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Homoeologous Recombination: A Novel and Efficient System for Broadening the Genetic Variability in Wheat

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Abstract: Gene transfer from wild wheat relatives to bread wheat is restricted to homologous recombination. The presence of the Pairing homoeologous 1 (*Ph1*) gene in the long arm of wheat chromosome 5B allows only homologous chromosomes to pair and recombine, resulting in diploid inheritance of polyploid wheat. Previously, we identified a potent homoeologous pairing promotor gene(s) (*Hpp-5M^g*); its carrier chromosome 5M^g derived from *Aegilops geniculata* and its wheat homoeologous chromosome 5D freely recombined in the presence of the *Ph1* gene. In this study, we investigated the effect of *Hpp-5M^g* on homoeologous recombination in the absence of *Ph1*. In *Hpp-5M^g/ph1bph1b* plants, we observed a vast genome-wide increase in homoeologous recombination and multiple crossovers (CO), including CO breakpoints in proximal regions of the chromosomes where recombination is known to be suppressed. We tested the efficacy of *Hpp-5M^g/ph1bph1b*-induced homoeologous recombination by producing new recombinants for the wheat streak mosaic virus resistance gene, *Wsm3*, present in the wheat-*Thinopyrum intermedium* Robertsonian translocation (RobT T7BS.7S#3L). A recombination frequency of 6.5% was detected by screening the progenies double monosomic for T7BS.7S#3L and 7B by genomic in situ hybridization. This recombination frequency was about 100-fold higher compared with the recombinant frequency of 0.06% observed by using *ph1b*-induced homoeologous recombination alone. Our results indicate that chromosome 5M^g promotes homoeologous recombination between wheat and wild wheat relative chromosomes, which helps in the generation of pre-breeding materials thereby accelerating wheat crop improvement.

Keywords: bread wheat; *pairing homoeologous 1* (*Ph1*); homoeologous pairing promoter; homoeologous recombination; genomic in situ hybridization

1. Introduction

Bread wheat, *Triticum aestivum* L., is an allohexaploid species (2n = 6x = 42, genomes AABBDD) and its 16 Gb genome is one of the largest among crop plants. In perspective, a single wheat chromosome is twice the size of the entire rice genome. Wheat is the most important staple food worldwide providing more than 20% of the protein and calorie requirement of humans, occupying more acreage than any other food crop in the world. Bread wheat originated less than 10,000 years ago from the hybridization events between tetraploid emmer wheat (*T. turgidum* subsp. *dicoccum*, (Schrank ex Schübler) Thell., 2n = 4x = 28, genomes AABB) and *Aegilops tauschii* Coss. (2n = 14, genome DD) in a farmer's field (reviewed in Huang et al. [1]). This recent origin and sparse sampling of gametes during its origin could be attributed to the narrow genetic base that limits the genetic variability in wheat.

The success of gene transfer from wheat's wild relatives to bread wheat largely depends on the evolutionary distance of the species involved. Species belonging to the primary gene pool of wheat

share completely homologous genomes. This group includes landraces of *T. aestivum*, landraces and wild strains of *T. turgidum* and the D-genome wild ancestor *Ae. tauschii*. Gene transfers from these species are achieved easily by direct hybridization and homologous recombination. The A-genome species *T. monococcum* L. and *T. urartu* Tumanian ex Gandilyan share homology for six of the seven A-genome chromosomes except 4A of polyploid wheats, which is highly rearranged and does not pair with any chromosome of diploid wheats (for review, see [2]).

The secondary gene pool of wheat includes polyploid *Triticum/Aegilops* species that have at least one homologous genome in common with common bread wheat. If the target gene(s) is located on homologous chromosomes, it also can be transferred easily by homologous recombination. Species belonging to the tertiary gene pool are more distantly related and represent a large reservoir of agronomically useful genes that can be exploited in wheat improvement, including genes conferring resistance to biotic and abiotic stress tolerance (reviewed in Jiang et al. [3]; Friebe et al. [4]). However, their chromosomes are not homologous to wheat chromosomes but more distantly related homoeologous chromosomes. Therefore, the gene transfer from these species to wheat cannot be achieved by homologous recombination. Meiotic pairing analysis of wide hybrids showed that wild relative and wheat homoeologous chromosomes failed to pair and recombine because of stringent homoeologous pairing recombination barriers [3,5].

Wheat aneuploid analysis [6] provided the first major breakthrough in mapping genes that control homologous and homoeologous chromosome pairing and recombination in wheat (reviewed in Sears [7]). This led to the identification of a major pairing homoeologous gene (*Ph1*) in the long arm of chromosome 5B [8,9] that suppresses homoeologous pairing and ensures strict homologous chromosome pairing and diploid inheritance in hexaploid wheat. A second suppressor of homoeologous recombination in wheat, *Ph2*, also has been identified, which is less effective than *Ph1* [10]. The *Ph2* gene locus has many co-segregating genes, among them the DNA mismatch repair gene *TaMSH7* is considered as a promising candidate for *Ph2* [11]. Deletion of the *Ph1* gene in the mutant stock *ph1b* [12] allows homoeologous pairing to occur, leading to recombination among chromosomes of wheat and distantly related species permitting limited gene transfer and has been widely used for manipulation of homoeologous recombination and crop improvement [2,4,13–15]. However, the frequency of *ph1b*-induced homoeologous recombination is low and is usually restricted to distal chromosome regions because recombination is suppressed in proximal regions of chromosomes [2].

Earlier, we reported that chromosome $5M^g$ of *Ae. geniculata* Roth. (2n = 4x = 28, $U^gU^gM^gM^g$) escapes the diploid pairing control and freely recombines with homoeologous chromosomes of wheat in the presence of *Ph1*, even in proximal chromosome regions where recombination is usually suppressed [16,17]. We further showed that $5M^g$ harbors homoeologous pairing promotor gene(s) (*Hpp-5M^g*) in proximal regions of the short or long arm spanning the centromere [17]. In the present study, we investigated the effect of *Hpp-5M^g* on homoeologous recombination in the absence of *Ph1*. In *Hpp-5M^g/ph1bph1b* plants we observed a vast genome-wide increase in homoeologous recombination and multiple crossing-over (CO) breakpoints including those in the proximal regions, where COs are known to be suppressed. We tested the efficacy of *Hpp-5M^g/ph1bph1b*-induced homoeologous recombination by producing new recombinants for wheat streak mosaic virus resistance gene, *Wsm3* present in the wheat-*Thinopyrum intermedium* (Host) Barkworth and D.R. Dewey Robertsonian translocation, RobT T7BS.7S#3L [18]. Genomic in situ hybridization (GISH)-based progeny screening of *Hpp-5M^g/ph1bph1b* genotypes double monosomic for T7BS.7S#3L/7B identifies 6.5% wheat-*Th. intermedium* recombinants. This is a 100-fold increase in induced homoeologous recombinant frequency compared to 0.06% observed by using *ph1b* alone [18]. Our results indicate that chromosome $5M^g$ promotes homoeologous recombination between wheat and wild wheat relative chromosomes, which can greatly accelerate gene transfers from distantly related species to wheat.

2. Materials and Methods

2.1. Plant Material and Chromosome Preparations

The cytogenetic stocks and hybrid plants used in this study are listed in Table 1. Chromosome $5M^g$ was transferred to wheat from two different *Ae. geniculata* accessions and, thus, have been designated as $5M^g$#1 and $5M^g$#2. $5M^g$#1 is a complete *Ae. geniculata* chromosome whereas $5M^g$#2 has a tiny segment of 5D of wheat at the telomeric region of the long arm [17]. In the present study, all experiments were performed with $5M^g$#1.

Table 1. Cytogenetic stocks used for studying homoeologous recombination in wheat.

Accession	Chromosome Number	Chromosome Constitution	Description
TA6708	42	DS$5M^g$#1(5D)	One pair of 5D of wheat substituted by a pair of $5M^g$#1 from *Ae. geniculata*, TA1800
TA3809	42	*Ph1* mutation	Deletion mutant of *Ph1* locus induced by X-ray irradiation
TA5624	42	T7BS-7S#3L	One pair of wheat-*Th. intermedium* translocation chromosome, involving 7BS of wheat and 7S#3L of *Th. intermedium* substituting for chromosome 7B of wheat

For chromosome preparations, the seeds were germinated in petri dishes on moist filter paper. Root tips (1–2 cm long) were incubated overnight in ice water. The root tips were fixed overnight in an ethanol:glacial acetic acid (3:1) and the fixed root tips were squashed in a drop of 45% acetic acid [19]. All slides were stored at −70 °C until use.

2.2. Genomic In Situ Hybridization (GISH)

Genomic DNAs of parental genomes were used as probes (Table S1). Total genomic DNAs from *T. urartu* (A genome), *Ae. tauschii* (D genome) and *Ae. comosa* Sm. in Sibth. and Sm. (M genome) were isolated using a Qiagen DNeasy Plant Mini Kit (Qiagen Inc., Valencia, CA, USA) following manufacturer's instructions. The DNA concentration of each sample was quantified using a NanoDrop® 1000 spectrophotometer (Thermo Fisher Scientific, Walthem, MA, USA). Approximately 1 µg of genomic DNA of each species was labeled with either digoxigenin-11-dUTP or biotin-16-dUTP according to the manufacturer's instructions (Roche, Indianapolis, IN, USA). Probes were purified with the QIAquick nucleotide removal kit (Qiagen Inc., Valencia, CA, USA). The GISH hybridization solution contains 50% formamide, 10% dextran sulfate, 2× SSC, 2 µg/mL of each of 2 labeled genomic DNA probes, and unlabeled total genomic DNA of wheat as a blocker. The probe:blocker ratio was about 1:50. After post-hybridization washes, the probes were detected with Alexafluor 488 streptavidin (Invitrogen, Grand Island, NY, USA) for biotin-labeled probes, and rhodamine-conjugated anti-digoxigenin (Roche) for dig-labeled probes. Chromosomes were counterstained with 4',6-diamidino-2-phenylindole (DAPI) in Vectashield antifade solution (Vector Laboratories, Burlingame, CA, USA). The images were captured with a Zeiss Axioplan 2 microscope using a cooled CCD camera CoolSNAP HQ2 (Photometrics, Tucson, AZ, USA) and AxioVision 4.8 software (Carl Zeiss Microscopy LLC, Thornwood, NY, USA). The final contrast of the images was processed using Adobe Photoshop CS5 software (Adobe, San Jose, CA, USA).

3. Results

3.1. Homoeologous Recombination in the Presence of $5M^g$ and Absence of Ph1

Previously, we identified chromosome $5M^g$ from *Ae. geniculata*, which escapes the diploid pairing control and freely recombines with 5D of wheat in the presence of *Ph1*, even in proximal chromosome regions where recombination is usually suppressed [17]. In this study, we investigated homoeologous

recombination of wheat in the presence of 5M^{g} and absence of *Ph1*. We crossed the *ph1b* mutant stock with the DS5M^{g}#1(5D) substitution line and then selected plants homozygous for *ph1b* and double monosomic for 5M^{g}#1 and 5D (Table 1). The recombination frequency was determined in the 57 self-progeny plants by GISH. Surprisingly, we observed 63 recombinant chromosomes between 5M^{g}#1 and 5D, or between 5M^{g}#1 and 5A or 5B. In the 57 plants analyzed, the observed homoeologous recombination frequency was higher than 100% (Figure 1), including plants that contained more than one recombinant chromosome. The recombinant frequency of the same cross in the presence of *Ph1* was 10% (11 recombinants out of 110 progenies screened) [17].

The GISH patterns of the 5M^{g}#1/5D recombinants revealed that 46 recombinants had more than two CO breakpoints per chromosome arm. Up to five CO sites were detected in two recombinant chromosomes (Figure 1b). In addition, we also observed recombinant chromosomes between D-genome and A- or B-genome chromosomes (Figure 1a and Figure S1). Recombinants with multiple COs and COs in the proximal regions were also detected (Figure 1a and Figure S1). In *ph1b* mutants, homoeologous CO breakpoints were restricted to distal region in few chromosomes with 2.0 ± 0.82 (n = 10) frequency of intergenomic exchanges per plant, and recombinants with multiple COs and CO in proximal region were not detected (Figure 2). Overall, these results support our previous hypothesis that chromosome 5M^{g} harbors homoeologous pairing promotor gene(s) (*Hpp-5M^{g}*) [17] that affect homoeologous recombination and CO interference, and this effect is more pronounced in the absence of the *Ph1* gene.

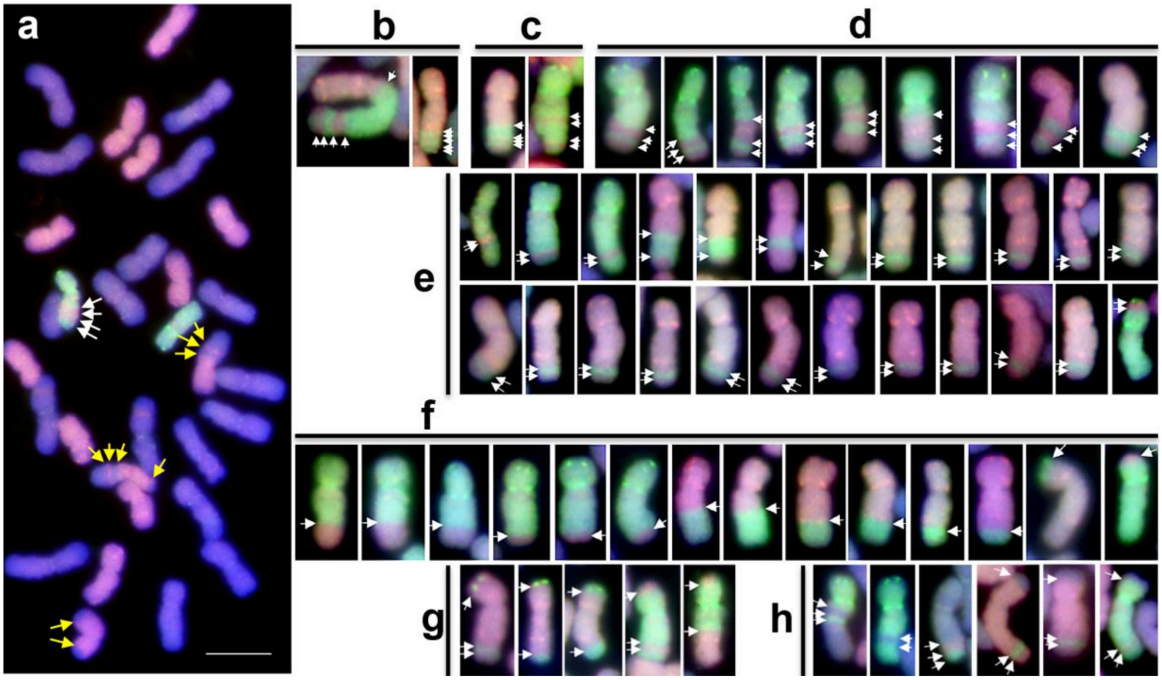

Figure 1. Genomic in situ hybridization (GISH)-based identification of recombinant chromosomes derived from plants with 5M^{g}#1 and without *Ph1* (*Hpp-5M^{g}/ph1bph1b*). (**a**) A partial mitotic metaphase cell having 4 recombinant chromosomes derived from homoeologous recombination between 5Mg#1 and 5D (white arrows), and between the wheat subgenomes (yellow arrows). (**b**–**f**) Recombinants with five (**b**), four (**c**), three (**d**), two (**e**), and one CO sites (**f**); (**g**) recombinants with COs in both the short and long arm; (**h**) recombinants derived from multiple homoeologous recombination events between 5M^{g}#1 and 5D, 5A, and 5B of wheat. A total of 63 recombinant chromosomes involving 5M^{g}#1 were identified, out of 57 plants screened. COs sites are indicated by arrows. 5M^{g}#1 is visualized in green, 5D in red, and 5A or 5B in blue fluorescence. Bar = 10 µm.

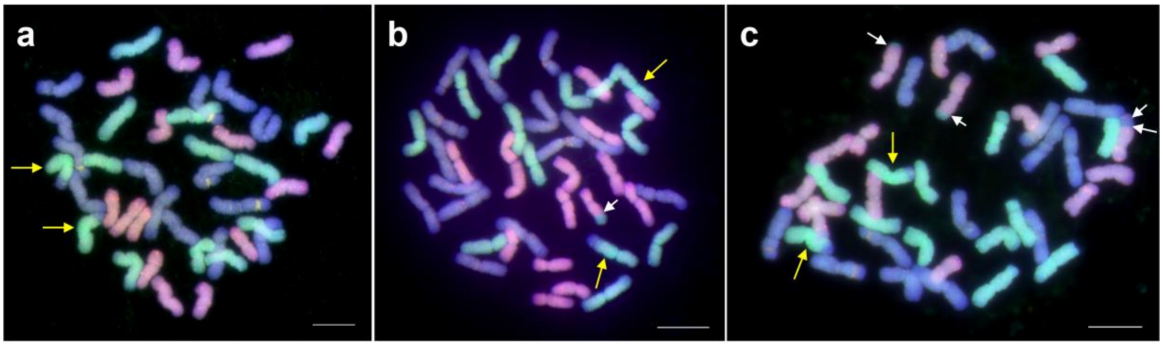

Figure 2. GISH patterns of mitotic metaphase chromosomes in the absence of 5M^g#1 and *Ph1* (*ph1bph1b*). (**a**) No recombinant chromosomes; (**b**) one recombinant chromosome; (**c**) three recombinant chromosomes. White arrows indicate the recombinant chromosomes; A-, D-, and B-genome chromosomes were visualized by green, red, and blue fluorescence, respectively. Recombinants with multiple COs and COs in the proximal region were not detected in 10 *ph1b* mutant plants analyzed. Yellow arrows point to the rearranged chromosome 4A. Bars = 10 μm.

3.2. Potential Use of Chromosome 5M^g in Wheat Improvement

We have studied *ph1b*-induced homoeologous recombination for producing recombinants for the wheat streak mosaic virus resistance gene, *Wsm3*, present in the wheat-*Thinopyrum intermedium* (RobT T7BS.7S#3L). Only one plant out of 1690 plants screened contained a wheat-*Th. intermedium* recombinant chromosome amounting to a recombinant frequency of 0.06% [18]. We tested the efficacy of *Hpp-5M^g/ph1bph1b*-induced homoeologous recombination by producing new recombinants for *Wsm3* present in RobT T7BS.7S#3L. The RobT line was crossed with the *ph1b* stock and the *ph1b* stock was also crossed with the disomic substitution line DS5M^g#1(5D). The F_1s were intercrossed and plants homozygous for *ph1b* and heterozygous for 5M^g were selected along with T7BS.7S#3L. The recombinant frequency was determined in the self-progenies by GISH. Two hundreds plants were screened out of which homoeologous recombination event between the RobT T7BS.7S#3L and chromosome 7B of wheat was detected in 13 plants amounting to a homoeologous recombination frequency of 6.5% (Figure 3). The homoeologous recombination frequency of 6.5% in the 5M^g/*ph1b*, *ph1b* stock was ~100-times greater compared to *ph1b* alone. Importantly, recombinants were recovered that had CO breakpoints in the proximal regions where COs are rarely observed in *ph1b*-induced recombination. Also, recombinants with double COs in interstitial regions were recovered (Figure 3e,f).

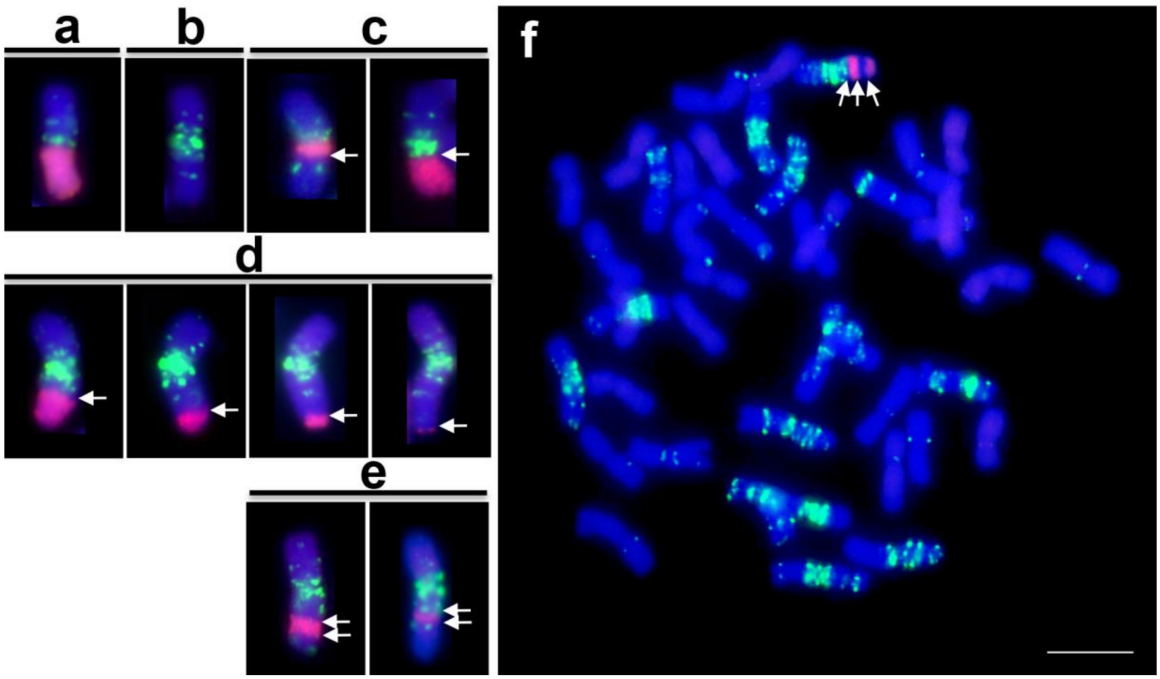

Figure 3. *Hpp-5M^{g}ph1bph1b*-induced homoeologous wheat-*Th. intermedium* recombinants. (**a**) RobT T7BS·7S#3L; (**b**) chromosome 7B; (**c**–**f**) recombinant chromosomes derived from *Hpp-5M^{g}ph1bph1b*-induced homoeologous recombination between (T7BS·7S#3L) and (7B); (**c**) COs in proximal region; (**d**) COs in interstitial and distal regions; (**e**,**f**) recombinants having more than two CO sites. Four recombinants involving translocation at distal region are not shown in the figure. Total genomic DNA of *Th. Intermedium* was used as a probe to detect the *Th. Intermedium* chromatin (red fluorescence). GAA repeats (green fluorescence) were used to identify chromosome 7B of wheat. Bar = 10 µm.

4. Discussion

Gene transfer from distantly related species of the tertiary gene pool to wheat cannot be achieved by homologous recombination because the *Ph1* gene on chromosome arm 5B suppresses homoeologous recombination [8,9]. Previously, we had identified a potent homoeologous pairing promotor gene(s) (*Hpp-5M^g*) and showed that its carrier chromosome 5M^g of *Ae. geniculata* and its wheat homoeologous chromosome 5D freely recombined in the presence of *Ph1* [17]. Similarly, a few studies have shown that homoeologous recombination can occur in the presence of *Ph1* particularly in hybrids between wheat and *Ae. speltoides* Tausch or *Amblyopyrum muticum* (Boiss.) Eig [20–22]. Chromosome 5U in *Ae. umbellulata* Zhuk. [23] and chromosome 5E in *Elytrigia elongata* (Host) Nevski have also been shown to promote recombination between homoeologous chromosomes [24], implying that the activity of *Ph1* in wheat can be suppressed by the genes of wild wheat relatives.

Distal localization of COs/chiasmata is a very common feature of wheat chromosomes and those of its close relatives *Aegilops*, barley, rye, and oat [25]. In wheat and barley, the distal halves of the arms represent nearly the entire length of the genetic maps [26–28]. Molecular cytological analysis using immunuofluorescence of MLH3 (barley MutL homologue, a marker for class-I interfering COs) on pachytene chromosomes of barley also revealed that the distribution of CO events is strongly biased towards the distal chromosomal regions [29]. This bias limits the genetic variability and reduces the efficiency of map-based cloning and breeding approaches in these crops. Hence, identification of a potential route to manipulate COs distribution toward the proximal region would be highly valuable for generating pre-breeding materials for plant breeders and would accelerate crop improvement. In *Hpp-5M^g/ph1bph1b* plants, we found a massive increase in homoeologous recombination and multiple COs per chromosome arm (Figure 1 and Figure S1) including in proximal regions in the chromosomes where COs are never observed even in homologous recombination. Thus,

manipulation of recombination between wheat and its wild relatives can be achieved by using *Hpp-5M^g* in wide crosses.

We tested the efficacy of the *Hpp-5M^g* mechanism by producing new recombinants for the wheat streak mosaic virus resistance gene *Wsm3* present in the wheat-*Th. intermedium* (RobT) T7BS.7S#3L (Figure 3). Progeny screening revealed that 6.5% were wheat-*Th. intermedium* recombinants with CO breakpoints covering the entire length of the *Th. intermedium* chromosome arm (Figure 3c–f), which is about 100-times higher compared to that observed by using the *ph1b* mutant alone. The frequency of *ph1b*-induced recombination is genome and chromosome specific. Friebe et al. [14] reported a frequency of *ph1b*-induced recombinants for the short arm of the *Th. intermedium* chromosome 4J^s of 2% (5 recombinants out of 245 progenies screened), whereas Danilova et al. [18] reported a much lower frequency of *ph1b*-induced recombinants for the wheat-*Th. intermedium* (RobT) 7S#3 (1 recombinant out of 1690 progenies screened, 0.06%). The difference in recombination frequencies observed for the 4J^{s}S and 7SL arms may indicate that the J^s genome has a greater genomic affinity to the B and D genomes of wheat compared to that of the S genome of *Th. intermedium*. However, observations in the cultivated rye, *Secale cereale* L. showed that even different arms of the same chromosome can have drastic differences in *ph1b*-induced recombinants frequencies. Lukaszewski et al. [30] observed recombinant frequency of 0.6% for the short arm and 16.3% for the long arm of rye chromosome 2R. In addition, a higher frequency of 6.7% was also reported for the short arm of rye chromosome 1R [31].

The COs and the process of recombination generate novel combination of parental alleles at each generation and this genetic variability plays a central role in evolution, speciation and selection of improved cultivars in plant breeding [32–36]. Recent studies in *Arabidopsis* meiosis showed that natural variation in CO frequency between different ecotypes was controlled by a procrossover E3 ligase gene *HEI10* [37]. Genotypes with extra copies of *HEI10* had higher CO frequencies in euchromatin but not in pericentromeric heterochromatic regions. It would be interesting to detect the similar pattern of increased copy numbers of *HEI10* gene corresponding to increased CO frequencies in wheat. The quantitative trait loci affecting the recombination frequency in wheat was detected in 6A and 6B at 50.2 and 47.8 cM respectively. *HEI10* is the candidate gene in these regions, which favors the increase in recombination frequencies in wheat [38]. Therefore, it might be intriguing to know that CO frequency in wheat nullisomic-6D-tetrasomic-6A or 6B which will reveal the effect of *HEI10* in increasing in CO frequency of wheat.

The RECQ4A and RECQ4B proteins in *Arabidopsis* are reported to have anticrossover activity [39,40]. Serra et al. [41] generated *Arabidopsis recq4a recq4b* double mutants and combined them with duplicated *HEI10* gene and observed a massive increase in CO frequency in euchromatic chromosome regions, providing a genetic framework for engineering meiotic recombination landscapes in plant genomes [41]. However, recombination remained suppressed in the pericentromeric regions similar to wild-type genotypes. Underwood et al. [42] noticed increased recombination in pericentromeric regions in H3K9me2 and non-CG DNA methylation pathway mutants in *Arabidopsis*. Similar procrossover and anticrossover genes and epigenetic mutants remain to be identified in wheat.

Generally, the presence of one CO in a chromosomal region suppresses the formation of another CO in the nearby regions and this phenomenon is termed as class I CO interference [32]. However, in *Hpp-5M^g/ph1bph1b* plants the phenomenon of class I CO interference is absent resulting in the clustering of several CO events at a close proximity (Figure 1 and Figure S1). In *5M^g/ph1bph1b*-induced homoeologous recombination of the wheat-*Th. intermedium* (RobT) T7BS.7S#3L, we also observed recombinants with double COs in interstitial and proximal regions (Figure 3e,f). This opens the possibility of transferring small desired alien segments from wild species to wheat with reduced linkage drag. Further studies on the molecular cloning of *Hpp-5M^g* gene(s) and its interaction with *Ph1* gene will revolutionize the transfer of desired genes from species of tertiary gene pool to wheat, making it more efficient and also allow the transfer of target genes that are located in interstitial and proximal regions of the chromosomes. We do not know if *Hpp-5M^g* also effects homologous recombination, which is presently under investigation.

Supplementary Materials: The following are available online at http://www.mdpi.com/2073-4395/10/8/1059/s1. Figure S1: Genomic in situ hybridization (GISH)-based identification of recombinant chromosomes derived from plants with 5M^{g}#1 and without *Ph1* (*Hpp-5M^{g}/ph1bph1b*). Table S1: Plant materials used in preparing the chromosome painting probes.

Author Contributions: D.-H.K. performed most of the experiments; D.-H.K., B.F. and B.S.G. wrote the manuscript; D.-H.K., B.F. and B.S.G. designed the experiments and analyzed the data. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflict of interest.

References

1. Huang, S.; Sirikhachornkit, A.; Su, X.; Faris, J.D.; Gill, B.S.; Haselkorn, R.P.; Gornicki, P. Phylogenetic analysis of the acetyl-CoA carboxylase and 3-phosphoglycerate kinase of the *Triticum/Aegilops* complex and the evolutionary history of polyploid wheat. *Proc. Natl. Acad. Sci. USA* **2002**, *12*, 8133–8138. [CrossRef] [PubMed]
2. Qi, L.L.; Friebe, B.; Gill, B.S. Homoeologous recombination, chromosome engineering and crop improvement. *Chromosome Res.* **2007**, *15*, 3–19. [CrossRef]
3. Jiang, J.; Friebe, B.; Gill, B.S. Recent advances in alien gene transfer in wheat. *Euphytica* **1994**, *73*, 199–212. [CrossRef]
4. Friebe, B.; Jiang, J.; Raupp, W.J.; McIntosh, R.A.; Gill, B.S. Characterization of wheat-alien translocations conferring resistance to diseases and pests: Current status. *Euphytica* **1996**, *91*, 59–87. [CrossRef]
5. Molnár-Láng, M.; Linc, G.; Szakács, É. Wheat–barley hybridization: The last 40 years. *Euphytica* **2014**, *195*, 315–329. [CrossRef]
6. Sears, E.R. *Aneuploids of Common Wheat*; Research Bulletin; Missouri Agricultural Experiment Station: Columbia, MO, USA, 1954; Volume 572, p. 59.
7. Sears, E.R. Genetic control of chromosome pairing in wheat. *Annu. Rev. Genet.* **1976**, *10*, 31–51. [CrossRef]
8. Riley, R.; Chapman, V. Genetic control of the cytologically diploid behavior of hexaploid wheat. *Nature* **1958**, *182*, 713–715. [CrossRef]
9. Sears, E.R.; Okamoto, M. Intergenomic chromosome relationship in hexaploid wheat. In Proceeding of the 10th International Congress of Genetics, Montreal, QC, Canada, 20–27 August 1958; pp. 258–259.
10. Mello-Sampayo, T. Genetic regulation of meiotic chromosome pairing by chromosome 3D of *Triticum aestivum*. *Nat. New Biol.* **1971**, *230*, 23–24. [CrossRef]
11. Sutton, T.; Whitford, R.; Baumann, U.; Dong, C.; Able, J.A.; Langridge, P. The *Ph2* pairing homoeologous locus of wheat (*Triticum aestivum*): Identification of candidate meiotic genes using a comparative genetics approach. *Plant J.* **2003**, *36*, 443–456. [CrossRef]
12. Sears, E.R. An induced mutant with homoeologous pairing in common wheat. *Can. J. Genet. Cytol.* **1977**, *19*, 585–593. [CrossRef]
13. Gill, B.S.; Friebe, B.; Raupp, W.J.; Wilson, D.L.; Cox, T.S.; Brown-Guedira, G.L.; Sears, R.S.; Fritz, A.K. Wheat Genetics Resource Center: The first 25 years. *Adv. Agron.* **2006**, *85*, 73–135.
14. Friebe, B.; Qi, L.L.; Wilson, D.L.; Chang, Z.L.; Seifers, D.L.; Martin, T.J.; Fritz, A.K.; Gill, B.S. Wheat-*Thinopyrum intermedium* recombinants resistant to wheat streak mosaic virus and *Triticum* mosaic virus. *Crop Sci.* **2009**, *49*, 1221–1226. [CrossRef]
15. Lukaszewski, A.J. Manipulation of homologous and homoeologous chromosome recombination in wheat. *Methods Mol. Biol.* **2016**, *1429*, 77–89. [PubMed]
16. Liu, W.; Rouse, M.; Friebe, B.; Jin, Y.; Gill, B.S.; Pumphrey, M.O. Discovery and molecular mapping of a new gene conferring resistance to stem rust, *Sr53*, derived from *Aegilops geniculata* and characterization of spontaneous translocation stocks with reduced alien chromatin. *Chromosome Res.* **2011**, *19*, 669–682. [CrossRef]
17. Koo, D.-H.; Liu, W.; Friebe, B.; Gill, B.S. Homoeologous recombination in the presence of *Ph1* gene in wheat. *Chromosoma* **2017**, *126*, 531–540. [CrossRef]

18. Danilova, T.V.; Zhang, G.; Liu, W.; Friebe, B.; Gill, B.S. Homoeologous recombination-based transfer and molecular cytogenetic mapping of a wheat streak mosaic virus and *Triticum* mosaic virus resistance gene *Wsm3* from *Thinopyrum intermedium* to wheat. *Theor. Appl. Genet.* **2017**, *130*, 549–556. [CrossRef]
19. Koo, D.-H.; Sehgal, S.K.; Friebe, B.; Gill, B.S. Structure and stability of telocentric chromosomes in wheat. *PLoS ONE* **2015**, *10*, e0137747. [CrossRef]
20. Riley, R. The diploidization of polyploid wheat. *Heredity* **1960**, *15*, 407–429. [CrossRef]
21. Dover, G.A.; Riley, R. Prevention of pairing of homoeologous meiotic chromosomes of wheat by an activity of supernumerary chromosomes of *Aegilops*. *Nature* **1972**, *240*, 159–161. [CrossRef]
22. Dvorak, J.; Deal, K.R.; Luo, M.-C. Discovery and mapping of wheat *Ph1* suppressors. *Genetics* **2006**, *174*, 17–27. [CrossRef]
23. Riley, R.; Chapman, V.; Miller, T.E. The determination of meiotic chromosome pairing. In Proceedings of the 4th International Wheat Genetics Symposium, Columbia, MO, USA, 6–11 August 1973; pp. 713–738.
24. Dvorak, J. Chromosomal distribution of genes in diploid *Elytriga elongata* that promote or suppress pairing of wheat homoeologous chromosomes. *Genome* **1987**, *29*, 34–40. [CrossRef]
25. Lukaszewski, A.J. Unexpected behavior of an inverted rye chromosome arm in wheat. *Chromosoma* **2008**, *117*, 569–578. [CrossRef] [PubMed]
26. Gill, K.S.; Gill, B.S.; Endo, T.R.; Boyko, E.V. Identification and high density mapping of gene-rich regions in chromosome group-1 of wheat. *Genetics* **1996**, *143*, 1001–1012. [PubMed]
27. Künzel, G.; Korzun, L.; Meister, A. Cytologically integrated physical restriction fragment length polymorphism maps for the barley genome based on translocation breakpoints. *Genetics* **2000**, *154*, 397–412. [PubMed]
28. Saintenac, C.; Falque, M.; Martin, O.C.; Paux, E.; Feuillet, C.; Sourdille, P. Detailed recombination studies along chromosome 3B provide new insights on crossover distribution in wheat (*Triticum aestivum* L.). *Genetics* **2009**, *181*, 393–403. [CrossRef]
29. Phillips, D.; Wnetrzak, J.; Nibau, C.; Barakate, A.; Ramsay, L.; Wright, F.; Higgins, J.D.; Perry, R.M.; Jenkins, G. Quantitative high resolution mapping of HvMLH3 foci in barley pachytene nuclei reveals a strong distal bias and weak interference. *J. Exp. Bot.* **2013**, *64*, 2139–2154. [CrossRef]
30. Lukaszewski, A.J.; Rybka, K.; Korzun, V.; Malyshev, S.V.; Lapinski, B.; Whitkus, R. Genetic and physical mapping of homoeologous recombination points involving wheat chromosome 2B and rye chromosome 2R. *Genome* **2004**, *47*, 36–45. [CrossRef]
31. Mercier, R.; Mézard, C.; Jenczewski, E.; Macaisne, N.; Grelon, M. The molecular biology of meiosis in plants. *Annu. Rev. Plant Biol.* **2015**, *66*, 297–327. [CrossRef]
32. Lukaszewski, A.J. Manipulation of the 1RS.1BL translocation in wheat by induced homoeologous recombination. *Crop Sci.* **2000**, *40*, 216–225. [CrossRef]
33. Wijnker, E.; de Jong, H. Managing meiotic recombination in plant breeding. *Trends Plant Sci.* **2008**, *13*, 640–646. [CrossRef]
34. Lambing, C.; Franklin, F.C.H.; Wang, C.-J.R. Understanding and manipulating meiotic recombination in plants. *Plant Physiol.* **2017**, *173*, 1530–1542. [CrossRef] [PubMed]
35. Lambing, C.; Heckmann, S. Tackling plant meiosis: From model research to crop improvement. *Front. Plant Sci.* **2018**, *9*, 1–15. [CrossRef]
36. Wang, Y.; Copenhaver, G.P. Meiotic recombination: Mixing it up in plants. *Annu. Rev. Plant Biol.* **2018**, *69*, 577–609. [CrossRef] [PubMed]
37. Ziolkowski, P.A.; Underwood, C.J.; Lambing, C.; Martinez-Garcia, M.; Lawrence, E.J.; Ziolkowska, L.; Griffin, C.; Choi, K.; Franklin, F.C.H.; Martienssen, R.A.; et al. Natural variation and dosage of the HEI10 meiotic E3 ligase control *Arabidopsis* crossover recombination. *Genes Dev.* **2017**, *31*, 306–317. [CrossRef] [PubMed]
38. Jordan, K.W.; Wang, S.; He, F.; Chao, S.; Lun, Y.; Paux, E.; Sourdille, P.; Sherman, J.; Akhunova, A.; Blake, N.K.; et al. The genetic architecture of genome-wide recombination rate variation in allopolyploid wheat revealed by nested association mapping. *Plant J.* **2018**, *95*, 1039–1054. [CrossRef]
39. Seguela-Arnaud, M.; Crismani, W.; Larcheveque, C.; Mazel, J.; Froger, N.; Choinard, S.; Lemhemdi, A.; Macaisne, N.; van Leene, J.; Gevaert, K.; et al. Multiple mechanisms limit meiotic crossovers: TOP3α and two BLM homologs antagonize crossovers in parallel to FANCM. *Proc. Natl. Acad. Sci. USA* **2015**, *112*, 4713–4718. [CrossRef]

40. Seguela-Arnaud, M.; Choinard, S.; Larcheveque, C.; Girard, C.; Froger, N.; Crismani, W.; Mercier, R. RMI1 and TOP3α limit meiotic CO formation through their C-terminal domains. *Nucleic Acids Res.* **2017**, *45*, 1860–1871. [CrossRef]
41. Serra, H.; Lambing, C.; Griffin, C.H.; Topp, S.D.; Nageswaran, D.C.; Underwood, C.J.; Ziolkowski, P.A.; Sequela-Arnaud, M.; Fernandes, J.B.; Mercier, R.; et al. Massive crossover elevation via combination of *HEI10* and *recq4a recq4b* during Arabidopsis meiosis. *Proc. Natl. Acad. Sci. USA* **2018**, *115*, 2437–2442. [CrossRef]
42. Underwood, C.J.; Choi, K.; Lambing, C.; Zhao, X.; Serra, H.; Borges, F.; Simorowski, J.; Ernst, E.; Jacob, R.; Henderson, I.R.; et al. Epigenetic activation of meiotic recombination near *Arabidopsis thaliana* centromeres via loss of H3K9me2 and non-CG DNA methylation. *Genome Res.* **2018**, *28*, 1–13. [CrossRef]