major goal in food supply for growing populations worldwide and under conditions of global warming for crop breeding programs. Many genes for the control of heading date have been identified in rice (Gramene; http://www.gramene.org), and a genetic network for heading date has been proposed (Hori *et al.* 2016, Tsuji *et al.* 2011). However, it is unclear which genotype exhibits the best fit to local environmental conditions for expanding the range of rice.

Asian cultivated rice, *Oryza sativa* L., originated in the tropics (Choi *et al.* 2017, Fuller 2011, Huang *et al.* 2012, Yang *et al.* 2012). Favoraüble alleles for adaptability to various environmental conditions have been acquired by artificial selection through a combination of mutations in natural populations (Hua *et al.* 2015, Jin *et al.* 2016, Konishi *et al.* 2008). Extensive efforts in rice breeding programs to optimize heading date have made rice production possible in various climatic conditions at latitudes ranging from 53°N to 40°S (Fujino *et al.* 2015a, 2015b, 2017, Lu and Chang 1980, Shinada *et al.* 2014). Early heading date, through a decrease in photoperiod sensitivity, may have played an important role in expanding the range of rice (Izawa 2007, Fujino *et al.* 2019a, 2019b Shrestha *et al.* 2014, Zheng *et al.* 2016).

Based on a series of genetic analyses for heading date in rice, we identified QTLs/genes for extremely early heading date behavior using unique natural variations originating from Hokkaido (41–45°N latitude), Japan, which has a long natural day length of more than 15 hours (Fujino and Sekiguchi 2005a, 2005b, 2008, Fujino *et al.* 2013, 2019a, 2019b, 2019c, Nonoue *et al.* 2008). In addition to the adaptability to local environmental conditions, genes for stable rice production have been selected for agriculture. Three genes, *Heading date 1* (*hd1*), *Oryza sativa Pseudo-Response Regulator37* (*osprr37*), and *Grain number, plant height and heading date 7* (*ghd7*), accounted for extremely early heading date as EARLY-Trio, which was specific to local environmental conditions in Hokkaido (Fujino *et al.* 2019c). *Hd1* is the rice ortholog of the *Arabidopsis* floral activator *CONSTANS* (Yano *et al.* 2000). *Ghd7* encodes a CO, CO-LIKE, and TIMING OF CAB1 (CCT) domain protein (Xue *et al.* 2008). *OsPRR37* is an ortholog of the circadian clock genes *PRR3/7* in *Arabidopsis* (Gao *et al.* 2014, Koo *et al.* 2013, Murakami *et al.* 2007, Nakamichi

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Table 1. Heading date of parental varieties

Variety	Genotype[a]	Average (day)	SD[b]	Range	
				Minimum	Maximum
Daichinohoshi (DH)	*Hd1ghd7osprr37DTH8*	86.8	1.2	84	88
Hoshinoyume (HS)	*Hd1ghd7osprr37DTH8*	93.8	0.6	92	94
HShd5	*Hd1ghd7osprr37dth8*	79.4	0.9	78	80

[a] Genotype is cited from Fujino *et al.* (2019b).
[b] SD: standard deviation.

et al. 2005).

Along with human migration in Japan, *de novo* mutations causing loss-of-function for extremely early heading date representing the rice population from Hokkaido were selected (Fujino and Sekiguchi 2005a, 2005b, Fujino *et al.* 2019b, 2019c). Previously, we identified the gene responsible for earlier heading date among local populations from Hokkaido with extremely early heading date (Fujino 2003, Fujino *et al.* 2013, 2019a, 2019b). A loss-of-function of *Heading date 5* (*Hd5*), *hd5*, accounted for this earlier heading date among a population with extremely early heading date (Fujino 2003, Fujino *et al.* 2013). *Hd5* is allelic to *Days to heading 8* (*DTH8*) encoding a putative HAP3 subunit of a CCAAT-box-binding transcription factor (Fujino *et al.* 2013, Wei *et al.* 2010).

The genetic base of heading date in rice varieties in Hokkaido clearly indicated the limitation of the variation of heading date during the short growth period (Fujino *et al.* 2019a, 2019b). Now, rice breeding programs in Hokkaido focused on good eating quality and successfully developed commercial varieties (Fujino *et al.* 2019a). Development of rice varieties with high quality and yield will explore rice production in Hokkaido. Optimum heading date by novel genotype for heading date is critical in rice breeding programs in Hokkaido. Here, we identified a single QTL for earlier heading date other than *dth8*. Then, we designed a genotype with pyramiding of these five genes: the QTL identified in this study, *dth8*, *Hd1*, *osprr37*, and *ghd7* for earlier heading date. We selected plants with the five genes and designated this combination as DATTO5. Finally, we discussed about the role of DATTO5 on rice breeding programs in Hokkaido.

Materials and Methods

Plant material

Two *japonica* elite rice varieties, Hoshinoyume (HS) and Daichinohoshi (DH), were used as the parental varieties. Both varieties were bred in rice breeding programs in Hokkaido for the current market class in Japan. HS was registered in 1996. DH is a progeny of HS and was registered in 1999 (**Supplemental Fig. 1**). To identify QTLs controlling the earlier heading date in DH than that in HS, we developed an F_2 population (n = 96) derived from the cross between HS and DH as a mapping population. In addition, a near isogenic line for *dth8*, HShd5 with the genetic background of HS, was used (Fujino *et al.* 2013, 2019c). All varieties used in this study had the EARLY-Trio, comprising *Hd1*, *ghd7*, and *osprr37* (**Table 1**).

Next, we designed a genotype pyramiding with the known genes for earlier heading date. The QTL for earlier heading date detected in this study was combined with *dth8*. DH was crossed with HShd5. A total of 191 F_2 plants were classified into four genotype classes based on genotypes for both the QTL detected in this study and *DTH8*. The agronomic traits were measured and compared among the four genotype classes.

Seeds of rice varieties were provided by the Local Independent Administrative Agency Hokkaido Research Organization Hokkaido Central Agricultural Experiment Station (Takikawa, Japan). All plant materials were cultivated in an experimental paddy field at Hokkaido Agricultural Research Center (Sapporo, Hokkaido, Japan, 43°00′ N latitude) in 2015 with 15.0 cm spacing between plants within each row and 30.0 cm spacing between rows. Cultivation management followed the standard procedures used at Hokkaido Agricultural Research Center. Sowing and transplanting were performed on 27 April and 21 May 2015, respectively.

Trait evaluation

Heading date was measured as days to heading (DTH) of the earliest heading panicle on individuals and recorded. We observed no plants showing heading at 74 days in this experiment. We measured DTH of plants every 2 days after 78 days.

Mean values of the yield-related traits, culm length (CL), panicle length (PL), panicle number (PN), and total seeds number (TS) were evaluated in accordance with Fujino *et al.* (2017) and shown for each line/variety. We counted the number of spikelets on the panicle as the TS independent of their fertility. In addition, internode length and panicle components, number of primary and secondary branches and seeds on the branch, were measured in the tiller of the longest culm per individual plant. Phenotypes were averaged for each line/variety. These values were compared using the Tukey–Kramer HSD test and statistically examined by two-way analysis of variance (ANOVA), for the epistatic interaction between the genes.

Re-sequencing

Genomic DNA extracted from <20 seedlings of DH was used for pair-end sequencing using an Illumina Hiseq2000. Raw sequence data were deposited in the DDBJ BioProject database under accession number DRA008496. The filtering procedure for polymorphism in the genome sequence was performed as described in Fujino *et al.* (2018).

DNA analysis

Total DNA was isolated from young leaves using the CTAB method (Murray and Thompson 1980). A total of 38 markers over the whole genome were used to detect polymorphisms among the F_2 populations derived from the cross between HS and DH (**Supplemental Table 1**). These markers had been developed using the myINDEL procedure (Fujino *et al.* 2018). In addition, to determine the alleles in the *DTH8* gene, a DNA marker tagged on the 19 bp deletion for gene function, HD519del, was used (Fujino *et al.* 2013). The amplification and polymorphisms with the designed primers were studied using a conventional PCR technique. PCR, electrophoresis, and sequencing were performed as described previously (Fujino *et al.* 2004, 2005).

QTL analysis

A linkage map of the F_2 population derived from the cross between HS and DH was constructed using the 38 markers. Linkage analyses were performed with MAPMAKER/EXP using the Kosambi function (Kosambi 1944, Lander *et al.* 1987). Detection of QTLs for heading date was conducted by composite interval mapping with QTL Cartographer 2.5 (Wang *et al.* 2012). The threshold to detect QTLs for heading date was determined using 1,000 permutation tests at a probability level of 0.05, LOD = 3.2.

Results

QTLs for early heading date in Daichinohoshi

There was a difference in heading date between the varieties (**Fig. 1**, **Table 1**). The heading date of HS was 93.8 ± 0.6 days, while those of HShd5 and DH were 79.4 ± 0.9 and 86.8 ± 1.2 days, respectively. The loss-of-function allele of *DTH8*, *dth8*, in HShd5 promoted heading date by 14.4 days. To identify QTLs controlling earlier heading date in DH, 7.0 days earlier than HS, we developed a mapping population derived from the cross between HS and DH. A wide variation with continuous distribution was observed in the frequency of heading date, ranging from 86 to 98 days (**Fig. 1**).

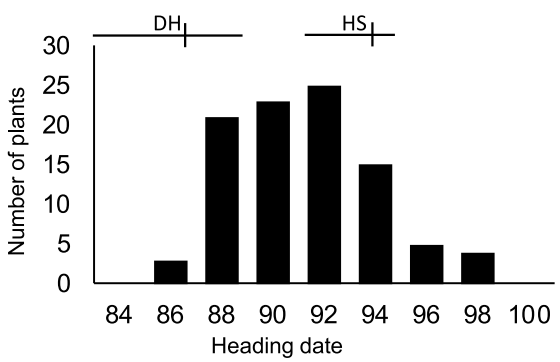

Fig. 1. Frequency distribution of heading date in the F_2 population (n = 96) derived from a cross between Hoshinoyume (HS) and Daichinohoshi (DH). Horizontal and vertical bars indicate the range and average of heading date.

According to the myINDEL procedure (Fujino *et al.* 2018), a total of the 38 InDel markers were developed, which showed clear polymorphisms between HS and DH (**Supplemental Table 2**). A single QTL with large effect on heading date was detected near INDEL05109 on chromosome 3, *qDTH3*, which accounted for 45.8% of total phenotypic variation. The DH allele, $qDTH3^{DH}$, promoted heading date, by 2.7 days, compared with the HS allele, $qDTH3^{HS}$ (**Fig. 2**, **Table 2**, **Supplemental Tables 2**, **3**).

Design of genotype pyramiding of five genes for earlier heading date

To combine the alleles for earlier heading date in both $qDTH3^{DH}$ of *qDTH3* and *dth8* of *DTH8*, an F_2 population from the cross between HShd5 and DH was developed. Heading date in this population showed a bimodal distribution ranging from 78 to 94 days (**Fig. 3A**). According to the genotype of *qDTH3* and *DTH8*, plants in this population were classified into nine genotypes (**Fig. 3B**, **Supplemental Table 4**).

Finally, we selected plants with genotype pyramiding of

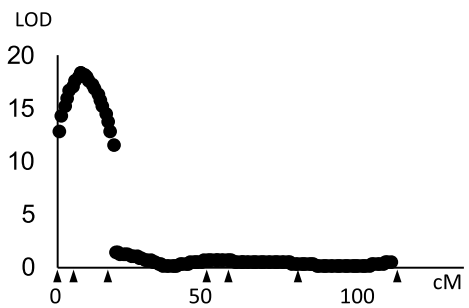

Fig. 2. LOD curve for QTL analysis for heading date. X-axis indicates the position of seven molecular markers (closed triangle) on chromosome 3 in the linkage map.

Table 2. QTLs for heading date detected in the F_2 population derived from the cross between Hoshinoyume (HS) and Daichinohoshi (DH)

Name	Interval	Chr[a]	LOD	Effect[b] (days)	PVE[c] (%)
qDTH3	3SHSDC01–INDEL05109*	3	18.5	–2.7	45.8

* indicates the nearest molecular marker.
[a] Chromosome.
[b] Effect of the DH allele, $qDTH3^{DH}$, are shown, which is compared with that of the HS allele, $qDTH3^{HS}$.
[c] Phenotipic variation explained.

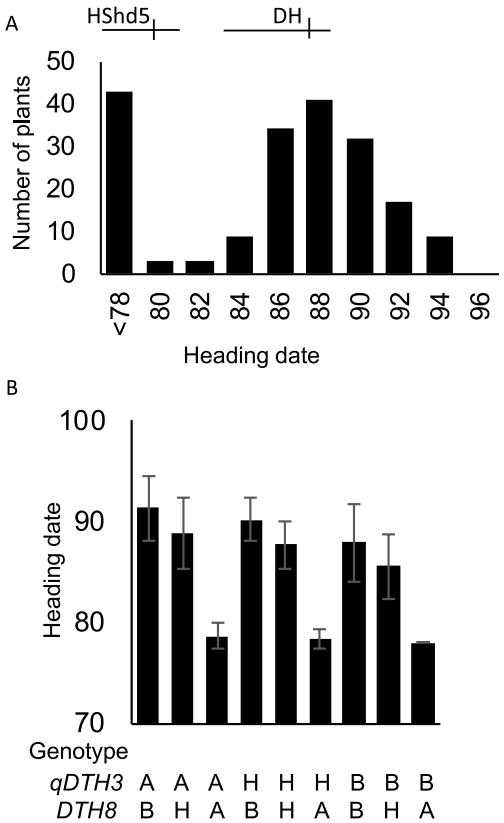

Fig. 3. Variation in heading date in the F_2 population (n = 191) derived from a cross between Daichinohoshi (DH) and HShd5. A; frequency distribution of heading date. Horizontal and vertical bars indicate the range and average of heading date. B; comparison of heading date between plants with the nine different genotypes of *qDTH3* and *DTH8*. Genotypes A, B, and H of *qDTH3* and *DTH8* indicate HShd5, DH, and heterozygous alleles, respectively. Bars with lines show average and standard deviation (SD) of heading date, respectively.

alleles for earlier heading date in homozygotes of both *qDTH3* and *DTH8*. The heading date of each genotype was significantly different depending on the genotype for heading date, *qDTH3* or *DTH8* (**Table 3**). When the genotype $qDTH3^{HS}DTH8$ in HS was defined as a wild-type (WT), $qDTH3^{DH}$ and *dth8* promoted heading date by 2.8 and 12.9 days, respectively, versus WT. $qDTH3^{DH}$ and *dth8* acted additively on the promotion of heading date by 13.4 days versus WT. We designated the genotype of $qDTH3^{DH}dth8$ with EARLY-trio, *Hd1ghd7osprr37*, as DATTO5.

Table 4. Coefficient among genotypes in the F_2 population in five traits

Trait	HD	CL	PL	PN	TS
HD	1				
CL	0.962	1			
PL	0.975	0.998	1		
PN	–0.837	–0.852	–0.871	1	
TS	0.990	0.984	0.993	–0.890	1

HD: heading date, CL: culm length, PL: panicle length, PN: panicle number, TS: total seeds on a panicle.
All values indicate significant differences at a 0.05 level.

Evaluation of yield-related traits

To elucidate the role of genes for heading date on agronomic traits, we compared four yield-related traits between the four genotypes of *qDTH3* and *DTH8* with EARLY-trio (**Table 3**). No abnormality in the evaluated traits was observed with genotype pyramiding of the four or three recessive alleles for heading date genes, $qDTH3^{DH}$, *dth8*, *osprr37*, and *ghd7*. Significant differences in CL and PL were detected additively with *qDTH3* and *DTH8* (**Table 3**). Additionally, a significant difference in TS was detected epistatically with *qDTH3* and *DTH8* (**Table 3**). Although no significant difference in PN was detected, a phenotypic trend depending on genotype of *qDTH3* and *DTH8* was observed (**Table 3**). $qDTH3^{DH}$ reduced PN, but *dth8* increased PN. Furthermore, DTH showed high coefficient values with PL, CL, and TS in positive and PN in negative, more than 0.837 (**Table 4**).

We measured CL and TS in detail. CL was expressed as the sum of the length of internode I–IV. Lengths of internodes I and II accounted for more than 80% of CL among any genotype (**Supplemental Fig. 2**). The lengths of internodes I and II were regulated additively by *qDTH3* and *DTH8* (**Supplemental Table 5**). $qDTH3^{DH}$ reduced internode

Table 3. Yield-related traits between plants with genotype for heading date among the F_2 population derived from the cross between Daichinohoshi (DH) and HShd5

Genotype in *qDTH3* and *DTH8*	n	Heading date		Culm length (CL)		Panicle length (PL)		Panicle number (PN)		Total seeds (TS)	
		Average ± SD (day)	Ratio to WT[a]	Average ± SD (cm)	Ratio to WT	Average ± SD (cm)	Ratio to WT	Average ± SD (number)	Ratio to WT	Average ± SD (number)	Ratio to WT
$qDTH3^{HS}dth8$	11	78.5 ± 1.3b	(85.9)	57.4 ± 5.2b	(82.5)	13.1 ± 1.1b	(78.9)	25.0 ± 3.9a	(110.1)	43.1 ± 10.9b	(56.3)
$qDTH3^{HS}DTH8$	7	91.4 ± 3.2a	(100)	69.6 ± 5.5a	(100)	16.6 ± 0.9a	(100)	22.7 ± 8.7a	(100)	76.6 ± 19.5a	(100)
$qDTH3^{DH}dth8$	11	78.0 ± 0b	(85.3)	51.4 ± 2.6b	(73.9)	11.7 ± 0.9b	(70.5)	26.9 ± 3.2a	(118.5)	35.2 ± 5.3b	(46)
$qDTH3^{DH}DTH8$	13	88.6 ± 2.8a	(96.9)	65.6 ± 4.9a	(94.3)	15.7 ± 1.3a	(94.6)	20.3 ± 6.1a	(89.4)	71.4 ± 13.4a	(93.2)

[a] Ratio to WT shows phenotypic value comparing that in WT, $qDTH^{HS}DTH8$, as a standard of 100.
Different letters indicate significant differences at $p < 0.05$.
Genotype of the *qDTH3* and *DTH8* genes in DH and Hoshinoyume (HS) carries $qDTH3^{DH}dth8$ and $qDTH3^{HS}DTH8$, respectively.

I by 3.4 cm and internode II by 2.0 cm versus WT (**Supplemental Table 5**). *dth8* reduced internodes I and II by 6.8 and 2.2 cm, respectively, versus WT (**Supplemental Table 5**). *qDTH3*^{DH}*dth8* additively reduced internodes I and II by 9.8 and 4.5 cm, respectively, versus WT (**Supplemental Tables 5**, **6**).

TS was expressed as the sum of seeds on the primary and secondary branches, which accounted for approximately 60% and 40%, respectively (**Supplemental Fig. 2**). The numbers of primary branches (Pb) and seeds on Pb (SPb) were additively regulated by *qDTH3* and *DTH8* (**Supplemental Table 7**). Whereas, the number of the secondary branches (Sb) and seeds on Sb (SSb) were dramatically reduced (**Supplemental Table 7**). *qDTH3*^{DH} showed 1.1- and 3.1-fold reductions in Sbs and SSbs, respectively, versus WT (**Supplemental Table 7**). *dth8* reduced Sbs and SSbs by 6.2- and 16.5-fold, respectively, versus WT (**Supplemental Table 7**). *qDTH3*^{DH}*dth8* additivelly reduced Sbs and SSbs by 7.7- and 21.7-fold, respectively, versus WT (**Supplemental Tables 6**, **7**). High positive coefficient values of DTH with these traits for CL and TS, more than 0.815 (**Supplemental Tables 8**, **9**).

Discussion

Heading date control is a major determinant of adaptability in crop species. Understanding the genetic mechanisms involved in the adaptability to species range can facilitate adaptive divergence within genetically improved local populations, thereby expanding the species range. In this study, we identified a single QTL for earlier heading date, *qDTH3*^{DH}, in rice variety DH in a local population with extremely early heading date (**Table 2**). *dth8* headed too early to keep enough spikelet number (**Table 3**). *qDTH3*^{DH} is useful to develop new variety with cropping season for early heading date-type in the current climatic conditions in Hokkaido.

Previously, we identified a QTL for heading date in a similar chromosomal region in rice varieties among the ancestral population of DH (Fujino and Sekiguchi 2008). The origin and pedigree of *qDTH3*^{DH} identified in this study may clarify the genetic complexity of agronomic traits among local populations with genetic diversity during rice breeding programs (Fujino *et al.* 2015a, 2015b, 2017, Shinada *et al.* 2014).

Next, we designed a genotype for early flowering time by pyramiding five alleles, *qDTH3*^{DH}, *hd5*, *Hd1*, *osprr37*, and *ghd7* and designated this combination as DATTO5. DATTO5 selected in this study exhibited earlier heading date than genotypes with *qDTH3*^{DH} or *dth8* alone but it wed a reduction of fitness due to smaller panicles with lower numbers of seeds compared with the rice variety HS representing the local population with extremely early heading date (**Table 3**). The short generation time, small plant architecture, high propagation, and easy cultivation are major advantages for a model variety/line in plant species. In particular, varieties/lines with small plant size and fast heading date may be suitable for model genetic systems in plant/crop research. Here, we described the development of a faster heading date rice line, which included pyramiding of five genes for earlier heading date by marker-assisted selection. The five alleles additively and epistatically acted on early heading date.

Rice varieties/lines with DATTO5 may be a useful tool in rice functional genomics due to its fast heading date and small stature. Furthermore, the phenotype of DATTO5 may have advantages as an educational tool and for food production in restricted spaces. DATTO5 might be useful for rice functional genomics similar to the rice variety Kitaake (Guotian *et al.* 2017, Kim *et al.* 2013, Rodrigues *et al.* 2013).

Rice is a major crop for human use. If global warming proceeded and the duration for rice growing seasons were expanded, *dth8* and DATTO5 might be turning useful for practical rice production in the future. The lower fitness found in *dth8* and DATTO5 under the current climatic conditions needs to be improved through the breeding of QTLs for yield-related traits (Wang *et al.* 2019, Xing and Zhang 2010, Gramene; http://www.gramene.org). Expression of the phenotype including heading date and yield results from interactions between genotype and environmental conditions where the plants are grown. The rice varieties/lines selected for local environmental conditions may have suitable heading date with fitness.

Author Contribution Statement

Conceived and designed the experiments and wrote the manuscript: KF. Performed the experiments and analyzed the data: KF, TI. Approved the final manuscript: KF, TI.

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