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Wheat genomic study for genetic improvement of traits in China

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Bread wheat (*Triticum aestivum* L.) is a major crop that feeds 40% of the world's population. Over the past several decades, advances in genomics have led to tremendous achievements in understanding the origin and domestication of wheat, and the genetic basis of agronomically important traits, which promote the breeding of elite varieties. In this review, we focus on progress that has been made in genomic research and genetic improvement of traits such as grain yield, end-use traits, flowering

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regulation, nutrient use efficiency, and biotic and abiotic stress responses, and various breeding strategies that contributed mainly by Chinese scientists. Functional genomic research in wheat is entering a new era with the availability of multiple reference wheat genome assemblies and the development of cutting-edge technologies such as precise genome editing tools, high-throughput phenotyping platforms, sequencing-based cloning strategies, high-efficiency genetic transformation systems, and speed-breeding facilities. These insights will further extend our understanding of the molecular mechanisms and regulatory networks underlying agronomic traits and facilitate the breeding process, ultimately contributing to more sustainable agriculture in China and throughout the world.

Key words: wheat, genomics, genetic improvement, China

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Introduction

Bread wheat is one of the first crops to be domesticated, and has been a staple food for humans for thousands of years. Wheat is now the most widely grown crop throughout the world, with a trade value greater than all other crops combined (Curtis, 2019). Wheat is also a source of micronutrients and dietary fiber; it contains minerals, vitamins, and fats (Shiferaw et al., 2013; Lafiandra et al., 2014). Wheat originated from a small area within the Fertile Crescent, later expanding to diverse environments around the globe (Salamini et al., 2002). Bread wheat is an allohexaploid species, comprising A, B, and D subgenomes. It originated from two successive rounds of polyploidization within the genera *Triticum* and *Aegilops*, forming tetraploid wheat (AABB) and hexaploid wheat (AABBDD), respectively (IWGSC, 2014) (Figure 1A). Polyploidization through fusion of genomes from different environments broadened the adaptability of bread wheat; however, this process, combined with a domestication bottleneck, severely reduced genetic diversity (Akhunov et al., 2010; Dubcovsky and Dvorak, 2007). Human selection for agronomic traits resulted in a general convergence of adaptations at the global level, with variation remaining in some specific characteristics to optimize fitness for different growth regions. The mechanisms of wheat evolution, speciation, and domestication therefore hold great interest for both basic and applied research purposes.

Recent advances in DNA sequencing technology, data analysis algorithms, and pipelines for assembling genomes have greatly facilitated understanding of large crop genomes, especially of wheat (Brenchley et al., 2012). The genomes of the ancestral wheat species *Triticum urartu* (AA) and *Aegilops tauschii* (DD) and of potential candidates for the B genome progenitor have been assembled since 2013 (Jia et al., 2013; Li et al., 2022a; Ling et al., 2013; Luo et al., 2013). Since then, wheat genomes with different ploidy levels have been assembled and released, including those of wild emmer, durum wheat, and multiple varieties of hexaploid wheat (Avni et al., 2017; Guo et al., 2020; IWGSC, 2014; IWGSC, 2018; Ling et al., 2018; Maccaferri et al., 2019; Sato et al., 2021; Walkowiak et al., 2020). A population-wide re-sequencing strategy has also been used to characterize introgression among wheat cultivars with different ploidy levels, yielding insights into environmental adaptation and the selection effects of modern breeding (Guo et al., 2020; Hao et al., 2020a; He et al., 2019; Zhou et al., 2020). The *Triticum* genus is a rich source of genetic diversity for sustained wheat improvement, comprising gene pools of different degrees. Recently, genome assemblies have been released for other species in the *Triticeae* tribe (Avni et al., 2022; Bauer et al., 2017; Chen et al., 2020c; Gao et al., 2021a), which could further accelerate the identification of elite genes/alleles and their application in wheat improvement.

Wheat is a major staple food in China, which currently leads the world in both production and consumption of wheat; approximately 17% of the world's wheat production is made in China (FAO, 2018) (Figure 1B). However, China still imports wheat from the United States, Canada, and Australia (data from General Administration of Customs, China). This is largely due to the need for high-quality wheat for specialized end-use products. Flour demands increase each year for an ever-wider range of end uses as living standards rise in China. Research has been undertaken to clarify the regulation of gluten accumulation and starch biosynthesis (the two major components that determine the end-use value of wheat flour) with respect to both abundance and quality (Liu et al., 2021). Such discoveries provide useful targets for modification of gluten function, allowing diversification of end-use properties through breeding practices.

The average wheat yield in China increased from 1840.5 kg ha^{-1} in 1978 to 5740.5 kg ha^{-1} in 2021, which is ~1.6 times of the current global average (United States Department of Agriculture). Two major breakthroughs in breeding have contributed to the sharp increase in average wheat yield over the past half century. First was the Green Revolution, which saw the rise of dwarf plant breeding, and the second was distant hybridization between wheat and wild

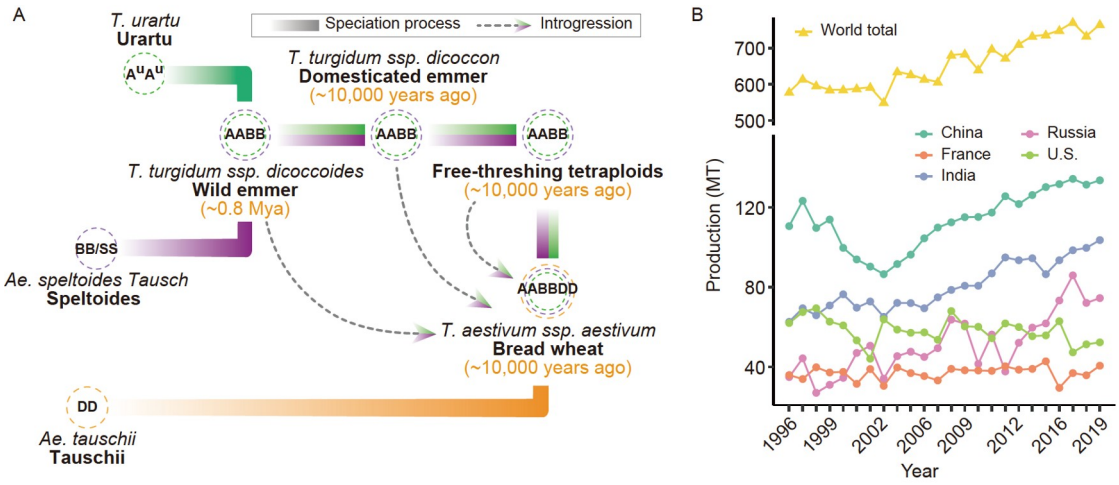

Figure 1 Speciation and production of hexaploid wheat. A, The speciation of bread wheat from polyploidization and introgression of ancestral species. B, Annual wheat production for global and the top five countries in the last fifteen years. MT: Millions of tons.

relatives (Gale et al., 1985; Gupta, 2016; Molnár-Láng et al., 2015). Recent progress has been made in identifying the *Reduced height* (*Rht*) Green Revolution genes, including both gibberellic acid (GA)-sensitive and GA-insensitive loci (McIntosh et al., 2020; Zhao et al., 2018). In addition to reducing plant height, some *Rht* loci also affect inflorescence architecture and thus affect grain yield (Mo et al., 2018; Tian et al., 2017). Better understanding of *Rht* loci can provide novel genetic resources for dwarf breeding applications, further increasing yield. To overcome the genetic bottleneck effect resulting from domestication and breeding, distant hybridization between wheat and wild relatives has been used for agronomic trait improvement (Molnár-Láng et al., 2015). Chinese scientists have made remarkable progress in generating elite varieties from wheat-alien hybrids. For example, Xiaoyan 6 was derived from hybridization between wheat and *Thinopyrum ponticum* (Li, 2018); it has excellent yield and resistance to disease and drought stress. Elite agronomic traits from rye, *Aegilops ventricosa*, *Agropyron cristatum*, and other wild relatives have also been transferred to wheat (Gao et al., 2021a; Gupta, 2016; Zhang et al., 2019d; Zhao and Bao, 1995). With the release of additional *Triticeae* genomes and rapid development of biological technologies, more elite gene resource from wild relatives could be efficiently introduced into the breeding process to improve yield and other agronomic traits.

Yield is a complex, polygenic, and quantitative trait composed of multiple elements, including effective tiller number, grain number per spike (GN), and grain weight. Many factors have been determined to affect yield using two main approaches: reverse genetics (e.g., studies of homologs in rice [*Oryza sativa*] and *Arabidopsis thaliana*) and forward genetics (e.g., biparental linkage analysis or genome-wide association study/studies [GWAS]) (Xiao et al., 2021; Yu et al., 2019). These approaches not only illustrate the underlying molecular mechanisms that govern yield traits in wheat, but also uncover elite alleles for breeding. Aside from genetic factors, yield performance can also be improved by application of fertilizers such as nitrogen (N), phosphorous (P), and potassium (K). However, fertilizer utilization increases farming costs, and over-fertilization has serious negative environmental impacts; this is particularly true in wheat cultivation in China. Thus, breeding of wheat varieties with high nutrient use efficiency is an urgent requirement. Several key determinants of nutrient use efficiency have been identified through quantitative trait locus (QTL) mapping, GWAS, and reverse genetic approaches (Lei et al., 2018; Qu et al., 2015; Ryan et al., 2015; Shao et al., 2017; Wang et al., 2013); most loci are linked to regulation of root development under different nutrient conditions. Modification of factors involved in nutrient uptake, assimilation, and redistribution could significantly improve nutrient use efficiency (Guttieri et al., 2017; He et al., 2015; Li et al., 2021e; Yang et al., 2019). As novel elite alleles for genes in nutrient utilization pathways are identified, wheat varieties with high nutrient use efficiency can be developed.

Flowering time is an important environmental adaptation that influences yield. Seasonal change of temperature is one of the main factors regulating heading date (Chouard, 1960; Shrestha et al., 2014). Wheat varieties are generally categorized as winter or spring wheat, based on whether they require long-term cold exposure prior to flowering (vernalization). Decades of effort have uncovered numerous genes that are known to separately mediate vernalization requirements, low temperature perception, signaling transduction, maintenance of vernalized status, and resetting the vernalization requirement between generations. Examples of such genes in cereals include *VERNALIZATION-Related 2* (*VER2*), *VERNALIZATION1* (*VRN1*), and *Glycine-rich RNA binding Protein* 2 (*TaGRP2*) (Luo and He, 2020; Xu and

Chong, 2018). Comparison of the regulatory mechanisms that control vernalization between species will extend our understanding of wheat adaptations and provide potential gene resources to meet the threats posed by global warming.

The long growing period of wheat, particularly winter wheat, increases the chances of exposure to environmental stresses such as diseases and pests (Gong et al., 2020; Lobell and Tebaldi, 2014). Drought, turbulent temperatures, and soil salinity are examples of abiotic stresses that impact wheat production (Gong et al., 2020). These stressors are becoming more severe due to global climate change. Identification of the genes responsible for tolerance to drought, high and low temperatures, and salinity will enable breeding of environmentally adaptable, resilient varieties. Understanding the signaling pathways that balance growth and stress tolerance will contribute to the goal of breeding resilient crops (Langridge and Reynolds, 2021; Tian et al., 2020; Wang et al., 2018d). Wheat production is constantly threatened by various diseases and pests, such as rust diseases, powdery mildew, Fusarium head blight/scab (FHB), aphids, Hessian flies (*Mayetiola destructor*), and orange wheat blossom midge (OWBM) (*Sitodiplosis mosellana*). Remarkable progress has been made in cloning genes that confer resistance to several diseases and the avirulence (Avr) proteins of the corresponding pathogens (Ma et al., 2020; Wang et al., 2020b). For known resistance genes or loci, marker-assisted selection (MAS) has been widely employed in breeding programs to improve disease resistance with great success. Recently, a notable breakthrough was made with the targeted deletion of a large region containing the susceptibility gene *mildew resistance locus O* (*TaMlo*) using clustered regularly interspaced short palindromic repeat (CRISPR)-mediated genome editing; furthermore, the local chromatin structure was altered to activate a flanking gene, *TaTMT3*, generating broad resistance to powdery mildew without yield penalty (Li et al., 2022b). This breakthrough and breeding successes at the International Maize and Wheat Improvement Center (CIMMYT) have provided new breeding strategies to promote high yield and broad-spectrum disease resistance.

Early in the 21st century, the rice genome sequence was released, and development of systems for mutant library generation and transformation were underway. This led to an explosion of greatly successful rice functional genomics studies by scientists from China and around the world over the past 15 years. These advances also drove continual improvements in the rice breeding process, such as molecular module breeding and molecule design, which have contributed to food security in China (Chen et al., 2022). There have since been advances in wheat genome sequencing, increased availability of large germplasm collections, generation of multiple types of mutant libraries, upgraded gene cloning strategies, new genome editing tools, development of high-efficiency transformation systems (Debernardi et al., 2020b; Wang et al., 2019a; Wang et al., 2022a), speed-breeding facilities (Watson et al., 2018), and precise, large-scale phenotyping platforms (Zhou et al., 2021). These factors portend the beginning of a "golden age" of gene functional studies in wheat, comparable to that of rice research over the past decade and a half.

We here review the research achievements in wheat genomics and molecular biology over the past several decades, focusing on eight areas. Furthermore, we propose future directions for functional genomic studies and breeding of sustainable wheat varieties.

Wheat genomics and domestication

A reference genome is the foundation for genetic and gene functional studies in any species. Wheat genomes are relatively large compared with other major cereal crops; diploid einkorn wheat is ~5.0 gigabases (Gb), tetraploid emmer is >10 Gb, and hexaploid bread wheat is ~16 Gb. Wheat genomes are also complex in composition, with more than 80% of each genome comprising repetitive DNA sequences. Sequencing and assembly of whole wheat genomes are therefore challenging. However, significant progress has been made over the last decade in generating accurate wheat genome assemblies. A series of reference-quality pseudomolecule genome assemblies have now been published for bread wheat, durum wheat, diploid wheat progenitors (*T. urartu* and *Ae. tauschii*), the tetraploid progenitor (*Triticum turgidum* ssp. *dicoccoides*), and other related species (Table 1).

Genomes of diploid wheat progenitors

For the wheat A genome progenitor *T. urartu*, a draft genome was generated using a whole-genome shotgun sequencing strategy on the Illumina HiSeq 2000 platform (Ling et al., 2013). Later, a chromosome-scale, high-quality reference genome was generated for *T. urartu* with an integrated strategy, including bacterial artificial chromosome (BAC)-to-BAC sequencing, single molecule real time whole-genome shotgun sequencing, linked reads, and optical mapping (Ling et al., 2018). Based on the estimated genome size of 4.94 Gb, 98.4% (4.86 Gb) of the *T. urartu* genome has been sequenced and assembled. Of the assembled sequences, 81.2% were annotated as transposable elements (Table 1). Furthermore, 37,516 high-confidence and 3,991 low-confidence genes were predicted, with an average transcript length of 1,453 bp and an average protein length of 332 amino acids (Ling et al., 2018).

For the wheat D genome progenitor *Ae. tauschii*, the accession AL8/78 was selected for genome sequencing and analysis. Luo et al. (2013) fingerprinted 461,706 BAC clones and constructed a 4.03 Gb physical map. Jia et al. (2013)

Table 1 Species and varieties sequenced in the genus of *Triticum* and its relatives

Species	Varieties/ accession	Genome type	Chr. No.	Genome size (Gb)	Gene No.	TE (%)	Proportion of Gypsy/Copia/ CACTA (%)	IT LTR-RT (Mya)	Ass. quality	References
T. urartu	PI428198	AA	7	4.94	41,507	81.4	42.7/24.3/5.0	1	Ref.	Ling et al., 2018
Ae. taushii	AL8/78	DD	7	4.36 4.31	39,622 42,828	84.4 85.9	40.8/16.1/10.8 38.3/16.5/16.8	NA 1	Ref. Ref.	Luo et al., 2017; Zhao et al., 2017
T. turgidum ssp. *dicoccoides*	Zavitan	BBAA	14	12	65,012	82.2	32.4/16.5/11.0	1.4	Chr-scale	Avni et al., 2017
T. turgidum ssp. *durum*	Svevo	BBAA	14	10.45	66,559	82.2	32.5/16.4/10.9	NA	Chr-scale	Maccaferri et al., 2019
T. aestivum	Chinese Spring	BBAADD	21	15.8	107,891	84.7	46.7/16.7/15.5	1	Ref.	IWGSC, 2014; IWGSC, 2018
	Norin 61	BBAADD	21	14.8	118,734	81.3	NA	NA	Ref.	Walkowiak et al., 2020
	Jagger	BBAADD	21	14.5	119,461	81.3	NA	NA	Ref.	
	Julius	BBAADD	21	14.4	119,135	81.3	NA	NA	Ref.	
	Arina*LrFor*	BBAADD	21	14.6	120,967	81	NA	NA	Ref.	
	SY Mattis	BBAADD	21	14.9	120,827	80.8	NA	NA	Ref.	
	LongReach Lancer	BBAADD	21	14.3	120,045	81	NA	NA	Ref.	
	CDC Stanley	BBAADD	21	14.5	119,377	81.4	NA	NA	Ref.	
	CDC Landmark	BBAADD	21	14.4	119,027	81.4	NA	NA	Ref.	
	Mace	BBAADD	21	14.4	119,772	81.1	NA	NA	Ref.	
	PI190962 (spelt wheat)	BBAADD	21	14.4	120,104	80.9	NA	NA	Ref.	
	Claire	BBAADD	21	14.3	NA	NA	NA	NA	Scaffolds	
	Cadenza	BBAADD	21	14.1	NA	NA	NA	NA	Scaffolds	
	Paragon	BBAADD	21	14.4	NA	NA	NA	NA	Scaffolds	
	Robigus	BBAADD	21	14.5	NA	NA	NA	NA	Scaffolds	
	Weebill 1	BBAADD	21	14.2	NA	NA	NA	NA	Scaffolds	
	Fielder	BBAADD	21	15	116,480	81	30.5/16/1/12.4	NA	Chr-scale	Sato et al., 2021
T. aestivum ssp. *tibetanum*	Zang 1817	BBAADD	21	14.71	118,078	82.74	44.2/15.3/17.2	NA	Chr-scale	Guo et al., 2020
H. vulgare	Morex	HH	7	4.79	39,734	80.8	21.3/16.0/4.7	2	Ref.	Mascher et al., 2017
S. cereale	Weining	RR	7	7.74	45,596	90.3	54.9/15.3/10.6	0.5	Ref.	Li et al., 2021a
	Lo7	RR	7	6.74	34,441	82.4	35.4/17.1/5.4	NA	Ref.	Rabanus-Wallace et al., 2021
Th. elongatum		EE	7	4.63	44,474	81.3	45.0/13.0/16.4	1.2	Chr-scale	Wang et al., 2020b
Ae. bicornis		SS	7	5.54	40,222	86%	46.1/16.6/15.6	NA	Chr-scale	
Ae. longissima		SS	7	6.02	37,201	88.1	49.3/17.8/14.0	NA	Chr-scale	
Ae. searsii		SS	7	5.37	37,995	86.9	44.8/16.7/17.8	NA	Chr-scale	Li et al., 2022a
Ae. sharonensis		SS	7	5.95	38,440	88.1	49.6/17.5/14.1	NA	Chr-scale	
Ae. speltoides		SS	7	4.45	37,607	86.1	43.7/22.8/11.1	NA	Chr-scale	

used the whole-genome shotgun sequencing strategy to generate a draft genome. Subsequently, Luo et al. (2017) combined data from ordered BAC clone sequencing, whole-genome shotgun sequencing, and BioNano optical genome mapping to build a chromosome-scale reference genome (4.225 Gb). Zhao et al. (2017) simultaneously assembled a high-quality reference genome (4.31 Gb) using short-read sequences generated on the Illumina HiSeq 2000 and HiSeq 2500 sequencing platforms combined with long-read PacBio RS II sequencing data. Based on the estimated genome size

of 4.5 Gb, these efforts together have produced sequences and assemblies covering more than 93% of the *Ae*. *tauschii* AL8/78 genome. Approximately 85% of the assembled sequences are annotated as transposable elements (Table 1), of which 59.9% are retrotransposons and 19.6% are DNA transposons. More than 40,000 high-confidence genes have been identified (Luo et al., 2017; Zhao et al., 2017).

The wheat B genome progenitor remains unidentified. *De novo* genome sequencing was recently conducted for all five species in the *Sitopsis* section of the *Aegilops* genus; comparative analysis with the B subgenome of polyploid wheat accessions refuted the previous widely-held opinion that *Aegilops speltoides* was the progenitor (Li et al., 2022a). The same study also excluded the possibility of any other *Sitopsis* species (*Aegilops bicornis*, *Aegilops longissima*, *Aegilops searsii*, or *Aegilops sharonensis*) being the donor, and the results were also inconsistent with the polyphyletic origin hypothesis. Instead, it posits that the B genome was donated by a single diploid species belonging to the B-lineage of *Aegilops*, which was most closely related to *Ae*. *speltoides* but likely went extinct soon after the formation of wild emmer wheat (*T*. *turgidum* ssp. *dicoccoides*) (Li et al., 2022a).

Genomes of tetraploid wild emmer and durum wheat

Wild emmer is the tetraploid progenitor of bread wheat. Avni et al. (2017) sequenced the accession Zavitan, which was collected from the Zavitan natural reserve in Israel (Nave et al., 2016). A 10.5-Gb genome was assembled using whole-genome shotgun sequencing data from libraries with various insert sizes and the software package DenovoMAGIC2^{TM} (NRGene, Nes Ziona, Israel). Fourteen chromosome-scale pseudomolecule sequences were constructed with a genetic map and Hi-C data. In the accession Zavitan, 82.2% of the genome consisted of transposable elements, including 69.9% long terminal repeat (LTR) retrotransposons and 11.5% DNA transposons; 65,012 high-confidence genes were identified (Table 1). Using the same strategy as for Zavitan, the durum wheat variety Svevo was sequenced and a 10.45-Gb genome assembled (Maccaferri et al., 2019). Of the assembled sequences, 82.2% were repetitive DNA and 66,559 high-confidence genes were identified (Table 1). Comparative analysis revealed that the genomes of the cultivated durum Svevo and the wild emmer accession Zavitan displayed strong overall synteny, with high similarity in the total numbers of high-confidence genes, chromosome structure, and transposable element composition (Table 1).

Bread wheat genomes

Bread wheat is allohexaploid and has a very large genome size (~16 Gb). To overcome the difficulties caused by the genome size and the complexities of the hexaploid genome, the International Wheat Genome Sequencing Consortium (IWGSC) employed a flow cytometry sorting approach to separate each chromosome arm of aneuploid wheat lines derived from double ditelosomic stocks of Chinese Spring (a wheat landrace widely used for cytogenetic studies), constructed BAC libraries, sequenced them on Illumina platforms, and produced a draft genome of 10.2 Gb (IWGSC, 2014). In 2018, IWGSC further generated chromosome-scale pseudomolecule sequences of Chinese Spring by incorporating additional genetic and physical data with a draft *de novo* whole-genome assembly. The total assembled genome was 14.5 Gb with a contig N50 of 51.8 kb and a scaffold N50 of 7.0 Mb. Approximately 97% (14.1 Gb) of the contigs could be assigned and were ordered along 21 chromosomes. Approximately 85% of the genome was annotated as repetitive DNA, including CACTA DNA transposons (15.5%) and the LTR retrotransposons Gypsy (46.7%) and Copia (16.7%). In total, 105,200 high-confidence genes and 154,780 low-confidence genes were predicted (Table 1) (IWGSC, 2018).

More recently, Sato et al. (2021) established a high-quality, chromosome-level genome assembly of the bread wheat variety Fielder. This variety is known for its ease of transformation with *Agrobacterium tumefaciens* or alteration via genome editing. The genome was sequenced using PacBio circular consensus sequencing with the HiFi approach. To determine the genetic basis of Tibetan wheat adaptation to high-altitude conditions, Guo et al. (2020) generated a draft genome sequence of a Tibetan semi-wild wheat accession (*Triticum aestivum* ssp. *tibetanum* Zang1817) (Table 1) and re-sequenced 245 wheat accessions, including landraces and varieties from across the world and Tibet. They found that high-altitude environments can trigger extensive reshaping of wheat genomes, and that Tibetan wheat accessions had accumulated high-altitude-adapted haplotypes of related genes in response to harsh environmental constraints. Based on their findings, they speculated that the Tibetan semi-wild wheat was a de-domesticated descendent of local landraces.

To reveal the genome variation of bread wheat used in modern breeding worldwide, Walkowiak et al. (2020) selected eight and seven spring and winter varieties, respectively, from different regions and derived from different breeding programs; they generated reference-quality pseudomolecule assemblies of ten varieties (Norin 61, Jagger, Julius, Arina*LrFor*, SY Mattis, LongReach Lancer, PI190962, CDC Stanley, CDC Landmark, and Mace) and scaffold-level assemblies of five varieties (Cadenza, Paragon, Robigus, Claire, and Weebill 1) using a whole-genome shotgun sequencing strategy with next- and third-generation sequencing technologies (Table 1). By comparative analysis of the assembled genomes, they identified extensive structural rearrangements, introgression from wild wheat re-

latives, differences in gene content, and sequence variations. These differences resulted from complex breeding histories aimed at improving adaptation to diverse environments, stress resistance, grain yield, and quality. These are valuable resources for functional gene discovery and breeding of novel wheat varieties that have high yield and adaptability to a broad range of challenging environments.

Comparative genomics of wheat and other monocots

Bread wheat belongs to the genus *Triticum* in the *Poaceae* family of monocots. Compared to other major cereals (e.g., rice and maize), bread wheat has a larger genome size (~16 Gb) and higher ploidy. There have been an estimated five rounds of polyploidization events in the evolutionary history of the wheat lineage, namely three well-acknowledged ancient polyploidization events (τ, σ, and ρ) shared by all of the grass lineages, and two recent allopolyploidization events in wheat (Jiao et al., 2014; Paterson et al., 2004; Salse et al., 2008; Tang et al., 2010; Wang et al., 2015c). A series of chromosomal fissions and fusions are inferred to have followed the evolution of monocots. There are estimated to have been five proto-chromosomes in the pre-τ ancestral monocot karyotype (AMK), nine proto-chromosomes in the pre-σ ancestral karyotype, and seven proto-chromosomes in the pre-ρ ancestral grass karyotype (AGK) (Murat et al., 2017). Two chromosome fusion events occurred after the ρ event, which led to 12 pairs of ancestral chromosomes in the common ancestor of grass species. Additional chromosomal rearrangements (CRs) later occurred, resulting in seven chromosomes in diploid *Triticeae* species (Ling et al., 2018; Murat et al., 2017). Although the chromosome number is conserved in *Triticeae* species, it has been concluded that a 4AL/5AL reciprocal translocation (RT) occurred at the diploid stage and that a 4AL/7BS RT, a 4A pericentric inversion, and a 4AL paracentric inversion took place at the tetraploid stage (Dvorak et al., 2018; Ma et al., 2013). A considerable number of CRs have been identified in the rye genome compared to wheat (Devos et al., 1993; Li et al., 2021a; Martis et al., 2013). In addition, some variety- or accession-specific translocations have been found in *Ae. tauschii* (e.g., accession AY61) and bread wheat (e.g., ArinaLrFor and SY Mattis) (Walkowiak et al., 2020; Zhou et al., 2021). The potential mechanism, selection and importance of these ancient and recent CRs, however, remain largely unclear.

Genome sizes differ significantly between grass species. The genomes of *Brachypodium distachyon*, rice, and sorghum are relatively small at ~270, 370, and 730 Mb, respectively; in contrast, maize, barley, rye, and hexaploid bread wheat have genomes of ~2.4, 5.1, 7.9, and 16 Gb, respectively (IWGSC, 2018; Haberer et al., 2016; Li et al., 2021a; The International Brachypodium Initiative, 2010). The variation in genome size seems to be correlated with the abundance of repetitive sequences. The *Brachypodium*, rice, and sorghum genomes contain 28.1%, 48.6%, and 61.0% repetitive sequences, respectively, whereas the maize, barley, rye, and hexaploid wheat genomes all contain > 80% repetitive sequences (Li et al., 2021a; Ling et al., 2018; Luo et al., 2017; Mascher et al., 2017; Paterson et al., 2009; Stein et al., 2018; The International Brachypodium Initiative, 2010). Although the largest grass genomes are more than ten times larger than the smallest grass genomes, they contain comparable numbers of annotated protein-coding genes; these range from 34,118 to 44,747 for diploid genomes (e.g., rice, sorghum, maize, and barley) compared to ~66,000 for tetraploid wheat and ~115,000 for hexaploid bread wheat. Gene families associated with fertility, abiotic stress responses, and morphological traits affecting yield are known to be specifically expanded in wheat species (IWGSC, 2018). However, the underlying mechanisms and functional significance of these expanded gene families require further investigation.

Whole-genome sequencing has deepened understanding of wheat domestication

The domestication of wheat ~10,000 BP in the Fertile Crescent marked the dawn of agriculture, enabling the transition from the hunter-gatherer lifestyle to sedentary societies (Lev-Yadun et al., 2000; Salamini et al., 2002; Zhao et al., 2022). Two of the essential traits in the evolution of bread wheat were the development of non-shattering seeds and the loss of tough glumes (Dubcovsky and Dvorak, 2007). The former trait prevents natural seed dispersal, allowing humans to harvest seeds at the optimal time. The non-shattering seed trait is determined by mutations in the *brittle rachis* (*Br*) gene (Avni et al., 2017; Pourkheirandish et al., 2015). The second meaningful change, from hulled to free-threshing grains, allows efficient large-scale grain harvesting. The primary genetic determinants of the free-threshing trait are a recessive mutation of the *Q* gene (Simons et al., 2006), accompanied by the modifying effects of a recessive mutation at the *tenacious glume* (*Tg*) locus (Jantasuriyarat et al., 2004). Cultivated forms of diploid, tetraploid, and hexaploid wheat all have tough rachises. Similarly, the early domesticated forms of einkorn, emmer, spelt, and macha wheat were hulled, whereas modern tetraploid and hexaploid wheat varieties are free-threshing (Zhao et al., 2021).

Several important genes associated with wheat domestication have been cloned using QTL and linkage disequilibrium (LD) mapping. However, little is known about bread wheat adaptation during domestication. Recently, whole-genome re-sequencing and GWAS (Cheng et al., 2019; Gaurav et al., 2022; Guo et al., 2020; Hao et al., 2020a; Wang et al., 2020d; Zhou et al., 2020; Zhou et al., 2021) have

generated insights into the initial domestication and subsequent diversification of the wheat lineage (Figure 1B). The phylogenetic relationship and population structure revealed the origins of bread wheat. In wild tetraploid progenitors, the monophyletic origin of domesticated emmer was wild emmer from the northern Levant (Cheng et al., 2019). The evolutionary relationship between domesticated emmer and threshing tetraploids (and to bread wheat) has been further clarified (Zhou et al., 2020). Using cytoplasmic evidence, it was shown that domesticated polyploid wheat emerged from the admixture of six dispersed founder wild emmer lineages (Wang et al., 2022d). In wild diploid progenitors, *Ae*. *tauschii* ssp. *strangulata* is the closest subspecies to the D subgenome of bread wheat (Zhou et al., 2021). In hexaploids, the bread wheat landrace was eventually split into Asian and European groups, with modern Asian varieties derived from intensive use of the European landrace (Hao et al., 2020a). Furthermore, whole-genome sequences of diverse accessions from across the globe allowed tracing of the genetic sources of adaptation (Meyer and Purugganan, 2013). Wild populations were introgressed into the bread wheat genome to form large sections of the modern wheat genome (Cheng et al., 2019; Zhou et al., 2020). These introgressions contained a great deal of phenotypic variability from both diploid and tetraploid progenitors, allowing bread wheat to adapt to human selection in the face of diverse environmental stressors (He et al., 2019). Genomic regions containing candidate genes for agronomic traits have also been identified, including those affecting extreme high-altitude tolerance (Guo et al., 2020), disease and pest resistance (Gaurav et al., 2022), starch synthesis (Hao et al., 2020a), and flowering time (Hao et al., 2020b). Transfer of adaptive alleles to elite varieties via genome editing technologies (Zhu et al., 2020) and rapid transformation systems (Zhou et al., 2021) could enrich the wheat germplasm pool. Together, these studies illustrate the functions of genes involved in bread wheat evolution through the course of domestication, and show the convergence of mutations occurring independently in the same genes and pathways.

Using whole-genome re-sequencing data and population genomic approaches combined with environmental and archaeobotanical data (Purugganan and Fuller, 2009), it may be possible to examine the evolutionary adaptations employed by bread wheat as it spread to new environments. This could allow us to identify traits and genes to support future efforts to breed plants that are tolerant of changing climate conditions.

Triticeae genome sequencing accelerates gene pool exploitation and wheat improvement

Triticeae is an important tribe in the grass family *Poaceae*; it includes staple food crops such as wheat, rye, and barley and forage crops such as Chinese wild rye (sheep grass). *Triticeae* species are important genetic resources with high diversity, constituting a primary, secondary, and tertiary gene pool (GP-1, GP-2, and GP-3, respectively) (Figure 2A, Table 2). *Triticeae* genome sequencing (TGS) has brought the study of *Triticeae* species to a new era, called Genomic *Triticeae*. This has greatly accelerated comparative structural and functional genomic studies conducted in monocot plants in the last several years, allowing for improvement of major cereal crops, especially wheat.

Triticeae genome sequencing

For the following discussion of *Triticeae* genomes, we merged genera containing the same genomes, retaining only 25 genera and 34 unique genomes (Table 2). Seven unique genomes (A, B, D, E, H, R, and S) have been sequenced in the *Triticum*, *Thinopyrum*, *Hordeum*, *Secale*, and *Aegilops* genera (Avni et al., 2022; Bauer et al., 2017; IWGSC, 2018; Jia et al., 2013; Li et al., 2021a; Li et al., 2022a; Luo et al., 2017; Mascher et al., 2017; Sato et al., 2021; Walkowiak et al., 2020; Wang et al., 2020c). Twelve unique genomes (F, G, I, Ns, P, St, U, Xa, Xm, Xu, V, and Y) may soon be published. The remaining 15 unique genomes from 11 genera have not yet been sequenced to our knowledge (Table 2).

Of the 34 unique genomes, 26 (76.5%) are present in polyploid *Triticeae*, although the number of polyploid genomes generated varies greatly. The St genome in *Pseudoroegneria* produced 10 polyploid genomes which were distributed among five genera of perennial Triticeae. The D genome from *Ae*. *tauschii* generated nine polyploid genomes in two annual genera, *Aegilops* and *Triticum*. The A genome from *T*. *urartu* has contributed to four polyploid *Triticum* genomes (Table 2). This implies the existence of genes that have promoted adaptation and polyploidization in these unique genomes. Although polyploid genomes evolved much later than diploids, their abundance demonstrates heterosis in natural environments. For example, it is the tetraploid species of Chinese wild rye (*Leymus chinensis*) and *Agropyron* that have spread worldwide, although there are diploid relatives of *Agropyron* and *Leymus*. The 34 unique *Triticeae* genomes represent rich GP-2 and GP-3 resources to produce new polyploids such as triticale by artificial construction (i.e., synthetic polyploids) or by future spontaneous occurrence, contributing to improvement of key agronomic traits.

Several web-based databases have been established to allow access to *Triticeae* genomes and other related data, including whole-genome sequencing (WGS), transcriptomic, epigenomic, and proteomic data (Blake et al., 2019; Colmsee et al., 2015; Ran et al., 2020; Spannagl et al., 2016; Walkowiak et al., 2020). The Wheat Genome Variation Database (WGVD, https://db.cngb.org/WGVD/), SnpHub (http://

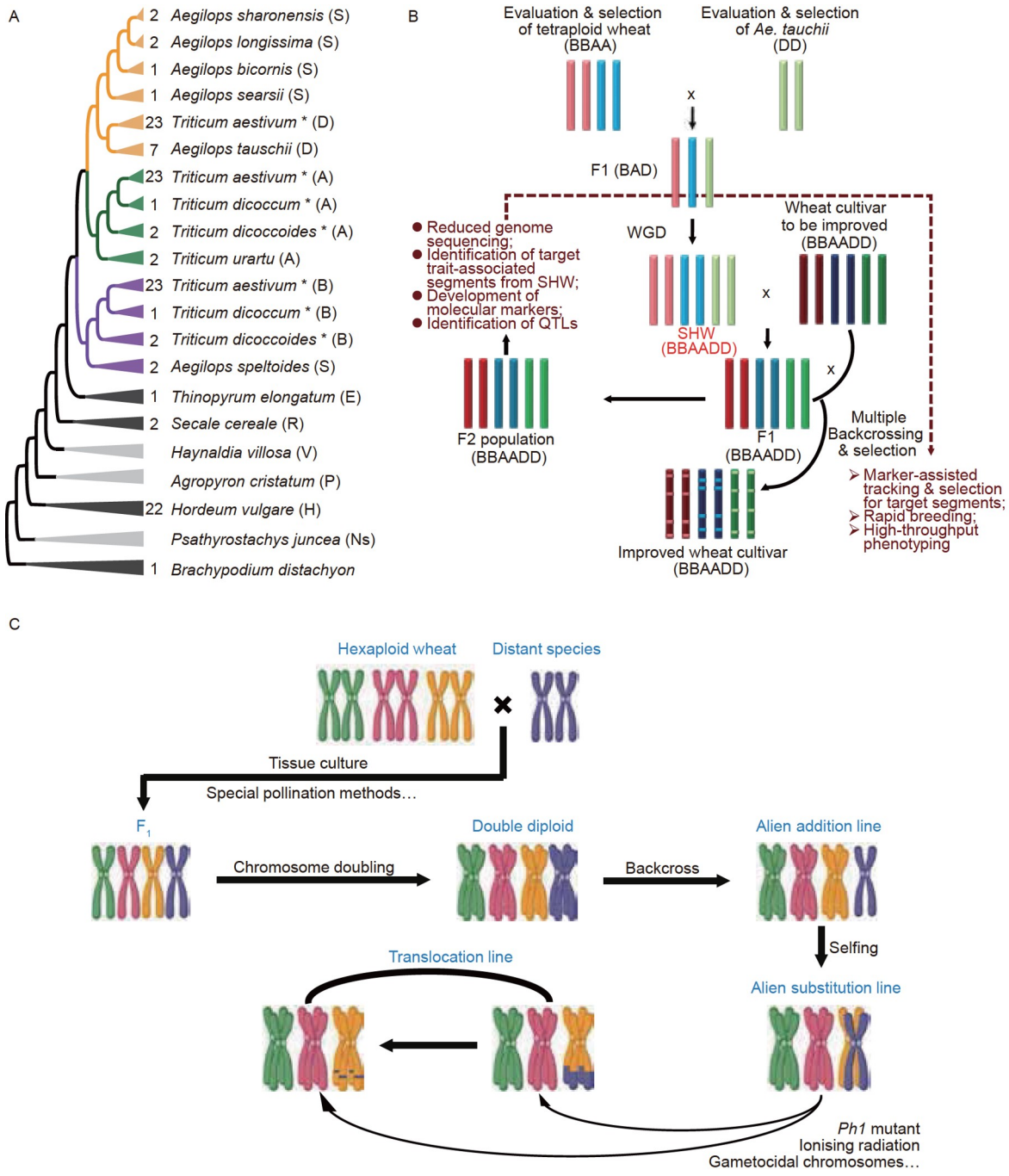

Figure 2 Genomic *Triticeae* facilitates gene pool exploitation and wheat improvement. A, Phylogenetic relationship of core species within *Triticeae* tribe. Digits indicate the number of published genomes. The asterisk indicates polyploidy species. B, Construction of synthetic hexaploid wheat and its utilization in wheat improvement. C, Diagrammatic illustration of alien gene transfer from wild species into wheat by distant hybridization.

wheat.cau.edu.cn/Wheat_SnpHub_Portal), and *Triticeae* Gene Tribe (TGT, http://wheat.cau.edu.cn/TGT/) have collected published whole genome re-sequencing data from more than 1,000 wheat and other *Triticeae* species and accessions; they have also collected selective signatures from wheat domestication and improvement and collinearity-incorporating homology information (Chen et al., 2020c; Ran et al., 2020; Wang et al., 2020d). Wheat Proteome and Plant Regulomics (http://bioinfo.sibs.ac.cn/plant-regulomics/index.php) and WheatOmics (http://wheatomics.sdau.edu.cn/) have provided proteomic and epigenomic information, respectively, for wheat and many other *Triticeae* species (Duncan et al., 2017; Ran et al., 2020). A range of useful tools have been integrated in some databases, such as a bulked segregant analysis (BSA)-based gene mapping module in WheatGmap (Zhang et al., 2021b) and a network-

Table 2 Unique genomes in *Triticeae* and advances in genome sequencing

Genome	Genera (genome)	*D*/*P*[a)]	Available[b)]
A	*Triticum* (A, AB, ABD, AG)	*D*/*P*	1
B	*Triticum* (AB,ABD)	*P*	1
D	*Aegilops* (D, CD, D^cS^sX, DN/DM^V, DMS/D^cS^sX, D^cXc, DD^cXc, D^cZcU), *Triticum* (ABD)	*D*/*P*	1
E	*Thinopyrum* (*Lophopyrum*) (E^b, E^e), *Psammopyrum* (EL)	*D*/*P*	1
H	*Hordeum* (H), *Elymus* (StH, StHY), *Stenostachys* (HW), *Pascopyrum* (StHNsXm)	*D*/*P*	1
R	*Secale* (R)	*D*/*P*	1
S	*Aegilops* (S, S^b, S^l, S^s)	*D*/*P*	1
F(Xe)	*Eremopyrum* (F, Fs, Xe, FXe, FsF, FXe)	*D*/*P*	2
G	*Triticum* (AG)	*P*	2
I	*Hordium* (I)	*D*	2
Ns	*Psathyrostachys* (Ns), *Pascopyrum* (StHNsXm), *Leymus* (NsXm)	*D*/*P*	2
P	*Agropyron* (P), *Elymus* (StPY)	*D*/*P*	2
St	*Pseudoroegneria* (St), *Pascopyrum* (StHNsXm), *Roegneria* (StY) *Elymus* (StH, StY, StHY, StPY, StWY, StStY), *Trichopyrum* (StE)	*D*/*P*	2
U	*Aegilop*s (U, UM ,UC, UMN, UMX, DZcU)	*D*/*P*	2
V	*Dasypyrum* (V, Xv, VXv)	*D*/*P*	2
Xm	*Leymus* (NsXm)	*P*	2
Xa	*Hordium* (XaXu)	*P*	2
Xu	*Hordium* (XaXu)	*P*	2
Y	*Roegneria* (StY), *Elymus* (StY, StHY, StPY, StWY, StStY)	*P*	2
C	*Aegilops* (C, CD, CU)	*D*/*P*	3
M	*Aegilops* (M, UM, UMN)	*D*/*P*	3
T	*Aegilops* (T)	*D*	3
Zc	*Aegilops* (D^cZcU)	*P*	3
O	*Henrardia* (O)	*D*	3
Q	*Heteranthelium* (Q)	*D*	3
Ta	*Taeniatherum* (Ta)	*D*	3
Xc	*Ae.crassa* (DcXc/Dmer)	*D*/*P*	3
X	*T.syriacum* (UMX/DMS)	*P*	3
K	*Crithopsis* (K)	*D*	3
L	*Festucopsis*, *Psammopyrum* (L)	*D*	3
W	*Ausralopyrum* (W), *Stenostachys* (HW)	*D*/*P*	3
Xo	*Hordelymus* (XoXr)	*P*	3
Xr	*Hordelymus* (XoXr)	*P*	3
Xp	*Peridictyon sanctum* (Xp)	*D*	3

a) D, diploid; P, polyploid; b) genome data 1, available; 2, will be available; 3, unknown.

based functional prediction pipeline in WheatNet (Lee et al., 2017). These websites provide convenient and user-friendly access to published resources, contributing substantially to *Triticeae* functional genomic studies.

Utilization of synthetic wheat in breeding

The bread wheat secondary gene pool includes the direct progenitor species *T*. *turgidum* and *Ae*. *tauschii*. Use of these resources has the potential to introduce novel genetic variation, especially genes involved in disease resistance and abiotic tolerance (Hao et al., 2019). Bread wheat is derived from a relatively small group of founder plants, and elite alleles and genes are limited. Hybridization of *T*. *turgidum* with *Ae*. *tauschii* to produce so-called synthetic wheats (SHWs) has been applied to enlarge the genetic base of bread wheat (Figure 2B) (Hao et al., 2019). In contrast to other methods used to surmount the constraints of limited intraspecific genetic diversity in crops, "synthetic crops" can by definition only be produced for allopolyploid crops

with extant diploid or lower-ploidy progenitors. The term synthetic crops refers to *ab initio* crop synthesis; this method can simultaneously harness genetic variations from more than one species and allow immediate transfer to the target allopolyploid crop. Bread wheat is a young allohexaploid species (BBAADD) with both its diploid progenitor (*Ae. tauschii*, genome DD) and tetraploid progenitor (*T. turgidum*, genome BBAA) available. Thus, it is perhaps not surprising that the synthetic crop approach was first tested in bread wheat.

It is imperative to broaden the genetic base of wheat. Genetic bottlenecks are commonly associated with domesticated crops (Olsen and Wendel, 2013). However, an allopolyploid crop further tightens the bottleneck due to the intrinsic lower intraspecific genetic variability; this is a result of the speciation model of allopolyploidization, which usually involves a very limited number of founder individuals and instantaneous reproductive isolation from its progenitors. Thus, wheat has lower levels of intraspecific genetic diversity compared with diploid crops such as maize and rice. Notably, however, the three subgenomes of wheat are not equally deprived of genetic variation; although genetic diversity in the D subgenome is mostly depleted, the A and B subgenomes are less depauperate. This is primarily because natural hybridization between tetraploid wheat and bread wheat occurred sporadically, which enabled genetic introgression from the BBAA subgenomes of tetraploid wheat into those of common wheat through a pentaploid intermediate (Deng et al., 2018). In contrast, hybridizations between bread wheat and the diploid *Ae. tauschii* (D genome) occurred very rarely (Zhou et al., 2021). Thus, the SHW approach, which enables simultaneous genetic introgression to all three subgenomes, holds great promise for augmenting the intraspecific diversity of bread wheat (Figure 2B). A constructed SHW possesses the same subgenomes as natural polyploid wheat. Thus, the two types of polyploid wheats, natural and synthetic, can easily be crossed with one another. In the resulting hybrids and their progenies, the corresponding homologous chromosomes (those from the same subgenome) of both sources would freely recombine, whereas homeologous chromosomes (those from different subgenomes) would not; this is because the homeologous pairing control loci, such as *Ph1* and *Ph2*, exist in both tetraploid and hexaploid wheat. Thus, upon selection, the intended beneficial variants of a SHW variety can be readily transferred and integrated into the already near-elite common wheat varieties (Figure 2B).

The first large-scale generation of SHWs intended for breeding was initiated at CIMMYT in the early 1980s (Mujeeb-Kazi and Hettel, 1995), and the resulting lines were used in breeding in various countries. Notably, Dong et al. (2010) also developed 22 SHWs in the 1980s using tetraploid wheat lines that carried genes for spontaneous chromosome doubling. Since then, at least 1577 primary SHWs comprising diverse combinations of durum varieties and *Ae. tauschii* accessions have been produced; using some of these as pre-breeding materials, 86 varieties have been released in 20 countries as of 2020 (Aberkane et al., 2020). These new SHW-derived varieties are characterized by increased resistance to biotic and abiotic stresses, high yield, improved quality, and enhanced biofortification capacity (Aberkane et al., 2020; Hao et al., 2020b).

The value of using SHWs to broaden the genetic base of bread wheat has been unequivocally documented. However, there remains ample space for further innovations to make the synthetic crop approach more effective and efficient. Of paramount significance is the combination of this approach with recent advances in genomics and genome editing technologies. As illustrated recently (Zhou et al., 2021), an integrated strategy for SHW that incorporates genomics, genome editing, and rapid breeding holds great promise for revolutionizing the current prevailing crop breeding method of inter-variety crossing.

Wheat improvement through distant hybridization

The genetic base of wheat has been continually narrowed as a result of long-term domestication and breeding efforts. The wild relatives of wheat have long been seen as potential sources of genomic diversity for abiotic and biotic stress resistance and other agronomically important traits. Distant hybridization is an efficient method of hybridizing these relatives with wheat, making them potential sources of novel genes for genetic improvement (Molnár-Láng et al., 2015). Since the 19th century, crosses have been successfully made between wheat and diverse genera in the *Triticeae* family, including *Secale*, *Aegilops*, *Thinopyrum*, *Hordeum*, *Agropyron*, *Psathyrostachys*, *Elymus*, *Leymus*, and *Dasypyrum*, successfully transferring elite agronomic traits into wheat (Gupta, 2016).

A pipeline has been established for creating wheat–alien hybrids (Figure 2C). Because there is inter-genus reproductive isolation in *Triticeae*, embryo rescue, colchicine treatment, and other methods have been used to improve the success rate of hybridization (Patial et al., 2021; Sirkka and Immonen, 1993; Subbarao et al., 2021). Extensive backcrossing, irradiation, callus culture-mediated translocation, and manipulation of *Ph* genes have also been performed to promote recombination of homeologous chromosomal segments; this produces wheat-alien compensating translocations with minimal alien chromatin, containing the desired gene(s) and decreasing the likelihood of linkage drag (Hao et al., 2020b).

Rye is an elite genetic resource that has been successfully applied in wheat improvement programs. Triticale is a new species generated by crossing wheat and rye, which com-

bines the cold resistance and nutrient utilization efficiency (NUtE) of rye with the high yield and nutritional quality of wheat (Dennett and Trethowan, 2013; Furman et al., 1997). Octoploid triticale was also bred successfully in China in the 1960s (Zhao and Bao, 1995; Zhao and Li, 1994). In 2019, a report showed that more than 3.8 million ha of triticale were grown worldwide, with total production exceeding 140,000 tons (https://www.fao.org/home/en). Researchers further created a series of substitution, addition, and translocation lines between rye and wheat through chromosome engineering methods. The most successful line was the one containing the 1RS chromosome segment, which occurred through 1AL.1RS, 1BL.1RS, and 1DL.1RS translocations (Rabinovich, 1998). This line has contributed several resistance genes for powdery mildew, leaf stripe, and stem rusts, and wheat varieties derived from these lines have been widely cultivated throughout the world.

The *Thinopyrum* genus is another of the most successful wheat relatives used in wheat distant hybridization. Many substitution, addition, and translocation lines between *Thinopyrum* species and wheat have been created in the last century. Zhensheng Li developed a milestone variety, Xiaoyan 6, through distant hybridization between wheat and *Th. ponticum* (Li, 2018). Recently, the FHB resistance gene *Fhb7* derived from *Th. ponticum* and the *Fhb-7EL* gene derived from *Thinopyrum elongatum* were introduced into mainstream wheat varieties in China. Several lines carrying *Fhb7* were developed and showed intermediate resistance to FHB; these lines are expected to greatly contribute to breeding for FHB resistance in wheat (Guo et al., 2015a; Wang et al., 2020b). A newly authorized winter wheat variety (Zhongke 166) carrying *Fhb-7EL* was identified as intermediately resistant to FHB (DOI: 10.1101/2021.02.03.429547).

Dasypyrum villosum has strong resistance to both biotic and abiotic stresses; it is therefore regarded as an important genetic resource for wheat improvement. Chen et al. (1995) developed T6AL·6VS, T6DL·6VS, and some small fragment translocation lines through gamma ray treatment. These translocation lines were immune or highly resistant to nearly all races of powdery mildew (Chen et al., 1995). Chen et al. (2006) further obtained diploids by crossing durum wheat with *D. villosum*, then introduced the powdery mildew resistance genes *Pm21* and *PmV* from 6VS of *D. villosum* #2 and *D. villosum* #4, respectively. *Pm21* encodes a typical coiled coil (CC)-nucleotide binding site (NBS)-leucine-rich repeat (LRR) protein (He et al., 2018). In addition, several translocation lines with powdery mildew resistance were developed from 5V, 2V, and 1V addition and substitution lines of durum wheat-*D. villosum* double diploid (Zhang et al., 2016b; Zhang et al., 2018a; Zhang et al., 2021c). *D. villosum* was reported to contain stem rust-resistance genes (Qi et al., 2011). A novel Robertsonian translocation event led to the transfer of a stem rust-resistance gene (*Sr52*), which was effective against the stem rust race Ug99, from *D. villosum* into bread wheat. The cereal cyst nematode resistance gene *CreV*, which is effective against *Heterodera filipjevi*, was transferred from chromosome 6VL of *D. villosum* to bread wheat (Zhang et al., 2016). Resistance to wheat spindle streak mosaic virus was transferred to wheat through a 4VS chromosome recombination with *Haynaldia villosa* (Zhao et al., 2013). Utilization of the *Ae. ventricosa* 2NvS translocation segment was first reported in the early 1990s; this segment contains key resistance genes for several wheat diseases, including root knot nematode; leaf, stripe, and stem rust; and wheat blast. More recently, researchers found that the frequency of the 2NS segment was increasing in Europe and in CIMMYT breeding programs, and that this increase was positively correlated with grain yield (Gao et al., 2021a). Utilization of *A. cristatum* 6PL segments has significantly increased GN and exhibits strong potential for increasing yield (Zhang et al., 2019b). Other wheat relatives, such as species in the genera *Psathyrostachys*, *Elymus*, and *Leymus*, have also been used in wheat breeding programs in recent years. Many bridge materials were created for these genera and wheat, promoting both basic research and the applied introduction of desired chromatin into wheat (Bai et al., 2020; Gong et al., 2019; Li et al., 2020a).

Due to rapidly-developing biological technologies, great progress has been achieved in wheat distant hybridization. However, the number of wild *Triticeae* relatives used in wheat improvement is still limited, and transferred alien genetic materials usually contain undesirable chromatin that affects the quality and yield of wheat. With recent advances in high-throughput genotyping and phenotyping platforms and efficient gene editing tools such as CRISPR/Cas9, more efficient and useful wheat breeding efforts are expected to be achieved in the near future.

Network of high-yield traits and the Green Revolution genes

Increasing grain yield is a priority in wheat breeding. Grain yield is a complex quantitative trait that is genetically determined by three individual components: spike number per unit area, grain size, and GN (Figure 3). Spike number per unit area is mainly determined by the number of fertile tillers. Tillering takes place from approximately the three-leaf seedling stage to the onset of stem elongation, and fertile tiller number is determined at anthesis in wheat (Zadoks et al., 1974). Both spikelet number and floret fertility are associated with GN. Spikelet initiation occurs in concert with tillering (Borràs-Gelonch et al., 2012); spikelet number peaks at the terminal spikelet stage, at which time the meristem at the top of a spike transforms to a terminal spikelet.

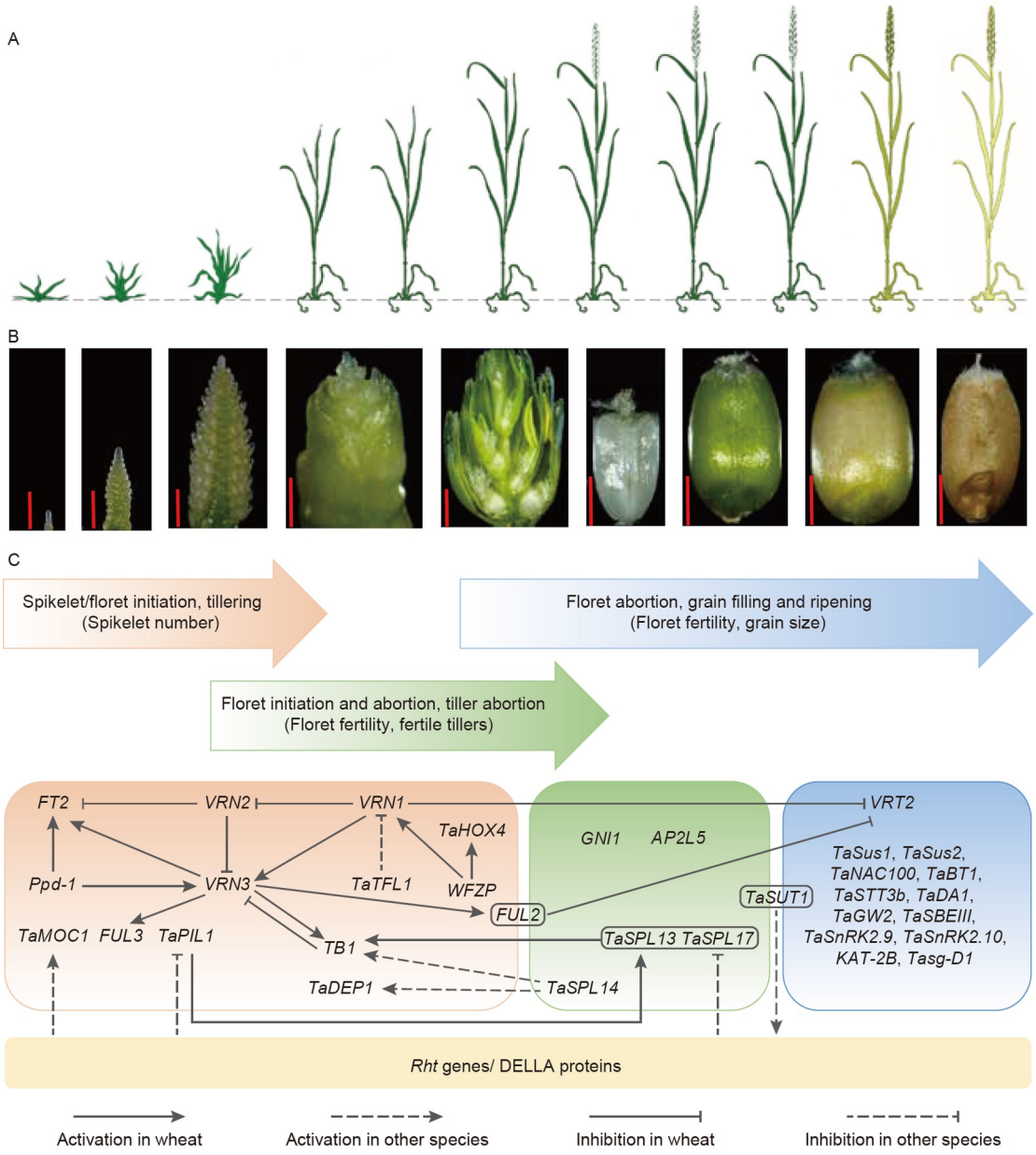

Figure 3 Gene regulatory networks for yield traits in wheat. A, The wheat life cycle. B, The shoot apex of wheat and spike, spikelet, grain morphology at different developmental stages. The bars indicate 1 mm, 1 mm, 1 mm, 400 μm, 2 mm, 2 mm, 2 mm, 2 mm, 2 mm, respectively. C, The genetic interaction of genes controlling grain size, spike number and tiller number in wheat.

Individual spikelets may produce more than eight florets in hexaploid wheat, but usually less than half of the florets set grain at physiological maturity (Guo and Schnurbusch, 2015). Floret fertility is affected by floret abortion, which mainly occurs during the pre-anthesis phase (Guo and Schnurbusch, 2015). Grain size is primarily determined during the post-anthesis phase (Brinton and Uauy, 2019; Ugarte et al., 2007). Attempts to increase grain yield have been hampered by the trade-off between grain size and grain number. The negative association between these two traits has become a bottleneck in improving grain yield (Bustos et al., 2013; Quintero et al., 2018).

Grain size

Grain size is an important target for increasing grain yield. Starch accounts for ~70% of dry wheat grain weight (Dale and Housley, 1986). Starch synthesis should therefore have significant effects on grain size. Wheat sucrose synthases (TaSus1 and TaSus2) catalyze the conversion of sucrose to fructose and UDP-glucose. *TaSus1* and *TaSus2* are associated with grain size (Jiang et al., 2011; Hou et al., 2014). Enhanced expression of *TaNAC100* increases *TaSus2* expression and grain starch contents (Li et al., 2021c). BRITTLE1 (BT1) transports ADP-glucose and is essential for starch

synthesis in crop grains (Kirchberger et al., 2007; Li et al., 2017b). Knocking down *TaBT1* in wheat decreases the grain size and starch content (Wang et al., 2019c). In addition, *TaSTT3b*, *TaDA1*, and *TaGW2* are involved in the starch biosynthesis pathway and in grain size (Liu et al., 2020b; Zhu et al., 2022). Starch branching enzymes (SBEs) catalyze the formation of branch points by hydrolyzing α-1,4-linkages and reattaching the chain via an α-1,6-linkage (Yu et al., 2021). Single nucleotide polymorphisms (SNPs) in TaSBEIII are associated with individual grain weight (Irshad et al., 2021). These results indicate the key role of starch synthesis in the regulation of wheat grain size.

Sucrose non-fermenting 1-related protein kinase 2 (SnRK2) family members have a conserved N-terminal kinase domain and a C-terminal domain that is rich in acidic amino acids (Mao et al., 2020b). The wheat protein kinase genes *TaSnRK2.9* and *TaSnRK2.10* are involved in regulating grain size (Feng et al., 2019; Zhang et al., 2017c). Three genes, *VEGETATIVE TO REPRODUCTIVE TRANSITION 2* (*VRT2*), *keto-acyl thiolase 2B* (*KAT-2B*), and *Tasg-D1* have been shown to be associated with grain size. Ectopic expression of *VRT2* in Polish wheat elongates the glume and grain, leading to an increase in grain size (Adamski et al., 2021; Liu et al., 2021a; Xiao et al., 2021). However, *Tasg-D1* negatively regulates grain size by repressing brassinosteroid (BR) signaling (Cheng et al., 2020). Interestingly, *Tasg-D1* promotes formation of erect leaves; plants with this trait can be planted more densely. Overexpression of *KAT-2B*, which is involved in β-oxidation during jasmonic acid (JA) synthesis, increases grain size (Chen et al., 2020b). Thus, *VRT2*, *Tasg-D1*, and *KAT-2B* all demonstrate great potential for high-yield breeding.

Grain number

Genetic increases in grain number are difficult to obtain because grain number is very sensitive to abiotic stress (Liu et al., 2020a). Grain number per spike depends on floret fertility and spikelet number per spike. The heritability of spikelet number per spike is relatively high in wheat. Spikelet number is determined at an early stage of spike development, and environmental conditions can affect it over a short period of time (Kuzay et al., 2019; Waddington et al., 1983; Zhang et al., 2018b). Some QTLs for spikelet number have been characterized in multiple genetic backgrounds (Chen et al., 2020d; Cui et al., 2012; Deng et al., 2011; Kuzay et al., 2019; Ma et al., 2019; Wang et al., 2011; Yao et al., 2019; Zhou et al., 2017). Floret abortion and fertility are highly sensitive to abiotic stresses such as heat and drought. Due to the strong sensitivity of grain number per spikelet to environmental stress, the QTLs known to be associated with floret fertility exhibit small effects (Prasad and Djanaguiraman, 2014; Wang et al., 2010).

Manipulation of spike development (e.g., spikelet/floret primordial initiation and enlargement) is an important strategy for the regulation of spikelet number and floret fertility (Chen et al., 2020d; Finnegan et al., 2018; Ochagavía et al., 2018; Pérez-Gianmarco et al., 2019; Prieto et al., 2018). Known flowering time genes are valuable resources for controlling the timing of spike development and the rate of spikelet/floret initiation and enlargement. Photoperiod insensitive (*Ppd-1a*) alleles accelerate spikelet primordial initiation, which can be partially compensated for by a short reproductive phase (Ochagavía et al., 2018; Prieto et al., 2018; Pérez-Gianmarco et al., 2019). Allelic variations of wheat *FRIZZY PANICLE* (*WFZP*) are associated with spikelet number per spike (Li et al., 2021f). *WFZP* activates *VRN1* and wheat *HOMEOBOX4* (*TaHOX4*) to regulate spikelet initiation and development (Li et al., 2021f). Deletion or mutation of *FLOWERING LOCUS T1* (*FT1*/*VRN3*) and *FLOWERING LOCUS T2* (*FT2*) extends the duration of spikelet initiation and development, which further significantly increases spikelet number per spike (Chen et al., 2022; Finnegan et al., 2018; Shaw et al., 2019). *VRN1* and *Ppd-1* positively regulate both *VRN3*/*FT1* and *FT2*, whereas *VRN2* acts as a transcriptional repressor of those genes (Shaw et al., 2019). *VRN1* downregulates *VRN2* (Chen and Dubcovsky, 2012). *VRN1* and *FUL2* act as repressors of *VRT2* (Li et al., 2021d; Liu et al., 2021a). *VRN1*, *FUL2*, and *FUL3* have redundant functions in spike development and interact with one another, and FUL2 and FUL3 are positive transcriptional regulators of *VRN3*/*FT1* (Li et al., 2019a; Li et al., 2021d). Allelic diversity in *TEOSINTE BRANCHED1* (*TB1*) is associated with paired spikelet development and tiller number (Boden et al., 2015; Dixon et al., 2018). The paired spikelets induced by *TB1* can be explained by the interaction between *TB1* and *FT1*, which can increase *TB1* expression to downregulate meristem identity genes (Boden et al., 2015; Dixon et al., 2018). The earliness per se locus *Eps-A^{m}1* affects the duration of early developmental phases and spikelet number in wheat (Lewis et al., 2008b; Faricelli et al., 2010). More recently, it was found that the late flowering alleles of *Eps* produce more fertile florets (Basavaraddi et al., 2021). Thus, flowering time genes have been employed consistently and successfully in regulating spikelet number and floret fertility by controlling the rate and duration of spike development events in wheat.

Genes in addition to those controlling flowering time also affect grain number. *Grain Number Increase 1* (*GNI1*), which encodes a homeodomain leucine zipper class I (HD Zip I) transcription factor (TF), is an ortholog of the barley gene *VRS1*/*HvHOX1* (Sakuma et al., 2019). Decreased expression of *GNI1* may increase floret fertility in wheat (Sakuma et al., 2019). *Q* (*AP2L5*) confers the square spike and free-threshing characteristics that developed during wheat domestication (Simons et al., 2006). A recent study showed

that *ap2l5* mutants have obvious decreases in spikelet number, which may be attributed to a premature transition of the spike meristem to a terminal spikelet (Debernardi et al., 2020a).

In rice, *IPA1* (*OsSPL14*) represses tillers and shapes ideal plant architecture (Jiao et al., 2010), whereas *OsSPL13* controls grain size (Si et al., 2016). Overexpression of *TaSPL13* in wheat may increase floret fertility (Li et al., 2020c). *TaPIL1* physically interacts with *TaSPL3* and *TaSPL17* (an ortholog of *OsSPL14*), which can activate *TB1* expression (Zhang et al., 2021a). The wheat gene *DWARF53* (*TaD53*) directly interacts with *TaSPL3*/*17*, which is controlled by miR156, to repress *TaSPL3*/*17*-mediated activation of *TaBA1* and *TB1* (Liu et al., 2017).

TaSUT1 and *TaSPL14* both regulate spikelet and grain number and thousand grain weight (TGW) in wheat (Al-Sheikh Ahmed et al., 2018; Cao et al., 2021). In *Arabidopsis*, *SUT1* is a suppressor of *TYPE ONE PROTEIN PHOSPHATASE 4* (*TOPP4*), which can promote DELLA protein degradation (Qin et al., 2014; Yan et al., 2019). DELLAs can prevent PIF3 from binding to target genes, including *PIL1* (Feng et al., 2008; Li et al., 2016). *TaPIL1* represses wheat tillering (Zhang et al., 2021a). Downregulation of *TaDEP1* increases spike length and reduces spikelet number in wheat (Huang et al., 2009). *OsSPL14* can increase *OsTB1* and *OsDEP1* expression by binding to their promoters (Duan et al., 2019). *GS3* acts antagonistically with *DEP1* to regulate grain size in rice (Sun et al., 2018). In tetraploid wheat, the *DEP1-B* mutant has significantly reduced spikelet number per spike (Kong et al., 2022). Mutation of *DEP1* reduces expression of *Cytokinin oxidase 2* (*OsCKX2*) in rice. Silencing *TaCKX1* significantly increases grain number and TGW, whereas silencing *TaCKX2* slightly decreases grain number in wheat (Jablonski et al., 2021). Overexpression of *TERMINAL FLOWER 1* (*TaTFL1*)*-2D* results in an increase in spikelet number and GN (Wang et al., 2017). In rice, *ABERRANT PANICLE ORGANIZATION 1* (*APO1*) positively controls spikelet number (Ikeda et al., 2007). *TaAPO-A1*, a wheat ortholog of *APO1*, is associated with spikelet number (Chen et al., 2020d; Kuzay et al., 2022; Muqaddasi et al., 2019). *TFL1* represses expression of *APETALA 1* (*AP1*), which is an ortholog of *VRN1* (Hanano and Goto, 2011). Haplotype analyses indicated that *TaTEF-7A* is probably associated with GN in wheat (Zheng et al., 2014).

Tillering

Spike number per unit area plays an important role in determining grain yield, and is closely associated with tiller survival and tiller number per unit area. Tiller number is a determinant of spike number, and tillers are initiated by the growth of axillary meristems (Moeller et al., 2014; Naruoka et al., 2011). Generally, an increase in the number of fertile tillers with spikes enhances grain yield (Naruoka et al., 2011). However, an excessive tiller number can lead to yield losses because the tillers compete with one another for resources and do not set fertile spikes at physiological maturity. Tiller number optimization plays an important role in efforts to increase yield.

Many QTLs associated with tiller number have been identified in wheat (Kato et al., 2000; Li et al., 2002; Moeller et al., 2014; Nasseer et al., 2016; Xu et al., 2017). Five tiller inhibition genes (*Tin1*, *Tin2*, *Tin3*, *Tin4*, and *Ftin*) have been mapped to chromosomes 1A, 2A, 2D, and 3A (Kuraparthy et al., 2007; Peng et al., 1998; Spielmeyer and Richards, 2004; Wang et al., 2022e; Zhang et al., 2013). *Tin1* has been cloned and is predicted to encode a cellulose synthase-like (Csl) protein homologous to members of the CslA clade (Hyles et al., 2017). *Tin1* increases spike size and grain weight (Atsmon and Jacobs, 1977), but its effects on yield traits vary across genetic backgrounds and environments (Duggan et al., 2005; Mitchell et al., 2012; Mitchell et al., 2013). Overexpression of the maize gene *TB1* in wheat decreases tiller number (Lewis et al., 2008a), whereas overexpression of tae-miR156 in wheat leads to an increase in tillering (Liu et al., 2017). *TaPIN1* expression levels are associated with tiller number, grain number, and grain size in wheat (Yao et al., 2021).

In rice, *MONOCULM1* (*MOC1*) was the first identified key regulator of tiller number. *MOC1* encodes a putative GRAS family nuclear protein. It is primarily expressed in axillary buds, in which it promotes outgrowth (Li et al., 2003). *MOC1 interacting protein1* (*MPI1*) overexpression results in enhanced tillering (Sun et al., 2010). Binding of MOC1 with the DELLA protein SLENDER RICE 1 (SLR1) can protect it from degradation (Liao et al., 2019). GA triggers the degradation of *SLR1* and *MOC1*, leading to a decrease in rice tiller number (Liao et al., 2019). *MOC3*, a rice ortholog of *WUSCHEL*, is required for tiller bud formation (Lu et al., 2015). An interaction between MOC1 and MOC3 upregulates *FLORAL ORGAN NUMBER1* (*FON1*) to control tiller bud outgrowth in rice (Shao et al., 2019). Moreover, rice anaphase-promoting complex (APC/C), a multi-subunit E3 ligase, controls tillering by mediating degradation of MOC1 (Lin et al., 2012; Xu et al., 2012). In wheat, genetic analysis of *TaMOC1* indicated that it is associated with spikelet number (Zhang et al., 2015). However, less is known about the effects of *TaMOC1* and associated genes on tiller number.

Effects of Rht genes on grain yield

Dwarf and semi-dwarf alleles of *Rht* loci significantly reduce plant height and improve harvest index and lodging resistance, ultimately leading to higher grain yields in wheat (Gale et al., 1985). The introduction of semi-dwarf genes

substantially increased grain yield during the Green Revolution. To date, 25 *Rht* genes have been identified in wheat (McIntosh et al., 2020). Genome loci have not been identified for four of those genes: *Rht6*, *Rht15*, *Rht19*, and *Rht20*; the other 21 genes were identified on chromosomes in groups of two to seven (McIntosh et al., 2020). Some of the 25 genes are alleles of the others. For example, *Rht3* (*Rht-B1c*), *Rht11* (*Rht-B1e*), and *Rht17* (*Rht-B1p*) are allelic to *Rht1* (Worland and Petrovic, 1988; Li et al., 2012; Bazhenov et al., 2015; Mo et al., 2018). Based on their responses to exogenous GA application, they are classified as GA-sensitive (*Rht4*, *Rht5*, *Rht6*, *Rht7*, *Rht8*, *Rht9*, *Rht12*, *Rht13*, *Rht14*, *Rht15*, *Rht16*, *Rht18*, *Rht24*, and *Rht25*) or GA-insensitive (*Rht1*/*Rht-B1b*, *Rht2*/*Rht-D1b*, *Rht3*/*Rht-B1c*, *Rht10*/*Rht-D1c*, *Rht11*/*Rht-B1e*, *Rht-B1h*, and *Rht17*/*Rht-B1p*) (Ellis et al., 2004; McIntosh et al., 2020), and have variable effects on plant height.

Only a few *Rht* genes (e.g., *Rht1*, *Rht2*, *Rht8*, *Rht11*, *Rht12*, and *Rht24*) have been used in wheat breeding to date (Mohan et al., 2021; Tian et al., 2022b; Würschum et al., 2017). Three GA-insensitive *Rht* genes and alleles, *Rht-A1*, *Rht-B1*, and *Rht-D1*, are located on chromosomes 4A, 4B, and 4D, respectively; these are the major sources of semi-dwarfism in modern wheat breeding and their utilization led to increased grain yield during the Green Revolution (Flintham et al., 1997). An important alternative to the GA-insensitive dwarfing alleles is the GA-responsive *Rht8* (Chai et al., 2022; Gasperini et al., 2012; Korzun et al., 1998; Xiong et al., 2022). *Rht8* is well-adapted to hot and dry environments (Korzun et al., 1998), providing semi-dwarf stature with the benefits of early seedling vigor and a longer coleoptile (Ellis et al., 2004). It increases spike compactness by 15% and decreases spike length without altering spikelet number (Kowalski et al., 2016). *Rht12*, *Rht18*, *Rht23*, *Rht24*, and *Rht25* are all GA-sensitive dwarfing genes. *Rht12* originated from a gamma ray-induced mutation (Viglasi, 1968). It was reported that *Rht12* reduced plant height by ~46%, reduced grain weight, and increased grain yield, harvest index, and lodging resistance (Rebetzke et al., 2012). *Rht18* influences spikelet number per spike, GN, and TGW (Yang et al., 2015). *Rht23* likely encodes a Q homolog and shows clear effects on plant height, spikelet density, spike shape, spikelet number, and glume toughness (Zhao et al., 2018). The frequency of the *Rht24b* allele has greatly increased over the last several decades, suggesting that it has been used in wheat breeding programs worldwide (Würschum et al., 2017; Tian et al., 2019). *Rht24b* is closely associated with increased TGW, GN, spike number, and nitrogen use efficiency (NUE), and photosynthetic rate (Li et al., 2015b; Tian et al., 2017; Tian et al., 2022b). *Rht25* significantly affects spike length, spike compactness, grain number, grain weight, and heading date (Mo et al., 2018). *Rht-B1b* and *Rht-D1b* reduce plant height by 15%–20% and increase grain yield by 5%–10% (Flintham et al., 1997; Hoogendoorn et al., 1990). These positive effects on grain yield are attributed to the increased number of productive tillers (Lanning et al., 2012; Sherman et al., 2014). It is notable that neither gene affects the number of organs. Some genes controlling wheat grain yield and *Rht* genes are connected to each other; a network has been elucidated based on the associations among these genes (Figure 3).

Potential of Green Revolution genes in modern breeding

Natural allelic variations in *Rht* genes are critical for improving grain yield in wheat. Previous studies have identified rich genetic diversity in *Rht* genes and verified that these allelic variations greatly contribute to wheat production worldwide (Wen et al., 2013; Würschum et al., 2015). Notably, some reports provided information about *Rht-1* allele distribution in Chinese germplasm, which facilitated understanding of the diversity of *Rht-1* and greatly enriched the resource pool for wheat breeding in China (Li et al., 2013a).

Greater photosynthetic capacity

Dwarf/semi-dwarf varieties have greater photosynthetic capacities than taller varieties (Bishop and Bugbee, 1998; LeCain et al., 1989). Relevant studies have hypothesized that because semi-dwarfism is associated with a reduction in leaf cell size, there is a higher concentration of photosynthetic machinery in each cell, and thus an increase in the photosynthetic capacity per unit leaf area or weight (Morgan et al., 1990). The positive effects of *Rht-B1c* on chlorophyll levels are likely due to upregulation of genes involved in chlorophyll biosynthesis and chloroplast development (Wen et al., 2013). However, other studies reported no difference in photosynthetic rates between tall and semi-dwarf varieties (Dobrikova et al., 2017; Nenova et al., 2014). Reports have been consistent in showing that dwarf lines have increased chlorophyll content. Validating the effects of *DELLA* genes on photosynthetic capacity is a promising potential tool for grain yield improvement in wheat breeding.

Efficient utilization of nitrogen fertilizer

Nitrogen fertilization can improve grain yield, but over-fertilization increases the risk of environmental pollution. A recent study suggested that enhanced DELLA protein function, which is characteristic in Green Revolution varieties, competitively inhibits the interaction between GIBBERELLIN INSENSITIVE DWARF1 (GID1) and NITROGEN-MEDIATED TILLER GROWTH RESPONSE 5 (NGR5); this effect stabilizes NGR5, improving grain yield and NUE by increasing the tiller number (Wu et al., 2020). GROWTH-REGULATING FACTOR 4 (OsGRF4) promotes nitrogen assimilation in rice and is inhibited by interactions with DELLA proteins, suggesting that DELLA accumulation re-

duces NUE (Li et al., 2018b). These findings reveal the potential of *DELLA* genes for altering NUE in wheat, which should be validated *in vivo* in the future.

Regulation of inflorescence meristem size

The size of the inflorescence meristem limits yield potential in crops (Xu et al., 2015; Guo et al., 2016; Je et al., 2016). DELLA proteins have genetically distinct roles in the regulation of stem growth and inflorescence meristem initiation, not only in *Arabidopsis* but also in barley (Serrano-Mislata et al., 2017). Therefore, the effects of *DELLA* genes on meristem size may allow improvement of grain yield in the wheat varieties carrying Green Revolution genes.

Regulation of end-use quality

As the Chinese population grows and living standards rise, consumers and industries are increasing the demand for wheat flour for a wider range of end uses. Demand is especially high for hard wheat flour (to be used in bread and noodles) and for soft wheat flour (to be used in cakes and biscuits). The end-use value of wheat flour primarily depends on the quantity and properties of the constituent gluten proteins and starch (Figure 4A). Gluten proteins are complex and mainly consist of two types of seed proteins, the polymeric glutenins and the monomeric gliadins, which together confer unique viscoelastic properties to wheat dough (Biesiekierski, 2017; Payne et al., 1987). For pan bread, noodles, and steamed bread, the breeding objectives are to improve the color, starch viscosity, and qualities that confer strength and extensibility to dough. For cookies and sponge cakes, the breeding objectives are to reduce the protein content and dough strength. High molecular weight (HMW)-glutenin subunits (GSs) account for approximately 10% of gluten proteins, but variation in their composition explains up to 70% of quality variation in breadmaking (Eagles et al., 2002; Liu et al., 2005; Payne et al., 1987). Thus, HMW-GS genes are the major functional targets for quality improvement in wheat.

Molecular mechanisms regulating gluten protein accumulation

The genes encoding gluten proteins are specifically expressed in the endosperm of developing wheat grains. They are primarily regulated at the transcriptional level through interactions between *cis*-acting motifs and *trans*-acting factors (Figure 4B). Considerable progress has been made in genomic analysis of *cis*- and *trans*-elements that affect gluten gene expression. The conserved *cis*-elements in the promoter regions of gluten genes have been identified (e.g., HMW-GSs, low molecular weight [LMW]-GSs, and gliadins) (Li et al., 2019d). A 300-bp promoter region containing the conserved *cis*-regulatory module 1 (CCRM1) (−300 to −101 bp) is sufficient to confer endosperm expression of HMW-GS genes. CCRM2 (−650 to −400 bp) and CCRM3 (−950 to −750 bp) enhance HMW-GS gene expression (Ravel et al., 2014; Li et al., 2019d). CCRM1-1 (−208 to −101 bp) appears to be indispensable for HMW-GS gene expression in the endosperm tissues, whereas CCRM1-2 (−300 to −209 bp) is required for the timely onset of HMW-GS gene expression in the endosperm (Li et al., 2019d). A variety of TFs that regulate gluten gene expression have been characterized. Storage protein activator (SPA) proteins, which are opaque2-like basic leucine zipper (bZIP) TFs, bind the GCN4-like motif (GLM; 5′-ATGAG/CTCAT-3′) of gluten genes and activate their expression (Ravel et al., 2014). SPA heterodimerizing protein (SHP), a protein interactor of SPA, represses transcription of HMW-GS and LMW-GS genes (Boudet et al., 2019). The prolamin box (P-box) (5′-TGTAAAG-3′) is recognized by prolamin-box binding factor (PBF), which is a DNA-binding with one zinc finger (DOF) TF (Diaz et al., 2005). The promoter regions of wheat alpha-gliadin and LMW-GS genes possess a typical P-box, whereas the promoters of HMW-GS genes contain only a P-like box (Dong et al., 2007). The wheat DOF TF P-box binding factor interacts with TaQM to activate transcription of LMW-GS and gliadin genes (Dong et al., 2007; Moehs et al., 2019; Ravel et al., 2006). Another DOF TF, PBF-D, binds a P-box element in the promoters of the HMW-GS genes *Glu-1By8* and *Glu-1Dx2*; PBF-D overexpression significantly increases HMW-GS accumulation in the grains (Zhu et al., 2018). Binding of the AACA motif (5′-AACA/TA-3′) by R2R3-type MYB TFs (Diaz et al., 2002; Wu et al., 2000), or of the RY repeat (5′-CATGCATG-3′) by the B3 protein FUSCA3 (Bäumlein et al., 1992; Moreno-Risueno et al., 2008), has also been shown to affect gluten gene expression. TaGAMyb, an R2R3 MYB TF, interacts with the histone acetyltransferase TaGCN5 to activate expression of the HMW-GS gene *Glu-1Dy* by acetylating histone H3 (Guo et al., 2015b). TaFUSCA3 transactivates the promoter of the HMW-GS gene *Glu-1Bx7* through binding to the *cis*-element RY repeat (Sun et al., 2017). The chromatin remodeling gene *TaDME*, which encodes 5-methylcytosine DNA glycosylase, is required for efficient expression of LMW-GS and gliadin genes through active demethylation of the promoters in developing wheat grains (Wen et al., 2012). The wheat endosperm-specific transcription factor TaNAC019 binds to the promoters of HMW-GS genes in cooperation with TaGAMyb to activate storage protein accumulation. *TaNAC019-BI* was identified as an elite allele for flour processing quality, establishing TaNAC019 as a candidate gene for breeding wheat with improved quality (Gao et al., 2021b). In addition, a novel NAC TF, SPR, was validated as a suppressor of seed storage protein synthesis in wheat (Shen et al., 2021). Taken together, these data suggest that tran-

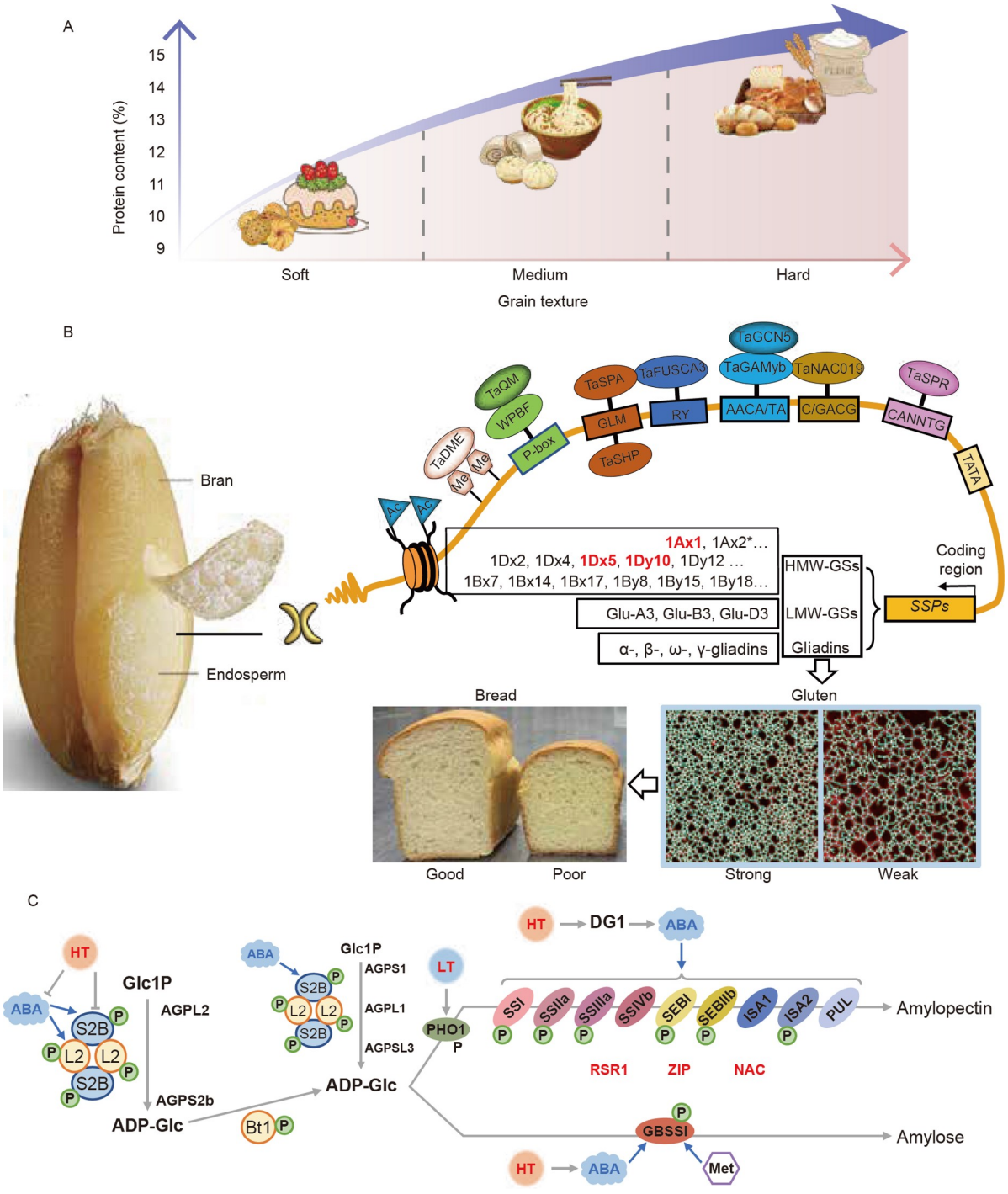

Figure 4 Wheat end-use quality determination and molecular regulation. A, The various end-use value of wheat flour depends on quantity and properties of gluten proteins. B, Transcriptional regulation of gluten genes involves complex interactions between *cis*- and *trans*-acting factors. C, Molecular regulatory mechanisms of starch biosynthesis in wheat.

scriptional regulation of gluten genes involves complex interactions between *cis*- and *trans*-acting factors. Differences in these interactions may underlie variations in the expression patterns of gluten genes and their effects on wheat end-use quality. Insights related to glutenin and gliadin gene expression may yield useful targets for modifying gluten protein function to improve wheat end-use properties.

Starch biosynthesis regulation

Starch biosynthesis in wheat grains requires multiple enzymes and transporters (Kumar et al., 2018) (Figure 4C). A total of 28 key enzymes and non-enzymatic proteins have been found to participate in starch biosynthesis during wheat endosperm development, namely five ADP-glucose pyr-

ophosphorylases (AGPases), one ADP-glucose (ADPG) transporter, two granule-bound starch synthases (GBSSs), seven starch synthases (SSs), four SBEs, four debranching enzymes (DBEs), two starch/α-glucan phosphorylases (PHOs), two disproportionating enzymes (DPEs), and one protein targeting to starch (PTST) (Huang et al., 2021). AGPase is the first key rate-limiting enzymatic step in the starch biosynthesis pathway (Biesiekierski, 2017); it catalyzes the conversion of glucose-1-phosphate and ATP to ADPG, which is the major substrate for starch biosynthesis (Pfister and Zeeman, 2016). GBSS catalyzes the transfer of ADPG to linear chains of α-(1, 4)-linked glucose residues, which are the main components of amylose. Amylopectin biosynthesis is more complex, involving at least SS, SBE, and DBE (Crofts et al., 2015). SS uses ADPG to elongate glucan chains, which form amylopectin molecules with branched structures that are jointly shaped by SBE and DBE (Hannah and James, 2008; Jeon et al., 2010). TaSBEIII is associated with the formation of both A and B starch granules in grains (Kang et al., 2013). TaSSIV and B-GRANULE CONTENT 1 (TaBGC1) are required for proper granule initiation in wheat endosperm amyloplasts. This was confirmed by a mutation in *TaSSIVb-D* that led to a reduction in the number of starch granules in chloroplasts (Guo et al., 2017). Furthermore, mutation of either *TaSSIV* or *TaBGC1* results in multiple initiations of amyloplasts and the formation of compound granules (Hawkins et al., 2021). Modifications to starch biosynthesis-related enzymes can have profound effects on the nutritional quality of wheat grains, which may have desirable health benefits. For example, Li et al. modified the composition, structure, and properties of starch by editing *TaSBEIIa* with CRISPR/Cas9; they generated transgene-free high-amylose wheat lines with increased levels of resistant starch, a dietary fiber with proven beneficial health effects (Li et al., 2021b).

Several TFs that regulate starch biosynthesis in developing wheat grains have been reported (Figure 4C). TaRSR1 is an important negative regulator of starch synthesis in wheat grains that temporally regulates the expression of specific starch biosynthesis-related enzyme-encoding genes (Liu et al., 2016). TubZIP28/TabZIP28 binds to promoters of the genes encoding cytosolic AGPases; knocking out *TabZIP28* in bread wheat causes significant declines in both the expression and activity levels of cytosolic AGPase. This results in a decrease in total starch content of ~4% in mature grains (Song et al., 2020). The endosperm-specific TF TaNAC019 regulates both glutenin and starch accumulation by directly activating the examined genes involved in seed storage protein accumulation and starch metabolism (Gao et al., 2021b). However, another study showed that overexpression of the A genome homoeolog of TaNAC019 (TaNAC019-A1) downregulated seed starch content and grain weight (Liu et al., 2020d). Thus, regulation of gluten protein accumulation and starch biosynthesis by TaNAC019 in wheat grains appears more complex than other known regulatory mechanisms and requires further study to be fully understood.

In addition to transcriptional regulation, post-translational modifications (PTMs) may also regulate starch accumulation (Figure 4C). PTMs have been revealed to occur extensively in starch biosynthesis proteins (Tappiban et al., 2021). To date, five types of PTMs have been found on plant starch biosynthesis proteins: phosphorylation, lysine acetylation, succinylation, lysine 2-hydroxyisobutyrylation, and malonylation. However, the functional effects of these modifications are generally not well understood (Tappiban et al., 2021). In wheat, phosphorylation has been detected in GBSSI, SSIIa, SSIII, and AGPS in developing grains, and reduced phosphorylation is correlated with decreased total starch content and yield in water-stressed plants (Cao et al., 2015a; Chen et al., 2014; Chen et al., 2017a). However, further study is required to better understand the molecular processes and functional consequences of different types of PTMs on wheat starch biosynthesis. A deeper understanding of such PTMs will facilitate appropriate genetic manipulation to improve starch accumulation and yield potential.

Breeding for end-use quality improvement

Advances in functional genomic studies of quality-related traits and the development of MAS have greatly accelerated the improvement of end-use quality in wheat. Many genes that contribute to quality-related traits have been utilized in breeding. Gene-specific markers corresponding to various glutenin subunit alleles have been developed for gene tagging and marker-assisted transfer. Specifically, markers mapped to *Glu-1* loci on chromosomes 1A, 1B, and 1D that encode HMW-GSs and to *Glu-3* loci encoding LMW-GSs have been developed. Superior HMW-GS genes, including Glu-1Dx5 + 1Dy10 and Glu-1Bx17 + 1Dy18, have been pyramided together to improve dough quality (Hernández et al., 2012; Liang et al., 2009). Notably, a mutant of HMW-GS 1Ax1 ($1Ax1^{G330E}$), which was induced by chemical mutagenesis with ethyl methane sulfonate (EMS), can significantly improve dough strength and bread-making quality compared to the wild-type allele (Li et al., 2015c); the mutant was used to breed the strong-gluten cultivar Kexing 3302 in China. The *Hardness* (*Ha*) locus carries the *Puroindoline A* (*Pina*) and *Puroindoline B* (*Pinb*) genes. These genes control wheat grain hardness, which is very important for milling and end-use traits. Single and double loss-of-function mutants for *Pina* and *Pinb* have been used to select for harder grain texture. Polyphenol oxidase (PPO) activity is responsible for the brown discoloration of wheat products, especially Asian noodles. PPO gene markers can be used to identify genotypes with lower PPO activity (Liang et al., 2009). The promoter of the gene *wbm*, identified based on its

high expression in the transcriptome of developing wheat seed (Furtado et al., 2015), has been shown to contain polymorphisms among different quality varieties. Wild wheat relatives have also been used as a source of genes to improve quality traits via backcrossing to modern varieties. For example, *Grain protein content* (*Gpc*)-*B1*, originally identified in wild emmer, has been introduced into durum and bread wheat lines to increase grain protein levels (Distelfeld et al., 2006).

Improvement of quality traits via conventional breeding requires a great deal of time and labor because the relevant phenotypic evaluations are complicated and laborious. MAS is useful for transferring a small number of genes with high impacts on quality traits. However, more specific markers for diverse target genes remain to be developed for future wheat quality improvement programs. Whole-genome level selection is effective for improving complex traits controlled by polygenes because it can simultaneously tag and transfer multiple genes. Once a genomic selection model is validated, it can be implemented in combination with MAS in breeding programs. Genome editing tools allow the introduction of elite variations to specific genes that are related to quality in elite varieties, which will reduce the time required for backcrossing and allow improvement of a variety within 2–3 years. It is therefore highly desirable to develop more efficient methods for improvement of wheat quality traits.

Vernalization regulation in wheat

Many species that grow in temperate climates, including wheat and barley, require prolonged cold exposure in the winter to acquire flowering competence for the coming spring; this process is known as vernalization (Chouard, 1960). Such a requirement ensures that flowering occurs in spring, when the higher temperatures and longer day lengths that are critical for successive reproductive growth and seed production will occur (Amasino, 2010; Luo et al., 2019; Xu and Chong, 2018). Vernalization not only controls flowering time but also impacts spikelet development. Several genes related to vernalization are involved in shaping spikelet development and spike architecture, directly contributing to wheat yield (Li et al., 2019a; Li et al., 2021d). The key components that remain to be fully understood are the molecular mechanisms underlying vernalization requirements, initiation, responses, maintenance, and resetting.

Determination of vernalization requirements in cereals

Winter wheat varieties have a longer growth period than spring wheat, and generally also have superior grain yield and quality (Cann et al., 2020; Coventry et al., 1993; Penrose, 1993). However, the time periods during which chilling temperatures occur can vary a great deal between regions, which limits the geographic regions in which winter wheat can be planted. Wheat has evolved mechanisms to fine-tune the requirements for the duration of chilling by adjusting vernalization needs. Varieties can thus be categorized as strong winter wheat, facultative wheat, or spring wheat. The natural variation in vernalization requirements is mainly determined by *VERNALIZATION* (*VRN*) loci, including *VRN1*, *VRN2*, and *VRN3*, which were first named in wheat (Yan et al., 2003) (reviewed by Luo and He, 2020; Xu and Chong, 2018). Although these genes bear the same names as *Arabidopsis* genes, *AtVRNs* encode entirely different types of proteins. *VRN1* is an APETALA1 (AP1)-like MADS-type TF that is induced by long-term cold exposure and promotes flowering (Yan et al., 2003). *VRN2* encodes a protein containing zinc-finger and CCT domains; it is a floral repressor that inhibits flowering prior to cold exposure (Yan et al., 2004). *VRN3*, an ortholog of the *Arabidopsis* gene *FT*, integrates both photoperiod and vernalization signals and accelerates flowering (Yan et al., 2006). In the autumn, prior to cold exposure, *VRN1* expression is low; in contrast, *VRN2* is highly expressed, repressing *VRN3* expression in leaves and preventing flowering (Chen and Dubcovsky, 2012). In the winter, *VRN1* expression increases with the duration of cold exposure. *VRN2* is gradually downregulated by cold exposure and is maintained at low levels after vernalization partly through direct repression by *VRN1*, which allows *VRN3* expression (Chen and Dubcovsky, 2012; Deng et al., 2015; Oliver et al., 2013). Moreover, VRN1 directly induces *VRN3* expression in leaves, and VRN3 moves to the shoot apical meristem to further promote *VRN1* expression by forming a florigen activation complex (FAC) with FLOWRING LOCUS D like 2 (FDL2) and 14-3-3C (Li and Dubcovsky, 2008; Li et al., 2015a). *VRN3* expression is also regulated by photoperiod pathway factors, including PHYTOCHROME C (PHYC), PHOTOPERIOD1 (PPD1), CONSTANS (CO), and NULCEAR FACTOR Y (NF-Y) (reviewed by Xu and Chong, 2018).

In addition to the core VRN1-VRN2-VRN3 regulatory module, orthologs of the key *Arabidopsis* gene *FLOWERING LOCUS C* (*FLC*) have been shown to function in the vernalization process of monocots (Ruelens et al., 2013; reviewed by Kennedy and Geuten, 2020). *TaOS2* (*TaODDSOC2*/*TaAGL33*) is downregulated by vernalization, and it remains lowly expressed after vernalization (Sharma et al., 2017; Winfield et al., 2009). This expression pattern in response to cold exposure is comparable to that of *FLC* in *Arabidopsis* (Luo and He, 2020). Knocking out the *TaOS2* D-homeolog causes slightly early flowering (three days earlier than in the wild type) (IWGSC, 2018). In barley and *Brachypodium*, gene expression patterns and genetic evidence also support that *BdOS2* and *HvOS2* function as floral repressors in the vernalization process (Greenup et al., 2010;

Sharma et al., 2017). The functions of the other two *FLC* orthologs in monocots, *TaOS1*/*TaAGL42* and *MADS37*/*TaAGL12*, require further investigation (reviewed by Kennedy and Geuten, 2020). In barley, HvVRN1 can directly downregulate *HvOS2* through binding of the promoter region, which releases HvOS2-mediated repression of *FPF1-like* genes to promote flowering (Deng et al., 2015; Greenup et al., 2010). In *Brachypodium*, *BdOS2* expression is elevated in *BdVRN1* RNAi lines and in *BdVRN2* overexpression lines (Woods et al., 2016), further confirming that VRN1 represses *TaOS2* in monocots.

Genetic variation at the *VRN1* locus is one of the major sources of differences in vernalization requirements between wheat varieties. One dominant *VRN1* allele in either the A, B, or D subgenome (or in the trans-located *VRN-D4* on chromosome 5DS) is sufficient to generate a spring growth habit. Spring alleles of *VRN-A1*, *VRN-B1*, and *VRN-D1* exhibit varied basal transcription levels prior to cold exposure and have different responses to vernalization (Fu et al., 2005; Kippes et al., 2015). An active *VRN2* allele is necessary for a vernalization requirement; the lack of *VRN2* or a mutation in the conserved CCT domain alters a winter growth habit to a spring growth habit (Yan et al., 2004; Dubcovsky et al., 2005). Constant activation of *VRN3* allele (early flowering) also allows plants to bypass the vernalization requirement (Yan et al., 2006). The majority of diploid wheat ancestors were of the winter type, especially those contributing to the A genome (e.g., *Triticum boeoticum* and *T. urartu*). After polyploidization, particularly in cultivated hexaploid bread wheat, spring forms were artificially selected for adaptation to different climatic conditions. Interestingly, the spring forms of polyploid wheat are primarily associated with a dominant allele at the *VRN1* locus (reviewed by Shcherban and Salina, 2017). This is likely due to the gain-of dominance of spring allele by mutation at *VRN1* while recessive for *VRN2* and *VRN3* loci. The expression pattern of *TaOS2* in winter and spring wheat varieties over the course of cold exposure suggests that it is a candidate locus for mediating the vernalization requirement (Sharma et al., 2017). However, more genetic evidence and sequence variation analyses must be performed to validate this hypothesis.

In addition to the requirement for vernalization, the degree of cold exposure needed to achieve vernalization saturation is an important consideration for the production and distribution of wheat varieties. DNA sequence polymorphisms and copy number variation at the *VRN1* locus have been studied to understand their contributions to the strength of the vernalization response (Chen et al., 2009; Díaz et al., 2012; Eagles et al., 2011; Fu et al., 2005; Li et al., 2013b; Kippes et al., 2015; Kippes et al., 2018; Muterko and Salina, 2018). A SNP in the first intron of *VRN-A1* is associated with differences in the vernalization requirement and response (Kippes et al., 2015; Kippes et al., 2018), likely resulting from altered binding strength of the flowering repressor TaGRP2 (Xiao et al., 2014). SNPs in the *VRN1* exon that cause amino acid substitutions (e.g., L117F and A180V) affect the length of cold exposure that is required to complete vernalization; these substitutions have distinct geographical distributions (Díaz et al., 2012; Eagles et al., 2011; Li et al., 2013b; Muterko and Salina, 2018). The L117F mutation occurs in the conserved K-domain, affecting vernalization duration via *VRN-A1* expression in winter wheat varieties that carry multiple copies of *VRN-A1* (Díaz et al., 2012; Dixon et al., 2019). The A180V mutation regulates vernalization duration through the strength of the interaction with its binding partner TaHOMEOBOX protein 1 (HOX1) (Li et al., 2013b). *VRN1* copy number variation and the differences in response kinetics between *VRN-A1*, *-B1*, and *-D1* may also influence the required duration of vernalization (Díaz et al., 2012; Loukoianov et al., 2005), although the details of the mechanisms involved remain unclear. Beyond sequence variation *per se*, increasing evidence supports the idea that epigenetic regulation may be involved in mediating differences in vernalization duration; this may include non-coding (nc)RNA, histone modifications, and local variations in chromatin structure (Huan et al., 2018; Oliver et al., 2009; Xiao et al., 2014; Xu et al., 2021). Further studies are required to fully understand differences in vernalization duration among winter wheat varieties, and to identify genetic variants that can be used in breeding to adapt wheat production and distribution to meet the threats of global climate change.

Perception and sensing of long-term cold exposure during vernalization

During vernalization, long-term low temperature exposure (0–10°C for more than one month) enables winter cereals to acquire flowering competency. This process includes two phases: sensing the environmental chilling signal and measuring the duration of cold exposure (Figure 5B). The mechanism by which wheat perceives the environmental chilling signal is not clear. In rice, the COLD1–G-protein α subunit 1 (RGA1) complex is a critical sensor in activating the cold-induced defense response. COLD1, a regulator of G-protein signaling (RGS), interacts with RGA1 to activate Ca^{2+} influx into the cytoplasm and to trigger downstream responses for chilling tolerance; these include activating the cold-responsive *INDUCER OF CBF EXPRESSION 1* (*ICE1*)–*C-REPEAT-BINDING FACTORS* (*CBF*)–*COLD REGULATED* (*COR*) gene module, and altering accumulation of metabolites such as sugar and proline (reviewed by Xu and Chong, 2018; Zhang et al., 2019c). Winter wheat is planted in the autumn to allow gradual acclimation to lower temperatures so that plants can later tolerate prolonged cold during the winter. The cold-activated *ICE1–CBF–COR* gene

module, which is conserved in wheat, may help to acquire freezing tolerance before winter (Li et al., 2018a; Pearce et al., 2013). Short-term cold exposure can also slightly upregulate *VRN1*, regardless of whether it is the winter or spring allele (Oliver et al., 2013). Multiple putative CBF- and ICE1-binding sites have been found in the *VRN1* promoter (Alonso-Peral et al., 2011). Interestingly, natural variations in loci for frost tolerance have been mapped to vernalization genes such as *VRN1* and *CBF*s (Zhu et al., 2014). Indeed, *VRN1* expression is negatively correlated with frost tolerance and with expression of *CBF* and *COR* genes (reviewed by Galiba et al., 2009). This is consistent with the observations that winter wheat is more resistant to freezing than spring wheat, but that this capability is reduced after vernalization treatment. VRN1 directly regulates *CBF* expression in barley (Deng et al., 2015), further confirming the relationship between vernalization and cold acclimation. Such interconnection is of great importance for overwintering, particularly for biennial and perennial plants. The mechanism by which a sensed chilling stress signal is transduced to vernalization is worthy of future study.

Although the mechanism for cold perception is unclear in wheat, the loci involved in sensing cold and triggering the vernalization response have long been sought. In the 1930s, a grafting assay suggested that shoot apices are responsible for perception of cold with respect to flowering (Curtis and Chang, 1930). However, due to limitations of the technique applied, it was difficult to distinguish between shoot apical meristems and young leaves. It was later reported that flowering competency could be acquired from vernalized leaves in sugar beet (Crosthwaite and Jenkins, 1993), *Luannari biennis* (Wellensiek, 1962), and *Thlaspi arvense* (Metzger, 1988). *In situ* RNA hybridization showed that some genes induced by vernalization were first expressed in immature leaves. This is true of *VER2*, for example, which encodes the lectin jacalin (Yong et al., 1999; Yong et al., 2003) and is a positive regulator of *VRN1*, accelerating vernalization and promoting flowering (Xiao et al., 2014). This evidence supports the hypothesis that young leaves serve as the primary tissue for perception of vernalization signals in wheat. *VRN1* expression is induced by cold in both the shoot apex and the leaves; it will therefore be informative to compare the transcriptional activation in both tissues at single-cell resolution *in situ*.

One major difference between chilling stress and vernalization is the duration of cold exposure. This raises the question of how plants quantitatively sense this parameter. It has long been known that glucose addition at the early stage of vernalization can significantly accelerate flowering, an effect that is reduced or totally absent at later stages (Li et al., 1987). A small proportion of intracellular glucose enters the hexosamine biosynthetic pathway, which ultimately produces UDP-N-acetylglucosamine (UDP-GlcNAc) (Zachara and Hart, 2004). UDP-GlcNAc levels fluctuate during vernalization but accumulate over time, as do global *O*-GlcNAcylation levels (Xing et al., 2009; Xu et al., 2019). For instance, TaGRP2 is gradually *O*-GlcNAcylated during the process of vernalization, de-repressing *VRN1* to promote flowering in wheat (Xiao et al., 2014). Dysfunction of *O*-GlcNAc transferase1 (OGT1) can fine-tune the flowering time of winter wheat (Fan et al., 2021). Thus, *O*-GlcNAcylation and phosphorylation of key proteins, combined with metabolic changes resulting from prolonged low temperature, may generate an effectively quantitative signal by which plants can measure chilling duration (Figure 5B). However, detailed mechanistic insights will require additional studies. A recent study in *Arabidopsis* suggested that the rate of NTM1-LIKE8 (NTL8) dilution would decrease at chilling temperatures due to the reduced plant growth rate but persistent protein stability. This would result in accumulation of NTL8, which can directly bind to *VERNALIZATION INSENSITIVE3* (*VIN3*) and activate its expression. *VIN3* encodes a PHD protein that functions together with Polycomb repressive complex 2 (PRC2) to epigenetically silence *FLC* during vernalization in *Arabidopsis* (Antoniou-Kourounioti et al., 2021; Zhao et al., 2021). Protein dilution levels dependent on temperature-dependent growth are thus exploited to provide long-term thermosensory information. This indicates that there are diverse mechanisms by which plants sense long-term cold and translate cold sensing into developmental signaling. It also demonstrates differences in the vernalization gene network between monocotyledons such as wheat and dicotyledons such as *Arabidopsis*.

Establishment and memory of vernalization

VRN1 is the major factor that mediates vernalization to promote flowering (Trevaskis, 2010; Yan et al., 2003). Prior to cold exposure, the winter allele of *VRN1* is silenced by a repressive histone modification, methylation of lysine 27 in histone H3 (H3K27me3), at both the promoter and a critical region in the first intron (Oliver et al., 2009; Xiao et al., 2014). Mutation of ENHANCER OF ZESTE-LIKE 1 (EZL1), a "writer" of H3K27me3, reduces the vernalization requirement through elevated *VRN1* expression and rapid flowering in *Brachypodium* (Lomax et al., 2018). A BAH- and TFIIS-domain-containing factor, REPRESSOR OF VERNALIZATION1 (RVR1), reportedly represses *VRN1* before vernalization related to H3K27me3 coverage (Woods et al., 2017) (Figure 5C). The "VRN" box in the promoter and the critical region within the first intron of *VRN1* are both important for repression of *VRN1* before vernalization; mutation of either region leads to de-repression of *VRN1* without cold exposure (Fu et al., 2005; Muterko et al., 2016; Yan et al., 2004; Strejčková et al., 2021). Recently, a genic loop between the promoter and the first intron was identified in

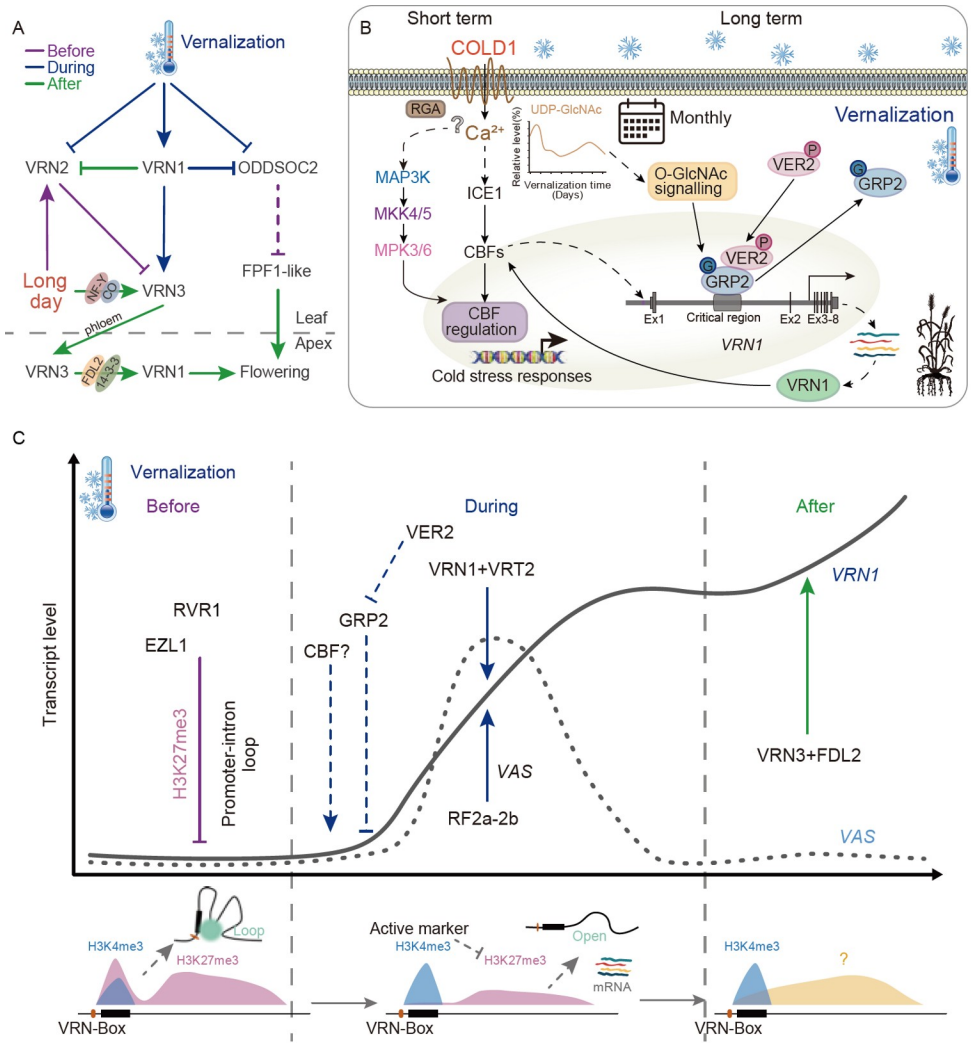

Figure 5 Vernalization regulated flowering transition in winter wheat. A, Genetic relationship among major vernalization requirement determination loci. B, Perception and sensing of short and long-term cold exposure during vernalization. C, Induction of *VRN1* expression during different stages of vernalization treatment via transcriptional regulation in the context of dynamic chromatin status.

the winter *VRN1* allele (Xu et al., 2021), suggesting a potential function of local chromatin structure in maintaining transcriptional silence of *VRN1* in winter wheat.

VRN1 transcription is quantitatively activated during long-term cold exposure with different accelerations at various vernalization stages (Figure 5C). Short-term cold exposure (hours to days) can induce defense-responsive factors such as CBFs to bind the *VRN1* promoter and activate or de-repress its expression, but only to a moderate degree (Alonso-Peral et al., 2011; Oliver et al., 2013). This is likely independent of the VRN-box that mediates the vernalization requirement (Oliver et al., 2013). TaVRT2, an SVP-like MADS TF, may also be involved in activation of *VRN1* at early stages (Xie et al., 2021). *TaVRT2* expression is rapidly increased upon cold exposure but sharply declines after cold exposure is ended. TaVRT2 may directly bind to the CArG box of the *VRN1* promoter (Kane et al., 2007; Xie et al., 2021). However, the actual function of TaVRT2 in activating *VRN1* during short term cold exposure, and whether the CArG box is necessary for initial activation of *VRN1* rather than vernalization response, requires further investigation (Kane et al., 2007; Pidal et al., 2009; Xie et al., 2021). It is currently unknown whether induction of *VRN1* expression requires a transcriptional activator, or whether alteration of the local chromatin environment by cold exposure is sufficient to initiate basal transcription of *VRN1*.

Short-term cold exposure can induce moderate *VRN1* expression, but the gene is downregulated via post-transcriptional regulation (Figure 5C). An RNA-binding protein, TaGRP2, has been shown to bind the RIP3 site of the critical first intron region in *VRN1* pre-mRNA, inhibiting *VRN1* activation in response to early vernalization treatment. TaGRP2 also influences the histone modification dynamic during cold exposure, decreasing H3K27me3 and increasing H3K4me3 at the first intron of *VRN1* (Xiao et al., 2014). This ensures that flowering does not occur without adequate vernalization. As

cold exposure is extended, *O*-GlcNAcylation of TaGRP2 is increased, likely mediated by TaOGT1 (Fan et al., 2021). Vernalization also induces phosphorylation of VER2 and promotes its translocation to the nucleus (Xing et al., 2009). VER2 interacts with *O*-GlcNAcylated TaGRP2, either inhibiting binding of TaGRP2 to *VRN1* pre-mRNA or facilitating TaGRP2 exportation to the cytoplasm; this removes inhibition of *VRN1* transcription (Xiao et al., 2014). The ncRNA *VAS* (a spliceoform of *VRN1*) is detected mainly in winter wheat. *VAS* is induced by cold exposure earlier than the full-length *VRN1* transcript; it functions as a long non-coding (lnc)RNA, accelerating activation of *VRN1* to promote flowering. *VAS* is recognized by the transcription factor RF2b and facilitates RF2b-RF2a dimer binding to the *VRN1* promoter via the Sp1 motif, further activating *VRN1*. This is also associated with breakage of the repressive genic loop between the promoter and the first intron of *VRN1* (Xu et al., 2021). Thus, longer cold exposure (~10–20 d) causes alterations in the chromatin environment, including histone modification changes from repressive to active, and a local genic loop break; this facilitates further full induction of *VRN1*. An insufficient vernalization process can be reversed by interruption with high temperature exposure (~35°C) in a process known as devernalization (Gregory and Purvis, 1948; Yong et al., 2003). A possible explanation for this phenomenon is reactivation of the floral repressors *VRN2* and *TaOS2* by warm temperatures during vernalization (Dixon et al., 2019).

After winter, plants must maintain the vernalized status through rounds of mitotic division to allow flowering in the spring. Such memory is thought to be dependent on epigenetic regulation. In *Arabidopsis*, memory of vernalization is achieved by spreading H3K27me3 through the entire *FLC* gene body region to maintain transcriptional silence (reviewed by Whittaker and Dean, 2017). In barley and wheat, winter-induced *VRN1* expression is maintained by active histone modifications; for instance, H3K27m3 is low in *VRN1*, whereas H3K4me3 and H3K36me3 are high (Oliver et al., 2009; Diallo et al., 2012), a state that is reenforced by the VRN1–VRN3 feed-forward loop (reviewed by Xu and Chong, 2018) (Figure 5C). Notably, the epigenetic memory of flowering competency gained from the vernalization process may also be retained at other loci, such as *VRN3* and *ODDSOC2* (Huan et al., 2018; Nelson et al., 2017). Whether the active chromatin state requires specific factors to maintain or is propagated by default should be further characterized in the future.

Resetting vernalization requirements for the next generation

After flowering, the "memory" of vernalization must be erased or otherwise reset in the offspring to prevent transgenerational inheritance of the vernalized state (Crevillén et al., 2014, reviewed by Finnegan et al., 2021; Luo and He, 2020). The erasure of cold memory involves resetting epigenetic modifications, which are the major factors mediating the vernalization response in cereals and *Arabidopsis* (reviewed by Luo and He, 2020; Xu and Chong, 2018).

In *Arabidopsis*, the flowering repressor *FLC* is repressed during vernalization and is maintained at low levels after cold exposure via chromatin-based silencing. *FLC* silencing persists through meiosis to gametes, with little or no expression in the mature pollen or female gametophytes of vernalized plants (Choi et al., 2009; Sheldon et al., 2008). Interestingly, the repressed state of *FLC* is maternally transmitted to early embryos (Luo et al., 2020). Reactivation or resetting of *FLC* expression is initiated in the proembryo at ~2–3 d after pollination (DAP). This process is initiated by the pioneer TF LEAFY COTYLEDON (LEC)1, which is expressed in the zygote within 1 DAP (Tao et al., 2017). LEC1 binds to the 5′ promoter region of *FLC* with repressive chromatin status, likely through its function as a "pioneer factor". Three B3-domain TFs (LEC2, FUSCA3/FUS3, and ABA-INSENSITIVE 3/ABI3) are also essential for resetting *FLC* expression in the progenies of vernalized plants (Tao et al., 2019; Xu et al., 2022). These B3 TFs function combinatorially to recognize the CME region, competing with VIVIPAROUS 1/ABI3-LIKE factors/ VAL1/2 and preventing the PHD–PRC2 association and recruiting active chromatin modifiers to switch the chromatin environment from the repressive H3K27me3 to the active H3K4me3 and H3K36me3 (Li et al., 2018c; Tao et al., 2017; Tao et al., 2019). LEC1 is partially responsible for activation of *LEC2*, *FUS3*, and *ABI3* expression in developing embryos (Jo et al., 2019), and thus facilitates the *FLC* resetting process. Following resetting during embryogenesis, *FLC* is further activated by ABI3, which acts with ABI5 during embryo maturation in response to abscisic acid (ABA) accumulation via active histone modification deposition (Xu et al., 2022). Active demethylation of H3K27me3 by histone demethylases plays a limited role in resetting *FLC* expression during embryogenesis (Crevillén et al., 2014; Tao et al., 2017).

Resetting of vernalization requirements in wheat is likely linked to re-silencing of *VRN1* transcription during embryogenesis through re-deposition of H3K27me3 (unpublished data); active expression of *VRN1* can still be observed in male and female gametes (Xiang et al., 2019). The molecular mechanisms underlying *VRN1* re-silencing during embryogenesis at both the genetic and epigenetic levels are a promising area for future research.

Fine-tuning the vernalization response through wheat breeding

Across the ten agro-ecological zones in China (He et al., 2001), the differing vernalization requirements between

wheat varieties are largely dependent on genetic variation at the *VRN1* and *VRN3* loci (Chen et al., 2013; Zhang et al., 2008; Zhang et al., 2015). This is likely because disruption of the recessive winter allele of *VRN1* in different homoeologs (*vrn-A1*, *vrn-B1* and *vrn-D1*) resulted in varied reduction of the vernalization requirement. In recent years, global climate change has caused increases in average temperatures and the occurrence of extreme weather events (Field et al., 2012). Warmer temperatures and temperature fluctuations restrict the growing area for some wheat varieties; furthermore, they affect the degree of vernalization completeness and the flowering competence of specific cultivars that were previously well-adapted to the agro-ecological zones in which they are grown. Identification of additional genetic loci controlling the vernalization response and generation of more genetic variations in known vernalization regulation factors would increase the capability of wheat to adequately withstand environmental changes. Recombination of current genetic variation in *VRN* loci by hybridization could also provide options for fine-tuning flowering time, as suggested by a study in barley (Fernández-Calleja et al., 2022). In addition to seasonal temperature, flowering time is also regulated by photoperiod. Several key regulatory loci with rich genetic variation have been identified that mediate flowering time based on photoperiod inputs (reviewed by Brambilla et al., 2017; Fernández-Calleja et al., 2021). Integration of both factors is a possible direction for adjusting vernalization requirements in specific wheat cultivars (Cha et al., 2022).

Importantly, elevated average temperatures could generally promote the growth and development of winter wheat, accelerating the transition of jointing and heading stages, thus increasing the threats posed by frost damage and late spring freezes. Vernalization comprises two interconnected processes: short-term chilling stress defense, then acquisition of flowering competence through long-term cold exposure. Future research should focus on identification of additional genetic loci that contribute to frost tolerance and flowering time in wheat, and on understanding the detailed mechanisms by which wheat senses short- and long-term cold exposure. This would enable breeders to pyramid appropriate genetic resources to adjust the vernalization response and duration requirements of individual wheat varieties based on their specific growth environments. Furthermore, dissecting the regulatory network underlying the balance between chilling stress defenses and flowering development could provide a genetic basis for molecular design of future wheat varieties that are resilient despite harsh conditions caused by global climate change.

Targeting nutrient use efficiency to increase yield traits

Genetic improvements and fertilizer application are both important strategies for increasing yield. However, historically, the increase in wheat yield in China was mainly due to overuse of chemical fertilizers rather than genetic gains in nutrient uptake efficiency (NUpE) and NUtE. Thus, improving nutrient use efficiency is an urgent need to achieve more sustainable agriculture. Here, we briefly summarize the genetic gains in nutrient-use traits obtained through past breeding efforts, the physiological and molecular mechanisms for efficient use of macronutrients, and strategies for improving nutrient use efficiency in future breeding.

Past improvements in traits related to nutrient use

Nutrient use efficiency encompasses both NUpE, i.e., nutrient acquisition from the soil, and NUtE, i.e., yield per unit of nutrient acquired. Nutrient use efficiency is affected by the uptake, assimilation, remobilization, and storage of nutrients (Figure 6A). In China, the rate of genetic gain for wheat yield was 0.65% per year from 1937 to 2012, contributing 47% to the total increase in wheat yield over that time period (Liu et al., 2021c). These gains were mainly due to reductions in plant height, improvements in harvest index, increases in TGW (0.38% per year) and, to a lesser degree, increases in GN (0.16% per year). Although nutrient use efficiency was not a target of past breeding efforts, traits related to nutrient use were nevertheless improved; these included NUpE, NUtE, nutrient harvest index (NHI), nutrient partial factor productivity (PFPN, yield per unit fertilizer rate) and nutrient agronomic efficiency (AEN, yield increases per unit fertilizer rate). However, the rates of genetic gain for NUpE (0.25% per year) and NUtE (0.31% per year) were lower than the rate for yield (0.65% per year), and no significant gain was observed for grain protein concentration (GPC) (Liu et al., 2021c).

Root morphology affects NUpE

To respond to variations in soil nutrient availability, plants can change the architecture of roots and aboveground tissues. N-, P-, and K-based fertilizers are well known to increase plant height, tiller number per plant, GN, and grain yield in wheat. Plants can adapt to nutrient availability by altering root-system architecture (RSA) to efficiently seek out nutrients. Fertilizer application can form nutrient-rich patches in soils, and the concentrated nitrate and phosphate patches can stimulate lateral root (LR) branching in wheat (Weligama et al., 2008). Low N availability can also stimulate LR branching and primary root (PR) elongation in wheat plants (Dissanayake et al., 2019; Shao et al., 2017). Wheat has developed highly specialized responses to P deficiency at the morphological, physiological, and biochemical levels to modify RSA and function. The adaptive changes include: (i) increased LR branching, increased root hair length and

density, and establishment of symbiotic relationships with arbuscular-mycorrhizal (AM) fungi; (ii) increased secretion of P-mobilizing exudates; and (iii) upregulation of high-affinity Pi transporters (Teng et al., 2013; Teng et al., 2017; Wen et al., 2019; Zheng et al., 2021).

Nitrate, which has highly dynamic distribution in the soil, is the main soluble N source for wheat growth. Thus, a large and deep root system is considered the ideal root architecture for efficient N acquisition (Garnett et al., 2009; Mi et al., 2010; Trachsel et al., 2013). The recovery rate of ^{15}N-labeled nitrate for the wheat varieties Xiaoyan54 (generated by distant hybridization between wheat and *Th. ponticum*) and Jing411 were positively correlated with the root length density (RLD) in the corresponding soil layers (Zhang et al., 2005). The major QTL *qMrl-7B* for primary root length increases RLD in both upper and deeper soil layers, and consequently enhances N uptake and grain yield under both low- and high-N conditions (Liu et al., 2021b). Root hairs can increase the area of root-soil contact with low carbon input, demonstrating the crucial role of efficient Pi acquisition in wheat (Keyes et al., 2013; Singh Gahoonia et al., 1997). Most of the P fertilizer applied to soil cannot be taken up by plants due to adsorption, precipitation, or conversion to organic forms (Holford, 1997); thus, root morphological and P-mobilizing exudation traits are important for efficient P acquisition in wheat (Manske et al., 2000).

There are several key determinants of wheat development that play crucial roles in RSA. Modern wheat varieties feature a reduced root size because they incorporate the Green Revolution gene *Rht1*; this root size is considered too small for optimum uptake of nutrients and maximum grain yield (Waines and Ehdaie, 2007). QTL mapping combined with analysis of near-isogenic lines (NILs) containing different *Rht1* alleles showed that the dwarf alleles of *Rht-B1* and *Rht-D1* reduced shoot and root biomass at high and low P conditions, but did not reduce the efficiency of P acquisition per unit of root dry weight (RDW) (Ryan et al., 2015). Introducing the 1RS alien chromosome translocation from rye into modern wheat varieties greatly increased shallow and deep root biomass and the uptake of N, P, and K (Ehdaie et al., 2010; Ryan et al., 2015; Waines and Ehdaie, 2007). The *VRN1* gene, which is responsible for spring/winter growth habits, is a key controller of RSA and NUE in wheat. The winter allele of *VRN1* consistently reduces root angle (Voss-Fels et al., 2018). Because of the high mobility of nitrate, large amounts of nitrate have accumulated in soil profiles in recent decades due to the excessive use of fertilizers; it has been measured as high as 453 kg N ha^{-1} in soil at 0–4 m during the wheat growing season in a semi-humid area in China (Zhou et al., 2016). A narrower root angle may be favorable for efficient uptake of nitrate in deep soils in winter wheat growth regions. The *VRN-A1a* allele has been suggested as a candidate gene for the major QTL controlling NUE on chromosome 5A (Lei et al., 2018). Because the prevalent *VRN1* alleles differ between wheat ecological regions across China (Sun et al., 2009), there may be differences in RSA and NUE between varieties in different ecological regions.

The auxin biosynthetic factor *TRYPTOPHAN AMINOTRANSFERASE-RELATED* (*TaTAR2.1*) is upregulated in roots by low N availability, and is required for LR growth under low-N conditions. *TaTAR2.1-3A* overexpression in wheat enhances LR branching, spike number, grain yield, and N uptake under low- and high-N conditions (Shao et al., 2017). *TaNFYA-B1* is a low-N- and low-P-inducible CCAAT box-binding TF; *TaNFYA-B1* overexpression upregulates *TaTAR2* in roots and improves root growth and grain yield of wheat with less N and P input (Qu et al., 2015). The MYB-CC type TF PHR1 and its homologs play key roles in regulating the Pi-starvation response in plants. In wheat, *TaPHR1* overexpression increases RDW and the root/shoot ratio under low-P conditions and LR branching under both low- and high-P conditions (Wang et al., 2013). Knocking down *TaPHR3* through RNAi reduces root length and root hair length under low-P conditions (Zheng et al., 2020). These results indicate that *PHR* genes are essential for RSA reprogramming in response to P availability.

Efficient nutrient uptake via transporters

Nitrate uptake by roots is mediated by the low-affinity transport system encoded by the *NRT1*/*NPF* gene family and the high-affinity transport system encoded by the *NRT2* gene family (Figure 6B). Only a few *NPF* and *NRT2* genes in wheat have been functionally characterized to date. When ectopically expressed in *Xenopus* oocytes, two *NPF* genes (TraesCS1B02G038700 and TraesCS1D02G214200) and one *NRT2* gene (TraesCS6A02G030800) exhibited nitrate transport activity (Li et al., 2021e). However, TaNRT2.5-3B requires a partner protein, TaNAR2.1, to allow nitrate transport activity in oocytes (Li et al., 2020e). *TaNRT2.5* mediates long-distance transportation of nitrate and post-anthesis N uptake (PANU). *TaNRT2.5-3B* overexpression increases PANU, grain nitrate concentration, and grain yield under field conditions (Li et al., 2020e).

GPC is a key element of wheat end-use value. It is difficult to simultaneously improve both yield and GPC due to the strong negative correlation between these two traits (Taulemesse et al., 2015). Many studies have demonstrated the importance of PANU in simultaneous improvement of both yield and GPC (Bogard et al., 2010; Guttieri et al., 2017; Monaghan et al., 2001; Taulemesse et al., 2015). In addition to *TaNRT2.5*, several other *TaNRT2* family members were found to be associated with PANU, including *TaNRT2.1* (Lamichhane et al., 2021; Li et al., 2020e; Taulemesse et al., 2015). The nitrate-inducible NAC transcription factor Ta-

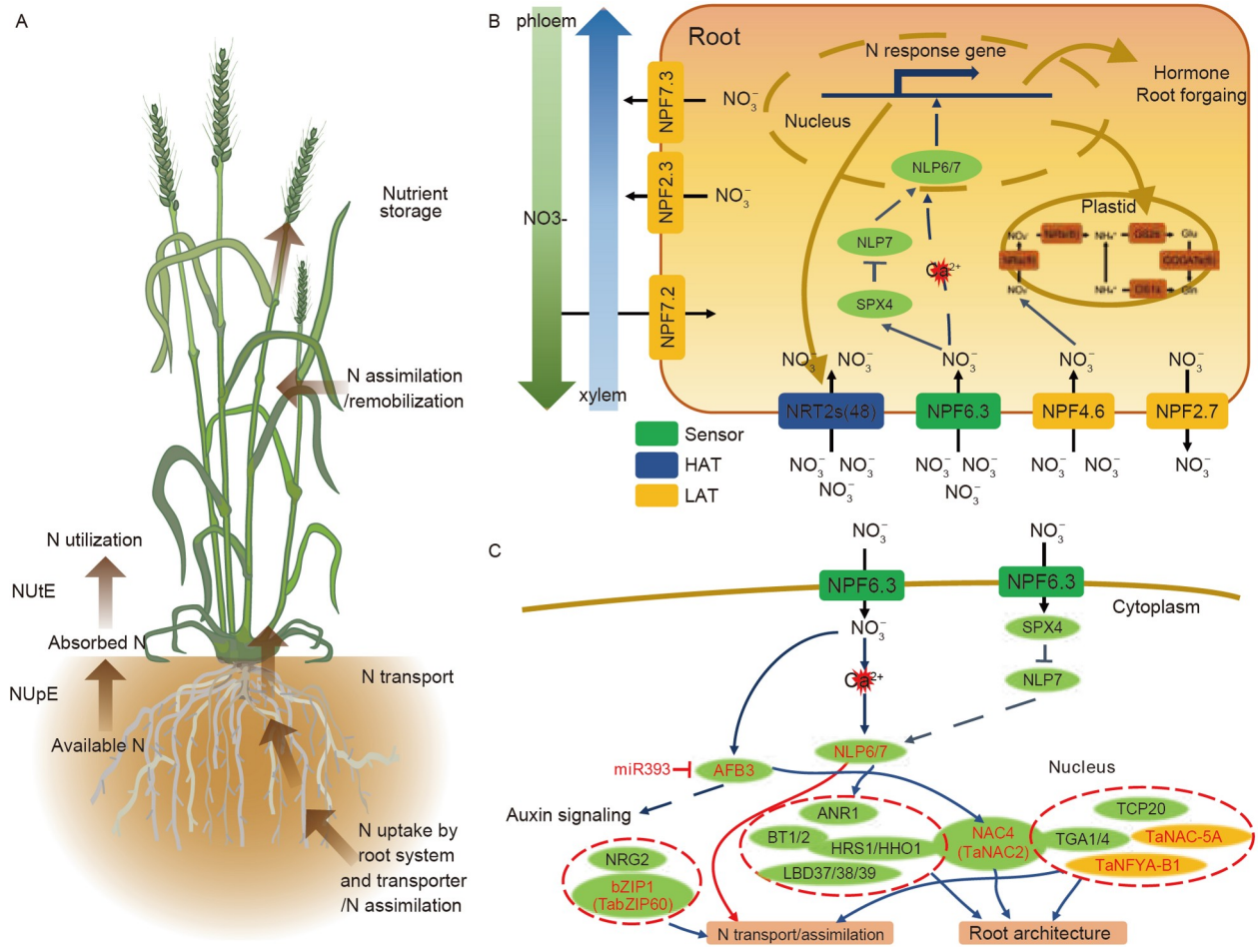

Figure 6 Regulation of nutrient use efficiency in crops. A, Nutrient uptake, assimilation, remobilization and storage in wheat and their effects on root system architecture. B, Regulation of nitrate uptake, assimilation, remobilization by specific transporters, key enzymes and transcription factors. C, Nitrate signaling transduction pathway and gene regulation network for nitrate transport and assimilation, as well as regulation of root architecture.

NAC2-5A positively regulates *TaNRT2.5* and *TaNRT2.1* expression in wheat. *TaNAC2-5A* overexpression significantly increases the nitrate influx rate, N uptake, grain N concentration (GNC), and grain yield under both low- and high-N conditions (He et al., 2015). Thus, manipulation of *TaNRT2* expression shows great potential for increasing wheat yield and GPC simultaneously.

The PHT1 transporters mediate P uptake and re-mobilization in plants. *TaPHT1.1*/*1.9*, *TaPHT1.2*, and *TaPHT1.10* expression were shown to be root-specific and positively correlated with P uptake across multiple P application rate treatments and wheat varieties (Teng et al., 2017). *TaPHT1.9-4B* is required for P uptake, especially under low-P conditions, and sequence variations in the promoter are associated with *TaPHT1.9* mRNA levels and with wheat growth performance and P content under P-limited conditions (Wang et al., 2021b). *PHT1* gene expression is positively regulated by the transcription factors *TaNFYA-B1*, *TaPHR1*, *TaPHR3* and *TaMYB4*, but negatively regulated by *PHOSPHATE 2* (*TaPHO2*), which encodes an ubiquitin-conjugating E2 enzyme. Knocking out *TaPHO2-A1* and overexpressing *TaNFYA-B1*, *TaPHR1*, or *TaMYB4* both increased P uptake and grain yield under low- and high-P conditions (Ouyang et al., 2016; Qu et al., 2015; Wang et al., 2013; Wang et al., 2021b), whereas knocking down *TaPHR3* had the reverse effects (Zheng et al., 2020).

Efficient nutrient utilization through redistribution and assimilation

A wheat variety with ideal nutrient use efficiency would not only efficiently obtain nutrients from the soil, but also use the absorbed nutrients efficiently to increase yield. Nitrate reductase (NR), glutamine synthetase (GS), and glutamine synthase (GOGAT) are key enzymes in primary N assimilation (Figure 6B). Several studies have demonstrated the contribution of N assimilation efficiency to wheat yield improvement in China. Analysis of 413 data points from 11 field experiments in China showed that yield increases from 7–9 Mg ha^{-1} to > 9 Mg ha^{-1} could mainly be attributed to

increased dry matter and N accumulation in winter wheat from stem elongation to anthesis (Meng et al., 2013). Consistent with those results, a study of 32 varieties that were widely planted in the Yangtze River Basin from 1950 to 2005 revealed that genetic gains in N uptake were primarily due to increased total N accumulation and increased N accumulation rate from stem elongation to anthesis; furthermore, wheat breeding increased leaf NR and GS activities during the same developmental stages (Tian et al., 2016). Thus, genetic improvement in N assimilation before anthesis contributed to increased yield and N uptake during breeding. Haplotype analysis of *TaGS2* genes, which encode the plastic GS isoforms, revealed that *TaGS2-2A*, *-2B*, and *-2D* were subject to breeding selection (Li et al., 2011). Transgenic expression of a favorable allele of *TaGS2-2A* in wheat increased root capacity to acquire N; N uptake before and after flowering; remobilization of N to grains and NHI; and increased grain yield and yield components under both low- and high-N conditions (Hu et al., 2018a). *TaGS2* expression is positively regulated by TaNAC2-5A (He et al., 2015).

TaNADH-GOGAT-3B may contribute to the NUE meta-QTL on chromosome 3B (Quraishi et al., 2011). Recently, interactions between TabZIP60 and TaNADH-GOGAT have shown their essential roles in mediating N use and wheat growth. TabZIP60 can bind the *TaNADH-GOGAT-3B* promoter and negatively regulate its expression. Decreasing *TabZIP60* expression or overexpressing *TaNADH-GOGAT-3B* increases grain yield and N uptake (Yang et al., 2019). OsARE1 is a genetic suppressor of a rice *fd-gogat* mutant defective in N assimilation (Wang et al., 2018c), and knockout of *ARE1* in rice or wheat increases grain yield under both low- and high-N conditions (Wang et al., 2018c; Guo et al., 2021).

Improved P utilization efficiency (PUtE) will lead to higher yield while reducing P removal from soils, supporting the sustainable use of non-renewable P resources. In barley, low-affinity P transporter expression (*HvPHT1.6* and *HvHPT1.3*) is positively correlated with genotypic differences in PUtE (Huang et al., 2011). In wheat, expression of *TaPHT1.6* in the roots, stems, leaves, spikes, and grains suggests that it may have a role in mediating P redistribution (Teng et al., 2017). The wheat variety SJZ8 displays higher expression of *TaPHT1.6* in the roots at the flowering stage and has higher PUtE than KN9204 under multiple levels of P availability (Teng et al., 2017). This suggests that higher expression of *PHT1* genes involved in P retranslocation may enhance economical use of absorbed P to produce grains.

Genes controlling yield response to nutrient availability

Fertilizers can increase plant height, tiller/spike number, and grain number. To date, only a few genes have been characterized with respect to their roles in mediating the responses of agronomic traits to fertilizers (Figure 6C). The *Rht1* alleles (DELLA alleles) reduce plant height and improve lodging resistance, substantially increasing wheat yield under higher fertilizer rates. Nitrate enhances cell proliferation (in a DELLA-dependent manner) and elongation (in a DELLA-independent manner) (Camut et al., 2021). Nitrate can increase GA biosynthesis, thus degrading DELLA proteins and increasing wheat height (Camut et al., 2021). Hormones such as auxin, cytokinin, GA, strigolactone, and ABA are involved in the control of tillering in wheat (Shang et al., 2021). *TaTAR2.1*-mediated auxin biosynthesis has been shown to be required for spike formation under both low- and high-N conditions (Shao et al., 2017). Wheat growth is closely related to plant N status; this is demonstrated by the fact that the nitrate transporter gene *TaNRT2.5* and the N assimilating genes *TaGS2* and *TaNADH-GOGAT* positively regulate tiller/spike number (Hu et al., 2018a; Li et al., 2020e; Yang et al., 2019), and that overexpressing *TaGS2* increases GN and TGW regardless of N supply levels (Hu et al., 2018a). Expression levels of *TaNFYA1*, *TaNAC2*, and *TabZIP60* are regulated by N availability. *TabZIP60-RNAi* and overexpression of *TaNFYA1* and *TaNAC2* increase tiller/spike number per plant under low- and high-N conditions, possibly by upregulating the genes that function in N uptake and assimilation (He et al., 2015; Qu et al., 2015; Yang et al., 2019). The P-starvation response regulators TaPHR1 and TaPHR3 have positive effects on GN under both low- and high-P conditions (Wang et al., 2013; Zheng et al., 2020). The elite allele of *TaPHR3-A1* is associated with higher GN, and was positively selected through wheat breeding (Zheng et al., 2020).

The genetic gain rate for GN is much lower than that of TGW (Liu et al., 2021c). GN is regarded as a promising selection criterion for future breeding programs in most Chinese wheat production zones (Wu et al., 2014). Due to the substantial effect of fertilizer on GN, it is necessary to explore the genes that control nutrient allocation to developing spikes and to more fully understand nutrient signaling in developing spikes, especially under sub-optimal fertilizer conditions. The *dep1-1* allele increases both GN and NUE (Sun et al., 2014), and the P-starvation response regulators TaPHR1 and TaPHR3 positively regulate both GN and P uptake in wheat; increasing GN therefore has great potential in breeding to improve yield and nutrient use efficiency (Wang et al., 2013; Zheng et al., 2020). GPC is a key determinant of end-use quality. However, traditional wheat breeding has greatly increased yield but not GPC. This phenomenon is associated with smaller genetic gains in NUpE and NUtE than in yield (Liu et al., 2021c), and with the lack of genetic gain for leaf NR and GS activities during grain filling (Tian et al., 2016). Transgenic expression of *TaGS2-2Ab* reportedly increases leaf GS activity during grain filling, N uptake before and after anthesis, N re-

mobilization, NHI, and grain yield (Hu et al., 2018a). Understanding the gene network governing N uptake and remobilization, especially during grain filling, will facilitate the design of wheat with improved yield, GPC, and NUE. *RHT1* and *VRN1* are key determinants of wheat development and adaptation to local growth conditions through control of RSA and nutrient use. It is crucial to understand the interactions between nutrient signaling and key wheat developmental genes; this will allow precise design of nutrient-efficient wheat varieties specific to different ecological regions based on the prevalent alleles of developmental genes in those areas.

Improving abiotic stress tolerance by focusing on yield

The long growing period of wheat, especially winter wheat, exposes it to more environmental stresses (such as salt, drought, and heat) than are faced by most crops. Genetic bottlenecks also make cultivated wheat increasingly vulnerable to environmental stresses (Wang et al., 2018b). However, the bread wheat genome is very complex (extremely large, hexaploid, and highly repetitive), which presents further obstacles to molecular breeding (Wang et al., 2015b). With the rapid development of wheat genomics in recent years, it has become possible to identify superior genes and favorable haplotypes for abiotic stress tolerance; to elucidate the functional mechanisms of these genes; to determine how to balance stress responses with high yield; and to ultimately use this information to directly select more stress-tolerant varieties. Here, we summarize the progress made in understanding the relationship between abiotic stress tolerance and yield and highlight areas for future study.

Discovering favorable variations for both abiotic stress tolerance and high yield via population genetics

Over the past five years, wheat population genetics has greatly advanced for several reasons: (i) multiple high-density and ultra-high-density SNP arrays have been constructed; (ii) large volumes of high-resolution omics data have been collected and published; and (iii) high-throughput and automatic phenome studies have been initiated. More importantly, traits can now be measured not only in growth chambers but also in the field, paving the way for discovery of yield-related variations under abiotic stress conditions. For example, GWAS were recently performed in wheat that directly used harvest index as the target trait under different temperature conditions. This revealed multiple stable genetic loci that govern grain weight under high-temperature stress, providing opportunities to develop new varieties with stable yield even under heat stress (Lou et al., 2021; Wang et al., 2021c). Similarly, GWAS for yield-related traits under salt stress (Hu et al., 2021; Li et al., 2020b), drought stress (Wang et al., 2019b), and combined heat and drought stress (Li et al., 2019e) were also recently conducted in wheat. These studies highlight that yield should be the parameter used to evaluate wheat tolerance to abiotic stress. Notably, the novel genetic loci uncovered by these studies, which were directly associated with yield-related traits under environmental stresses, are more practical than stress tolerance loci *per se* in breeding.

As more details of the genetic bases of yield-related traits have been revealed in wheat, the genetic interplay between yield-related traits and traditional stress-tolerance traits (such as root biomass) has become an intriguing area of research. Some GWAS have simultaneously investigated both types of traits in the same natural populations, highlighting pleiotropy or co-localization of loci for yield and abiotic stress tolerance. For example, 23 agronomic and drought tolerance traits were genetically analyzed via GWAS in a large durum wheat population comprising 493 accessions. The study revealed a genetic locus governing both yield traits and drought tolerance. Although the candidate genes were different (*Rht-B1* for yield and a gene encoding a WD40 protein for drought tolerance), the gene hitchhiking effect led to a directional selection of the elite *WD40* allele for drought tolerance during the Green Revolution (Wang et al., 2019b). Similarly, a recent GWAS using a panel of 307 bread wheat accessions suggested that linkage drag between the genetic loci on chromosome 6B responsible for yield, kernel length and seed germination under salt stress had a positive effect on salinity stress tolerance in the Chinese breeding process (Yu et al., 2020). Another GWAS performed by Li et al. (2019e) used 277 wheat accessions to study drought and heat stress tolerance. In contrast to the results described above, they found that breeding in China during the past several decades increased the frequency of elite alleles governing yield-related traits in four loci within selection sweep regions but diminished favorable genetic variation governing abiotic stress tolerance located in the same loci. In another GWAS, 269 salt-tolerant loci were studied in 323 accessions and 150 double haploid lines (Li et al., 2020b). At the genic level, one natural allelic gene of *TaNAC071-A* was identified in a natural population of 430 individuals; this gene is activated by TaMYBL1 to improve drought resistance and yield (Mao et al., 2022a). Within the same population, TaNAC8-6A was discovered to induce both auxin signaling and drought responses, to stimulate lateral root development and water use efficiency, and to contribute to drought resistance in wheat (Mao et al., 2020a).

In summary, recent population genetic studies have revealed the importance of positive and negative effects resulting from genetic linkages between loci affecting yield-related traits and those affecting abiotic stress tolerance.

These studies have provided direct genetic evidence of the interplay between agricultural traits and stress tolerance, revealing deep insights into the molecular mechanisms underlying the stress tolerance–productivity trade-off (Li et al., 2019e). Furthermore, the identification of natural allelic variation provides potential targets for molecular breeding via targeted genome editing.

Somatic introgression provides novel genetic variation for salt stress resistance

In addition to positional cloning based on biparental populations and GWAS with natural accessions, other approaches can be used to introduce artificial variations at both the genetic and epigenetic levels; an example is artificial mutagenesis, such as genomic shock-based mutagenesis (Liu et al., 2015; Wang et al., 2014a; Wang et al., 2015a; Wang et al., 2018a). A pioneering attempt was made to use asymmetric somatic hybridization to introgress genetic materials from a donor species (*Th. ponticum*) into a recipient species (common wheat cv. JN177). The co-emergence of biparental nuclear/cytoplasmic genomes and the introgression of donor chromosomal fragments results in "genomic shock", inducing novel genetic variations (e.g., SNPs and insertion/deletion mutations [Indels]) and epigenetic variation (DNA methylation) in wheat (Liu et al., 2015; Wang et al., 2015a; Wang et al., 2018a). With this "somatic introgression" approach, the Shanrong series of wheat introgression derivatives were generated, which have diverse elite agronomic traits; for example, Shanrong No. 3 (SR3) showed both robust growth and high yield in high-saline conditions (Xia et al., 2003). Over the past 15 years, SR3 has been promoted for use in the saline-alkali land of the Yellow River Delta. Thus, asymmetric somatic hybridization induced allelic variation and was effectively used for the identification of salt-resistant genes.

Two major mechanisms underlying salinity tolerance in wheat have been genetically dissected (Figure 7A). One is sodium exclusion by high-affinity K^+ transporters (HKT1;5), with an ancestral Na^+ transporter significantly increasing grain yield in saline soils. The other mechanism is regulation of reactive oxygen species (ROS) homeostasis, which was revealed by genetic analysis in SR3 (reviewed by Wang et al., 2018b). Through QTL mapping and omics analyses, a wheat poly(ADP ribose) polymerase (PARP) gene, *TaSRO1*, was identified as the candidate gene in a salt-tolerant QTL in SR3. Two amino acid variations in TaSRO1 confer two elite traits, superior salt tolerance and vigorous growth ability, to SR3. These effects were attributed to the higher genomic stability and superior maintenance of ROS homeostasis; ROS levels were elevated through regulation of genes governing both ROS production and scavenging (Liu et al., 2014). Additionally, a set of ROS homeostasis-associated genes with differential expression patterns were shown to possess epigenetic variation in SR3 (Wang et al., 2014a; Wang et al., 2020e). TaSOD2 enhances salt tolerance by lowering H_2O_2 product levels but elevating O_2^- substrate levels to alter ROS homeostasis (Wang et al., 2016). Accumulation of methionine sulfoxide reductase (MSR 4.1) offers wheat a stronger capacity for alleviating ROS damage of sulfur-containing amino acids under saline stress (Ding et al., 2019). The alpha-linolenic acid metabolism pathway for salt stress response in SR3 is associated with ROS neutralization induced by lipid peroxidation (Dong et al., 2013; Zhao et al., 2014). The wheat pyruvate transporter BASS2 enhances salt tolerance by promoting ABI4-mediated plastid retrograde signaling to modulate ROS homeostasis in chloroplasts (Zhao et al., 2016). These findings show that regulation of ROS homeostasis has implications far beyond decreasing ROS levels, revealing a potential new strategy for enhancing salt tolerance.

Hormone signals are also associated with salt tolerance in SR3. The allene oxide cyclase (AOC) gene *TaAOC1* enhances salt tolerance by promoting the JA-synthesis branch of the alpha-linolenic acid metabolism pathway, whereas the 12-oxo-phytodienoic acid reductase TaOPR3 enhances salt tolerance by promoting ABA signaling in a JA-independent manner (Dong et al., 2013; Zhao et al., 2014). *TaCHP* encodes a DC2-domain containing TF that has allelic variation in the promoter; higher expression of this gene in SR3 enhances salt tolerance in an ABA-dependent manner (Li et al., 2010). TaGBF1 negatively regulates salt tolerance by linking pathways associated with light and ABA (Sun et al., 2015). Thus, artificial mutations via asymmetric somatic hybridization can provide excellent genetic resources for mining elite genes and elucidating the mechanisms of abiotic stress resistance in wheat.

Functional dissection of genes and their responses to high temperature and drought

Many genes involved in responses to abiotic stress such as drought and heat have been identified in wheat (Figure 7B). Temperature signaling in wheat shares similar cascades with other plant species (Winfield et al., 2010; Willick et al., 2018; Wang et al., 2019b). Heat signaling is transduced by TaHsfA1b (Tian et al., 2020), TaHsfA6f (Xue et al., 2015), and TaHsfC2a (Hu et al., 2018b); it is mediated by TaMBF1c (Qin et al., 2015; Tian et al., 2022a), triggering the heat-responsive proteins TaFER-5B (Zang et al., 2017) and Ta2CP (Mishra et al., 2021) to control oxidative stress. The heat-induced TaHSP proteins enhance protein folding and confer general thermotolerance for maintenance of physiological processes under heat stress (Lyu et al., 2020). The key photosynthetic enzyme rubisco activase (RCA) is highly sensitive to heat (Degen et al., 2020; Degen et al., 2021;

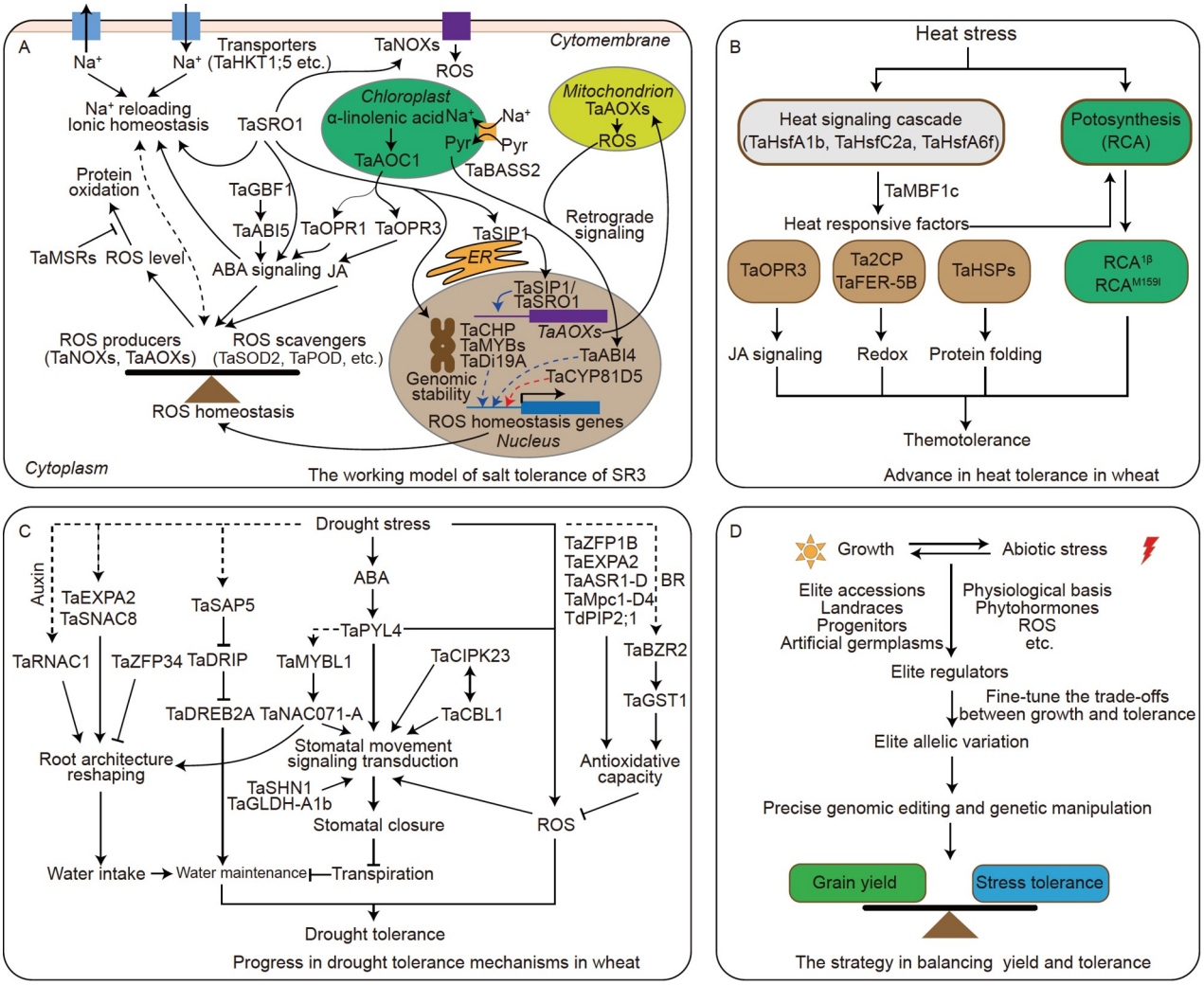

Figure 7 Working model of abiotic stress tolerance to salt, heat and drought in wheat. A, The mechanisms for regulating ionic and ROS homeostasis, two major physiological bases, in wheat. B, Advance in research on heat-tolerant genes in wheat. C, Progress in drought tolerance mechanism of wheat. D, The strategy for balancing grain yield and tolerance to abiotic stress in future molecular breeding of wheat.

Ristic et al., 2009). Selecting for the higher thermotolerant isoform, RCA1β (Degen et al., 2020; Degen et al., 2021; Scafaro et al., 2019), and the amino acid substitution RCA-M159I (Degen et al., 2020) can significantly improve wheat thermotolerance. This highlights the fact that protecting heat sensitive processes is a promising strategy to improve overall wheat thermotolerance. ABA and JA play key roles in modulating heat resistance (Hu et al., 2018b; Tian et al., 2020). This suggests the existence of an intersection of gene regulatory networks involved in responses to different abiotic stresses in wheat; it also indicates that the complex signaling pathways controlling heat tolerance in wheat must be verified.

Controlling water evaporation is a general drought response in plants. A series of genes are involved in regulating stomatal aperture to reduce water loss and improve drought tolerance; these include TaSHN1 (Bi et al., 2018), TaGLDH-A1b (Zhang et al., 2016a), TaCIPK23, TaCBL1 (Cui et al., 2018), TaSNAC8 (Mao et al., 2020a), and TaNAC071 (Mao et al., 2022a) (Figure 7C). Stomatal closure is generally accepted to function through ABA signaling. Recently, an allelic variation of the ABA receptor TaPYL1-1B was proven to be associated with drought tolerance in wheat (Mao et al., 2022b). Enhancing the capacity for water intake is another important approach to improve wheat drought tolerance. TaZFP34 (Chang et al., 2016), TaRNAC1 (Chen et al., 2018a), and TaEXPA2 (Chen et al., 2018a) enhance wheat root development, increasing water intake and thus enhancing drought tolerance. Controlling drought-induced ROS is another critical mechanism for drought tolerance. The key TF TaBZR2 in the BR signaling pathway positively activates *TaGST1* to promote scavenging of drought-induced superoxide anions (Cui et al., 2019). TaZFP1B (Cheuk et al., 2020), TdPIP2;1 (Ayadi et al., 2019), TaMpc1-D4 (Li et al., 2020e), and TaASR1-D (Qiu et al., 2021) also increase antioxidant capacity to improve drought tolerance. The domi-

nant mutant of the GSK3-like kinase TaBIN2 blocks BR signaling in wheat and was recently shown to affect the drought response (Cheng et al., 2020; Gupta et al., 2021). However, the known regulatory network of wheat drought tolerance remains incomplete. For example, the key Ta-DREB TFs involved in the drought response (Morran et al., 2011) are regulated by TaSAP5 and TaDRIP (Zhang et al., 2017a), but the components of the related signaling cascade are still unknown.

Breeding strategies to address trade-offs between yield and abiotic stress resistance

Natural variation offers elite agricultural traits that can be exploited during crop domestication and breeding. It is desirable to mine elite allelic variations of stress tolerance genes to allow plants to respond to adverse environmental stimuli without imposing trade-offs between yield and stress tolerance (Silva et al., 2019). Although many genetic populations have been used in QTL analyses in wheat, only a few alleles that are responsive to abiotic stress tolerance have been mined, and they have rarely been utilized in breeding (Wang et al., 2018b). *TmHKT1;5-A* was identified as a candidate gene for the *Nax2* locus; it is an elite gene that encodes a selective Na^+ transporter. This gene was retained only in the wheat relative *Triticum monococcum*. Introducing *TmHKT1;5-A* into durum wheat via hybridization significantly reduced leaf Na^+ content and increased grain yield by 25% compared to NILs without the *Nax2* locus (Munns et al., 2012). Moreover, because wheat is hexaploid, epigenetic modifications of genes in the three subgenomes comprise the predominant dosage regulation machinery in wheat. For example, *TaCYP81D5* expression is associated with epigenetic variations; it contributes to salinity tolerance at both the seedling and reproductive stages of bread wheat and is a candidate for crop improvement (Wang et al., 2020e).

The next phase of research in wheat molecular breeding should be devoted to determining the mechanisms by which superior genes coordinate stress responses with development, then to fully elucidating the related signaling pathways (Figure 7D). A specific focus should be understanding how elite genes regulate cross-talk between phytohormones and redox/secondary signaling molecules such as ROS, reactive nitrogen species (RNS), and Ca^{2+}, which have the potential to balance stress tolerance and plant development. For example, TaSRO1 functions as such regulator, linking upstream ROS signals and downstream stress responsive signals to fine-tune plant growth and stress tolerance. TaSRO1 serves as a "brake" and interacts with the key regulator of mitochondrial retrograde signaling in wheat, TaSIP1, to prevent prolonged or excessive activation of mitochondrial retrograde signaling; TaSRO1 thus coordinates development and salt tolerance in saline-alkali soil (Wang et al., 2022b). In addition, ABA is the central regulator of stomatal opening, which affects both transpiration and photosynthetic activity; overexpression of a wheat ABA receptor was shown to significantly increase grain production per liter of water and to protect plant productivity during water deficit (Mega et al., 2019).

Exploring the most suitable and predominant phenotypes, which may be correlated with stress tolerance capacity, is a crucial prerequisite for mining superior genes and their elite variations. High-throughput platforms and methods for phenotypic screening of stress tolerance traits during the entire plant lifecycle (from germination to reproduction) must be developed for wheat. Advances in population genetics will yield novel QTLs and genetic/epigenetic variations affecting abiotic stress tolerance, particularly from wheat landraces, progenitors, and relatives, and will then be available for breeding (Wang et al., 2018b). Co-separated markers related to QTLs that are responsible for abiotic stress tolerance can also be identified and developed in wheat, promoting the breeding of abiotic stress tolerance from traditional to marker-assisted approaches. More importantly, identification of natural or artificial variations in stress tolerance genes will provide targets for modern breeding strategies such as genome editing. Further identification of signaling "hub" genes and the molecular pathways they mediate will allow successful pyramiding to increase stress tolerance.

Breeding for disease and pest resistance

Wheat production is consistently threatened by many types of diseases and pests; these include FHB, stripe rust, leaf rust, stem rust, powdery mildew, leaf blotch, wheat blast, cereal cyst nematodes (CCN), Hessian flies, aphids, OWBM, curl mites, stem sawflies, and several viral diseases (Figure 8A). Geneticists, breeders, and phytopathologists have worked for centuries to identify and characterize pathogens and host resistance genes to better understand host-parasite relationships; the ultimate goal would be to apply disease- and pest-resistance genes in breeding programs. In recent years, abundant genomics resources and research tools have accelerated molecular mapping and cloning of wheat disease- and pest-resistance genes and the corresponding Avr proteins in pathogens. Progress in understanding the genetic bases and pathological mechanisms of wheat disease and pest resistance are helpful for breeding resistant varieties.

Genetic mechanisms of disease and pest resistance

Wheat FHB resistance

FHB is primarily caused by the *Fusarium graminearum* species complex. It is a destructive spike disease of wheat

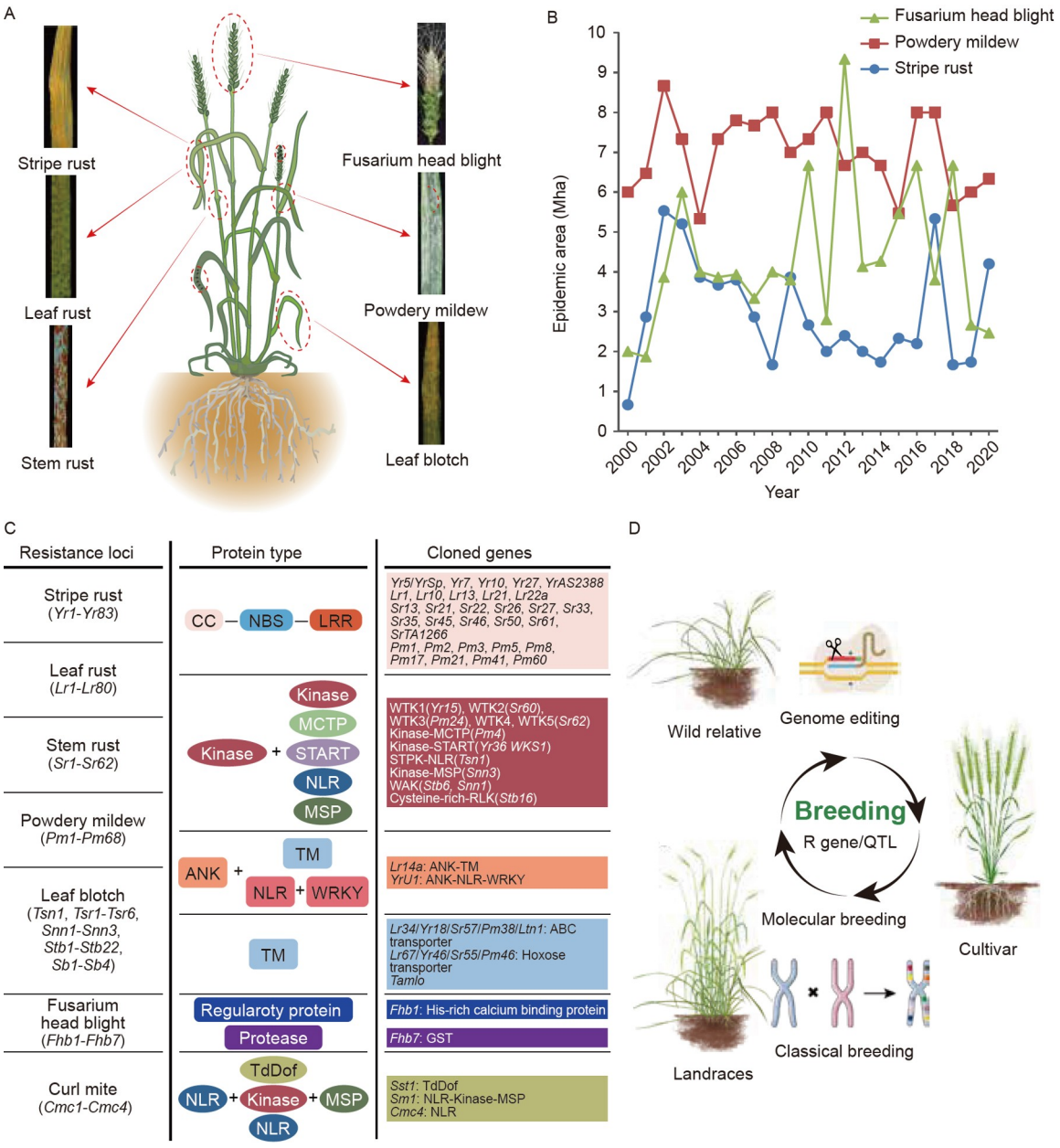

Figure 8 Cloning of wheat disease and pest resistance genes and application for breeding. A, Morphology of various diseases threatens wheat growth and yield. B, The epidemic regions for Fusarium head blight, stripe rust and powdery mildew in China for the past two decades. C, Summary of resistance gene cloning for various diseases and pest in wheat. D, Strategies used for breeding wheat with disease resistance.

that occurs worldwide, causing not only severe yield and quality losses in epidemic years, but also posing serious threats to humans and animals who consume the infected grains, which contain mycotoxins produced by the pathogens (Parry et al., 1995). Due to climate change and continuous rotation of wheat and maize, FHB epidemics have become increasingly frequent in China over recent years (Figure 8B) (Ma et al., 2020). To overcome FHB, China launched the largest ever nationwide screening for FHB-resistant germplasm in 1974, which laid a solid foundation for modern FHB resistance research (CCRWS, 1984).

Wheat is not immune to infection with *Fusarium* species; however, different levels of FHB resistance exist in wheat lines and relatives. This resistance is controlled by multiple genes and is greatly affected by environmental factors (Ma et al., 2020). Over 579 QTLs for FHB resistance have been reported in resistant lines such as Sumai 3 and Wangshuibai, and even in susceptible lines (Jia et al., 2018). These QTLs are distributed across all wheat chromosomes, but can be grouped into 45 chromosomal bins (Ma et al., 2020). Most of the identified QTLs were associated with multiple FHB resistance types. Evaluation of a set of QTLs in NILs showed that *Fhb1* and *Fhb2* are responsible for resistance against within-spike disease spread (type II resistance), whereas

Fhb4 and *Fhb5* are responsible for resistance to initial infection (type I resistance) (Cuthbert et al., 2007; Ma et al., 2020; Xue et al., 2010; Xue et al., 2011). Three chromosome segments for FHB resistance have been transferred into wheat from *Leymus racemosus*, *Elymus tsukushiensis*, and *Th. ponticum*, and designated as *Fhb3* (Qi et al., 2008), *Fhb6* (Cainong et al., 2015), and *Fhb7* (Guo et al., 2015a), respectively. FHB-resistance QTLs usually have small effects and may not be detectable in all environments; nevertheless, 23 bins were repeatedly identified in ten or more lines, namely 1A-1, 1B-1, 2A-2, 2A-3, 2B-1, 2B-2, 2D-1, 2D-2, 3A-1, 3B-1, 3B-2, 4A-2, 4B-1, 4D-1, 5A-1, 5A-2, 5A-3, 5B-2, 5B-3, 5D-1, 6B-1, 7A-1, and 7A-2 (Ma et al., 2020).

Fhb1 (in the 3B-1 bin) was initially identified as a pore-forming toxin-like gene (Rawat et al., 2016), but was later shown to be a histidine-rich calcium-binding protein-like product (His) (Li et al., 2019c; Su et al., 2019). His proteins are highly conserved among members of the plant kingdom and may be essential in growth and development. *Fhb1* is a semi-dominant gene that positively regulates FHB resistance. It resulted from a 752-bp deletion at the 5′ end of the last exon of the His-coding gene on chromosome 3BS (Li et al., 2019c). It was recently reported that *Fhb7* from *Th. elongatum* encodes a glutathione S-transferase (GST) enzyme that plays a role in trichothecene detoxification (Wang et al., 2020b). In addition to *Fhb1* and *Fhb7*, *Fhb2* (6B-1 bin), *Fhb4* (4B-1 bin), *Fhb5* (5A-1 bin), *Qfhs.ndsu-3A* (3A-1 bin), and *Qfhb.nau-2B* (2B-2 bin) have also been fine-mapped (Li et al., 2019b; Li et al., 2019c; Li et al., 2019f; Ma et al., 2020; Xue et al., 2010; Xue et al., 2011). As more FHB resistance QTLs are characterized, a comprehensive understanding of host resistance mechanisms is expected to emerge.

Wheat rust resistance

Stem rust, stripe rust, and leaf rust are the three most economically impactful rust diseases in wheat (McIntosh et al., 1995) (Figure 8A). Under epidemic conditions, rust diseases can cause yield losses of ~20%–50% in the major crop producing regions (Wellings, 2011). Stem rust was once the most serious rust disease globally. Due to the development and wide application of the resistant germplasm Hope (*Sr2*) and the 1RS/1BL translocation (*Sr31*), stem rust was brought under control in most wheat production areas. However, a new virulent *Pgt* race group from Uganda, Ug99 (TTKSK), overcame the resistance of *Sr31*, resulting in a new global threat to wheat production (Singh et al., 2015). Stripe rust is a worldwide epidemic, with infections in susceptible wheat varieties following the seasonal winds in more than 60 countries. Stripe rust is one of the most important wheat diseases in China (Figure 8B), and major epidemics have broken out almost ten times since 1950. During the 2019–2020 and 2020–2021 seasons, stripe rust epidemics were observed in major wheat-producing areas such as Sichuan, Gansu, Hubei, and Henan provinces. This was mostly due to the prevalence of the virulent *Pst* race CYR34 (V26), which overcame the resistance of *Yr24*/*Yr26*/*YrCH42* and *Yr10* (McIntosh et al., 2018). Leaf rust occurs worldwide wherever wheat is grown. It is most severe in areas where dew is frequent during the jointing through flowering stages. Ideal conditions for leaf rust epidemics include mild days and nights with adequate moisture for dew development overnight. In China, leaf rust epidemics were often observed in the late grain filling stage in the major-producing wheat regions, but it has become more widespread due to the lack of leaf rust-resistance genes in commercial wheat varieties.

Rust pathogen resistance in wheat is broadly classified into two types: race-specific and race non-specific. Race-specific resistance, also known as all-stage resistance (ASR), tends to be controlled by a single gene or a few major genes, and to trigger the hypersensitive response (HR) to avirulent pathotypes (McIntosh et al., 1995). ASR is prone to circumvention by new virulent races of pathogens. In contrast, race non-specific resistance is usually conferred by several minor effect genes and provides partial resistance against a broad range of pathotypes. This type of resistance, often called adult plant resistance (APR), is considered more robust. Due to the rapid emergence of novel virulent rust races, it is essential to explore resistance genes in wheat and related species. Currently, 84 stripe rust resistance loci (*Yr1* to *Yr83*), 80 leaf rust resistance loci (*Lr1* to *Lr80*), and 62 stem rust resistance loci (*Sr1* to *Sr62*) have been cataloged, and many temperately designated genes and alleles have also been identified (Figure 8C) (McIntosh et al., 2021; Klymiuk et al., 2022). Some of the documented rust resistance genes/alleles were derived from *T. aestivum*; the remainder were introgressed into *T. aestivum* from wheat relatives and alien species. Most of the cataloged genes confer ASR, but some confer APR. Several rust resistance genes also show high-temperature adult-plant (HTAP) resistance when exposed to high temperatures during the growing season; HTAP resistance is considered robust and is race non-specific.

To determine the molecular mechanisms underlying rust resistance in wheat, resistance genes must be cloned and characterized, and gene-specific markers must be developed for marker-assisted breeding. Relevant genes that have been cloned to date include six leaf rust resistance genes (*Lr1* [Cloutier et al., 2007], *Lr10* [Feuillet et al., 2003], *Lr13* [Hewitt et al., 2021b; Yan et al., 2021], *Lr14a* [Kolodziej et al., 2021], *Lr21* [Huang et al., 2003], and *Lr22a* [Thind et al., 2017]), 14 stem rust resistance genes (*Sr13* [Zhang et al., 2017b], *Sr21* [Chen et al., 2018b], *Sr22* [Steuernagel et al., 2016], *Sr26* [Zhang et al., 2020], *Sr27* [Upadhyaya et al., 2021], *Sr33* [Periyannan et al., 2013], *Sr35* [Saintenac et al., 2013], *Sr45* [Steuernagel et al., 2016], *Sr46* [Klymiuk et al., 2018], *Sr50* [Mago et al., 2015], *Sr60* [Chen et al., 2020a],

Sr61 [Zhang et al., 2020], *Sr62* [Yu et al., 2022], and *SrTA1266* [Arora et al., 2019]), eight stripe rust resistance genes (*Yr5*, *YrSp*, and *Yr7* [Marchal et al., 2018], *Yr15* [Klymiuk et al., 2018], *Yr27* [Athiyannan et al., 2022], *Yr36* [Fu et al., 2009], *YrAS2388* [Zhang et al., 2019a], and *YrU1* [Wang et al., 2020a]), and two pleiotropic APR genes (*Lr34*/*Yr18*/*Sr57*/*Pm38*/*Ltn1* [Krattinger et al., 2009] and *Lr67*/*Yr46*/*Sr55*/*Pm46* [Moore et al., 2015]) (Figure 8C). Most of the cloned rust resistance genes encode nucleotide-binding and leucine-rich repeat (NLR) domain proteins, which are race-specific and recognize secreted pathogen effectors. However, several cloned rust resistance genes encode other types of proteins that confer broad-spectrum and durable resistance. For example, *Lr14a* encodes a membrane-localized protein containing twelve ankyrin (ANK) repeats and is involved in calcium signaling (Kolodziej et al., 2021). *YrU1* from *T. urartu* encodes an ANK-NLR-WRKY protein (Wang et al., 2020a). *Yr15*, *Sr60*, and *Sr62* are tandem kinase proteins called *wheat tandem kinase* (*WTK*) *1*, *2*, and *5*, respectively (Chen et al., 2020a; Klymiuk et al., 2018; Yu et al., 2022). The protein encoded by *Yr36* (WKS1) contains kinase and putative START lipid-binding domains (Fu et al., 2009). The two pleiotropic APR genes encode an adenosine triphosphate-binding cassette (ABC) transporter and a predicted hexose transporter, respectively; they confer partial resistance to leaf rust, stripe rust, stem rust, and powdery mildew (Krattinger et al., 2009; Moore et al., 2015). The *Lr34*/*Yr18*/*Sr57*/*Pm38* gene also showed leaf tip necrosis (*Ltn1*) and resistance to spot blotch (*Sb1*) and barley yellow dwarf virus (BYDV) (*Bdv1*) (McIntosh, 2021). These genes are valuable in breeding for disease resistance due to their robust, broad-spectrum resistance.

Wheat powdery mildew resistance

Powdery mildew is a long-established foliar disease that is seriously affecting wheat production all over the world at present. It occurs primarily in tropical and subtropical climates that use both semi-dwarf/high-yield varieties and high levels of nitrogen fertilizer. Wheat powdery mildew has been relatively severe in China since the late 1970s, expanding over the last several decades from the southwestern part of the country into the eastern and northern regions. Destructive powdery mildew epidemics in 1990 and 1991 caused yield losses of up to 1.44 and 0.77 million tons, respectively; a novel virulent isolate, *Bgt*, had overcome the resistance conferred by the *Pm8* gene in 1RS/1BL wheat lines derived from the rye variety Petkus (Zou et al., 2018). From 2002 to 2020, powdery mildew outbreaks affected an average of 7 million ha of wheat each year in China, reaching a record high in 2021 (Figure 8B). The high frequency of outbreaks, extensive hospitable land area, and devastating nature of powdery mildew make it a great threat to wheat production.

Thus far, 65 permanently designated powdery mildew (*Pm*) resistance genes (*Pm1*–*Pm68*) and dozens of provisionally-named *Ml*-genes have been documented (McIntosh et al., 2021). However, only a few major *Pm* genes have been widely used in wheat breeding programs. In China, the most widely used powdery mildew resistance gene is *Pm8*, which is present in 50%–60% of the varieties in major wheat-producing regions such as Northern China Plain, Huang and Huai Rivers Valley Wheat Zones (Cao et al., 2015b). *Pm8*/*Yr9*/*Lr26* in 1RS/1BL do not confer resistance to the *Bgt*, *Pst*, and *Pt* isolates that prevailed in the 1990s. Due to the lack of resistance and the unfavorable effects of 1RS on gluten and bread-making quality, new powdery mildew resistance genes have been explored to replace *Pm8* in breeding programs. The most well-known is *Pm21*, which was derived from the 6VS/6AL translocation and confers resistance to all *Bgt* isolates that have been tested worldwide (Xing et al., 2018). The *Pm21* gene was successfully used in varieties in the Middle and Lower Yangtze River Valley Wheat Zone and the Southwest Wheat Zone that were adapted to local conditions with promising agronomic traits. Unfortunately, *Pm21* was not successfully used in the North China Plain, Huang-Huai River Valley Wheat Zones. Only a few commercial wheat varieties carry the *Pm21* gene in that region, partially due to the relatively low occurrence of powdery mildew disease and to the linkage drag of 6VS chromatin on agronomic traits (Cao et al., 2015b). Instead, *Pm2* and *Pm4* (*Pm4a* and *Pm4b*) have been widely applied in Henan Province, whereas *Pm2* and *Pm52* are dominant in wheat varieties grown in Shandong and Hebei provinces (Cao et al., 2015b; Shi et al., 2021).

Of the 65 documented *Pm* genes, only a few have been characterized by positional cloning, MutRenSeq/MutChromSeq strategies, or GWAS (Figure 8C): *Pm1* (Hewitt et al., 2021a), *Pm2* (Sánchez-Martín et al., 2016), *Pm3* (Yahiaoui et al., 2009), *Pm4* (Sánchez-Martín et al., 2021), *Pm5* (Xie et al., 2020), *Pm8* (Hurni et al., 2013), *Pm17* (Singh et al., 2018), *Pm21* (Xing et al., 2017; He et al., 2018), *Pm24*/*WTK3* (Lu et al., 2020), *Pm41* (Li et al., 2020d), *Pm60* (Zou et al., 2018), and *WTK4* (Gaurav et al., 2022). Most of these encode typical NLR proteins, except *Pm24*/*WTK3*, *WTK4*, and *Pm4* (kinase-MCTP), which have protein kinase domains. NLR proteins tend to recognize pathogen Avr proteins and express resistance through effector-triggered immunity (ETI) via a gene-for-gene resistance model. The occurrence of new virulent *Bgt* isolates often overcomes NLR resistance, resulting in susceptibility of commercial cultivars with a single NLR gene deployed in monoculture over a wide area. *Pm2* and *Pm4* are currently losing resistance in most of the wheat-growing areas in China, leaving only *Pm21* and *Pm52* in many of the currently grown cultivars and making it likely that more resistance will be lost in the future. “Backup” robust powdery mildew resistance genes such as *Pm5e*, *Pm12*, *Pm24*, *Pm36*, and *Pm64* are

available for breeders in China to integrate into commonly grown cultivars (Zhang et al., 2019b).

Wheat leaf spot and blotch resistance

Wheat leaf spot and blotch are types of foliar diseases that are caused by many species of necrotrophic fungal pathogens. The major diseases are tan spot, *Septoria tritici* blotch (STB), *Parastagonospora* (also known as *Septoria*) *nodorum* blotch (SNB), and *Bipolaris sorokiniana* blotch (spot blotch). Leaf spot and blotch have occurred in all wheat growing areas in China, causing major damage to the basal leaves and to upper leaves, including the flag leaf. Host plants have a range of defense mechanisms and immune responses that can be deployed against these pathogens. The stages of infection are usually as follows: host-pathogen contact; phytotoxin and cell wall degrading enzyme (CWDE) secretion; host penetration; primary lesion formation; lesion expansion; tissue maceration; and leaf necrosis. The infection activates plant immune responses either through Pathogen/Microbe Associated Molecular Pattern (P/MAMP), Effector Triggered Immunity (ETI), or even through Effector Triggered Susceptibility (ETS).

Many genes and QTLs for resistance to leaf spot and blotch have been identified in recent years. The major genes include the tan spot susceptibility gene *Tsn1*, the tan spot resistance genes *Tsr1–Tsr6*, the STB resistance genes *Stb1–Stb22*, the SNB resistance genes *Snn1–Snn3*, and the spot blotch resistance genes *Sb1–Sb4* (McIntosh et al., 2021; Zhang et al., 2020). Cloning of *Tsn1* (Faris et al., 2010), *Snn1* (Shi et al., 2016), *Snn3-D1* (Zhang et al., 2021f), *Stb6* (Saintenac et al., 2018), and *Stb16q* (Saintenac et al., 2021) has demonstrated the versatility of necrotrophic specialist pathogens such as *Pyrenophora tritici-repentis*, *P. nodorum*, and *S. tritici*; they can exploit a diverse range of host targets, hijacking the plant defense machinery for their own benefit. All of the cloned susceptibility genes encode products containing a protein kinase (PK) domain, suggesting that signal transduction through phosphorylation may be critical for their functions. However, a PK domain alone may not be sufficient for susceptibility. Some of these genes encode additional critical domains that likely function in the recognition or perception of the corresponding necrotrophic effectors (NEs) (Zhang et al., 2021f). In wheat breeding programs, these susceptibility genes can be eliminated from germplasm through conventional breeding with MAS, or by rendering the genes nonfunctional via precise genome editing techniques, abolishing NE recognition.

Wheat pest resistance

Aphids, Hessian flies, OWBM, CCN, curl mites, and stem sawflies are the major destructive wheat pests in China and throughout the world. Aphids are insects that belong to the superfamily Aphidoidea; they are small, soft-bodied insects that feed by piercing the phloem and consuming the sap. Sap removal itself often causes little direct damage, but it can indirectly damage wheat by transmitting viruses such as BYDV, which negatively affects growth and development. Hessian flies are important wheat pests that also feed on barley, rye, and some grasses. Injuries caused by Hessian fly larval feeding result in stunted wheat plants with weakened stems. OWBM larvae crawl into wheat florets and feed on the surface of developing wheat kernels. OWBM infestations often result in kernel damage, reducing the yield and decreasing grain quality. CCN, caused by *Heterodera avenae* and *H. filipjevi*, is an emerging threat in winter and spring wheat regions. The nematodes are attracted to and aggregate around wheat roots to initiate infection, causing stunted and poor wheat growth, reducing tiller number, and causing nematode cysts within bushy knots on the roots. Wheat curl mites can be found in protected areas of the plant, such as curled leaves or leaf whorls, axils, or sheaths; they are the vector of wheat streak mosaic virus and the High Plains virus.

There are resistant wheat varieties that prevent pest damage, and many major genes and QTLs for wheat pest resistance have been identified. For example, diverse wheat germplasm studies have yielded more than nine genes for Russian aphid resistance (*Dn1–Dn9*), 36 Hessian fly resistance genes (*H1–H36*), eight CCN resistance genes (*Cre1–Cre8*), and four genes for wheat curl mite resistance (*Cmc1–Cmc4*) (McIntosh et al., 2021). In addition to these major genes, an increasing number of QTLs for wheat pest resistance have been reported. For example, QTLs for OWBM resistance were reported on chromosomes 1A, 2D, 4A, 4D, and 7D (Zhang et al., 2020); major QTLs for Hessian fly resistance were reported on chromosomes 3B (Xu et al., 2021) and 7D (Winn et al., 2021); and *Qcre-ma7D* and *Qcre-ma2A* were found to provide resistance to *H. filipjevi* and *H. avenae*, respectively (Cui et al., 2019).

Wheat cultivars with resistance to OWBM (conferred by the *Sm1* gene, identified from the American variety Augusta) have become commercially available and are increasingly used to manage midge populations. Using multiple wheat genome sequences and high-resolution mapping, *Sm1* was shown to encode an NB-ARC-LRR-Kinase-MSP protein associated with insect resistance (Walkowiak et al., 2020). The NB-ARC domain was found to be indispensable for resistance. Using population genomics and GWAS methods in *Ae. tauschii*, resistance to wheat curl mite (*Cmc4*) was mapped to a 440-kb LD block on chromosome arm 6DS, within a region previously determined by biparental mapping. This interval contained ten genes, including an NLR immune receptor, which was a gene class previously reported to confer arthropod resistance in melon and tomato (Gaurav et al., 2022). Wheat stem sawfly (WSS, *Cephus cinctus* Norton) is another major pest in durum wheat-growing re-

gions of North America. Solid-stemmed wheat cultivars controlled by the major QTL *SSt1* on 3B are resistant to WSS. Using map-based cloning, Nilsen et al. (2020) found that the copy number of a DOF protein encoded by *TdDof* is correlated with increased expression and solid stems. *TdDof* regulates programmed cell death (PCD) in pith parenchyma cells, enhancing WSS resistance.

Interactions between disease resistance genes and pathogen effectors

The causal pathogens *Pgt*, *Pst*, *Pt*, and *Bgt* are obligate biotrophic fungi, meaning that they can only grow and reproduce in a living host. The interactions between most of the resistance genes to stem rust, stripe rust, leaf rust, and powdery mildew and the corresponding pathogen *Avr* genes are gene-for-gene relationships (Flor, 1971). In recent years, completion of the *Pgt* and *Bgt* genome assemblies and the availability of re-sequencing data for different pathotypes allowed isolation of several *Pgt* and *Bgt Avr* genes, including alleles of *AvrSr27* (Upadhyaya et al., 2021), *AvrSr35* (Salcedo et al., 2017), *AvrSr50* (Chen et al., 2017b), *AvrPm1* (Hewitt et al., 2021a), *AvrPm2* (Praz et al., 2017), and *AvrPm3* (Bourras et al., 2015; Bourras et al., 2019).

AvrSr35 encodes a secreted protein with an N-terminal signal that bears no similarity to any other known effectors. AvrSr35 is translocated into the host cytoplasm, where it interacts with the stem rust resistance protein Sr35, resulting in an incompatible interaction (Salcedo et al., 2017). *AvrSr50* was characterized after genomic comparison of the virulent isolate Pgt632 (derived from a spontaneous mutation) and the avirulent isolate Pgt279 (Chen et al., 2017b). *AvrSr27* was isolated through re-sequencing spontaneous virulent *Pgt* mutants and those with deletions in predicted secreted proteins. Two *AvrSr27* candidate genes (*AvrSr27-1* and *AvrSr27-2*) encode predicted secreted proteins of 144 amino acids in length. Both *AvrSr27-1* and *AvrSr27-2* were proven to be effectors that recognize *Sr27*, a CC-NBS-LRR protein. *AvrSr27-1* and *AvrSr27-2* encode a new type of secreted protein; they are closely related to each other and show no similarity to any proteins from other rust species (Upadhyaya et al., 2021).

In barley, the reaction to some *Mla* resistance alleles is controlled by multiple *Avr* genes in *Blumeria graminis* f. sp. *hordei* (Brown and Jessop, 1995). A similar situation was also observed in the interactions between the allelic series of the wheat powdery mildew resistance gene *Pm3* and the corresponding *Bgt* genes. For example, two powdery mildew fungus genes control avirulence in *Pm3f*; one gene is involved in recognition by the resistance protein, and the second is a suppressor. Resistance is only observed when the suppressor is inactive and the *Bgt* Avr is recognized (Bourras et al., 2016). Such suppressor/*Avr* gene combinations provide the basis of specificity in the wheat–*Bgt* interaction system. In wheat, more than 300 resistance genes have been described that confer resistance to rusts, powdery mildews, and leaf blotch, many of which have multiple known alleles (McIntosh et al., 2021). Identification and functional characterization of the Avr proteins corresponding to many of these resistance proteins will provide a unique biological opportunity to describe the network of interactions between wheat foliar disease pathogens and their hosts. Map-based cloning, GWAS, and re-sequencing approaches have been used to isolate *Avr* genes in wheat pathogens.

With rapid progress in next-generation sequencing (NGS) and new alternative sequencing technologies (such as PacBio), the *Pgt*, *Pst*, *Pt*, and *Bgt* reference genomes could be improved. This would greatly support map-based cloning and pave the way for GWAS in these pathogens through sequencing numerous isolates. It should also be possible to identify *Avr* genes encoding candidate secreted effector proteins (CSEPs) based on common features of the *Avr* genes in mildew and rust genomes. The population genetics and genomics of wheat mildew and rusts have been largely underexplored. Characterizing *Avr* diversity at the population level will shed light on the evolutionary forces driving host–pathogen co-evolution in these agronomically important pathosystems.

Breeding for disease resistance via MAS

Disease resistance has long been a primary goal of plant breeding. Breeders have applied many different types of resistance genes in developing new cultivars. Although many resistance genes have been identified and characterized, only a few are available in major commercial wheat cultivars. The pleiotropic APR genes *Lr34*/*Yr18*/*Sr57*/*Pm38*/*Ltn1*, *Lr46*/*Yr29*/*Sr58*/*Pm39*/*Ltn2*, *Lr67*/*Yr46*/*Sr55*/*Pm46*, and *Lr27*/*Yr30*/*Sr2* have been recommended for use in breeding programs either alone or pyramided with other major resistance genes or QTLs to archive broad spectrum, robust resistance. However, the frequency of these pleiotropic APR genes is very low in modern Chinese wheat cultivars, partially due to their minor resistance effects and the difficulty of selection via conventional breeding methods. The availability of functional and tightly-linked markers for these genes would greatly promote their application in wheat breeding.

An enormous amount of effort has been made to identify and map genes and QTLs for wheat disease resistance. This made it possible to utilize most of the identified disease resistance genes and QTLs by marker-assisted transfer and pyramiding (Figure 8D). Due to the higher accuracy, increased efficiency, lower total cost, and shorter breeding cycle compared to traditional selection, MAS has been implemented in breeding disease resistance in wheat since the beginning of this century. A major goal has been to develop

markers that are closely linked, easy to use (i.e., breeder-friendly), and suitable for high-throughput screening and validation/fine-mapping of target QTLs. The DNA markers available for MAS have evolved from restriction fragment length polymorphism (RFLP) markers to a series of easy-to-use PCR-based markers (e.g., the high-throughput SNP-based kompetitive allele-specific PCR [KASP] markers). Moreover, diagnostic functional markers are now available for over 20 resistance genes against powdery mildew, rusts, FHB, and other diseases (MASwheat [maswheat.ucdavis.edu]; GrainGenes [wheat.pw.usda.gov]).

MAS has been successfully used in wheat for the transfer and pyramiding of qualitative resistance genes, mainly focusing on resistance to powdery mildew and rusts. Moreover, benefitting from QTL validation and fine-mapping, an increasing number of studies have reported improvement of polygene-controlled resistance through MAS, such as adult-plant powdery mildew resistance, slow-rusting resistance, and FHB resistance. By pyramiding the slow-rusting resistance genes *Lr34*/*Yr18*/*Sr57*/*Pm38*, *Lr67*/*Yr46*/*Sr55*/*Pm46*, and *Lr46*/*Yr29*/*Sr58*/*Pm39*, resistance has been conferred against multiple rusts and powdery mildew; scientists from CIMMYT have thus successfully developed high-yield wheat cultivars with durable and broad-spectrum disease resistance (Singh et al., 2016). The *Ae. ventricosa* 2NS-2AS translocation carrying *Yr17*/*Lr37*/*Sr38*/*Cre5* has been successfully incorporated into wheat cultivars in China and the United States. *Yr15* from wild emmer and *YrAs2388* derived from *Ae. tauschii* were also highly resistant to the dominant races of *Pst*, and have been incorporated into commercial varieties in Sichuan Province. The leaf rust resistance gene *Lr13*/*LrZH22*/*Ne2* (Hewitt et al., 2021b; Yan et al., 2021) and the stripe rust resistance genes *YrZH22* and *YrZH84* were derived from the cornerstone parental line Zhou 8425B and are believed to have originated from the durum wheat donor of hexaploid triticale. These genes were often identified in wheat cultivars at Northern China, Huang-Huai River Valley Wheat Zone and conferred excellent leaf and stripe rust resistance. Furthermore, the pleiotropic APR gene *Lr27*/*Yr30*/*Sr2* has been found in many Chinese wheat cultivars. This evidence and current breeding practices suggest that pyramiding several major rust resistance genes into a pleiotropic APR gene backbone, such as *Lr27*/*Yr30*/*Sr2*, could provide strong and durable resistance. An alternative approach to develop transgenic wheat with stronger and potentially more durable resistance against rust diseases could be achieved by stacking five different rust resistance genes (*Sr22*, *Sr35*, *Sr45*, *Sr50*, and *Sr55*/*Lr67*/*Yr46*/ *Pm46*) in a single cassette (Luo et al., 2021).

MAS is a particularly useful strategy for FHB resistance, for which evaluation is difficult and cannot be conducted before flowering. At least ten FHB QTLs have been used in MAS; *Fhb1* is the most widely used. The lines with multiple FHB resistance QTLs typically showed greatly improved resistance (Li et al., 2019f; Zhang et al., 2021e). FHB-resistant cultivars developed using MAS have been registered in the United States (Anderson et al., 2012; Bernardo et al., 2014) and will soon be completed in China. In addition to use for improvement of resistance to a single pathogen or pathotype, MAS has also shown great potential in stacking genes that confer resistance to different types of pathogens (Mallick et al., 2015; Maré et al., 2020; Randhawa et al., 2019; Zeng et al., 2005). Genes or QTLs conferring resistance to multiple types of pathogens are highly attractive to breeders, and the list of known genes of this type is growing (Hu et al., 2019; Krattinger et al., 2009; Lagudah et al., 2009; Miedaner et al., 2012).

Far more target genes or QTLs that are currently suitable for MAS are available for breeding resistance to powdery mildew, rusts, and FHB than for any other diseases. For minor and developing diseases, resistance gene discovery and mapping is the key task at present, and progress is being made in this area (He et al., 2020; Saintenac et al., 2021; Singh et al., 2021; Su et al., 2021). Mapping and MAS can be conducted simultaneously (e.g., Li et al., 2014; Li et al., 2017a); this approach is becoming more feasible due to the availability of reference genome sequences, mapping technologies such as genotyping by sequencing, SNP-chip assays, and BSA-seq, among other advances. In the future, it is likely that MAS platforms will be developed that are high-throughput, technically easy to access, and low-cost, combining both foreground and background selections. This will drive genomics-assisted breeding for multiple traits, whether qualitative or quantitative, to a new level than was previously conceivable.

Genome editing for disease resistance

The development and application of genome editing tools has become a major focus of plant science and precision plant breeding. Such tools include zinc-finger nucleases (ZFNs), transcription activator-like effector nucleases (TALEN), and CRISPR/Cas9; these methods have contributed to genetic studies and engineering of crops with desirable traits (Figure 8D). The first reported genome-edited wheat was a line with the three homeologs of the barley gene *Mlo* (Büschges et al., 1997) knocked out, resulting in resistance to the powdery mildew pathogen *Bgt* (Wang et al., 2014b). Loss of *Mlo* function results in robust and broad-spectrum resistance to powdery mildew in barley, wheat, and many other plants (Kusch and Panstruga, 2017). However, negative pleiotropic effects related to accelerated senescence were often observed in such mutants, limiting their value in breeding programs. A new wheat *mlo* mutant, R32, was recently developed. This mutant maintains robust disease resistance without any undesirable growth defects (Li et al.,

2022b); a 304-kb targeted deletion in the *MLO-B1* locus rescues crop growth and yield. The deletion mutation altered the local chromatin landscape and resulted in ectopic activation of a nearby gene, *Tonoplast Monosaccharide Transporter 3* (*TaTMT3B*), alleviating the fitness costs associated with *TaMLO* disruption. Introducing *mlo* resistance from R32 into elite commercial wheat varieties via backcrossing and MAS produced powdery mildew-resistant lines with elite agronomic traits. Precision genome editing of this chromatin region via CRISPR/Cas9 also facilitated the rapid development of this new *mlo* mutation in elite wheat varieties, conferring excellent powdery mildew resistance without undesirable pleiotropic effects (Li et al., 2022b).

Mlo is a disease susceptibility gene, meaning that loss of function results in host disease resistance. Most recently, another wheat susceptible gene *TaPsIPK1*, a *P. striiformis* induced receptor-like cytoplasmic kinase, was found specifically recognizing the effectors of *PsSpg1* in *P. striiformis* and *PtSpg1* in *P. tritici* and triggering rust susceptibility (Wang et al., 2022c). Knocking out of *TaPsIPK1* homeologs in wheat cultivar Fielder by CRISPR-Cas9 technology confers broad-spectrum stripe rust and leaf rust resistance without loss of key agronomic traits. These results provide novel approach for exploring host susceptible genes for genome editing to develop excellent wheat cultivars for breeding broad-spectrum and durable resistance.

Among the wheat disease resistance genes that have been cloned thus far, most are resistance genes rather than susceptibility genes, and are therefore not suitable for a knockout approach via genome editing. Mining the allelic or haplotypic variation of cloned wheat disease resistance genes is necessary to identify a suitable target site for genome editing. For example, after surveying a worldwide wheat collection, Xie et al. (2020) identified a key single nucleotide variation (SNV), G3033A, in the NLR protein encoded by *Pm5e*, which could be used as a precise base editing site. Similarly, a 6-bp deletion identified in *Pm24*/*WTK3* (Lu et al., 2020) is an ideal target for precise deletion or exon replacement via CRISPR/Cas9 to confer powdery mildew resistance in elite wheat varieties. As more wheat disease resistance genes are cloned and the key sequence variations related to resistance are characterized, genome editing will be the most rapid and efficient approach for developing new disease-resistant and high-yield varieties.

Powerful genome editing tools with the capacity to precisely edit target genes effectively support molecular design for breeding as a feasible strategy. However, there are a series of key steps related to disease resistance that must be gone through. For example, exploitation of novel disease resistant germplasm resources; whole genome characterization of NLRs (NLRsome) and kinases in wheat and relative species and effectors in wheat pathogens; cloning and functional analysis of major genes/QTLs and the interaction network of genes related to resistance; pyramiding and stacking multiple disease resistance genes into elite wheat cultivars without yield penalty using MAS and transgenic approaches; higher efficiency genome editing and synthetic biology approach for disease resistance innovation.

Perspectives

Challenges in wheat breeding and production

With the human population projected to reach 9.9 billion by 2050, wheat production must increase by more than 2% annually to meet the increasing demand. However, the actual annual increase has only been ~1.2% over the past two decades, and this was mainly a result of new varieties and increasing water and nitrogen fertilizer supplies. In addition, global climate change poses a great threat to grain yield and quality, causing issues such as drought and intense heat during the grain filling stage (Figure 7). Increased temperatures in the winter and spring promote pathogen propagation and the spread of novel regional diseases, threatening wheat production. For example, the major diseases affecting wheat breeding and production were stripe rust and powdery mildew for several decades in the main wheat-producing areas in China (Huang-Huai River Valley wheat zones), but leaf rust and FHB have spread quickly over the past decade, becoming the major diseases to target in breeding resistance (Figure 8).

After the Green Revolution of the 1960s, semi-dwarf plants with resistance to lodging were widely adopted to increase cereal crop yields (Figure 3). However, semi-dwarf crops require high nitrogen fertilizer input to maximize yield. This increases farming costs, constitutes a large proportion of the energy consumed worldwide, and has detrimental effects on the environment, such as greenhouse gas emissions and eutrophication. Thus, enhancing crop production while decreasing N fertilizer usage is an urgent challenge; this can be accomplished by improving NUE (Figure 6). To meet the challenges resulting from human population growth, global warming, and requirements for sustainable agriculture, it is necessary to breed crops with high resistance to diseases and adaptability to stressful environments (such as low water and nutrient supplies) without yield penalties. The key strategies to achieve these goals are to discover and utilize genes and elite allelic resource from natural variations and to apply synthetic strategies.

Elucidating concerted evolution and subgenome asymmetry based on graph-based pan-genomes and epigenomes

Because wheat is a polyploid species, the subgenomes must work in concert to form a uni-nucleus for gene transcription and translation. Numerous structural variations (SVs) tend to

occur during the polyploidization process; thus, one or a few reference genomes cannot cover the full range of genetic diversity in species with high ploidy levels. Recently, a wheat pan-genome was constructed using primarily Illumina short reads and some PacBio data (Walkowiak et al., 2020). This study resulted in genome assemblies for more than ten varieties without further integration of the data. This approach does not sufficiently address research demands such as revealing the genotypes of different alleles at each locus and identifying larger SVs. The release of pan-genomes for rice and soybean provide blueprints for construction of a graph-based pan-genome for wheat (Liu et al., 2020c; Qin et al., 2021; Zhao et al., 2018). There will be additional technical difficulties to be overcome, such as abundant repeat sequences (>85%) and the hexaploid nature of wheat. However, it is imperative to construct a graph-based pan-genome resource for wheat to allow advanced evolutionary and functional genomic studies. In the context of evolutionary research, wild emmer, domesticated emmer, and emmer landraces should be a greater focus of research. For gene discovery and breeding, landmark varieties should be studied in more detail, including key landraces and ancestral collections.

In addition to DNA sequence variation, epigenomic diversity also contributes to asymmetric gene expression between subgenomes and relative process of wheat development and response to environmental conditions (Li et al., 2019g; Wang et al., 2021a; Zhao et al., 2022). Histone modifications, specifically H3K27me2, and chromatin accessibility dynamics contributed to genome stability and genetic recombination during wheat speciation (Liu et al., 2021d; Yuan et al., 2022). Interactions between epigenetic regulatory elements and high-order chromatin architecture shape the wheat transcriptional regulatory network and specify subgenome chromosome territories following polyploidization and introgression (Jia et al., 2021; Zhang et al., 2021d). However, the analyses conducted to date mainly describe the correlation between epigenomic variation and subgenome divergence during the course of evolution. Understanding the causality of epigenomic diversification-driven wheat speciation requires additional detailed study in the future.

Integration and expansion of strategies for gene discovery to pyramid in elite varieties

Discovering and pyramiding favorable alleles has long been a staple of molecular breeding. The main strategies for gene discovery are currently GWAS in natural collections and fine-mapping QTLs followed by cloning the crucial genes in a bi-parental population. To bridge genomics and breeding, advanced backcross-nested association mapping (AB-NAM) populations and AB-NAM plus inter-crossed (AB-NAMIC) populations are alternatively used to increase the genome contents of founder genotypes. This is accomplished by backcrossing at early stages with medium breeding selection to control the population size for efficient and economical phenotyping and genotyping. This has been proven as an efficient method for introgression from wild barley to cultivated varieties and from landrace to elite varieties in wheat (Zhang et al., unpublished data). Integration of GWAS/QTL analysis with other high-throughput multi-dimensional information has the potential to accelerate gene discovery and functional research and generate improvements in wheat agronomic traits. Relevant multi-dimensional data types include population-wide transcriptomes, metabolomes, proteomes, and epigenomes (e.g., accessible chromatin regions, DNA methylation, and dynamic chromatin modification signals). Such a multi-omic data integration strategy has been shown to work efficiently in maize (Gui et al., 2020).

To date, the majority of wheat research has been based on only a few reference genomes, with Chinese Spring being the most prevalent (IWGSC, 2018). This lack of diversity causes difficulties in capturing the hidden genetic, genomic, and molecular mechanisms of founder genotypes in breeding. This again emphasizes the urgent requirement for wheat pan-genome information, which will assist in mapping and isolating unique genes. In addition, the dispensable genome is anticipated to contain hotspots for gene discovery and could provide major support for the formation of super-characters in elite varieties. However, characterization of the dispensable genome requires a pan-genome reference. Due to the unusually large genome size of wheat, epigenetic regulatory elements are largely distributed in the non-coding intergenic regions (Li et al., 2019g; Zhao et al., 2022), forming rich resources for manipulation of gene expression and improvement of agronomic traits.

Strengthen bioinformatics database infrastructure

The wheat research community has been deluged with massive genome assemblies, emerging high-throughput multi-omics sequencing data, and phenotypic data for varieties, landrace, ancestors, and relatives within *Triticeae*. Unprecedented demand for exploiting the published, massively diversified data necessitates development of wheat-specific bioinformatics databases to accelerate scientific discoveries. Several databases were recently published by Chinese teams, such as the Wheat-SnpHub-Portal (Wang et al., 2020d), Triticeae-GeneTribe (Chen et al., 2020c), WGVD (Wang et al., 2020d), WheatGmap (Zhang et al., 2021b), WheatGene (Garcia et al., 2021), and the widely-used database WheatOmics (http://wheatomics.sdau.edu.cn/) (Ma et al., 2021). In addition to the significantly increased requirements for computing resources due to the large genome size of wheat, the pervasive SVs and introgressions in

the wheat genome create an urgent need for methodological innovations in diverse dimensions, including algorithms, interactions, and data curation. A powerful database must be developed for wheat, similar to ENCODE, that takes into account the need for data uniformity, bench effects, user-friendliness of the interface, design compatibility, and functional extendibility. These tasks will require interdisciplinary backgrounds to effectively combine computational technologies and biological knowledge of wheat. Maintaining a popular database also presents unique challenges compared to other types of research, such as considerable long-term investments of both time and money, which would be particularly challenging for a single research team. Thus, gathering data and training experts skilled in developing bioinformatics databases should be equally prioritized. To this end, a sustainable funding source and a stable non-profit team with professional skills are essential for developing and maintaining such databases, particularly due to the relatively large wheat genome size. It would be beneficial for the wheat research community to work towards construction of a comprehensive, expandable central database by integrating resources and talents through a long-term funded collaborative project. Constructing purpose-specific databases with methodological innovations must be encouraged. Moreover, a widely accepted data-sharing mechanism is vital to balance competition and cooperation, which will ultimately benefit the wheat research community.

Intelligent breeding for the next Green Revolution

In the near future, innovations in sequencing technologies and bioinformatics analysis pipelines are expected to enable high-throughput genotyping of germplasm at low cost, which will in turn allow the generation of a reference pan-genome comprising landmark genetically diverse varieties, landraces, and distant relatives of wheat. Agronomic phenotypes with multi-dimensional parameters will be acquired by robotics and drones in the field and analyzed with deep learning algorithms to intelligently quantify trait measurements. Key trait-regulating genes will be identified from GWAS and the rapid growth multi-omics data collection and analysis. Functionally characterized core factors could be used for directional improvements in desired traits through precision gene editing, synthetic biology, and transgenic approaches. Complex associations between genotypes, phenotypes, and the environment will be uncovered by machine learning models to direct germplasm selection and plan hybridization schemes. Supported by these data, it may soon be feasible to assemble all possible superior alleles at QTLs into a single virtual, optimized genome to simulate optimal phenotypes, a concept called genomic design breeding (GDB). Instead of pyramiding individual genes with explicit functions to facilitate introgression breeding, the GDB strategy encompasses a group of genes (i.e., a haplotype block) in ideal combinations.

This new type of "intelligent breeding" will be characterized by the integration of modern genomics, phenomics, genome editing, and synthetic biology, combined with artificial intelligence (AI) technology. This framework is expected to accelerate the cultivation of novel wheat varieties that not only have high yield, superior quality, and multi-stress resistance, but are also ecologically and environmentally friendly.

Compliance and ethics *The author(s) declare that they have no conflict of interest.*

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References

Aberkane, H., Payne, T., Kishi, M., Smale, M., Amri, A., and Jamora, N. (2020). Transferring diversity of goat grass to farmers' fields through the development of synthetic hexaploid wheat. Food Sec 12, 1017–1033.

Adamski, N.M., Simmonds, J., Brinton, J.F., Backhaus, A.E., Chen, Y., Smedley, M., Hayta, S., Florio, T., Crane, P., Scott, P., et al. (2021). Ectopic expression of *Triticum polonicum VRT-A2* underlies elongated glumes and grains in hexaploid wheat in a dosage-dependent manner. Plant Cell 33, 2296–2319.

Akhunov, E.D., Akhunova, A.R., Anderson, O.D., Anderson, J.A., Blake, N., Clegg, M.T., Coleman-Derr, D., Conley, E.J., Crossman, C.C., Deal, K.R., et al. (2010). Nucleotide diversity maps reveal variation in diversity among wheat genomes and chromosomes. BMC Genomics 11, 702.

Al-Sheikh Ahmed, S., Zhang, J., Ma, W., and Dell, B. (2018). Contributions of *TaSUTs* to grain weight in wheat under drought. Plant Mol Biol 98, 333–347.

Alonso-Peral, M.M., Oliver, S.N., Casao, M.C., Greenup, A.A., and Trevaskis, B. (2011). The promoter of the cereal *VERNALIZATION1* gene is sufficient for transcriptional induction by prolonged cold. PLoS ONE 6, e29456.

Amasino, R. (2010). Seasonal and developmental timing of flowering. Plant J 61, 1001–1013.

Anderson, J.A., Wiersma, J.J., Linkert, G.L., Kolmer, J.A., Jin, Y., Dill-Macky, R., Wiersma, J.V., and Hareland, G.A. (2012). Registration of 'Sabin' wheat. J Plant regist 6, 174–179.

Antoniou-Kourounioti, R.L., Zhao, Y., Dean, C., and Howard, M. (2021). Feeling every bit of winter - distributed temperature sensitivity in vernalization. Front Plant Sci 12, 628726.

Arora, S., Steuernagel, B., Gaurav, K., Chandramohan, S., Long, Y., Matny, O., Johnson, R., Enk, J., Periyannan, S., Singh, N., et al. (2019). Resistance gene cloning from a wild crop relative by sequence capture and association genetics. Nat Biotechnol 37, 139–143.

Athiyannan, N., Abrouk, M., Boshoff, W.H.P., Cauet, S., Rodde, N.,

Kudrna, D., Mohammed, N., Bettgenhaeuser, J., Botha, K.S., Derman, S.S., et al. (2022). Long-read genome sequencing of bread wheat facilitates disease resistance gene cloning. Nat Genet 54, 227–231.
Atsmon, D., and Jacobs, E. (1977). A newly bred 'Gigas' form of bread wheat (*Triticum aestivum* L.): morphological features and thermo-photoperiodic responses. Crop Sci 17, 31–35.
Avni, R., Lux, T., Minz-Dub, A., Millet, E., Sela, H., Distelfeld, A., Deek, J., Yu, G., Steuernagel, B., Pozniak, C., et al. (2022). Genome sequences of three *Aegilops* species of the section Sitopsis reveal phylogenetic relationships and provide resources for wheat improvement. Plant J 110, 179–192.
Avni, R., Nave, M., Barad, O., Baruch, K., Twardziok, S.O., Gundlach, H., Hale, I., Mascher, M., Spannagl, M., Wiebe, K., et al. (2017). Wild emmer genome architecture and diversity elucidate wheat evolution and domestication. Science 357, 93–97.
Ayadi, M., Brini, F., and Masmoudi, K. (2019). Overexpression of a wheat aquaporin gene, *Td*PIP2;1, enhances salt and drought tolerance in transgenic durum wheat cv. Maali. Int J Mol Sci 20, 2389.
Bai, S., Yuan, F., Zhang, H., Zhang, Z., Zhao, J., Yang, Q., Wu, J., and Chen, X. (2020). Characterization of the wheat-*Psathyrostachys huashania* Keng 2Ns/2D substitution line H139: a novel germplasm with enhanced resistance to wheat take-all. Front Plant Sci 11, 233.
Basavaraddi, P.A., Savin, R., Wingen, L.U., Bencivenga, S., Przewieslik-Allen, A.M., Griffiths, S., and Slafer, G.A. (2021). Interactions between two QTLs for time to anthesis on spike development and fertility in wheat. Sci Rep 11, 2451.
Bauer, E., Schmutzer, T., Barilar, I., Mascher, M., Gundlach, H., Martis, M. M., Twardziok, S.O., Hackauf, B., Gordillo, A., Wilde, P., et al. (2017). Towards a whole-genome sequence for rye (*Secale cereale* L.). Plant J 89, 853–869.
Bäumlein, H., Nagy, I., Villarroel, R., Inze, D., and Wobus, U. (1992). *Cis*-analysis of a seed protein gene promoter: the conservative RY repeat CATGCATG within the legumin box is essential for tissue-specific expression of a legumin gene.. Plant J 2, 233–239.
Bazhenov, M.S., Divashuk, M.G., Amagai, Y., Watanabe, N., and Karlov, G.I. (2015). Isolation of the dwarfing *Rht-B1p* (*Rht17*) gene from wheat and the development of an allele-specific PCR marker. Mol Breeding 35, 213.
Bernardo, A., Bai, G., Yu, J., Kolb, F., Bockus, W., and Dong, Y. (2014). Registration of near-isogenic winter wheat germplasm contrasting in *Fhb1* for fusarium head blight resistance. J Plant Registrat 8, 106–108.
Bi, H., Shi, J., Kovalchuk, N., Luang, S., Bazanova, N., Chirkova, L., Zhang, D., Shavrukov, Y., Stepanenko, A., Tricker, P., et al. (2018). Overexpression of the *TaSHN1* transcription factor in bread wheat leads to leaf surface modifications, improved drought tolerance, and no yield penalty under controlled growth conditions. Plant Cell Environ 41, 2549–2566.
Biesiekierski, J.R. (2017). What is gluten? J Gastroenterol Hepatol 32, 78–81.
Bishop, D.L., and Bugbee, B.G. (1998). Photosynthetic capacity and dry mass partitioning in dwarf and semi-dwarf wheat (*Triticum aestivum* L.). J Plant Physiol 153, 558–565.
Blake, V.C., Woodhouse, M.R., Lazo, G.R., Odell, S.G., Wight, C.P., Tinker, N.A., Wang, Y., Gu, Y.Q., Birkett, C.L., Jannink, J.L., et al. (2019). GrainGenes: centralized small grain resources and digital platform for geneticists and breeders. Database: J Biol Databases Curation 2019, baz065.
Boden, S.A., Cavanagh, C., Cullis, B.R., Ramm, K., Greenwood, J., Jean Finnegan, E., Trevaskis, B., and Swain, S.M. (2015). *Ppd-1* is a key regulator of inflorescence architecture and paired spikelet development in wheat. Nat Plants 1, 14016.
Bogard, M., Allard, V., Brancourt-Hulmel, M., Heumez, E., Machet, J.M., Jeuffroy, M.H., Gate, P., Martre, P., and Le Gouis, J. (2010). Deviation from the grain protein concentration–grain yield negative relationship is highly correlated to post-anthesis N uptake in winter wheat. J Exp Bot 61, 4303–4312.
Borràs-Gelonch, G., Rebetzke, G.J., Richards, R.A., and Romagosa, I. (2012). Genetic control of duration of pre-anthesis phases in wheat (*Triticum aestivum* L.) and relationships to leaf appearance, tillering, and dry matter accumulation. J Exp Bot 63, 69–89.
Boudet, J., Merlino, M., Plessis, A., Gaudin, J.C., Dardevet, M., Perrochon, S., Alvarez, D., Risacher, T., Martre, P., and Ravel, C. (2019). The bZIP transcription factor SPA Heterodimerizing Protein represses glutenin synthesis in *Triticum aestivum*. Plant J 97, 858–871.
Bourras, S., Kunz, L., Xue, M., Praz, C.R., Müller, M.C., Kälin, C., Schläfli, M., Ackermann, P., Flückiger, S., Parlange, F., et al. (2019). The *AvrPm3-Pm3* effector-NLR interactions control both race-specific resistance and host-specificity of cereal mildews on wheat. Nat Commun 10, 2292.
Bourras, S., McNally, K.E., Ben-David, R., Parlange, F., Roffler, S., Praz, C.R., Oberhaensli, S., Menardo, F., Stirnweis, D., Frenkel, Z., et al. (2015). Multiple avirulence loci and allele-specific effector recognition control the *Pm3* race-specific resistance of wheat to powdery mildew. Plant Cell 27, 2991–3012.
Bourras, S., McNally, K.E., Müller, M.C., Wicker, T., and Keller, B. (2016). Avirulence genes in cereal powdery mildews: the Gene-for-Gene hypothesis 2.0. Front Plant Sci 7, 241.
Brambilla, V., Gomez-Ariza, J., Cerise, M., and Fornara, F. (2017). The importance of being on time: regulatory networks controlling photoperiodic flowering in cereals. Front Plant Sci 8, 665.
Brenchley, R., Spannagl, M., Pfeifer, M., Barker, G.L.A., D'Amore, R., Allen, A.M., McKenzie, N., Kramer, M., Kerhornou, A., Bolser, D., et al. (2012). Analysis of the bread wheat genome using whole-genome shotgun sequencing. Nature 491, 705–710.
Brinton, J., and Uauy, C. (2019). A reductionist approach to dissecting grain weight and yield in wheat. J Integr Plant Biol 61, 337–358.
Brown, J.K.M., and Jessop, A.C. (1995). Genetics of avirulences in *Erysiphe graminis* f.sp. *hordei*. Plant Pathol 44, 1039–1049.
Büschges, R., Hollricher, K., Panstruga, R., Simons, G., Wolter, M., Frijters, A., van Daelen, R., van der Lee, T., Diergaarde, P., Groenendijk, J., et al. (1997). The barley *Mlo* gene: a novel control element of plant pathogen resistance. Cell 88, 695–705.
Bustos, D.V., Hasan, A.K., Reynolds, M.P., and Calderini, D.F. (2013). Combining high grain number and weight through a DH-population to improve grain yield potential of wheat in high-yielding environments. Field Crops Res 145, 106–115.
Cainong, J.C., Bockus, W.W., Feng, Y., Chen, P., Qi, L., Sehgal, S.K., Danilova, T.V., Koo, D.H., Friebe, B., and Gill, B.S. (2015). Chromosome engineering, mapping, and transferring of resistance to Fusarium head blight disease from *Elymus tsukushiensis* into wheat. Theor Appl Genet 128, 1019–1027.
Camut, L., Gallova, B., Jilli, L., Sirlin-Josserand, M., Carrera, E., Sakvarelidze-Achard, L., Ruffel, S., Krouk, G., Thomas, S.G., Hedden, P., et al. (2021). Nitrate signaling promotes plant growth by upregulating gibberellin biosynthesis and destabilization of DELLA proteins. Curr Biol 31, 4971–4982.
Cann, D.J., Schillinger, W.F., Hunt, J.R., Porker, K.D., and Harris, F.A.J. (2020). Agroecological advantages of early-sown winter wheat in semi-arid environments: a comparative case study from Southern Australia and Pacific Northwest United States. Front Plant Sci 11, 568.
Cao, H., Yan, X., Chen, G., Zhou, J., Li, X., Ma, W., and Yan, Y. (2015a). Comparative proteome analysis of A- and B-type starch granule-associated proteins in bread wheat (*Triticum aestivum* L.) and Aegilops crassa. J Proteomics 112, 95–112.
Cao, J., Liu, K., Song, W., Zhang, J., Yao, Y., Xin, M., Hu, Z., Peng, H., Ni, Z., Sun, Q., et al. (2021). Pleiotropic function of the *SQUAMOSA PROMOTER-BINDING PROTEIN-LIKE* gene *TaSPL14* in wheat plant architecture. Planta 253, 44.
Cao, T.J., Chen, Y.X., Li, D., Zhang, Y., Wang, X.C., Zhao, H., and Liu, Z. Y. (2015b). Identification and molecular detection of powdery mildew resistance of new bred wheat varieties (lines) in Henan province, China. Acta Agronomica Sin 41, 1172–1182.
CCRWS. (1984). Evaluation of wheat varietal germplasm for scab resistance (in Chinese). Zuowu Pinzhong Ziyuan 4, 2–7.

Cha, J.K., O'Connor, K., Alahmad, S., Lee, J.H., Dinglasan, E., Park, H., Lee, S.M., Hirsz, D., Kwon, S.W., Kwon, Y., et al. (2022). Speed vernalization to accelerate generation advance in winter cereal crops. Mol Plant 15, 1300–1309.

Chai, L., Xin, M., Dong, C., Chen, Z., Zhai, H., Zhuang, J., Cheng, X., Wang, N., Geng, J., Wang, X., et al. (2022). A natural variation in Ribonuclease H-like gene underlies *Rht8* to confer "Green Revolution" trait in wheat. Mol Plant 15, 377–380.

Chang, H., Chen, D., Kam, J., Richardson, T., Drenth, J., Guo, X., McIntyre, C.L., Chai, S., Rae, A.L., and Xue, G.P. (2016). Abiotic stress upregulated TaZFP34 represses the expression of type-B response regulator and *SHY2* genes and enhances root to shoot ratio in wheat. Plant Sci 252, 88–102.

Chen, A., and Dubcovsky, J. (2012). Wheat TILLING mutants show that the vernalization gene *VRN1* down-regulates the flowering repressor *VRN2* in leaves but is not essential for flowering. PLoS Genet 8, e1003134.

Chen, D., Chai, S., McIntyre, C.L., and Xue, G.P. (2018a). Overexpression of a predominantly root-expressed NAC transcription factor in wheat roots enhances root length, biomass and drought tolerance. Plant Cell Rep 37, 225–237.

Chen, F., Gao, M., Zhang, J., Zuo, A., Shang, X., and Cui, D. (2013). Molecular characterization of vernalization and response genes in bread wheat from the Yellow and Huai Valley of China. BMC Plant Biol 13, 199.

Chen, G.X., Zhen, S.M., Liu, Y.L., Yan, X., Zhang, M., and Yan, Y.M. (2017a). *In vivo* phosphoproteome characterization reveals key starch granule-binding phosphoproteins involved in wheat water-deficit response. BMC Plant Biol 17, 168.

Chen, G., Zhu, J., Zhou, J., Subburaj, S., Zhang, M., Han, C., Hao, P., Li, X., and Yan, Y. (2014). Dynamic development of starch granules and the regulation of starch biosynthesis in *Brachypodium distachyon*: comparison with common wheat and *Aegilops peregrina*. BMC Plant Biol 14, 198.

Chen, J., Upadhyaya, N.M., Ortiz, D., Sperschneider, J., Li, F., Bouton, C., Breen, S., Dong, C., Xu, B., Zhang, X., et al. (2017b). Loss of *AvrSr50* by somatic exchange in stem rust leads to virulence for *Sr50* resistance in wheat. Science 358, 1607–1610.

Chen, P.D., Qi, L.L., Zhou, B., Zhang, S.Z., and Liu, D.J. (1995). Development and molecular cytogenetic analysis of wheat-*Haynaldia villosa* 6VS/6AL translocation lines specifying resistance to powdery mildew. Theoret Appl Genet 91-91, 1125–1128.

Chen, S., Rouse, M.N., Zhang, W., Zhang, X., Guo, Y., Briggs, J., and Dubcovsky, J. (2020a). Wheat gene *Sr60* encodes a protein with two putative kinase domains that confers resistance to stem rust. New Phytol 225, 948–959.

Chen, S., Zhang, W., Bolus, S., Rouse, M.N., and Dubcovsky, J. (2018b). Identification and characterization of wheat stem rust resistance gene *Sr21* effective against the Ug99 race group at high temperature. PLoS Genet 14, e1007287.

Chen, Y., Yan, Y., Wu, T.T., Zhang, G.L., Yin, H., Chen, W., Wang, S., Chang, F., and Gou, J.Y. (2020b). Cloning of wheat *keto-acyl thiolase 2B* reveals a role of jasmonic acid in grain weight determination. Nat Commun 11, 6266.

Chen, Y., Carver, B.F., Wang, S., Zhang, F., and Yan, L. (2009). Genetic loci associated with stem elongation and winter dormancy release in wheat. Theor Appl Genet 118, 881–889.

Chen, Y., Song, W., Xie, X., Wang, Z., Guan, P., Peng, H., Jiao, Y., Ni, Z., Sun, Q., and Guo, W. (2020c). A collinearity-incorporating homology inference strategy for connecting emerging assemblies in the triticeae tribe as a pilot practice in the plant pangenomic era. Mol Plant 13, 1694–1708.

Chen, Y.P., Wang, H.Z., Cao, A.Z., Wang, C.M., and Chen, P.D. (2006). Cloning of a resistance gene analog from wheat and development of a codominant PCR marker for *Pm21*. J Integr Plant Biol 48, 715–721.

Chen, Z., Cheng, X., Chai, L., Wang, Z., Du, D., Wang, Z., Bian, R., Zhao, A., Xin, M., Guo, W., et al. (2020d). Pleiotropic QTL influencing spikelet number and heading date in common wheat (*Triticum aestivum* L.). Theor Appl Genet 133, 1825–1838.

Chen, Z., Ke, W., He, F., Chai, L., Cheng, X., Xu, H., Wang, X., Du, D., Zhao, Y., Chen, X., et al. (2022). A single nucleotide deletion in the third exon of *FT-D1* increases the spikelet number and delays heading date in wheat (*Triticum aestivum* L.). Plant Biotechnol J 20, 920–933.

Cheng, H., Liu, J., Wen, J., Nie, X., Xu, L., Chen, N., Li, Z., Wang, Q., Zheng, Z., Li, M., et al. (2019). Frequent intra- and inter-species introgression shapes the landscape of genetic variation in bread wheat. Genome Biol 20, 136.

Cheng, X., Xin, M., Xu, R., Chen, Z., Cai, W., Chai, L., Xu, H., Jia, L., Feng, Z., Wang, Z., et al. (2020). A single amino acid substitution in STKc_GSK3 kinase conferring semispherical grains and its implications for the origin of *Triticum sphaerococcum*. Plant Cell 32, 923–934.

Cheuk, A., Ouellet, F., and Houde, M. (2020). The barley stripe mosaic virus expression system reveals the wheat C2H2 zinc finger protein TaZFP1B as a key regulator of drought tolerance. BMC Plant Biol 20, 144.

Choi, J., Hyun, Y., Kang, M.J., In Yun, H., Yun, J.Y., Lister, C., Dean, C., Amasino, R.M., Noh, B., Noh, Y.S., et al. (2009). Resetting and regulation of *FLOWERING LOCUS C* expression during *Arabidopsis* reproductive development. Plant J 57, 918–931.

Chouard, P. (1960). Vernalization and its relations to dormancy. Annu Rev Plant Physiol 11, 191–238.

Cloutier, S., McCallum, B.D., Loutre, C., Banks, T.W., Wicker, T., Feuillet, C., Keller, B., and Jordan, M.C. (2007). Leaf rust resistance gene *Lr1*, isolated from bread wheat (*Triticum aestivum* L.) is a member of the large psr567 gene family. Plant Mol Biol 65, 93–106.

Colmsee, C., Beier, S., Himmelbach, A., Schmutzer, T., Stein, N., Scholz, U., and Mascher, M. (2015). BARLEX— the barley draft genome explorer. Mol Plant 8, 964–966.

Coventry, D.R., Reeves, T.G., Brooke, H.D., and Cann, D.K. (1993). Influence of genotype, sowing date, and seeding rate on wheat development and yield. Aust J Exp Agric 33, 751–757.

Crevillén, P., Yang, H., Cui, X., Greeff, C., Trick, M., Qiu, Q., Cao, X., and Dean, C. (2014). Epigenetic reprogramming that prevents transgenerational inheritance of the vernalized state. Nature 515, 587–590.

Crofts, N., Abe, N., Oitome, N.F., Matsushima, R., Hayashi, M., Tetlow, I. J., Emes, M.J., Nakamura, Y., and Fujita, N. (2015). Amylopectin biosynthetic enzymes from developing rice seed form enzymatically active protein complexes. J Exp Bot 66, 4469–4482.

Crosthwaite, S.K., and Jenkins, G.I. (1993). The role of leaves in the perception of vernalizing temperatures in sugar beet. J Exp Bot 44, 801–806.

Cui, F., Ding, A., Li, J., Zhao, C., Wang, L., Wang, X., Qi, X., Li, X., Li, G., Gao, J., et al. (2012). QTL detection of seven spike-related traits and their genetic correlations in wheat using two related RIL populations. Euphytica 186, 177–192.

Cui, X.Y., Du, Y.T., Fu, J.D., Yu, T.F., Wang, C.T., Chen, M., Chen, J., Ma, Y.Z., and Xu, Z.S. (2018). Wheat CBL-interacting protein kinase 23 positively regulates drought stress and ABA responses. BMC Plant Biol 18, 93.

Cui, X.Y., Gao, Y., Guo, J., Yu, T.F., Zheng, W.J., Liu, Y.W., Chen, J., Xu, Z.S., and Ma, Y.Z. (2019). BES/BZR transcription factor TaBZR2 positively regulates drought responses by activation of *TaGST1*. Plant Physiol 180, 605–620.

Curtis, B.C. (2019). Wheat in the World. Available online: http://www.fao.org/3/y4011e/y4011e4004.htm.

Curtis, O.F., and Chang, H.T. (1930). The relative effectiveness of the temperature of the crown as contrasted with that of the rest of the plant upon the flowering of celery plants. Am J Bot 17, 1047–1048.

Cuthbert, P.A., Somers, D.J., and Brulé-Babel, A. (2007). Mapping of *Fhb2* on chromosome 6BS: a gene controlling Fusarium head blight field resistance in bread wheat (*Triticum aestivum* L.). Theor Appl Genet 114, 429–437.

Dale, E.M.D., and Housley, T.L. (1986). Sucrose synthase activity in developing wheat endosperms differing in maximum weight. Plant Physiol 82, 7–10.
Debernardi, J.M., Greenwood, J.R., Jean Finnegan, E., Jernstedt, J., and Dubcovsky, J. (2020a). *APETALA 2*-like genes *AP2L2* and *Q* specify lemma identity and axillary floral meristem development in wheat. Plant J 101, 171–187.
Debernardi, J.M., Tricoli, D.M., Ercoli, M.F., Hayta, S., Ronald, P., Palatnik, J.F., and Dubcovsky, J. (2020b). A GRF-GIF chimeric protein improves the regeneration efficiency of transgenic plants. Nat Biotechnol 38, 1274–1279.
Degen, G.E., Orr, D.J., and Carmo-Silva, E. (2021). Heat-induced changes in the abundance of wheat Rubisco activase isoforms. New Phytol 229, 1298–1311.
Degen, G.E., Worrall, D., and Carmo-Silva, E. (2020). An isoleucine residue acts as a thermal and regulatory switch in wheat Rubisco activase. Plant J 103, 742–751.
Deng, S., Wu, X., Wu, Y., Zhou, R., Wang, H., Jia, J., and Liu, S. (2011). Characterization and precise mapping of a QTL increasing spike number with pleiotropic effects in wheat. Theor Appl Genet 122, 281–289.
Deng, W., Casao, M.C., Wang, P., Sato, K., Hayes, P.M., Finnegan, E.J., and Trevaskis, B. (2015). Direct links between the vernalization response and other key traits of cereal crops. Nat Commun 6, 5882.
Deng, X., Sha, Y., Lv, Z., Wu, Y., Zhang, A., Wang, F., and Liu, B. (2018). The capacity to buffer and sustain imbalanced D-subgenome chromosomes by the BBAA component of hexaploid wheat is an evolved dominant trait. Front Plant Sci 9, 1149.
Dennett, A.L., and Trethowan, R.M. (2013). Milling efficiency of triticale grain for commercial flour production. J Cereal Sci 57, 527–530.
Devos, K.M., Atkinson, M.D., Chinoy, C.N., Francis, H.A., Harcourt, R.L., Koebner, R.M.D., Liu, C.J., Masojć, P., Xie, D.X., and Gale, M.D. (1993). Chromosomal rearrangements in the rye genome relative to that of wheat. Theoret Appl Genet 85-85, 673–680.
Diallo, A.O., Ali-Benali, M.A., Badawi, M., Houde, M., and Sarhan, F. (2012). Expression of vernalization responsive genes in wheat is associated with histone H3 trimethylation. Mol Genet Genomics 287, 575–590.
Díaz, A., Zikhali, M., Turner, A.S., Isaac, P., and Laurie, D.A. (2012). Copy number variation affecting the *Photoperiod-B1* and *Vernalization-A1* genes is associated with altered flowering time in wheat (*Triticum aestivum*). PLoS ONE 7, e33234.
Diaz, I., Martinez, M., Isabel-LaMoneda, I., Rubio-Somoza, I., and Carbonero, P. (2005). The DOF protein, SAD, interacts with GAMYB in plant nuclei and activates transcription of endosperm-specific genes during barley seed development. Plant J 42, 652–662.
Diaz, I., Vicente-Carbajosa, J., Abraham, Z., Martínez, M., Isabel-La Moneda, I., and Carbonero, P. (2002). The GAMYB protein from barley interacts with the DOF transcription factor BPBF and activates endosperm-specific genes during seed development. Plant J 29, 453–464.
Ding, P., Fang, L., Wang, G., Li, X., Huang, S., Gao, Y., Zhu, J., Xiao, L., Tong, J., Chen, F., et al. (2019). Wheat methionine sulfoxide reductase A4.1 interacts with heme oxygenase 1 to enhance seedling tolerance to salinity or drought stress. Plant Mol Biol 101, 203–220.
Dissanayake, I., Rodriguez-Medina, J., Brady, S.M., and Tanurdžić, M. (2019). Transcriptional dynamics of bread wheat in response to nitrate and phosphate supply reveal functional divergence of genetic factors involved in nitrate and phosphate signaling. BioRxiv:10.1101/551069.
Distelfeld, A., Uauy, C., Fahima, T., and Dubcovsky, J. (2006). Physical map of the wheat high-grain protein content gene *Gpc-B1* and development of a high-throughput molecular marker. New Phytol 169, 753–763.
Dixon, L.E., Greenwood, J.R., Bencivenga, S., Zhang, P., Cockram, J., Mellers, G., Ramm, K., Cavanagh, C., Swain, S.M., and Boden, S.A. (2018). *TEOSINTE BRANCHED1* regulates inflorescence architecture and development in bread wheat (*Triticum aestivum*). Plant Cell 30, 563–581.
Dixon, L.E., Karsai, I., Kiss, T., Adamski, N.M., Liu, Z., Ding, Y., Allard, V., Boden, S.A., and Griffiths, S. (2019). *VERNALIZATION1* controls developmental responses of winter wheat under high ambient temperatures. Development 146, dev172684.
Dobrikova, A.G., Yotsova, E.K., Börner, A., Landjeva, S.P., and Apostolova, E.L. (2017). The wheat mutant DELLA-encoding gene (*Rht-B1c*) affects plant photosynthetic responses to cadmium stress. Plant Physiol Biochem 114, 10–18.
Dong, G., Ni, Z., Yao, Y., Nie, X., and Sun, Q. (2007). Wheat Dof transcription factor WPBF interacts with *TaQM* and activates transcription of an alpha-gliadin gene during wheat seed development. Plant Mol Biol 63, 73–84.
Dong, W., Wang, M., Xu, F., Quan, T., Peng, K., Xiao, L., and Xia, G. (2013). Wheat oxophytodienoate reductase gene *TaOPR1* confers salinity tolerance via enhancement of abscisic acid signaling and reactive oxygen species scavenging. Plant Physiol 161, 1217–1228.
Dong, Y.C., Xu, S.J., Zhou, R.H., Yang, X.M., Li, X.Q., and Li, L.H. (2010). Discovery and study on chromosome natural doubling germplasm of intergeneric hybrids in wheat (in Chinese). In: DongYuChen Anthology of Papers. Beijing: China Agricultural Press. 325–331.
Duan, E., Wang, Y., Li, X., Lin, Q., Zhang, T., Wang, Y., Zhou, C., Zhang, H., Jiang, L., Wang, J., et al. (2019). OsSHI1 regulates plant architecture through modulating the transcriptional activity of IPA1 in rice. Plant Cell 31, 1026–1042.
Dubcovsky, J., Chen, C., and Yan, L. (2005). Molecular characterization of the allelic variation at the *VRN-H2* vernalization locus in barley. Mol Breeding 15, 395–407.
Dubcovsky, J., and Dvorak, J. (2007). Genome plasticity a key factor in the success of polyploid wheat under domestication. Science 316, 1862–1866.
Duggan, B.L., Richards, R.A., van Herwaarden, A.F., and Fettell, N.A. (2005). Agronomic evaluation of a tiller inhibition gene (*tin*) in wheat. I. Effect on yield, yield components, and grain protein. Aust J Agric Res 56, 169–178.
Duncan, O., Trösch, J., Fenske, R., Taylor, N.L., and Millar, A.H. (2017). Resource: mapping the *Triticum aestivum* proteome. Plant J 89, 601–616.
Dvorak, J., Wang, L., Zhu, T., Jorgensen, C.M., Luo, M.C., Deal, K.R., Gu, Y.Q., Gill, B.S., Distelfeld, A., Devos, K.M., et al. (2018). Reassessment of the evolution of wheat chromosomes 4A, 5A, and 7B. Theor Appl Genet 131, 2451–2462.
Eagles, H.A., Cane, K., and Trevaskis, B. (2011). Veery wheats carry an allele of *Vrn-A1* that has implications for freezing tolerance in winter wheats. Plant Breeding 130, 413–418.
Eagles, H.A., Hollamby, G.J., and Eastwood, R.F. (2002). Genetic and environmental variation for grain quality traits routinely evaluated in southern Australian wheat breeding programs. Aust J Agric Res 53, 1047–1057.
Ehdaie, B., Merhaut, D.J., Ahmadian, S., Hoops, A.C., Khuong, T., Layne, A.P., and Waines, J.G. (2010). Root system size influences water-nutrient uptake and nitrate leaching potential in wheat. J Agronomy Crop Sci 196, 455–466.
Ellis, M.H., Rebetzke, G.J., Chandler, P., Bonnett, D., Spielmeyer, W., and Richards, R.A. (2004). The effect of different height reducing genes on the early growth of wheat. Funct Plant Biol 31, 583–589.
Fan, M., Miao, F., Jia, H., Li, G., Powers, C., Nagarajan, R., Alderman, P. D., Carver, B.F., Ma, Z., and Yan, L. (2021). *O*-linked *N*-acetylglucosamine transferase is involved in fine regulation of flowering time in winter wheat. Nat Commun 12, 2303.
FAO. (2018). Food Outlook: Biannual Report on Global Food Markets. Rome, 67–74.
Faricelli, M.E., Valárik, M., and Dubcovsky, J. (2010). Control of flowering time and spike development in cereals: the earliness *per se Eps-1* region in wheat, rice, and *Brachypodium*. Funct Integr Genomics 10, 293–306.
Faris, J.D., Zhang, Z., Lu, H., Lu, S., Reddy, L., Cloutier, S., Fellers, J.P., Meinhardt, S.W., Rasmussen, J.B., Xu, S.S., et al. (2010). A unique

wheat disease resistance-like gene governs effector-triggered susceptibility to necrotrophic pathogens. Proc Natl Acad Sci USA 107, 13544–13549.
Feng, J., Wang, L., Wu, Y., Luo, Q., Zhang, Y., Qiu, D., Han, J., Su, P., Xiong, Z., Chang, J., et al. (2019). *TaSnRK2.9*, a sucrose non-fermenting 1-related protein kinase gene, positively regulates plant response to drought and salt stress in transgenic tobacco. Front Plant Sci 9, 2003.
Feng, S., Martinez, C., Gusmaroli, G., Wang, Y., Zhou, J., Wang, F., Chen, L., Yu, L., Iglesias-Pedraz, J.M., Kircher, S., et al. (2008). Coordinated regulation of *Arabidopsis thaliana* development by light and gibberellins. Nature 451, 475–479.
Fernández-Calleja, M., Casas, A.M., and Igartua, E. (2021). Major flowering time genes of barley: allelic diversity, effects, and comparison with wheat. Theor Appl Genet 134, 1867–1897.
Fernández-Calleja, M., Ciudad, F.J., Casas, A.M., and Igartua, E. (2022). Hybrids provide more options for fine-tuning flowering time responses of winter barley. Front Plant Sci 13, 827701.
Feuillet, C., Travella, S., Stein, N., Albar, L., Nublat, A., and Keller, B. (2003). Map-based isolation of the leaf rust disease resistance gene *Lr10* from the hexaploid wheat (*Triticum aestivum* L.) genome. Proc Natl Acad Sci USA 100, 15253–15258.
Field, C.B., Barros, V., Stocker, T.F., and Dahe, Q. (2012). Managing the Risks of Extreme Events and Disasters to Advance Climate Change Adaptation: Special Report of the Intergovernmental Panel on Climate Change. Cambridge: Cambridge University Press.
Finnegan, E.J., Ford, B., Wallace, X., Pettolino, F., Griffin, P.T., Schmitz, R.J., Zhang, P., Barrero, J.M., Hayden, M.J., Boden, S.A., et al. (2018). Zebularine treatment is associated with deletion of *FT-B1* leading to an increase in spikelet number in bread wheat. Plant Cell Environ 41, 1346–1360.
Finnegan, E.J., Robertson, M., and Helliwell, C.A. (2021). Resetting *FLOWERING LOCUS C* expression after vernalization is just activation in the early embryo by a different name. Front Plant Sci 11, 620155.
Flintham, J.E., Börner, A., Worland, A.J., and Gale, M.D. (1997). Optimizing wheat grain yield: effects of *Rht* (gibberellin-insensitive) dwarfing genes. J Agric Sci 128, 11–25.
Flor, H.H. (1971). Current status of the gene-for-gene concept. Annu Rev Phytopathol 9, 275–296.
Fu, D., Szucs, P., Yan, L., Helguera, M., Skinner, J.S., von Zitzewitz, J., Hayes, P.M., and Dubcovsky, J. (2005). Large deletions within the first intron in *VRN-1* are associated with spring growth habit in barley and wheat. Mol Genet Genomics 273, 54–65.
Fu, D., Uauy, C., Distelfeld, A., Blechl, A., Epstein, L., Chen, X., Sela, H., Fahima, T., and Dubcovsky, J. (2009). A kinase-START gene confers temperature-dependent resistance to wheat stripe rust. Science 323, 1357–1360.
Furman, B.J., Qualset, C.O., Skovmand, B., Heaton, J.H., Corke, H., and Wesenberg, D.M. (1997). Characterization and analysis of North American triticale genetic resources. Crop Sci 37, 1951–1959.
Furtado, A., Bundock, P.C., Banks, P.M., Fox, G., Yin, X., and Henry, R.J. (2015). A novel highly differentially expressed gene in wheat endosperm associated with bread quality. Sci Rep 5, 10446.
Gale, M.D., Youssefian, S., and Russell, G. (1985). Dwarfing genes in wheat. Prog Plant Breeding 1, 1–35.
Galiba, G., Vágújfalvi, A., Li, C., Soltész, A., and Dubcovsky, J. (2009). Regulatory genes involved in the determination of frost tolerance in temperate cereals. Plant Sci 176, 12–19.
Gao, L., Koo, D.H., Juliana, P., Rife, T., Singh, D., Lemes da Silva, C., Lux, T., Dorn, K.M., Clinesmith, M., Silva, P., et al. (2021a). The *Aegilops ventricosa* 2N^{v}S segment in bread wheat: cytology, genomics and breeding. Theor Appl Genet 134, 529–542.
Gao, Y., An, K., Guo, W., Chen, Y., Zhang, R., Zhang, X., Chang, S., Rossi, V., Jin, F., Cao, X., et al. (2021b). The endosperm-specific transcription factor TaNAC019 regulates glutenin and starch accumulation and its elite allele improves wheat grain quality. Plant Cell 33, 603–622.
Garcia, D.F., Wang, Z., Guan, J., Yin, L., Geng, S., Li, A., and Mao, L. (2021). WheatGene: a genomics database for common wheat and its related species. Crop J 9, 1486–1491.
Garnett, T., Conn, V., and Kaiser, B.N. (2009). Root based approaches to improving nitrogen use efficiency in plants. Plant Cell Environ 32, 1272–1283.
Gasperini, D., Greenland, A., Hedden, P., Dreos, R., Harwood, W., and Griffiths, S. (2012). Genetic and physiological analysis of *Rht8* in bread wheat: an alternative source of semi-dwarfism with a reduced sensitivity to brassinosteroids. J Exp Bot 63, 4419–4436.
Gaurav, K., Arora, S., Silva, P., Sánchez-Martín, J., Horsnell, R., Gao, L., Brar, G.S., Widrig, V., John Raupp, W., Singh, N., et al. (2022). Population genomic analysis of *Aegilops tauschii* identifies targets for bread wheat improvement. Nat Biotechnol 40, 422–431.
Gong, B., Zhu, W., Li, S., Wang, Y., Xu, L., Wang, Y., Zeng, J., Fan, X., Sha, L., Zhang, H., et al. (2019). Molecular cytogenetic characterization of wheat-*Elymus repens* chromosomal translocation lines with resistance to *Fusarium* head blight and stripe rust. BMC Plant Biol 19, 590.
Gong, Z., Xiong, L., Shi, H., Yang, S., Herrera-Estrella, L.R., Xu, G., Chao, D.Y., Li, J., Wang, P.Y., Qin, F., et al. (2020). Plant abiotic stress response and nutrient use efficiency. Sci China Life Sci 63, 635–674.
Greenup, A.G., Sasani, S., Oliver, S.N., Talbot, M.J., Dennis, E.S., Hemming, M.N., and Trevaskis, B. (2010). *ODDSOC2* is a MADS box floral repressor that is down-regulated by vernalization in temperate cereals. Plant Physiol 153, 1062–1073.
Gregory, F.G., and Purvis, O.N. (1948). Reversal of vernalization by high temperature. Nature 161, 859–860.
Gui, S., Yang, L., Li, J., Luo, J., Xu, X., Yuan, J., Chen, L., Li, W., Yang, X., Wu, S., et al. (2020). ZEAMAP, a comprehensive database adapted to the maize multi-omics era. iScience 23, 101241.
Guo, H., Liu, Y., Li, X., Yan, Z., Xie, Y., Xiong, H., Zhao, L., Gu, J., Zhao, S., and Liu, L. (2017). Novel mutant alleles of the starch synthesis gene *TaSSIVb-D* result in the reduction of starch granule number per chloroplast in wheat. BMC Genomics 18, 358.
Guo, J., Zhang, X., Hou, Y., Cai, J., Shen, X., Zhou, T., Xu, H., Ohm, H.W., Wang, H., Li, A., et al. (2015a). High-density mapping of the major FHB resistance gene *Fhb7* derived from *Thinopyrum ponticum* and its pyramiding with *Fhb1* by marker-assisted selection. Theor Appl Genet 128, 2301–2316.
Guo, M., Wang, Q., Zong, Y., Nian, J., Li, H., Li, J., Wang, T., Gao, C., and Zuo, J. (2021). Genetic manipulations of *TaARE1* boost nitrogen utilization and grain yield in wheat. J Genet Genomics 48, 950–953.
Guo, W., Yang, H., Liu, Y., Gao, Y., Ni, Z., Peng, H., Xin, M., Hu, Z., Sun, Q., and Yao, Y. (2015b). The wheat transcription factor TaGAMyb recruits histone acetyltransferase and activates the expression of a high-molecular-weight glutenin subunit gene. Plant J 84, 347–359.
Guo, W., Xin, M., Wang, Z., Yao, Y., Hu, Z., Song, W., Yu, K., Chen, Y., Wang, X., Guan, P., et al. (2020). Origin and adaptation to high altitude of Tibetan semi-wild wheat. Nat Commun 11, 5085.
Guo, Z., and Schnurbusch, T. (2015). Variation of floret fertility in hexaploid wheat revealed by tiller removal. J Exp Bot 66, 5945–5958.
Guo, Z., Slafer, G.A., and Schnurbusch, T. (2016). Genotypic variation in spike fertility traits and ovary size as determinants of floret and grain survival rate in wheat. J Exp Bot 67, 4221–4230.
Gupta, A., Hua, L., Lin, G., Molnár, I., Doležel, J., Liu, S., and Li, W. (2021). Multiple origins of Indian dwarf wheat by mutations targeting the TREE domain of a GSK3-like kinase for drought tolerance, phosphate uptake, and grain quality. Theor Appl Genet 134, 633–645.
Gupta, P. (2016). Use of alien genetic variation for wheat improvement. In: Molecular Breeding for Sustainable Crop Improvement. Cham: Springer. 1–30.
Guttieri, M.J., Frels, K., Regassa, T., Waters, B.M., and Baenziger, P.S. (2017). Variation for nitrogen use efficiency traits in current and historical great plains hard winter wheat. Euphytica 213, 87.
Haberer, G., Mayer, K.F., and Spannagl, M. (2016). The big five of the monocot genomes. Curr Opin Plant Biol 30, 33–40.
Hanano, S., and Goto, K. (2011). *Arabidopsis* TERMINAL FLOWER1 is

involved in the regulation of flowering time and inflorescence development through transcriptional repression. Plant Cell 23, 3172–3184.
Hannah, L.C., and James, M. (2008). The complexities of starch biosynthesis in cereal endosperms. Curr Opin Biotechnol 19, 160–165.
Hao, C., Jiao, C., Hou, J., Li, T., Liu, H., Wang, Y., Zheng, J., Liu, H., Bi, Z., Xu, F., et al. (2020a). Resequencing of 145 landmark cultivars reveals asymmetric sub-genome selection and strong founder genotype effects on wheat breeding in China. Mol Plant 13, 1733–1751.
Hao, M., Zhang, L., Ning, S., Huang, L., Yuan, Z., Wu, B., Yan, Z., Dai, S., Jiang, B., Zheng, Y., et al. (2020b). The resurgence of introgression breeding, as exemplified in wheat improvement. Front Plant Sci 11, 252.
Hao, M., Zhang, L., Zhao, L., Dai, S., Li, A., Yang, W., Xie, D., Li, Q., Ning, S., Yan, Z., et al. (2019). A breeding strategy targeting the secondary gene pool of bread wheat: introgression from a synthetic hexaploid wheat. Theor Appl Genet 132, 2285–2294.
Hawkins, E., Chen, J., Watson-Lazowski, A., Ahn-Jarvis, J., Barclay, J.E., Fahy, B., Hartley, M., Warren, F.J., and Seung, D. (2021). STARCH SYNTHASE 4 is required for normal starch granule initiation in amyloplasts of wheat endosperm. New Phytol 230, 2371–2386.
He, F., Pasam, R., Shi, F., Kant, S., Keeble-Gagnere, G., Kay, P., Forrest, K., Fritz, A., Hucl, P., Wiebe, K., et al. (2019). Exome sequencing highlights the role of wild-relative introgression in shaping the adaptive landscape of the wheat genome. Nat Genet 51, 896–904.
He, H., Zhu, S., Zhao, R., Jiang, Z., Ji, Y., Ji, J., Qiu, D., Li, H., and Bie, T. (2018). *Pm21*, encoding a typical CC-NBS-LRR protein, confers broad-spectrum resistance to wheat powdery mildew disease. Mol Plant 11, 879–882.
He, X., Kabir, M.R., Roy, K.K., Anwar, M.B., Xu, K., Marza, F., Odilbekov, F., Chawade, A., Duveiller, E., Huttner, E., et al. (2020). QTL mapping for field resistance to wheat blast in the Caninde#1/Alondra population. Theor Appl Genet 133, 2673–2683.
He, X., Qu, B., Li, W., Zhao, X., Teng, W., Ma, W., Ren, Y., Li, B., Li, Z., and Tong, Y. (2015). The nitrate inducible NAC transcription factor TaNAC2-5A controls nitrate response and increases wheat yield. Plant Physiol 169, 1991–2005.
He, Z.H., Rajaram, S., Xin, Z.Y., and Huang, G.Z. (2001). A history of wheat breeding in China. Mexico, D.F.: CIMMYT.
Hernández, Z.J.E., Figueroa, J.D.C., Rayas-Duarte, P., Martínez-Flores, H. E., Arámbula, G.V., Luna, G.B., and Peña, R.J. (2012). Influence of high and low molecular weight glutenins on stress relaxation of wheat kernels and the relation to sedimentation and rheological properties. J Cereal Sci 55, 344–350.
Hewitt, T., Müller, M.C., Molnár, I., Mascher, M., Holušová, K., Šimková, H., Kunz, L., Zhang, J., Li, J., Bhatt, D., et al. (2021a). A highly differentiated region of wheat chromosome 7AL encodes a *Pm1a* immune receptor that recognizes its corresponding *AvrPm1a* effector from *Blumeria graminis*. New Phytol 229, 2812–2826.
Hewitt, T., Zhang, J., Huang, L., Upadhyaya, N., Li, J., Park, R., Hoxha, S., McIntosh, R., Lagudah, E., and Zhang, P. (2021b). Wheat leaf rust resistance gene *Lr13* is a specific *Ne2* allele for hybrid necrosis. Mol Plant 14, 1025–1028.
Holford, I.C.R. (1997). Soil phosphorus: its measurement, and its uptake by plants. Soil Res 35, 227–239.
Hoogendoorn, J., Rickson, J.M., and Gale, M.D. (1990). Differences in leaf and stem anatomy related to plant height of tall and dwarf wheat (*Triticum aestivum* L.). J Plant Physiol 136, 72–77.
Hou, J., Jiang, Q., Hao, C., Wang, Y., Zhang, H., and Zhang, X. (2014). Global selection on sucrose synthase haplotypes during a century of wheat breeding. Plant Physiol 164, 1918–1929.
Hu, M., Zhao, X., Liu, Q., Hong, X., Zhang, W., Zhang, Y., Sun, L., Li, H., and Tong, Y. (2018a). Transgenic expression of plastidic glutamine synthetase increases nitrogen uptake and yield in wheat. Plant Biotechnol J 16, 1858–1867.
Hu, P., Zheng, Q., Luo, Q., Teng, W., Li, H., Li, B., and Li, Z. (2021). Genome-wide association study of yield and related traits in common wheat under salt-stress conditions. BMC Plant Biol 21, 27.
Hu, W., He, X., Dreisigacker, S., Sansaloni, C.P., Juliana, P., and Singh, P. K. (2019). A wheat chromosome 5AL region confers seedling resistance to both tan spot and Septoria nodorum blotch in two mapping populations. Crop J 7, 809–818.
Hu, X.J., Chen, D., Lynne McIntyre, C., Fernanda Dreccer, M., Zhang, Z. B., Drenth, J., Kalaipandian, S., Chang, H., and Xue, G.P. (2018b). Heat shock factor C2a serves as a proactive mechanism for heat protection in developing grains in wheat via an ABA-mediated regulatory pathway. Plant Cell Environ 41, 79–98.
Huan, Q., Mao, Z., Chong, K., and Zhang, J. (2018). Global analysis of H3K4me3/H3K27me3 in *Brachypodium distachyon* reveals *VRN3* as critical epigenetic regulation point in vernalization and provides insights into epigenetic memory. New Phytol 219, 1373–1387.
Huang, C.Y., Shirley, N., Genc, Y., Shi, B., and Langridge, P. (2011). Phosphate utilization efficiency correlates with expression of low-affinity phosphate transporters and noncoding RNA, *IPS1*, in barley. Plant Physiol 156, 1217–1229.
Huang, L., Brooks, S.A., Li, W., Fellers, J.P., Trick, H.N., and Gill, B.S. (2003). Map-based cloning of leaf rust resistance gene *Lr21* from the large and polyploid genome of bread wheat. Genetics 164, 655–664.
Huang, L., Tan, H., Zhang, C., Li, Q., and Liu, Q. (2021). Starch biosynthesis in cereal endosperms: an updated review over the last decade. Plant Commun 2, 100237.
Huang, X., Qian, Q., Liu, Z., Sun, H., He, S., Luo, D., Xia, G., Chu, C., Li, J., and Fu, X. (2009). Natural variation at the *DEP1* locus enhances grain yield in rice. Nat Genet 41, 494–497.
Hurni, S., Brunner, S., Buchmann, G., Herren, G., Jordan, T., Krukowski, P., Wicker, T., Yahiaoui, N., Mago, R., and Keller, B. (2013). Rye *Pm8* and wheat *Pm3* are orthologous genes and show evolutionary conservation of resistance function against powdery mildew. Plant J 76, 957–969.
Hyles, J., Vautrin, S., Pettolino, F., MacMillan, C., Stachurski, Z., Breen, J., Berges, H., Wicker, T., and Spielmeyer, W. (2017). Repeat-length variation in a wheat cellulose synthase-like gene is associated with altered tiller number and stem cell wall composition. J Exp Bot 68, 1519–1529.
Ikeda, K., Ito, M., Nagasawa, N., Kyozuka, J., and Nagato, Y. (2007). Rice *ABERRANT PANICLE ORGANIZATION 1*, encoding an F-box protein, regulates meristem fate. Plant J 51, 1030–1040.
Irshad, A., Guo, H., Ur Rehman, S., Wang, X., Gu, J., Xiong, H., Xie, Y., Zhao, L., Zhao, S., Wang, C., et al. (2021). Identification of single nucleotide polymorphism in *TaSBEIII* and development of KASP marker associated with grain weight in wheat. Front Genet 12, 697294.
International Wheat Genome Sequencing Consortium (IWGSC). (2014). A chromosome-based draft sequence of the hexaploid bread wheat (*Triticum aestivum*) genome. Science 345, 1251788.
International Wheat Genome Sequencing Consortium (IWGSC). (2018). Shifting the limits in wheat research and breeding using a fully annotated reference genome. Science 361, eaar7191.
Jablonski, B., Bajguz, A., Bocian, J., Orczyk, W., and Nadolska-Orczyk, A. (2021). Genotype-dependent effect of silencing of *TaCKX1* and *TaCKX2* on phytohormone crosstalk and yield-related traits in wheat. Int J Mol Sci 22, 11494.
Jantasuriyarat, C., Vales, M.I., Watson, C.J.W., and Riera-Lizarazu, O. (2004). Identification and mapping of genetic loci affecting the free-threshing habit and spike compactness in wheat (*Triticum aestivum* L.). Theor Appl Genet 108, 261–273.
Je, B.I., Gruel, J., Lee, Y.K., Bommert, P., Arevalo, E.D., Eveland, A.L., Wu, Q., Goldshmidt, A., Meeley, R., Bartlett, M., et al. (2016). Signaling from maize organ primordia via FASCIATED EAR3 regulates stem cell proliferation and yield traits. Nat Genet 48, 785–791.
Jeon, J.S., Ryoo, N., Hahn, T.R., Walia, H., and Nakamura, Y. (2010). Starch biosynthesis in cereal endosperm. Plant Physiol Biochem 48, 383–392.
Jia, H., Zhou, J., Xue, S., Li, G., Yan, H., Ran, C., Zhang, Y., Shi, J., Jia, L., Wang, X., et al. (2018). A journey to understand wheat Fusarium head

blight resistance in the Chinese wheat landrace Wangshuibai. Crop J 6, 48–59.
Jia, J., Xie, Y., Cheng, J., Kong, C., Wang, M., Gao, L., Zhao, F., Guo, J., Wang, K., Li, G., et al. (2021). Homology-mediated inter-chromosomal interactions in hexaploid wheat lead to specific subgenome territories following polyploidization and introgression. Genome Biol 22, 26.
Jia, J., Zhao, S., Kong, X., Li, Y., Zhao, G., He, W., Appels, R., Pfeifer, M., Tao, Y., Zhang, X., et al. (2013). *Aegilops tauschii* draft genome sequence reveals a gene repertoire for wheat adaptation. Nature 496, 91–95.
Jiang, Q., Hou, J., Hao, C., Wang, L., Ge, H., Dong, Y., and Zhang, X. (2011). The wheat (*T. aestivum*) sucrose synthase 2 gene (*TaSus2*) active in endosperm development is associated with yield traits. Funct Integr Genomics 11, 49–61.
Jiao, Y., Wang, Y., Xue, D., Wang, J., Yan, M., Liu, G., Dong, G., Zeng, D., Lu, Z., Zhu, X., et al. (2010). Regulation of *OsSPL14* by OsmiR156 defines ideal plant architecture in rice. Nat Genet 42, 541–544.
Jiao, Y., Li, J., Tang, H., and Paterson, A.H. (2014). Integrated syntenic and phylogenomic analyses reveal an ancient genome duplication in monocots. Plant Cell 26, 2792–2802.
Jo, L., Pelletier, J.M., and Harada, J.J. (2019). Central role of the LEAFY COTYLEDON1 transcription factor in seed development. J Integr Plant Biol 61, 564–580.
Kane, N.A., Agharbaoui, Z., Diallo, A.O., Adam, H., Tominaga, Y., Ouellet, F., and Sarhan, F. (2007). TaVRT2 represses transcription of the wheat vernalization gene *TaVRN1*. Plant J 51, 670–680.
Kang, G., Li, S., Zhang, M., Peng, H., Wang, C., Zhu, Y., and Guo, T. (2013). Molecular cloning and expression analysis of the starch-branching enzyme III gene from common wheat (*Triticum aestivum*). Biochem Genet 51, 377–386.
Kato, K., Miura, H., and Sawada, S. (2000). Mapping QTLs controlling grain yield and its components on chromosome 5A of wheat. Theor Appl Genet 101, 1114–1121.
Kennedy, A., and Geuten, K. (2020). The role of FLOWERING LOCUS C relatives in cereals. Front Plant Sci 11, 617340.
Keyes, S.D., Daly, K.R., Gostling, N.J., Jones, D.L., Talboys, P., Pinzer, B. R., Boardman, R., Sinclair, I., Marchant, A., and Roose, T. (2013). High resolution synchrotron imaging of wheat root hairs growing in soil and image based modelling of phosphate uptake. New Phytol 198, 1023–1029.
Kippes, N., Debernardi, J.M., Vasquez-Gross, H.A., Akpinar, B.A., Budak, H., Kato, K., Chao, S., Akhunov, E., and Dubcovsky, J. (2015). Identification of the *VERNALIZATION 4* gene reveals the origin of spring growth habit in ancient wheats from South Asia. Proc Natl Acad Sci USA 112, E5401.
Kippes, N., Guedira, M., Lin, L., Alvarez, M.A., Brown-Guedira, G.L., and Dubcovsky, J. (2018). Single nucleotide polymorphisms in a regulatory site of *VRN-A1* first intron are associated with differences in vernalization requirement in winter wheat. Mol Genet Genomics 293, 1231–1243.
Kirchberger, S., Leroch, M., Huynen, M.A., Wahl, M., Neuhaus, H.E., and Tjaden, J. (2007). Molecular and biochemical analysis of the plastidic ADP-glucose transporter (ZmBT1) from *Zea mays*. J Biol Chem 282, 22481–22491.
Klymiuk, V., Chawla, H.S., Wiebe, K., Ens, J., Fatiukha, A., Govta, L., Fahima, T., and Pozniak, C.J. (2022). Discovery of stripe rust resistance with incomplete dominance in wild emmer wheat using bulked segregant analysis sequencing. Commun Bio 5, 826.
Klymiuk, V., Yaniv, E., Huang, L., Raats, D., Fatiukha, A., Chen, S., Feng, L., Frenkel, Z., Krugman, T., Lidzbarsky, G., et al. (2018). Cloning of the wheat *Yr15* resistance gene sheds light on the plant tandem kinase-pseudokinase family. Nat Commun 9, 3735.
Kolodziej, M.C., Singla, J., Sánchez-Martín, J., Zbinden, H., Šimková, H., Karafiátová, M., Doležel, J., Gronnier, J., Poretti, M., Glauser, G., et al. (2021). A membrane-bound ankyrin repeat protein confers race-specific leaf rust disease resistance in wheat. Nat Commun 12, 956.
Kong, X., Wang, F., Geng, S., Guan, J., Tao, S., Jia, M., Sun, G., Wang, Z., Wang, K., Ye, X., et al. (2022). The wheat *AGL6*-like MADS-box gene is a master regulator for floral organ identity and a target for spikelet meristem development manipulation. Plant Biotechnol J 20, 75–88.
Korzun, V., Röder, M.S., Ganal, M.W., Worland, A.J., and Law, C.N. (1998). Genetic analysis of the dwarfing gene (*Rht8*) in wheat. Part I. Molecular mapping of *Rht8* on the short arm of chromosome 2D of bread wheat (*Triticum aestivum* L.). Theor Appl Genet 96, 1104–1109.
Kowalski, A.M., Gooding, M., Ferrante, A., Slafer, G.A., Orford, S., Gasperini, D., and Griffiths, S. (2016). Agronomic assessment of the wheat semi-dwarfing gene *Rht8* in contrasting nitrogen treatments and water regimes. Field Crops Res 191, 150–160.
Krattinger, S.G., Lagudah, E.S., Spielmeyer, W., Singh, R.P., Huerta-Espino, J., McFadden, H., Bossolini, E., Selter, L.L., and Keller, B. (2009). A putative ABC transporter confers durable resistance to multiple fungal pathogens in wheat. Science 323, 1360–1363.
Kumar, R., Mukherjee, S., and Ayele, B.T. (2018). Molecular aspects of sucrose transport and its metabolism to starch during seed development in wheat: a comprehensive review. Biotechnol Adv 36, 954–967.
Kuraparthy, V., Sood, S., Dhaliwal, H.S., Chhuneja, P., and Gill, B.S. (2007). Identification and mapping of a tiller inhibition gene (*tin3*) in wheat. Theor Appl Genet 114, 285–294.
Kusch, S., and Panstruga, R. (2017). *mlo*-Based resistance: an apparently universal "Weapon" to defeat powdery mildew disease. Mol Plant Microbe Interact 30, 179–189.
Kuzay, S., Lin, H., Li, C., Chen, S., Woods, D.P., Zhang, J., Lan, T., von Korff, M., and Dubcovsky, J. (2022). *WAPO-A1* is the causal gene of the 7AL QTL for spikelet number per spike in wheat. PLoS Genet 18, e1009747.
Kuzay, S., Xu, Y., Zhang, J., Katz, A., Pearce, S., Su, Z., Fraser, M., Anderson, J.A., Brown-Guedira, G., DeWitt, N., et al. (2019). Identification of a candidate gene for a QTL for spikelet number per spike on wheat chromosome arm 7AL by high-resolution genetic mapping. Theor Appl Genet 132, 2689–2705.
Lafiandra, D., Riccardi, G., and Shewry, P.R. (2014). Improving cereal grain carbohydrates for diet and health. J Cereal Sci 59, 312–326.
Lagudah, E.S., Krattinger, S.G., Herrera-Foessel, S., Singh, R.P., Huerta-Espino, J., Spielmeyer, W., Brown-Guedira, G., Selter, L.L., and Keller, B. (2009). Gene-specific markers for the wheat gene *Lr34*/*Yr18*/*Pm38* which confers resistance to multiple fungal pathogens. Theor Appl Genet 119, 889–898.
Lamichhane, S., Murata, C., Griffey, C.A., Thomason, W.E., and Fukao, T. (2021). Physiological and molecular traits associated with nitrogen uptake under limited nitrogen in soft red winter wheat. Plants 10, 165.
Langridge, P., and Reynolds, M. (2021). Breeding for drought and heat tolerance in wheat. Theor Appl Genet 134, 1753–1769.
Lanning, S.P., Martin, J.M., Stougaard, R.N., Guillen-Portal, F.R., Blake, N.K., Sherman, J.D., Robbins, A.M., Kephart, K.D., Lamb, P., Carlson, G.R., et al. (2012). Evaluation of near-isogenic lines for three height-reducing genes in hard red spring wheat. Crop Sci 52, 1145–1152.
LeCain, D.R., Morgan, J.A., and Zerbi, G. (1989). Leaf anatomy and gas exchange in nearly isogenic semidwarf and tall winter wheat. Crop Sci 29, 1246–1251.
Lee, T., Hwang, S., Kim, C.Y., Shim, H., Kim, H., Ronald, P.C., Marcotte, E.M., and Lee, I. (2017). WheatNet: a genome-scale functional network for hexaploid bread wheat, *Triticum aestivum*. Mol Plant 10, 1133–1136.
Lei, L., Li, G., Zhang, H., Powers, C., Fang, T., Chen, Y., Wang, S., Zhu, X., Carver, B.F., and Yan, L. (2018). Nitrogen use efficiency is regulated by interacting proteins relevant to development in wheat. Plant Biotechnol J 16, 1214–1226.
Lev-Yadun, S., Gopher, A., and Abbo, S. (2000). The cradle of agriculture. Science 288, 1602–1603.
Lewis, J.M., Mackintosh, C.A., Shin, S., Gilding, E., Kravchenko, S., Baldridge, G., Zeyen, R., and Muehlbauer, G.J. (2008a). Overexpression of the maize *Teosinte Branched1* gene in wheat suppresses tiller development. Plant Cell Rep 27, 1217–1225.
Lewis, S., Faricelli, M.E., Appendino, M.L., Valárik, M., and Dubcovsky, J.

(2008b). The chromosome region including the earliness *per se* locus *Eps-A^m1* affects the duration of early developmental phases and spikelet number in diploid wheat. J Exp Bot 59, 3595–3607.
Li, A., Yang, W., Lou, X., Liu, D., Sun, J., Guo, X., Wang, J., Li, Y., Zhan, K., Ling, H.Q., et al. (2013a). Novel natural allelic variations at the *Rht-1* loci in wheat. J Integr Plant Biol 55, 1026–1037.
Li, A., Yang, W., Guo, X., Liu, D., Sun, J., and Zhang, A. (2012). Isolation of a gibberellin-insensitive dwarfing gene, *Rht-B1e*, and development of an allele-specific PCR marker. Mol Breeding 30, 1443–1451.
Li, C., Lv, J., Zhao, X., Ai, X., Zhu, X., Wang, M., Zhao, S., and Xia, G. (2010). *TaCHP*: a wheat zinc finger protein gene down-regulated by abscisic acid and salinity stress plays a positive role in stress tolerance. Plant Physiol 154, 211–221.
Li, C., and Dubcovsky, J. (2008). Wheat FT protein regulates *VRN1* transcription through interactions with FDL2. Plant J 55, 543–554.
Li, C., Lin, H., Chen, A., Lau, M., Jernstedt, J., and Dubcovsky, J. (2019a). Wheat *VRN1* , *FUL2* and *FUL3* play critical and redundant roles in spikelet development and spike determinacy. Development 146, dev175398.
Li, C., Lin, H., and Dubcovsky, J. (2015a). Factorial combinations of protein interactions generate a multiplicity of florigen activation complexes in wheat and barley. Plant J 84, 70–82.
Li, G., Yu, M., Fang, T., Cao, S., Carver, B.F., and Yan, L. (2013b). Vernalization requirement duration in winter wheat is controlled by *Ta*VRN-A1 at the protein level. Plant J 76, 742–753.
Li, G.Q., Jia, L., Zhou, J.Y., Fan, J.C., Yan, H.S., Shi, J.X., Wang, X., Fan, M., Xue, S.L., Cao, S.Y., et al. (2019b). Evaluation and precise mapping of *QFhb.nau-2B* conferring resistance against Fusarium infection and spread within spikes in wheat (*Triticum aestivum* L.). Mol Breeding 39, 62.
Li, G., Zhou, J., Jia, H., Gao, Z., Fan, M., Luo, Y., Zhao, P., Xue, S., Li, N., Yuan, Y., et al. (2019c). Mutation of a histidine-rich calcium-binding-protein gene in wheat confers resistance to Fusarium head blight. Nat Genet 51, 1106–1112.
Li, G., Wang, L., Yang, J., He, H., Jin, H., Li, X., Ren, T., Ren, Z., Li, F., Han, X., et al. (2021a). A high-quality genome assembly highlights rye genomic characteristics and agronomically important genes. Nat Genet 53, 574–584.
Li, J., Jiao, G., Sun, Y., Chen, J., Zhong, Y., Yan, L., Jiang, D., Ma, Y., and Xia, L. (2021b). Modification of starch composition, structure and properties through editing of *TaSBEIIa* in both winter and spring wheat varieties by CRISPR/Cas9. Plant Biotechnol J 19, 937–951.
Li, J., Wang, K., Li, G., Li, Y., Zhang, Y., Liu, Z., Ye, X., Xia, X., He, Z., and Cao, S. (2019d). Dissecting conserved cis-regulatory modules of *Glu-1* promoters which confer the highly active endosperm-specific expression via stable wheat transformation. Crop J 7, 8–18.
Li, J., Zhao, L., Cheng, X., Bai, G., Li, M., Wu, J., Yang, Q., Chen, X., Yang, Z., and Zhao, J. (2020a). Molecular cytogenetic characterization of a novel wheat-*Psathyrostachys huashanica* Keng T3DS-5NsL•5NsS and T5DL-3DS•3DL dual translocation line with powdery mildew resistance. BMC Plant Biol 20, 163.
Li, J., Xie, L., Tian, X., Liu, S., Xu, D., Jin, H., Song, J., Dong, Y., Zhao, D., Li, G., et al. (2021c). TaNAC100 acts as an integrator of seed protein and starch synthesis exerting pleiotropic effects on agronomic traits in wheat. Plant J 108, 829–840.
Li, K., Debernardi, J.M., Li, C., Lin, H., Zhang, C., Jernstedt, J., Korff, M., Zhong, J., and Dubcovsky, J. (2021d). Interactions between SQUAMOSA and SHORT VEGETATIVE PHASE MADS-box proteins regulate meristem transitions during wheat spike development. Plant Cell 33, 3621–3644.
Li, K., Yu, R., Fan, L.M., Wei, N., Chen, H., and Deng, X.W. (2016). DELLA-mediated PIF degradation contributes to coordination of light and gibberellin signalling in *Arabidopsis*. Nat Commun 7, 11868.
Li, L., Mao, X., Wang, J., Chang, X., Reynolds, M., and Jing, R. (2019e). Genetic dissection of drought and heat-responsive agronomic traits in wheat. Plant Cell Environ 42, 2540–2553.
Li, L., Peng, Z., Mao, X., Wang, J., Li, C., Chang, X., and Jing, R. (2020b). Genetic insights into natural variation underlying salt tolerance in wheat. J Exp Bot 72, 1135–1150.
Li, L., Shi, F., Wang, Y., Yu, X., Zhi, J., Guan, Y., Zhao, H., Chang, J., Chen, M., Yang, G., et al. (2020c). TaSPL13 regulates inflorescence architecture and development in transgenic wheat (*Triticum aestivum* L.). Plant Sci 296, 110516.
Li, L.F., Zhang, Z.B., Wang, Z.H., Li, N., Sha, Y., Wang, X.F., Ding, N., Li, Y., Zhao, J., Wu, Y., et al. (2022a). Genome sequences of five Sitopsis species of *Aegilops* and the origin of polyploid wheat B subgenome. Mol Plant 15, 488–503.
Li, M., Tian, H., and Gao, Y. (2021e). A genome-wide analysis of NPF and NRT2 transporter gene families in bread wheat provides new insights into the distribution, function, regulation and evolution of nitrate transporters. Plant Soil 465, 47–63.
Li, M., Dong, L., Li, B., Wang, Z., Xie, J., Qiu, D., Li, Y., Shi, W., Yang, L., Wu, Q., et al. (2020d). A CNL protein in wild emmer wheat confers powdery mildew resistance. New Phytol 228, 1027–1037.
Li, N., Jia, H.Y., Kong, Z.X., Tang, W., Ding, Y.X., Liang, J.C., Ma, H.Q., and Ma, Z.Q. (2017a). Identification and marker-assisted transfer of a new powdery mildew resistance gene at the *Pm4* locus in common wheat. Mol Breeding 37, 79.
Li, N., Wen, Z., Wang, J., Fu, B., Liu, J., Xu, H., Kong, Z., Zhang, L., Jia, H., and Ma, Z. (2014). Transfer and mapping of a gene conferring later-growth-stage powdery mildew resistance in a tetraploid wheat accession. Mol Breeding 33, 669–677.
Li, Q., Byrns, B., Badawi, M.A., Diallo, A.B., Danyluk, J., Sarhan, F., Laudencia-Chingcuanco, D., Zou, J., and Fowler, D.B. (2018a). Transcriptomic insights into phenological development and cold tolerance of wheat grown in the field. Plant Physiol 176, 2376–2394.
Li, S., Tian, Y., Wu, K., Ye, Y., Yu, J., Zhang, J., Liu, Q., Hu, M., Li, H., Tong, Y., et al. (2018b). Modulating plant growth-metabolism coordination for sustainable agriculture. Nature 560, 595–600.
Li, S., Wei, X., Ren, Y., Qiu, J., Jiao, G., Guo, X., Tang, S., Wan, J., and Hu, P. (2017b). *OsBT1* encodes an ADP-glucose transporter involved in starch synthesis and compound granule formation in rice endosperm. Sci Rep 7, 40124.
Li, S., Lin, D., Zhang, Y., Deng, M., Chen, Y., Lv, B., Li, B., Lei, Y., Wang, Y., Zhao, L., et al. (2022b). Genome-edited powdery mildew resistance in wheat without growth penalties. Nature 602, 455–460.
Li, T., Zhang, H., Huang, Y., Su, Z., Deng, Y., Liu, H., Mai, C., Yu, G., Li, H., Yu, L., et al. (2019f). Effects of the *Fhb1* gene on Fusarium head blight resistance and agronomic traits of winter wheat. Crop J 7, 799–808.
Li, W., He, X., Chen, Y., Jing, Y., Shen, C., Yang, J., Teng, W., Zhao, X., Hu, W., Hu, M., et al. (2020e). A wheat transcription factor positively sets seed vigour by regulating the grain nitrate signal. New Phytol 225, 1667–1680.
Li, W.L., Nelson, J.C., Chu, C.Y., Shi, L.H., Huang, S.H., and Liu, D.J. (2002). Chromosomal locations and genetic relationships of tiller and spike characters in wheat. Euphytica 125, 357–366.
Li, X.P., Zhao, X.Q., He, X., Zhao, G.Y., Li, B., Liu, D.C., Zhang, A.M., Zhang, X.Y., Tong, Y.P., and Li, Z.S. (2011). Haplotype analysis of the genes encoding glutamine synthetase plastic isoforms and their association with nitrogen-use- and yield-related traits in bread wheat. New Phytol 189, 449–458.
Li, X.Z., Hao, N.B., and Tan, K.H. (1987). Changes of soluble protein components in winter wheat (*Triticum aestivum* L.) shoots during vernalization and its relation to morphogenesis (in Chinese). J Integr Plant Biol 29, 492–498.
Li, X., Xia, X., Xiao, Y., He, Z., Wang, D., Trethowan, R., Wang, H., and Chen, X. (2015b). QTL mapping for plant height and yield components in common wheat under water-limited and full irrigation environments. Crop Pasture Sci 66, 660–670.
Li, X., Qian, Q., Fu, Z., Wang, Y., Xiong, G., Zeng, D., Wang, X., Liu, X., Teng, S., Hiroshi, F., et al. (2003). Control of tillering in rice. Nature 422, 618–621.
Li, Y., An, X., Yang, R., Guo, X., Yue, G., Fan, R., Li, B., Li, Z., Zhang, K.,

Dong, Z., et al. (2015c). Dissecting and enhancing the contributions of high-molecular-weight glutenin subunits to dough functionality and bread quality. Mol Plant 8, 332–334.
Li, Y., Li, L., Zhao, M., Guo, L., Guo, X., Zhao, D., Batool, A., Dong, B., Xu, H., Cui, S., et al. (2021f). Wheat *FRIZZY PANICLE* activates *VERNALIZATION1-A* and *HOMEOBOX4-A* to regulate spike development in wheat. Plant Biotechnol J 19, 1141–1154.
Li, Z., Jiang, D., and He, Y. (2018c). FRIGIDA establishes a local chromosomal environment for *FLOWERING LOCUS C* mRNA production. Nat Plants 4, 836–846.
Li, Z., Wang, M., Lin, K., Xie, Y., Guo, J., Ye, L., Zhuang, Y., Teng, W., Ran, X., Tong, Y., et al. (2019g). The bread wheat epigenomic map reveals distinct chromatin architectural and evolutionary features of functional genetic elements. Genome Biol 20, 139.
Li, Z.S. (2018). Breeding of Xiaoyan series varieties and their derivatives (in Chinese). In: Li, J.Y., ed. LiZhenSheng Anthology of Papers. Beijing: Science Press. 78–91.
Liang, D., Tang, J., Peña, R.J., Singh, R., He, X., Shen, X., Yao, D., Xia, X., and He, Z. (2009). Characterization of CIMMYT bread wheats for high- and low-molecular weight glutenin subunits and other quality-related genes with SDS-PAGE, RP-HPLC and molecular markers. Euphytica 172, 235–250.
Liao, Z., Yu, H., Duan, J., Yuan, K., Yu, C., Meng, X., Kou, L., Chen, M., Jing, Y., Liu, G., et al. (2019). SLR1 inhibits MOC1 degradation to coordinate tiller number and plant height in rice. Nat Commun 10, 2738.
Lin, Q., Wang, D., Dong, H., Gu, S., Cheng, Z., Gong, J., Qin, R., Jiang, L., Li, G., Wang, J.L., et al. (2012). Rice APC/C^{TE} controls tillering by mediating the degradation of MONOCULM 1. Nat Commun 3, 752.
Ling, H.Q., Ma, B., Shi, X., Liu, H., Dong, L., Sun, H., Cao, Y., Gao, Q., Zheng, S., Li, Y., et al. (2018). Genome sequence of the progenitor of wheat A subgenome *Triticum urartu*. Nature 557, 424–428.
Ling, H.Q., Zhao, S., Liu, D., Wang, J., Sun, H., Zhang, C., Fan, H., Li, D., Dong, L., Tao, Y., et al. (2013). Draft genome of the wheat A-genome progenitor *Triticum urartu*. Nature 496, 87–90.
Liu, B., Liu, L., Asseng, S., Zhang, D., Ma, W., Tang, L., Cao, W., and Zhu, Y. (2020a). Modelling the effects of post-heading heat stress on biomass partitioning, and grain number and weight of wheat. J Exp Bot 71, 6015–6031.
Liu, G., Wu, Y., Xu, M., Gao, T., Wang, P., Wang, L., Guo, T., and Kang, G. (2016). Virus-induced gene silencing identifies an important role of the *TaRSR1* transcription factor in starch synthesis in bread wheat. Int J Mol Sci 17, 1557.
Liu, H., Li, H., Hao, C., Wang, K., Wang, Y., Qin, L., An, D., Li, T., and Zhang, X. (2020b). *TaDA1*, a conserved negative regulator of kernel size, has an additive effect with *TaGW2* in common wheat (*Triticum aestivum* L.). Plant Biotechnol J 18, 1330–1342.
Liu, J., Chen, Z., Wang, Z., Zhang, Z., Xie, X., Wang, Z., Chai, L., Song, L., Cheng, X., Feng, M., et al. (2021a). Ectopic expression of *VRT-A2* underlies the origin of *Triticum polonicum* and *Triticum petropavlovskyi* with long outer glumes and grains. Mol Plant 14, 1472–1488.
Liu, J., Cheng, X., Liu, P., and Sun, J. (2017). miR156-targeted SBP-box transcription factors interact with DWARF53 to regulate *TEOSINTE BRANCHED1* and *BARREN STALK1* expression in bread wheat. Plant Physiol 174, 1931–1948.
Liu, J., Yao, Y., Xin, M., Peng, H., Ni, Z., and Sun, Q. (2021). Shaping polyploid wheat for success: origins, domestication, and the genetic improvement of agronomic traits. Integrative Plant Biol 64, 536–563.
Liu, J., Zhang, Q., Meng, D., Ren, X., Li, H., Su, Z., Zhang, N., Zhi, L., Ji, J., Li, J., et al. (2021b). *QMrl-7B* enhances root system, biomass, nitrogen accumulation and yield in bread wheat. Plants 10, 764.
Liu, L., He, Z., Yan, J., Zhang, Y., Xia, X., and Peña, R.J. (2005). Allelic variation at the *Glu-1* and *Glu-3* loci, presence of the 1B.1R translocation, and their effects on mixographic properties in Chinese bread wheats. Euphytica 142, 197–204.
Liu, L., Sadras, V.O., Xu, J., Hu, C., Yang, X., and Zhang, S. (2021c). Chapter Five—Genetic improvement of crop yield, grain protein and nitrogen use efficiency of wheat, rice and maize in China. In: Sparks, D. L., ed. Advances in Agronomy, Vol 168. New York: Academic Press. 203–252.
Liu, R., Lu, J., Zhou, M., Zheng, S., Liu, Z., Zhang, C., Du, M., Wang, M., Li, Y., Wu, Y., et al. (2020c). Developing stripe rust resistant wheat (*Triticum aestivum* L.) lines with gene pyramiding strategy and marker-assisted selection. Genet Resour Crop Evol 67, 381–391.
Liu, S., Li, F., Kong, L., Sun, Y., Qin, L., Chen, S., Cui, H., Huang, Y., and Xia, G. (2015). Genetic and epigenetic changes in somatic hybrid introgression lines between wheat and tall wheatgrass. Genetics 199, 1035–1045.
Liu, S., Liu, S., Wang, M., Wei, T., Meng, C., Wang, M., and Xia, G. (2014). A wheat *SIMILAR TO RCD-ONE* gene enhances seedling growth and abiotic stress resistance by modulating redox homeostasis and maintaining genomic integrity. Plant Cell 26, 164–180.
Liu, Y., Hou, J., Wang, X., Li, T., Majeed, U., Hao, C., and Zhang, X. (2020d). The NAC transcription factor NAC019-A1 is a negative regulator of starch synthesis in wheat developing endosperm. J Exp Bot 71, 5794–5807.
Liu, Y., Yuan, J., Jia, G., Ye, W., Jeffrey Chen, Z., and Song, Q. (2021d). Histone H3K27 dimethylation landscapes contribute to genome stability and genetic recombination during wheat polyploidization. Plant J 105, 678–690.
Lobell, D.B., and Tebaldi, C. (2014). Getting caught with our plants down: the risks of a global crop yield slowdown from climate trends in the next two decades. Environ Res Lett 9, 074003.
Lomax, A., Woods, D.P., Dong, Y., Bouché, F., Rong, Y., Mayer, K.S., Zhong, X., and Amasino, R.M. (2018). An ortholog of *CURLY LEAF/ENHANCER OF ZESTE like-1* is required for proper flowering in *Brachypodium distachyon*. Plant J 93, 871–882.
Lou, H., Zhang, R., Liu, Y., Guo, D., Zhai, S., Chen, A., Zhang, Y., Xie, C., You, M., Peng, H., et al. (2021). Genome-wide association study of six quality-related traits in common wheat (*Triticum aestivum* L.) under two sowing conditions. Theor Appl Genet 134, 399–418.
Loukoianov, A., Yan, L., Blechl, A., Sanchez, A., and Dubcovsky, J. (2005). Regulation of *VRN-1* vernalization genes in normal and transgenic polyploid wheat. Plant Physiol 138, 2364–2373.
Lu, P., Guo, L., Wang, Z., Li, B., Li, J., Li, Y., Qiu, D., Shi, W., Yang, L., Wang, N., et al. (2020). A rare gain of function mutation in a wheat tandem kinase confers resistance to powdery mildew. Nat Commun 11, 680.
Lu, Z., Shao, G., Xiong, J., Jiao, Y., Wang, J., Liu, G., Meng, X., Liang, Y., Xiong, G., Wang, Y., et al. (2015). *MONOCULM 3*, an ortholog of *WUSCHEL* in rice, is required for tiller bud formation. J Genet Genomics 42, 71–78.
Luo, M.C., Gu, Y.Q., You, F.M., Deal, K.R., Ma, Y., Hu, Y., Huo, N., Wang, Y., Wang, J., Chen, S., et al. (2013). A 4-gigabase physical map unlocks the structure and evolution of the complex genome of *Aegilops tauschii*, the wheat D-genome progenitor. Proc Natl Acad Sci USA 110, 7940–7945.
Luo, M., Xie, L., Chakraborty, S., Wang, A., Matny, O., Jugovich, M., Kolmer, J.A., Richardson, T., Bhatt, D., Hoque, M., et al. (2021). A five-transgene cassette confers broad-spectrum resistance to a fungal rust pathogen in wheat. Nat Biotechnol 39, 561–566.
Luo, M.C., Gu, Y.Q., Puiu, D., Wang, H., Twardziok, S.O., Deal, K.R., Huo, N., Zhu, T., Wang, L., Wang, Y., et al. (2017). Genome sequence of the progenitor of the wheat D genome *Aegilops tauschii*. Nature 551, 498–502.
Luo, X., Chen, T., Zeng, X.L., He, D., and He, Y. (2019). Feedback regulation of FLC by FLOWERING LOCUS T (FT) and FD through a 5′ FLC promoter region in Arabidopsis. Mol Plant 12, 285–288.
Luo, X., and He, Y. (2020). Experiencing winter for spring flowering: a molecular epigenetic perspective on vernalization. J Integr Plant Biol 62, 104–117.
Luo, X., Ou, Y., Li, R., and He, Y. (2020). Maternal transmission of the epigenetic 'memory of winter cold' in *Arabidopsis*. Nat Plants 6, 1211–1218.

Lyu, J., Wang, D., Duan, P., Liu, Y., Huang, K., Zeng, D., Zhang, L., Dong, G., Li, Y., Xu, R., et al. (2020). Control of grain size and weight by the GSK2-LARGE1/OML4 pathway in rice. Plant Cell 32, 1905–1918.
Ma, J., Ding, P., Liu, J., Li, T., Zou, Y., Habib, A., Mu, Y., Tang, H., Jiang, Q., Liu, Y., et al. (2019). Identification and validation of a major and stably expressed QTL for spikelet number per spike in bread wheat. Theor Appl Genet 132, 3155–3167.
Ma, J., Stiller, J., Berkman, P.J., Wei, Y., Rogers, J., Feuillet, C., Dolezel, J., Mayer, K.F., Eversole, K., Zheng, Y.L., et al. (2013). Sequence-based analysis of translocations and inversions in bread wheat (*Triticum aestivum* L.). PLoS ONE 8, e79329.
Ma, S., Wang, M., Wu, J., Guo, W., Chen, Y., Li, G., Wang, Y., Shi, W., Xia, G., Fu, D., et al. (2021). WheatOmics: a platform combining multiple omics data to accelerate functional genomics studies in wheat. Mol Plant 14, 1965–1968.
Ma, Z., Xie, Q., Li, G., Jia, H., Zhou, J., Kong, Z., Li, N., and Yuan, Y. (2020). Germplasms, genetics and genomics for better control of disastrous wheat Fusarium head blight. Theor Appl Genet 133, 1541–1568.
Maccaferri, M., Harris, N.S., Twardziok, S.O., Pasam, R.K., Gundlach, H., Spannagl, M., Ormanbekova, D., Lux, T., Prade, V.M., Milner, S.G., et al. (2019). Durum wheat genome highlights past domestication signatures and future improvement targets. Nat Genet 51, 885–895.
Mago, R., Zhang, P., Vautrin, S., Šimková, H., Bansal, U., Luo, M.C., Rouse, M., Karaoglu, H., Periyannan, S., Kolmer, J., et al. (2015). The wheat *Sr50* gene reveals rich diversity at a cereal disease resistance locus. Nat Plants 1, 15186.
Mallick, N., Vinod, Sharma, J.B., Tomar, R.S., Sivasamy, M., and Prabhu, K.V. (2015). Marker-assisted backcross breeding to combine multiple rust resistance in wheat. Plant Breed 134, 172–177.
Manske, G.G.B., Ortiz-Monasterio, J.I., Van Ginkel, M., González, R.M., Rajaram, S., Molina, E., and Vlek, P.L.G. (2000). Traits associated with improved P-uptake efficiency in CIMMYT's semidwarf spring bread wheat grown on an acid Andisol in Mexico. Plant Soil 221, 189–204.
Mao, H., Li, S., Chen, B., Jian, C., Mei, F., Zhang, Y., Li, F., Chen, N., Li, T., Du, L., et al. (2022a). Variation in *cis*-regulation of a NAC transcription factor contributes to drought tolerance in wheat. Mol Plant 15, 276–292.
Mao, H., Li, S., Wang, Z., Cheng, X., Li, F., Mei, F., Chen, N., and Kang, Z. (2020a). Regulatory changes in *TaSNAC8-6A* are associated with drought tolerance in wheat seedlings. Plant Biotechnol J 18, 1078–1092.
Mao, H., Jian, C., Cheng, X., Chen, B., Mei, F., Li, F., Zhang, Y., Li, S., Du, L., Li, T., et al. (2022b). The wheat ABA receptor gene *TaPYL1-1B* contributes to drought tolerance and grain yield by increasing water-use efficiency. Plant Biotechnol J 20, 846–861.
Mao, X., Li, Y., Rehman, S.U., Miao, L., Zhang, Y., Chen, X., Yu, C., Wang, J., Li, C., and Jing, R. (2020b). The Sucrose Non-Fermenting 1-Related Protein Kinase 2 (SnRK2) genes are multifaceted players in plant growth, development and response to environmental stimuli. Plant Cell Physiol 61, 225–242.
Marchal, C., Zhang, J., Zhang, P., Fenwick, P., Steuernagel, B., Adamski, N.M., Boyd, L., McIntosh, R., Wulff, B.B.H., Berry, S., et al. (2018). BED-domain-containing immune receptors confer diverse resistance spectra to yellow rust. Nat Plants 4, 662–668.
Maré, A., Boshoff, W.H.P., and Herselman, L. (2020). Molecular breeding of wheat lines for multiple rust and Fusarium head blight resistance. Euphytica 216, 163.
Martis, M.M., Zhou, R., Haseneyer, G., Schmutzer, T., Vrána, J., Kubaláková, M., König, S., Kugler, K.G., Scholz, U., Hackauf, B., et al. (2013). Reticulate evolution of the rye genome. Plant Cell 25, 3685–3698.
Mascher, M., Gundlach, H., Himmelbach, A., Beier, S., Twardziok, S.O., Wicker, T., Radchuk, V., Dockter, C., Hedley, P.E., Russell, J., et al. (2017). A chromosome conformation capture ordered sequence of the barley genome. Nature 544, 427–433.
McIntosh, R., Mu, J., Han, D., and Kang, Z. (2018). Wheat stripe rust resistance gene *Yr24*/*Yr26*: a retrospective review. Crop J 6, 321–329.
McIntosh, R.A., Dubcovsky, J., Rogers, W.J., Xia, X.C., and Raupp, W.J. (2020). Catalogue of gene symbols for wheat: 2020 supplement. In: 13th Int Wheat Genet Symp.
McIntosh, R.A., Dubcovsky, J., Rogers, W.J., Xia, X.C., and Raupp, W.J. (2021). Catalogue of gene symbols for wheat: 2021 supplement. Annu Wheat Newsletter 67, 104–113.
McIntosh, R.A., Wellings, C.R., and Park, R.F. (1995). Wheat Rusts: An Atlas of Resistance Genes. CSIRO Publishing.
Mega, R., Abe, F., Kim, J.S., Tsuboi, Y., Tanaka, K., Kobayashi, H., Sakata, Y., Hanada, K., Tsujimoto, H., Kikuchi, J., et al. (2019). Tuning water-use efficiency and drought tolerance in wheat using abscisic acid receptors. Nat Plants 5, 153–159.
Meng, Q., Yue, S., Chen, X., Cui, Z., Ye, Y., Ma, W., Tong, Y., and Zhang, F. (2013). Understanding dry matter and nitrogen accumulation with time-course for high-yielding wheat production in China. PLoS ONE 8, e68783.
Metzger, J.D. (1988). Localization of the site of perception of thermoinductive temperatures in *Thlaspi arvense* L. Plant Physiol 88, 424–428.
Meyer, R.S., and Purugganan, M.D. (2013). Evolution of crop species: genetics of domestication and diversification. Nat Rev Genet 14, 840–852.
Mi, G.H., Chen, F.J., Wu, Q.P., Lai, N.W., Yuan, L.X., and Zhang, F.S. (2010). Ideotype root architecture for efficient nitrogen acquisition by maize in intensive cropping systems. Sci China Life Sci 53, 1369–1373.
Miedaner, T., Risser, P., Paillard, S., Schnurbusch, T., Keller, B., Hartl, L., Holzapfel, J., Korzun, V., Ebmeyer, E., and Utz, H.F. (2012). Broad-spectrum resistance loci for three quantitatively inherited diseases in two winter wheat populations. Mol Breeding 29, 731–742.
Mishra, D., Shekhar, S., Chakraborty, S., and Chakraborty, N. (2021). Wheat 2-Cys peroxiredoxin plays a dual role in chlorophyll biosynthesis and adaptation to high temperature. Plant J 105, 1374–1389.
Mitchell, J.H., Chapman, S.C., Rebetzke, G.J., Bonnett, D.G., and Fukai, S. (2012). Evaluation of a reduced-tillering (*tin*) gene in wheat lines grown across different production environments. Crop Pasture Sci 63, 128–141.
Mitchell, J.H., Rebetzke, G.J., Chapman, S.C., and Fukai, S. (2013). Evaluation of reduced-tillering (*tin*) wheat lines in managed, terminal water deficit environments. J Exp Bot 64, 3439–3451.
Mo, Y., Vanzetti, L.S., Hale, I., Spagnolo, E.J., Guidobaldi, F., Al-Oboudi, J., Odle, N., Pearce, S., Helguera, M., and Dubcovsky, J. (2018). Identification and characterization of *Rht25*, a locus on chromosome arm 6AS affecting wheat plant height, heading time, and spike development. Theor Appl Genet 131, 2021–2035.
Moehs, C.P., Austill, W.J., Holm, A., Large, T.A.G., Loeffler, D., Mullenberg, J., Schnable, P.S., Skinner, W., van Boxtel, J., Wu, L., et al. (2019). Development of decreased-gluten wheat enabled by determination of the genetic basis of *lys3a* barley. Plant Physiol 179, 1692–1703.
Moeller, C., Evers, J.B., and Rebetzke, G. (2014). Canopy architectural and physiological characterization of near-isogenic wheat lines differing in the *tiller inhibition* gene *tin*. Front Plant Sci 5, 617.
Mohan, A., Grant, N.P., Schillinger, W.F., and Gill, K.S. (2021). Characterizing reduced height wheat mutants for traits affecting abiotic stress and photosynthesis during seedling growth. Physiologia Plantarum 172, 233–246.
Molnár-Láng, M., Ceoloni, C., and Doležel, J. (2015). Alien Introgression in Wheat. Cham: Springer.
Monaghan, J.M., Snape, J.W., Chojecki, A.J.S., and Kettlewell, P.S. (2001). The use of grain protein deviation for identifying wheat cultivars with high grain protein concentration and yield. Euphytica 122, 309–317.
Moore, J.W., Herrera-Foessel, S., Lan, C., Schnippenkoetter, W., Ayliffe, M., Huerta-Espino, J., Lillemo, M., Viccars, L., Milne, R., Periyannan, S., et al. (2015). A recently evolved hexose transporter variant confers resistance to multiple pathogens in wheat. Nat Genet 47, 1494–1498.

Moreno-Risueno, M.A., González, N., Díaz, I., Parcy, F., Carbonero, P., and Vicente-Carbajosa, J. (2008). FUSCA3 from barley unveils a common transcriptional regulation of seed-specific genes between cereals and Arabidopsis. Plant J 53, 882–894.
Morgan, J.A., Lecain, D.R., and Wells, R. (1990). Semidwarfing genes concentrate photosynthetic machinery and affect leaf gas-exchange of wheat. Crop Sci 30, 602–608.
Morran, S., Eini, O., Pyvovarenko, T., Parent, B., Singh, R., Ismagul, A., Eliby, S., Shirley, N., Langridge, P., and Lopato, S. (2011). Improvement of stress tolerance of wheat and barley by modulation of expression of DREB/CBF factors. Plant Biotechnol J 9, 230–249.
Mujeeb-Kazi, A., and Hettel, G.P. (1995). Utilizing wild grass biodiversity in wheat improvement: 15 years of wide cross research at CIMMYT. CIMMYT.
Munns, R., James, R.A., Xu, B., Athman, A., Conn, S.J., Jordans, C., Byrt, C.S., Hare, R.A., Tyerman, S.D., Tester, M., et al. (2012). Wheat grain yield on saline soils is improved by an ancestral Na^+ transporter gene. Nat Biotechnol 30, 360–364.
Muqaddasi, Q.H., Brassac, J., Koppolu, R., Plieske, J., Ganal, M.W., and Röder, M.S. (2019). *TaAPO-A1*, an ortholog of rice *ABERRANT PANICLE ORGANIZATION 1*, is associated with total spikelet number per spike in elite European hexaploid winter wheat (*Triticum aestivum* L.) varieties. Sci Rep 9, 13853.
Murat, F., Armero, A., Pont, C., Klopp, C., and Salse, J. (2017). Reconstructing the genome of the most recent common ancestor of flowering plants. Nat Genet 49, 490–496.
Muterko, A., Kalendar, R., and Salina, E. (2016). Novel alleles of the V*ERNALIZATION1* genes in wheat are associated with modulation of DNA curvature and flexibility in the promoter region. BMC Plant Biol 16, 9.
Muterko, A., and Salina, E. (2018). Origin and distribution of the *VRN-A1* exon 4 and exon 7 haplotypes in domesticated wheat species. Agronomy 8, 156.
Naruoka, Y., Talbert, L.E., Lanning, S.P., Blake, N.K., Martin, J.M., and Sherman, J.D. (2011). Identification of quantitative trait loci for productive tiller number and its relationship to agronomic traits in spring wheat. Theor Appl Genet 123, 1043–1053.
Nasseer, A.M., Martin, J.M., Heo, H.Y., Blake, N.K., Sherman, J.D., Pumphrey, M., Kephart, K.D., Lanning, S.P., Naruoka, Y., and Talbert, L.E. (2016). Impact of a quantitative trait locus for tiller number on plasticity of agronomic traits in spring wheat. Crop Sci 56, 595–602.
Nave, M., Avni, R., Ben-Zvi, B., Hale, I., and Distelfeld, A. (2016). QTLs for uniform grain dimensions and germination selected during wheat domestication are co-located on chromosome 4B. Theor Appl Genet 129, 1303–1315.
Nelson, M.N., Książkiewicz, M., Rychel, S., Besharat, N., Taylor, C.M., Wyrwa, K., Jost, R., Erskine, W., Cowling, W.A., Berger, J.D., et al. (2017). The loss of vernalization requirement in narrow-leafed lupin is associated with a deletion in the promoter and de-repressed expression of a *Flowering Locus T* (*FT*) homologue. New Phytol 213, 220–232.
Nenova, V.R., Kocheva, K.V., Petrov, P.I., Georgiev, G.I., Karceva, T.V., Börner, A., and Landjeva, S.P. (2014). Wheat *Rht-B1* dwarfs exhibit better photosynthetic response to water deficit at seedling stage compared to the wild type. J Agro Crop Sci 200, 434–443.
Nilsen, K.T., Walkowiak, S., Xiang, D., Gao, P., Quilichini, T.D., Willick, I. R., Byrns, B., N'Diaye, A., Ens, J., Wiebe, K., et al. (2020). Copy number variation of *TdDof* controls solid-stemmed architecture in wheat. Proc Natl Acad Sci USA 117, 28708–28718.
Ochagavía, H., Prieto, P., Savin, R., Griffiths, S., and Slafer, G.A. (2018). Dynamics of leaf and spikelet primordia initiation in wheat as affected by *Ppd-1a* alleles under field conditions. J Exp Bot 69, 2621–2631.
Oliver, S.N., Deng, W., Casao, M.C., and Trevaskis, B. (2013). Low temperatures induce rapid changes in chromatin state and transcript levels of the cereal *VERNALIZATION1* gene. J Exp Bot 64, 2413–2422.
Oliver, S.N., Finnegan, E.J., Dennis, E.S., Peacock, W.J., and Trevaskis, B. (2009). Vernalization-induced flowering in cereals is associated with changes in histone methylation at the *VERNALIZATION1* gene. Proc Natl Acad Sci USA 106, 8386–8391.
Olsen, K.M., and Wendel, J.F. (2013). A bountiful harvest: Genomic insights into crop domestication phenotypes. Annu Rev Plant Biol 64, 47–70.
Ouyang, X., Hong, X., Zhao, X., Zhang, W., He, X., Ma, W., Teng, W., and Tong, Y. (2016). Knock out of the *PHOSPHATE 2* gene *TaPHO2-A1* improves phosphorus uptake and grain yield under low phosphorus conditions in common wheat. Sci Rep 6, 29850.
Parry, D.W., Jenkinson, P., and McLEOD, L. (1995). Fusarium ear blight (scab) in small grain cereals—a review. Plant Pathol 44, 207–238.
Paterson, A.H., Bowers, J.E., Bruggmann, R., Dubchak, I., Grimwood, J., Gundlach, H., Haberer, G., Hellsten, U., Mitros, T., Poliakov, A., et al. (2009). The *Sorghum bicolor* genome and the diversification of grasses. Nature 457, 551–556.
Paterson, A.H., Bowers, J.E., and Chapman, B.A. (2004). Ancient polyploidization predating divergence of the cereals, and its consequences for comparative genomics. Proc Natl Acad Sci USA 101, 9903–9908.
Patial, M., Chaudhary, H.K., Sharma, N., Sundaresha, S., Kapoor, R., Pal, D., Pramanick, K.K., Shukla, A.K., and Kumar, J. (2021). Effect of different in vitro and in vivo variables on the efficiency of doubled haploid production in *Triticum aestivum* L. using Imperata cylindrica-mediated chromosome elimination technique. CEREAL Res Commun 49, 133–140.
Payne, P.I., Nightingale, M.A., Krattiger, A.F., and Holt, L.M. (1987). The relationship between HMW glutenin subunit composition and the bread-making quality of British-grown wheat varieties. J Sci Food Agric 40, 51–65.
Pearce, S., Zhu, J., Boldizsár, Á., Vágújfalvi, A., Burke, A., Garland-Campbell, K., Galiba, G., and Dubcovsky, J. (2013). Large deletions in the *CBF* gene cluster at the *Fr-B2* locus are associated with reduced frost tolerance in wheat. Theor Appl Genet 126, 2683–2697.
Peng, Z.S., Yen, C., and Yang, J.L. (1998). Genetic control of oligo-culms character common wheat. Wheat Inform Serv 86, 6.
Penrose, L. (1993). Yield of early dryland sowing of wheat with winter and spring habit in southern and central New South Wales. Aust J Exp Agric 33, 601–608.
Pérez-Gianmarco, T.I., Slafer, G.A., and González, F.G. (2019). Photoperiod-sensitivity genes shape floret development in wheat. J Exp Bot 70, 1339–1348.
Periyannan, S., Moore, J., Ayliffe, M., Bansal, U., Wang, X., Huang, L., Deal, K., Luo, M., Kong, X., Bariana, H., et al. (2013). The gene *Sr33*, an ortholog of barley *Mla* genes, encodes resistance to wheat stem rust race Ug99. Science 341, 786–788.
Pfister, B., and Zeeman, S.C. (2016). Formation of starch in plant cells. Cell Mol Life Sci 73, 2781–2807.
Pidal, B., Yan, L., Fu, D., Zhang, F., Tranquilli, G., and Dubcovsky, J. (2009). The CArG-box located upstream from the transcriptional start of wheat vernalization gene *VRN1* is not necessary for the vernalization response. J Heredity 100, 355–364.
Pourkheirandish, M., Hensel, G., Kilian, B., Senthil, N., Chen, G., Sameri, M., Azhaguvel, P., Sakuma, S., Dhanagond, S., Sharma, R., et al. (2015). Evolution of the grain dispersal system in barley. Cell 162, 527–539.
Prasad, P.V.V., and Djanaguiraman, M. (2014). Response of floret fertility and individual grain weight of wheat to high temperature stress: sensitive stages and thresholds for temperature and duration. Funct Plant Biol 41, 1261–1269.
Praz, C.R., Bourras, S., Zeng, F., Sánchez-Martín, J., Menardo, F., Xue, M., Yang, L., Roffler, S., Böni, R., Herren, G., et al. (2017). *AvrPm2* encodes an RNase-like avirulence effector which is conserved in the two different specialized forms of wheat and rye powdery mildew fungus. New Phytol 213, 1301–1314.
Prieto, P., Ochagavía, H., Savin, R., Griffiths, S., and Slafer, G.A. (2018). Dynamics of floret initiation/death determining spike fertility in wheat as affected by *Ppd* genes under field conditions. J Exp Bot 69, 2633–2645.

Purugganan, M.D., and Fuller, D.Q. (2009). The nature of selection during plant domestication. Nature 457, 843–848.
Qi, L.L., Pumphrey, M.O., Friebe, B., Chen, P.D., and Gill, B.S. (2008). Molecular cytogenetic characterization of alien introgressions with gene *Fhb3* for resistance to Fusarium head blight disease of wheat. Theor Appl Genet 117, 1155–1166.
Qi, L.L., Pumphrey, M.O., Friebe, B., Zhang, P., Qian, C., Bowden, R.L., Rouse, M.N., Jin, Y., and Gill, B.S. (2011). A novel Robertsonian translocation event leads to transfer of a stem rust resistance gene (*Sr52*) effective against race Ug99 from *Dasypyrum villosum* into bread wheat. Theor Appl Genet 123, 159–167.
Qin, D., Wang, F., Geng, X., Zhang, L., Yao, Y., Ni, Z., Peng, H., and Sun, Q. (2015). Overexpression of heat stress-responsive *TaMBF1c*, a wheat (*Triticum aestivum* L.) multiprotein bridging factor, confers heat tolerance in both yeast and rice. Plant Mol Biol 87, 31–45.
Qin, P., Lu, H., Du, H., Wang, H., Chen, W., Chen, Z., He, Q., Ou, S., Zhang, H., Li, X., et al. (2021). Pan-genome analysis of 33 genetically diverse rice accessions reveals hidden genomic variations. Cell 184, 3542–3558.e16.
Qin, Q., Wang, W., Guo, X., Yue, J., Huang, Y., Xu, X., Li, J., and Hou, S. (2014). *Arabidopsis* DELLA protein degradation is controlled by a type-one protein phosphatase, TOPP4. PLoS Genet 10, e1004464.
Qiu, D., Hu, W., Zhou, Y., Xiao, J., Hu, R., Wei, Q., Zhang, Y., Feng, J., Sun, F., Sun, J., et al. (2021). TaASR1-D confers abiotic stress resistance by affecting ROS accumulation and ABA signalling in transgenic wheat. Plant Biotechnol J 19, 1588–1601.
Qu, B., He, X., Wang, J., Zhao, Y., Teng, W., Shao, A., Zhao, X., Ma, W., Wang, J., Li, B., et al. (2015). A wheat CCAAT box-binding transcription factor increases the grain yield of wheat with less fertilizer input. Plant Physiol 167, 411–423.
Quintero, A., Molero, G., Reynolds, M.P., and Calderini, D.F. (2018). Trade-off between grain weight and grain number in wheat depends on GxE interaction: a case study of an elite CIMMYT panel (CIMCOG). Eur J Agronomy 92, 17–29.
Quraishi, U.M., Abrouk, M., Murat, F., Pont, C., Foucrier, S., Desmaizieres, G., Confolent, C., Rivière, N., Charmet, G., Paux, E., et al. (2011). Cross-genome map based dissection of a nitrogen use efficiency ortho-metaQTL in bread wheat unravels concerted cereal genome evolution. Plant J 65, 745–756.
Rabanus-Wallace, M.T., Hackauf, B., Mascher, M., Lux, T., Wicker, T., Gundlach, H., Baez, M., Houben, A., Mayer, K.F.X., Guo, L., et al. (2021). Chromosome-scale genome assembly provides insights into rye biology, evolution and agronomic potential. Nat Genet 53, 564–573.
Rabinovich, S.V. (1998). Importance of wheat-rye translocations for breeding modern cultivars of *Triticum aestivum* L. (Reprinted from Wheat: Prospects for global improvement, 1998). Euphytica 100, 323–340.
Ran, X., Zhao, F., Wang, Y., Liu, J., Zhuang, Y., Ye, L., Qi, M., Cheng, J., and Zhang, Y. (2020). Plant Regulomics: a data-driven interface for retrieving upstream regulators from plant multi-omics data. Plant J 101, 237–248.
Randhawa, M.S., Bains, N.S., Sohu, V.S., Chhuneja, P., Trethowan, R.M., Bariana, H.S., and Bansal, U. (2019). Marker assisted transfer of stripe rust and stem rust resistance genes into four wheat cultivars. Agronomy 9, 497.
Ravel, C., Fiquet, S., Boudet, J., Dardevet, M., Vincent, J., Merlino, M., Michard, R., and Martre, P. (2014). Conserved *cis*-regulatory modules in promoters of genes encoding wheat high-molecular-weight glutenin subunits. Front Plant Sci 5, 621.
Ravel, C., Nagy, I.J., Martre, P., Sourdille, P., Dardevet, M., Balfourier, F., Pont, C., Giancola, S., Praud, S., and Charmet, G. (2006). Single nucleotide polymorphism, genetic mapping, and expression of genes coding for the DOF wheat prolamin-box binding factor. Funct Integr Genomics 6, 310–321.
Rawat, N., Pumphrey, M.O., Liu, S., Zhang, X., Tiwari, V.K., Ando, K., Trick, H.N., Bockus, W.W., Akhunov, E., Anderson, J.A., et al. (2016). Wheat *Fhb1* encodes a chimeric lectin with agglutinin domains and a pore-forming toxin-like domain conferring resistance to Fusarium head blight. Nat Genet 48, 1576–1580.
Rebetzke, G.J., Ellis, M.H., Bonnett, D.G., Mickelson, B., Condon, A.G., and Richards, R.A. (2012). Height reduction and agronomic performance for selected gibberellin-responsive dwarfing genes in bread wheat (*Triticum aestivum* L.). Field Crops Res 126, 87–96.
Ristic, Z., Momcilovic, I., Bukovnik, U., Prasad, P.V.V., Fu, J., Deridder, B. P., Elthon, T.E., and Mladenov, N. (2009). Rubisco activase and wheat productivity under heat-stress conditions. J Exp Bot 60, 4003–4014.
Ruelens, P., de Maagd, R.A., Proost, S., Theißen, G., Geuten, K., and Kaufmann, K. (2013). FLOWERING LOCUS C in monocots and the tandem origin of angiosperm-specific MADS-box genes. Nat Commun 4, 2280.
Ryan, P.R., Liao, M., Delhaize, E., Rebetzke, G.J., Weligama, C., Spielmeyer, W., and James, R.A. (2015). Early vigour improves phosphate uptake in wheat. J Exp Bot 66, 7089–7100.
Saintenac, C., Cambon, F., Aouini, L., Verstappen, E., Ghaffary, S.M.T., Poucet, T., Marande, W., Berges, H., Xu, S., Jaouannet, M., et al. (2021). A wheat cysteine-rich receptor-like kinase confers broad-spectrum resistance against *Septoria tritici* blotch. Nat Commun 12, 433.
Saintenac, C., Lee, W.S., Cambon, F., Rudd, J.J., King, R.C., Marande, W., Powers, S.J., Bergès, H., Phillips, A.L., Uauy, C., et al. (2018). Wheat receptor-kinase-like protein Stb6 controls gene-for-gene resistance to fungal pathogen *Zymoseptoria tritici*. Nat Genet 50, 368–374.
Saintenac, C., Zhang, W., Salcedo, A., Rouse, M.N., Trick, H.N., Akhunov, E., and Dubcovsky, J. (2013). Identification of wheat gene *Sr35* that confers resistance to Ug99 stem rust race group. Science 341, 783–786.
Sakuma, S., Golan, G., Guo, Z., Ogawa, T., Tagiri, A., Sugimoto, K., Bernhardt, N., Brassac, J., Mascher, M., Hensel, G., et al. (2019). Unleashing floret fertility in wheat through the mutation of a homeobox gene. Proc Natl Acad Sci USA 116, 5182–5187.
Salamini, F., Ozkan, H., Brandolini, A., Schäfer-Pregl, R., and Martin, W. (2002). Genetics and geography of wild cereal domestication in the Near East. Nat Rev Genet 3, 429–441.
Salcedo, A., Rutter, W., Wang, S., Akhunova, A., Bolus, S., Chao, S., Anderson, N., De Soto, M.F., Rouse, M., Szabo, L., et al. (2017). Variation in the *AvrSr35* gene determines *Sr35* resistance against wheat stem rust race Ug99. Science 358, 1604–1606.
Salse, J., Bolot, S., Throude, M., Jouffe, V., Piegu, B., Quraishi, U.M., Calcagno, T., Cooke, R., Delseny, M., and Feuillet, C. (2008). Identification and characterization of shared duplications between rice and wheat provide new insight into grass genome evolution. Plant Cell 20, 11–24.
Sánchez-Martín, J., Steuernagel, B., Ghosh, S., Herren, G., Hurni, S., Adamski, N., Vrána, J., Kubaláková, M., Krattinger, S.G., Wicker, T., et al. (2016). Rapid gene isolation in barley and wheat by mutant chromosome sequencing. Genome Biol 17, 221.
Sánchez-Martín, J., Widrig, V., Herren, G., Wicker, T., Zbinden, H., Gronnier, J., Spörri, L., Praz, C.R., Heuberger, M., Kolodziej, M.C., et al. (2021). Wheat *Pm4* resistance to powdery mildew is controlled by alternative splice variants encoding chimeric proteins. Nat Plants 7, 327–341.
Sato, K., Abe, F., Mascher, M., Haberer, G., Gundlach, H., Spannagl, M., Shirasawa, K., and Isobe, S. (2021). Chromosome-scale genome assembly of the transformation-amenable common wheat cultivar 'Fielder'. DNA Res 28, dsab008.
Scafaro, A.P., Bautsoens, N., den Boer, B., Van Rie, J., and Gallé, A. (2019). A conserved sequence from heat-adapted species improves rubisco activase thermostability in wheat. Plant Physiol 181, 43–54.
Serrano-Mislata, A., Bencivenga, S., Bush, M., Schiessl, K., Boden, S., and Sablowski, R. (2017). *DELLA* genes restrict inflorescence meristem function independently of plant height. Nat Plants 3, 749–754.
Shang, Q., Wang, Y., Tang, H., Sui, N., Zhang, X., and Wang, F. (2021). Genetic, hormonal, and environmental control of tillering in wheat. Crop J 9, 986–991.
Shao, A., Ma, W., Zhao, X., Hu, M., He, X., Teng, W., Li, H., and Tong, Y.

(2017). The auxin biosynthetic *TRYPTOPHAN AMINOTRANSFERASE RELATED TaTAR2.1-3A* increases grain yield of wheat. Plant Physiol 174, 2274–2288.
Shao, G., Lu, Z., Xiong, J., Wang, B., Jing, Y., Meng, X., Liu, G., Ma, H., Liang, Y., Chen, F., et al. (2019). Tiller bud formation regulators MOC1 and MOC3 cooperatively promote tiller bud outgrowth by activating *FON1* expression in rice. Mol Plant 12, 1090–1102.
Sharma, N., Ruelens, P., D'hauw, M., Maggen, T., Dochy, N., Torfs, S., Kaufmann, K., Rohde, A., and Geuten, K. (2017). A flowering locus C homolog is a vernalization-regulated repressor in *Brachypodium* and is cold regulated in wheat. Plant Physiol 173, 1301–1315.
Shaw, L.M., Lyu, B., Turner, R., Li, C., Chen, F., Han, X., Fu, D., and Dubcovsky, J. (2019). *FLOWERING LOCUS T2* regulates spike development and fertility in temperate cereals. J Exp Bot 70, 193–204.
Shcherban, A.B., and Salina, E.A. (2017). Evolution of VRN-1 homoeologous loci in allopolyploids of Triticum and their diploid precursors. BMC Plant Biol 17, 188.
Sheldon, C.C., Hills, M.J., Lister, C., Dean, C., Dennis, E.S., and Peacock, W.J. (2008). Resetting of *FLOWERING LOCUS C* expression after epigenetic repression by vernalization. Proc Natl Acad Sci USA 105, 2214–2219.
Shen, L., Luo, G., Song, Y., Xu, J., Ji, J.J., Zhang, C., Gregová, E., Yang, W., Li, X., Sun, J., et al. (2021). A novel NAC family transcription factor *SPR* suppresses seed storage protein synthesis in wheat. Plant Biotechnol J 19, 992–1007.
Sherman, J.D., Martin, J.M., Blake, N.K., Lanning, S.P., and Talbert, L.E. (2014). Genetic basis of agronomic differences between a modern and a historical spring wheat cultivar. Crop Sci 54, 1–13.
Shi, G., Zhang, Z., Friesen, T.L., Raats, D., Fahima, T., Brueggeman, R.S., Lu, S., Trick, H.N., Liu, Z., Chao, W., et al. (2016). The hijacking of a receptor kinase-driven pathway by a wheat fungal pathogen leads to disease. Sci Adv 2, e1600822.
Shi, X., Wu, P., Hu, J., Qiu, D., Qu, Y., Li, Y., Liu, Y., Gebremariam, T.G., Xie, J., Wu, Q., et al. (2021). Molecular characterization of all-stage and adult-plant resistance loci against powdery mildew in winter wheat cultivar Liangxing 99 using BSR-Seq technology. Plant Dis 105, 3443–3450.
Shiferaw, B., Smale, M., Braun, H.J., Duveiller, E., Reynolds, M., and Muricho, G. (2013). Crops that feed the world 10. Past successes and future challenges to the role played by wheat in global food security. Food Sec 5, 291–317.
Shrestha, R., Gómez-Ariza, J., Brambilla, V., and Fornara, F. (2014). Molecular control of seasonal flowering in rice, arabidopsis and temperate cereals. Ann Bot 114, 1445–1458.
Si, L., Chen, J., Huang, X., Gong, H., Luo, J., Hou, Q., Zhou, T., Lu, T., Zhu, J., Shangguan, Y., et al. (2016). *OsSPL13* controls grain size in cultivated rice. Nat Genet 48, 447–456.
Silva, A.C., Lima, M.F., Eloy, N.B., Thiebaut, F., Montessoro, P., Hemerly, A.S., and Ferreira, P.C.G. (2019). The Yin and Yang in plant breeding: the trade-off between plant growth yield and tolerance to stresses. Biotechnol Res Innovation 3, 73–79.
Simons, K.J., Fellers, J.P., Trick, H.N., Zhang, Z., Tai, Y.S., Gill, B.S., and Faris, J.D. (2006). Molecular characterization of the major wheat domestication gene *Q*. Genetics 172, 547–555.
Singh Gahoonia, T., Care, D., and Nielsen, N.E. (1997). Root hairs and phosphorus acquisition of wheat and barley cultivars. Plant Soil 191, 181–188.
Singh, P.K., Gahtyari, N.C., Roy, C., Roy, K.K., He, X., Tembo, B., Xu, K., Juliana, P., Sonder, K., Kabir, M.R., et al. (2021). Wheat blast: a disease spreading by intercontinental jumps and its management strategies. Front Plant Sci 12, 710707.
Singh, R.P., Hodson, D.P., Jin, Y., Lagudah, E.S., Ayliffe, M.A., Bhavani, S., Rouse, M.N., Pretorius, Z.A., Szabo, L.J., Huerta-Espino, J., et al. (2015). Emergence and spread of new races of wheat stem rust fungus: continued threat to food security and prospects of genetic control. Phytopathology 105, 872–884.
Singh, R.P., Singh, P.K., Rutkoski, J., Hodson, D.P., He, X., Jørgensen, L. N., Hovmøller, M.S., and Huerta-Espino, J. (2016). Disease impact on wheat yield potential and prospects of genetic control. Annu Rev Phytopathol 54, 303–322.
Singh, S.P., Hurni, S., Ruinelli, M., Brunner, S., Sanchez-Martin, J., Krukowski, P., Peditto, D., Buchmann, G., Zbinden, H., and Keller, B. (2018). Evolutionary divergence of the rye *Pm17* and *Pm8* resistance genes reveals ancient diversity. Plant Mol Biol 98, 249–260.
Sirkka, A., and Immonen, T. (1993). Comparison of callus culture with embryo culture at different times of embryo rescue for primary triticale production. Euphytica 70, 185–190.
Song, Y., Luo, G., Shen, L., Yu, K., Yang, W., Li, X., Sun, J., Zhan, K., Cui, D., Liu, D., et al. (2020). *TubZIP28*, a novel bZIP family transcription factor from *Triticum urartu*, and *TabZIP28*, its homologue from *Triticum aestivum*, enhance starch synthesis in wheat. New Phytol 226, 1384–1398.
Spannagl, M., Alaux, M., Lange, M., Bolser, D.M., Bader, K.C., Letellier, T., Kimmel, E., Flores, R., Pommier, C., Kerhornou, A., et al. (2016). transPLANT resources for Triticeae genomic data. Plant Genome 9, plantgenome2015.06.0038.
Spielmeyer, W., and Richards, R.A. (2004). Comparative mapping of wheat chromosome 1AS which contains the tiller inhibition gene (*tin*) with rice chromosome 5S. Theor Appl Genet 109, 1303–1310.
Stein, J.C., Yu, Y., Copetti, D., Zwickl, D.J., Zhang, L., Zhang, C., Chougule, K., Gao, D., Iwata, A., Goicoechea, J.L., et al. (2018). Genomes of 13 domesticated and wild rice relatives highlight genetic conservation, turnover and innovation across the genus *Oryza*. Nat Genet 50, 285–296.
Steuernagel, B., Periyannan, S.K., Hernández-Pinzón, I., Witek, K., Rouse, M.N., Yu, G., Hatta, A., Ayliffe, M., Bariana, H., Jones, J.D.G., et al. (2016). Rapid cloning of disease-resistance genes in plants using mutagenesis and sequence capture. Nat Biotechnol 34, 652–655.
Strejčková, B., Milec, Z., Holušová, K., Cápal, P., Vojtková, T., Čegan, R., and Šafář, J. (2021). In-depth sequence analysis of bread wheat *VRN1* genes. Int J Mol Sci 22, 12284.
Su, J., Zhao, J., Zhao, S., Li, M., Pang, S., Kang, Z., Zhen, W., Chen, S., Chen, F., and Wang, X. (2021). Genetics of resistance to common root rot (Spot Blotch), *Fusarium* crown rot, and sharp eyespot in wheat. Front Genet 12, 699342.
Su, Z., Bernardo, A., Tian, B., Chen, H., Wang, S., Ma, H., Cai, S., Liu, D., Zhang, D., Li, T., et al. (2019). A deletion mutation in *TaHRC* confers *Fhb1* resistance to Fusarium head blight in wheat. Nat Genet 51, 1099–1105.
Subbarao, G.V., Kishii, M., Bozal-Leorri, A., Ortiz-Monasterio, I., Gao, X., Ibba, M.I., Karwat, H., Gonzalez-Moro, M.B., Gonzalez-Murua, C., Yoshihashi, T., et al. (2021). Enlisting wild grass genes to combat nitrification in wheat farming: A nature-based solution. Proc Natl Acad Sci USA 118, e2106595118.
Sun, F., Liu, X., Wei, Q., Liu, J., Yang, T., Jia, L., Wang, Y., Yang, G., and He, G. (2017). Functional characterization of TaFUSCA3, a B3-superfamily transcription factor gene in the wheat. Front Plant Sci 8, 1133.
Sun, F., Zhang, W., Xiong, G., Yan, M., Qian, Q., Li, J., and Wang, Y. (2010). Identification and functional analysis of the MOC1 interacting protein 1. J Genet Genomics 37, 69–77.
Sun, H., Qian, Q., Wu, K., Luo, J., Wang, S., Zhang, C., Ma, Y., Liu, Q., Huang, X., Yuan, Q., et al. (2014). Heterotrimeric G proteins regulate nitrogen-use efficiency in rice. Nat Genet 46, 652–656.
Sun, Q.M., Zhou, R.H., Gao, L.F., Zhao, G.Y., and Jia, J.Z. (2009). The characterization and geographical distribution of the genes responsible for vernalization requirement in Chinese bread wheat. J Integr Plant Biol 51, 423–432.
Sun, S., Wang, L., Mao, H., Shao, L., Li, X., Xiao, J., Ouyang, Y., and Zhang, Q. (2018). A G-protein pathway determines grain size in rice. Nat Commun 9, 851.
Sun, Y., Xu, W., Jia, Y., Wang, M., and Xia, G. (2015). The wheat *TaGBF1* gene is involved in the blue-light response and salt tolerance. Plant J 84, 1219–1230.

Tang, H., Bowers, J.E., Wang, X., and Paterson, A.H. (2010). Angiosperm genome comparisons reveal early polyploidy in the monocot lineage. Proc Natl Acad Sci USA 107, 472–477.
Tao, Z., Hu, H., Luo, X., Jia, B., Du, J., and He, Y. (2019). Embryonic resetting of the parental vernalized state by two B3 domain transcription factors in *Arabidopsis*. Nat Plants 5, 424–435.
Tao, Z., Shen, L., Gu, X., Wang, Y., Yu, H., and He, Y. (2017). Embryonic epigenetic reprogramming by a pioneer transcription factor in plants. Nature 551, 124–128.
Tappiban, P., Ying, Y., Xu, F., and Bao, J. (2021). Proteomics and post-translational modifications of starch biosynthesis-related proteins in developing seeds of rice. Int J Mol Sci 22, 5901.
Taulemesse, F., Le Gouis, J., Gouache, D., Gibon, Y., and Allard, V. (2015). Post-flowering nitrate uptake in wheat is controlled by N status at flowering, with a putative major role of root nitrate transporter *NRT2.1*. PLoS ONE 10, e0120291.
Teng, W., Deng, Y., Chen, X.P., Xu, X.F., Chen, R.Y., Lv, Y., Zhao, Y.Y., Zhao, X.Q., He, X., Li, B., et al. (2013). Characterization of root response to phosphorus supply from morphology to gene analysis in field-grown wheat. J Exp Bot 64, 1403–1411.
Teng, W., Zhao, Y.Y., Zhao, X.Q., He, X., Ma, W.Y., Deng, Y., Chen, X.P., and Tong, Y.P. (2017). Genome-wide identification, characterization, and expression analysis of PHT1 phosphate transporters in wheat. Front Plant Sci 8, 543.
The International Brachypodium Initiative. (2010). Genome sequencing and analysis of the model grass *Brachypodium distachyon*. Nature 463, 763–768.
Thind, A.K., Wicker, T., Šimková, H., Fossati, D., Moullet, O., Brabant, C., Vrána, J., Doležel, J., and Krattinger, S.G. (2017). Rapid cloning of genes in hexaploid wheat using cultivar-specific long-range chromosome assembly. Nat Biotechnol 35, 793–796.
Tian, X., Qin, Z., Zhao, Y., Wen, J., Lan, T., Zhang, L., Wang, F., Qin, D., Yu, K., Zhao, A., et al. (2022a). Stress granule-associated TaMBF1c confers thermotolerance through regulating specific mRNA translation in wheat (*Triticum aestivum*). New Phytol 233, 1719–1731.
Tian, X., Wang, F., Zhao, Y., Lan, T., Yu, K., Zhang, L., Qin, Z., Hu, Z., Yao, Y., Ni, Z., et al. (2020). Heat shock transcription factor A1b regulates heat tolerance in wheat and Arabidopsis through OPR3 and jasmonate signalling pathway. Plant Biotechnol J 18, 1109–1111.
Tian, X., Xia, X., Xu, D., Liu, Y., Xie, L., Hassan, M.A., Song, J., Li, F., Wang, D., Zhang, Y., et al. (2022b). *Rht24b*, an ancient variation of *TaGA2ox-A9*, reduces plant height without yield penalty in wheat. New Phytol 233, 738–750.
Tian, X., Wen, W., Xie, L., Fu, L., Xu, D., Fu, C., Wang, D., Chen, X., Xia, X., Chen, Q., et al. (2017). Molecular mapping of reduced plant height gene *Rht24* in bread wheat. Front Plant Sci 8, 1379.
Tian, X., Zhu, Z., Xie, L., Xu, D., Li, J., Fu, C., Chen, X., Wang, D., Xia, X., He, Z., et al. (2019). Preliminary exploration of the source, spread, and distribution of *Rht24* reducing height in bread wheat. Crop Sci 59, 19–24.
Tian, Z., Li, Y., Liang, Z., Guo, H., Cai, J., Jiang, D., Cao, W., and Dai, T. (2016). Genetic improvement of nitrogen uptake and utilization of winter wheat in the Yangtze River Basin of China. Field Crops Res 196, 251–260.
Trachsel, S., Kaeppler, S.M., Brown, K.M., and Lynch, J.P. (2013). Maize root growth angles become steeper under low N conditions. Field Crops Res 140, 18–31.
Trevaskis, B. (2010). The central role of the *VERNALIZATION1* gene in the vernalization response of cereals. Funct Plant Biol 37, 479–487.
Ugarte, C., Calderini, D.F., and Slafer, G.A. (2007). Grain weight and grain number responsiveness to pre-anthesis temperature in wheat, barley and triticale. Field Crops Res 100, 240–248.
Upadhyaya, N.M., Mago, R., Panwar, V., Hewitt, T., Luo, M., Chen, J., Sperschneider, J., Nguyen-Phuc, H., Wang, A., Ortiz, D., et al. (2021). Genomics accelerated isolation of a new stem rust avirulence gene-wheat resistance gene pair. Nat Plants 7, 1220–1228.
Viglasi, P. (1968). Short-strawed mutants of karcag 522 winter wheat induced by gamma rays. Acta Agron Hung 17, 205.
Voss-Fels, K.P., Robinson, H., Mudge, S.R., Richard, C., Newman, S., Wittkop, B., Stahl, A., Friedt, W., Frisch, M., Gabur, I., et al. (2018). *VERNALIZATION1* modulates root system architecture in wheat and barley. Mol Plant 11, 226–229.
Waddington, S.R., Cartwright, P.M., and Wall, P.C. (1983). A quantitative scale of spike initial and pistil development in barley and wheat. Ann Bot 51, 119–130.
Waines, J.G., and Ehdaie, B. (2007). Domestication and crop physiology: roots of green-revolution wheat. Ann Bot 100, 991–998.
Walkowiak, S., Gao, L., Monat, C., Haberer, G., Kassa, M.T., Brinton, J., Ramirez-Gonzalez, R.H., Kolodziej, M.C., Delorean, E., Thambugala, D., et al. (2020). Multiple wheat genomes reveal global variation in modern breeding. Nature 588, 277–283.
Wang, H., Zou, S., Li, Y., Lin, F., and Tang, D. (2020a). An ankyrin-repeat and WRKY-domain-containing immune receptor confers stripe rust resistance in wheat. Nat Commun 11, 1353.
Wang, H., Sun, S., Ge, W., Zhao, L., Hou, B., Wang, K., Lyu, Z., Chen, L., Xu, S., Guo, J., et al. (2020b). Horizontal gene transfer of *Fhb7* from fungus underlies *Fusarium* head blight resistance in wheat. Science 368, eaba5435.
Wang, H., Yin, H., Jiao, C., Fang, X., Wang, G., Li, G., Ni, F., Li, P., Su, P., Ge, W., et al. (2020c). Sympatric speciation of wild emmer wheat driven by ecology and chromosomal rearrangements. Proc Natl Acad Sci USA 117, 5955–5963.
Wang, J., Liao, X., Li, Y., Zhou, R., Yang, X., Gao, L., and Jia, J. (2010). Fine mapping a domestication-related QTL for spike-related traits in a synthetic wheat. Genome 53, 798–804.
Wang, J., Sun, J., Miao, J., Guo, J., Shi, Z., He, M., Chen, Y., Zhao, X., Li, B., Han, F.P., et al. (2013). A phosphate starvation response regulator *Ta-PHR1* is involved in phosphate signalling and increases grain yield in wheat. Ann Bot 111, 1139–1153.
Wang, J., Fu, W., Wang, R., Hu, D., Cheng, H., Zhao, J., Jiang, Y., and Kang, Z. (2020d). WGVD: an integrated web-database for wheat genome variation and selective signatures. Database 2020, baaa090.
Wang, J., Liu, W., Wang, H., Li, L., Wu, J., Yang, X., Li, X., and Gao, A. (2011). QTL mapping of yield-related traits in the wheat germplasm 3228. Euphytica 177, 277–292.
Wang, K., Shi, L., Liang, X., Zhao, P., Wang, W., Liu, J., Chang, Y., Hiei, Y., Yanagihara, C., Du, L., et al. (2022a). The gene *TaWOX5* overcomes genotype dependency in wheat genetic transformation. Nat Plants 8, 110–117.
Wang, M., Ji, Y., Feng, S., Liu, C., Xiao, Z., Wang, X., Wang, Y., and Xia, G. (2018a). The non-random patterns of genetic variation induced by asymmetric somatic hybridization in wheat. BMC Plant Biol 18, 244.
Wang, M., Li, Z., Zhang, Y., Zhang, Y., Xie, Y., Ye, L., Zhuang, Y., Lin, K., Zhao, F., Guo, J., et al. (2021a). An atlas of wheat epigenetic regulatory elements reveals subgenome divergence in the regulation of development and stress responses. Plant Cell 33, 865–881.
Wang, M., Liu, C., Xing, T., Wang, Y., and Xia, G. (2015a). Asymmetric somatic hybridization induces point mutations and indels in wheat. BMC Genomics 16, 807.
Wang, M., Qin, L., Xie, C., Li, W., Yuan, J., Kong, L., Yu, W., Xia, G., and Liu, S. (2014a). Induced and constitutive DNA methylation in a salinity-tolerant wheat introgression line. Plant Cell Physiol 55, 1354–1365.
Wang, M., Wang, S., Liang, Z., Shi, W., Gao, C., and Xia, G. (2018b). From genetic stock to genome editing: gene exploitation in wheat. Trends Biotechnol 36, 160–172.
Wang, M., Wang, S., and Xia, G. (2015b). From genome to gene: a new epoch for wheat research? Trends Plant Sci 20, 380–387.
Wang, M., Zhao, X., Xiao, Z., Yin, X., Xing, T., and Xia, G. (2016). A wheat superoxide dismutase gene *TaSOD2* enhances salt resistance through modulating redox homeostasis by promoting NADPH oxidase activity. Plant Mol Biol 91, 115–130.
Wang, M., Wang, M., Zhao, M., Wang, M., Liu, S., Tian, Y., Moon, B., Liang, C., Li, C., Shi, W., et al. (2022b). TaSRO1 plays a dual role in

suppressing TaSIP1 to fine tune mitochondrial retrograde signalling and enhance salinity stress tolerance. New Phytol, , doi: 10.1111/nph.18340.
Wang, M., Yuan, J., Qin, L., Shi, W., Xia, G., and Liu, S. (2020e). *TaCYP81D5*, one member in a wheat cytochrome P450 gene cluster, confers salinity tolerance via reactive oxygen species scavenging. Plant Biotechnol J 18, 791–804.
Wang, N., Tang, C., Fan, X., He, M., Gan, P., Zhang, S., Hu, Z., Wang, X., Yan, T., Shu, W., et al. (2022c). Inactivation of a wheat protein kinase gene confers broad-spectrum resistance to rust fungi. Cell 185, 2961–2974.
Wang, P., Li, G., Li, G., Yuan, S., Wang, C., Xie, Y., Guo, T., Kang, G., and Wang, D. (2021b). TaPHT1;9-4B and its transcriptional regulator TaMYB4-7D contribute to phosphate uptake and plant growth in bread wheat. New Phytol 231, 1968–1983.
Wang, Q., Nian, J., Xie, X., Yu, H., Zhang, J., Bai, J., Dong, G., Hu, J., Bai, B., Chen, L., et al. (2018c). Genetic variations in *ARE1* mediate grain yield by modulating nitrogen utilization in rice. Nat Commun 9, 735.
Wang, S., Xu, S., Chao, S., Sun, Q., Liu, S., and Xia, G. (2019a). A genome-wide association study of highly heritable agronomic traits in durum wheat. Front Plant Sci 10, 919.
Wang, X., Chen, S., Shi, X., Liu, D., Zhao, P., Lu, Y., Cheng, Y., Liu, Z., Nie, X., Song, W., et al. (2019b). Hybrid sequencing reveals insight into heat sensing and signaling of bread wheat. Plant J 98, 1015–1032.
Wang, X., Guan, P., Xin, M., Wang, Y., Chen, X., Zhao, A., Liu, M., Li, H., Zhang, M., Lu, L., et al. (2021c). Genome-wide association study identifies QTL for thousand grain weight in winter wheat under normal- and late-sown stressed environments. Theor Appl Genet 134, 143–157.
Wang, X., Hou, L., Lu, Y., Wu, B., Gong, X., Liu, M., Wang, J., Sun, Q., Vierling, E., and Xu, S. (2018d). Metabolic adaptation of wheat grains contributes to a stable filling rate under heat stress. J Exp Bot 69, 5531–5545.
Wang, X., Wang, J., Jin, D., Guo, H., Lee, T.H., Liu, T., and Paterson, A.H. (2015c). Genome alignment spanning major poaceae lineages reveals heterogeneous evolutionary rates and alters inferred dates for key evolutionary events. Mol Plant 8, 885–898.
Wang, Y., Cheng, X., Shan, Q., Zhang, Y., Liu, J., Gao, C., and Qiu, J.L. (2014b). Simultaneous editing of three homoeoalleles in hexaploid bread wheat confers heritable resistance to powdery mildew. Nat Biotechnol 32, 947–951.
Wang, Y., Yu, H., Tian, C., Sajjad, M., Gao, C., Tong, Y., Wang, X., and Jiao, Y. (2017). Transcriptome association identifies regulators of wheat spike architecture. Plant Physiol 175, 746–757.
Wang, Y., Hou, J., Liu, H., Li, T., Wang, K., Hao, C., Liu, H., and Zhang, X. (2019c). *TaBT1*, affecting starch synthesis and thousand kernel weight, underwent strong selection during wheat improvement. J Exp Bot 70, 1497–1511.
Wang, Z., Wang, W., Xie, X., Wang, Y., Yang, Z., Peng, H., Xin, M., Yao, Y., Hu, Z., Liu, J., et al. (2022d). Dispersed emergence and protracted domestication of polyploid wheat uncovered by mosaic ancestral haploblock inference. Nat Commun 13, 3891.
Wang, Z., Wu, F., Chen, X., Zhou, W., Shi, H., Lin, Y., Hou, S., Yu, S., Zhou, H., Li, C., et al. (2022e). Fine mapping of the tiller inhibition gene *TIN4* contributing to ideal plant architecture in common wheat. Theor Appl Genet 135, 527–535.
Watson, A., Ghosh, S., Williams, M.J., Cuddy, W.S., Simmonds, J., Rey, M. D., Asyraf Md Hatta, M., Hinchliffe, A., Steed, A., Reynolds, D., et al. (2018). Speed breeding is a powerful tool to accelerate crop research and breeding. Nat Plants 4, 23–29.
Weligama, C., Tang, C., Sale, P.W.G., Conyers, M.K., and Liu, D.L. (2008). Localised nitrate and phosphate application enhances root proliferation by wheat and maximises rhizosphere alkalisation in acid subsoil. Plant Soil 312, 101–115.
Wellensiek, S.J. (1962). Dividing cells as the locus for vernalization. Nature 195, 307–308.
Wellings, C.R. (2011). Global status of stripe rust: a review of historical and current threats. Euphytica 179, 129–141.
Wen, S., Wen, N., Pang, J., Langen, G., Brew-Appiah, R.A.T., Mejias, J.H., Osorio, C., Yang, M., Gemini, R., Moehs, C.P., et al. (2012). Structural genes of wheat and barley 5-methylcytosine DNA glycosylases and their potential applications for human health. Proc Natl Acad Sci USA 109, 20543–20548.
Wen, W., Deng, Q., Jia, H., Wei, L., Wei, J., Wan, H., Yang, L., Cao, W., and Ma, Z. (2013). Sequence variations of the partially dominant DELLA gene *Rht-B1c* in wheat and their functional impacts. J Exp Bot 64, 3299–3312.
Wen, Z., Li, H., Shen, Q., Tang, X., Xiong, C., Li, H., Pang, J., Ryan, M.H., Lambers, H., and Shen, J. (2019). Tradeoffs among root morphology, exudation and mycorrhizal symbioses for phosphorus-acquisition strategies of 16 crop species. New Phytol 223, 882–895.
Whittaker, C., and Dean, C. (2017). The *FLC* locus: a platform for discoveries in epigenetics and adaptation. Annu Rev Cell Dev Biol 33, 555–575.
Willick, I.R., Takahashi, D., Fowler, D.B., Uemura, M., and Tanino, K.K. (2018). Tissue-specific changes in apoplastic proteins and cell wall structure during cold acclimation of winter wheat crowns. J Exp Bot 69, 1221–1234.
Winfield, M.O., Lu, C., Wilson, I.D., Coghill, J.A., and Edwards, K.J. (2010). Plant responses to cold: transcriptome analysis of wheat. Plant Biotechnol J 8, 749–771.
Winfield, M.O., Lu, C., Wilson, I.D., Coghill, J.A., and Edwards, K.J. (2009). Cold- and light-induced changes in the transcriptome of wheat leading to phase transition from vegetative to reproductive growth. BMC Plant Biol 9, 55.
Winn, Z.J., Acharya, R., Merrill, K., Lyerly, J., Brown-Guedira, G., Cambron, S., Harrison, S.H., Reisig, D., and Murphy, J.P. (2021). Mapping of a novel major effect Hessian fly field partial-resistance locus in southern soft red winter wheat line LA03136E71. Theor Appl Genet 134, 3911–3923.
Woods, D.P., McKeown, M.A., Dong, Y., Preston, J.C., and Amasino, R.M. (2016). Evolution of *VRN2/Ghd7*-like genes in vernalization-mediated repression of grass flowering. Plant Physiol 170, 2124–2135.
Woods, D.P., Ream, T.S., Bouché, F., Lee, J., Thrower, N., Wilkerson, C., and Amasino, R.M. (2017). Establishment of a vernalization requirement in *Brachypodium distachyon* requires *REPRESSOR OF VERNALIZATION1*. Proc Natl Acad Sci USA 114, 6623–6628.
Worland, A.J., and Petrovic, S. (1988). The gibberellic acid insensitive dwarfing gene from the wheat variety Saitama 27. Euphytica 38, 55–63.
Wu, C.Y., Washida, H., Onodera, Y., Harada, K., and Takaiwa, F. (2000). Quantitative nature of the Prolamin-box, ACGT and AACA motifs in a rice glutelin gene promoter: minimal *cis*-element requirements for endosperm-specific gene expression. Plant J 23, 415–421.
Wu, K., Wang, S., Song, W., Zhang, J., Wang, Y., Liu, Q., Yu, J., Ye, Y., Li, S., Chen, J., et al. (2020). Enhanced sustainable green revolution yield via nitrogen-responsive chromatin modulation in rice. Science 367, eaaz2046.
Wu, W., Li, C., Ma, B., Shah, F., Liu, Y., and Liao, Y. (2014). Genetic progress in wheat yield and associated traits in China since 1945 and future prospects. Euphytica 196, 155–168.
Würschum, T., Langer, S.M., and Longin, C.F.H. (2015). Genetic control of plant height in European winter wheat cultivars. Theor Appl Genet 128, 865–874.
Würschum, T., Langer, S.M., Longin, C.F.H., Tucker, M.R., and Leiser, W. L. (2017). A modern Green Revolution gene for reduced height in wheat. Plant J 92, 892–903.
Xia, G., Xiang, F., Zhou, A., Wang, H., and Chen, H. (2003). Asymmetric somatic hybridization between wheat (*Triticum aestivum* L.) and *Agropyron elongatum* (Host) Nevishi. Theor Appl Genet 107, 299–305.
Xiang, D., Quilichini, T.D., Liu, Z., Gao, P., Pan, Y., Li, Q., Nilsen, K.T., Venglat, P., Esteban, E., Pasha, A., et al. (2019). The transcriptional landscape of polyploid wheats and their diploid ancestors during embryogenesis and grain development. Plant Cell 31, 2888–2911.
Xiao, J., Chen, Y., Lu, Y., Liu, Z., Si, D., Xu, T., Sun, L., Wang, Z., Yuan, C., Sun, H., et al. (2021). A natural variation of an *SVP* MADS-box transcription factor in *Triticum petropavlovskyi* leads to its ectopic

expression and contributes to elongated glume. Mol Plant 14, 1408–1411.
Xiao, J., Xu, S., Li, C., Xu, Y., Xing, L., Niu, Y., Huan, Q., Tang, Y., Zhao, C., Wagner, D., et al. (2014). *O*-GlcNAc-mediated interaction between VER2 and TaGRP2 elicits *TaVRN1* mRNA accumulation during vernalization in winter wheat. Nat Commun 5, 4572.
Xie, J., Guo, G., Wang, Y., Hu, T., Wang, L., Li, J., Qiu, D., Li, Y., Wu, Q., Lu, P., et al. (2020). A rare single nucleotide variant in *Pm5e* confers powdery mildew resistance in common wheat. New Phytol 228, 1011–1026.
Xie, L., Zhang, Y., Wang, K., Luo, X., Xu, D., Tian, X., Li, L., Ye, X., Xia, X., Li, W., et al. (2021). *TaVrt2* , an SVP-like gene, cooperates with *TaVrn1* to regulate vernalization-induced flowering in wheat. New Phytol 231, 834–848.
Xing, L., Hu, P., Liu, J., Cui, C., Wang, H., Di, Z., Zhou, S., Xu, J., Gao, L., and Huang, Z. (2017). *NLR1-V*, a CC-NBS-LRR encoding gene, is a potential candidate gene of the wheat powdery mildew resistance gene *Pm21*. BioRxiv: 10.1101/114058.
Xing, L., Li, J., Xu, Y., Xu, Z., and Chong, K. (2009). Phosphorylation modification of wheat lectin VER2 is associated with vernalization-induced *O*-GlcNAc signaling and intracellular motility. PLoS ONE 4, e4854.
Xing, L., Hu, P., Liu, J., Witek, K., Zhou, S., Xu, J., Zhou, W., Gao, L., Huang, Z., Zhang, R., et al. (2018). *Pm21* from *Haynaldia villosa* encodes a CC-NBS-LRR protein conferring powdery mildew resistance in wheat. Mol Plant 11, 874–878.
Xiong, H., Zhou, C., Fu, M., Guo, H., Xie, Y., Zhao, L., Gu, J., Zhao, S., Ding, Y., Li, Y., et al. (2022). Cloning and functional characterization of Rht8, a "Green Revolution" replacement gene in wheat. Mol Plant 15, 373–376.
Xu, C., Liberatore, K.L., MacAlister, C.A., Huang, Z., Chu, Y.H., Jiang, K., Brooks, C., Ogawa-Ohnishi, M., Xiong, G., Pauly, M., et al. (2015). A cascade of arabinosyltransferases controls shoot meristem size in tomato. Nat Genet 47, 784–792.
Xu, C., Wang, Y., Yu, Y., Duan, J., Liao, Z., Xiong, G., Meng, X., Liu, G., Qian, Q., and Li, J. (2012). Degradation of MONOCULM 1 by APC/CTAD1 regulates rice tillering. Nat Commun 3, 750.
Xu, G., Tao, Z., and He, Y. (2022). Embryonic reactivation of *FLOWERING LOCUS C* by ABSCISIC ACID-INSENSITIVE 3 establishes the vernalization requirement in each Arabidopsis generation. Plant Cell 34, 2205–2221.
Xu, Y., La, G., Fatima, N., Liu, Z., Zhang, L., Zhao, L., Chen, M.S., and Bai, G. (2021). Precise mapping of QTL for Hessian fly resistance in the hard winter wheat cultivar 'Overland'. Theor Appl Genet 134, 3951–3962.
Xu, S., and Chong, K. (2018). Remembering winter through vernalisation. Nat Plants 4, 997–1009.
Xu, S., Dong, Q., Deng, M., Lin, D., Xiao, J., Cheng, P., Xing, L., Niu, Y., Gao, C., Zhang, W., et al. (2021). The vernalization-induced long non-coding RNA *VAS* functions with the transcription factor TaRF2b to promote *TaVRN1* expression for flowering in hexaploid wheat. Mol Plant 14, 1525–1538.
Xu, S., Xiao, J., Yin, F., Guo, X., Xing, L., Xu, Y., and Chong, K. (2019). The protein modifications of *O*-GlcNAcylation and phosphorylation mediate vernalization response for flowering in winter wheat. Plant Physiol 180, 1436–1449.
Xu, T., Bian, N., Wen, M., Xiao, J., Yuan, C., Cao, A., Zhang, S., Wang, X., and Wang, H. (2017). Characterization of a common wheat (*Triticum aestivum* L.) high-tillering dwarf mutant. Theor Appl Genet 130, 483–494.
Xue, G.P., Drenth, J., and McIntyre, C.L. (2015). TaHsfA6f is a transcriptional activator that regulates a suite of heat stress protection genes in wheat (*Triticum aestivum* L.) including previously unknown Hsf targets. J Exp Bot 66, 1025–1039.
Xue, S., Li, G., Jia, H., Xu, F., Lin, F., Tang, M., Wang, Y., An, X., Xu, H., Zhang, L., et al. (2010). Fine mapping *Fhb4*, a major QTL conditioning resistance to Fusarium infection in bread wheat (*Triticum aestivum* L.). Theor Appl Genet 121, 147–156.
Xue, S., Xu, F., Tang, M., Zhou, Y., Li, G., An, X., Lin, F., Xu, H., Jia, H., Zhang, L., et al. (2011). Precise mapping *Fhb5*, a major QTL conditioning resistance to Fusarium infection in bread wheat (*Triticum aestivum* L.). Theor Appl Genet 123, 1055–1063.
Yahiaoui, N., Kaur, N., and Keller, B. (2009). Independent evolution of functional *Pm3* resistance genes in wild tetraploid wheat and domesticated bread wheat. Plant J 57, 846–856.
Yan, J., Liu, Y., Huang, X., Li, L., Hu, Z., Zhang, J., Qin, Q., Yan, L., He, K., Wang, Y., et al. (2019). An unreported NB-LRR protein SUT1 is required for the autoimmune response mediated by type one protein phosphatase 4 mutation (topp4-1) in *Arabidopsis*. Plant J 100, 357–373.
Yan, L., Fu, D., Li, C., Blechl, A., Tranquilli, G., Bonafede, M., Sanchez, A., Valarik, M., Yasuda, S., and Dubcovsky, J. (2006). The wheat and barley vernalization gene *VRN3* is an orthologue of *FT*. Proc Natl Acad Sci USA 103, 19581–19586.
Yan, L., Loukoianov, A., Blechl, A., Tranquilli, G., Ramakrishna, W., SanMiguel, P., Bennetzen, J.L., Echenique, V., and Dubcovsky, J. (2004). The wheat *VRN2* gene is a flowering repressor down-regulated by vernalization. Science 303, 1640–1644.
Yan, L., Loukoianov, A., Tranquilli, G., Helguera, M., Fahima, T., and Dubcovsky, J. (2003). Positional cloning of the wheat vernalization gene *VRN1*. Proc Natl Acad Sci USA 100, 6263–6268.
Yan, X., Li, M., Zhang, P., Yin, G., Zhang, H., Gebrewahid, T.W., Zhang, J., Dong, L., Liu, D., Liu, Z., et al. (2021). High-temperature wheat leaf rust resistance gene *Lr13* exhibits pleiotropic effects on hybrid necrosis. Mol Plant 14, 1029–1032.
Yang, J., Wang, M., Li, W., He, X., Teng, W., Ma, W., Zhao, X., Hu, M., Li, H., Zhang, Y., et al. (2019). Reducing expression of a nitrate-responsive bZIP transcription factor increases grain yield and N use in wheat. Plant Biotechnol J 17, 1823–1833.
Yang, Z., Zheng, J., Liu, C., Wang, Y., Condon, A.G., Chen, Y., and Hu, Y. G. (2015). Effects of the GA-responsive dwarfing gene *Rht18* from tetraploid wheat on agronomic traits of common wheat. Field Crops Res 183, 92–101.
Yao, F.Q., Li, X.H., Wang, H., Song, Y.N., Li, Z.Q., Li, X.G., Gao, X.Q., Zhang, X.S., and Bie, X.M. (2021). Down-expression of *TaPIN1s* increases the tiller number and grain yield in wheat. BMC Plant Biol 21, 443.
Yao, H., Xie, Q., Xue, S., Luo, J., Lu, J., Kong, Z., Wang, Y., Zhai, W., Lu, N., Wei, R., et al. (2019). *HL2* on chromosome 7D of wheat (*Triticum aestivum* L.) regulates both head length and spikelet number. Theor Appl Genet 132, 1789–1797.
Yong, W., Chong, K., Liang, T., Xu, Z., Tan, K., and Zhu, Z. (1999). Cloning and characterization of vernalization-related gene (ver203F) cDNA 3′ end. Chin Sci Bull 44, 1289–1294.
Yong, W., Xu, Y., Xu, W., Wang, X., Li, N., Wu, J., Liang, T., Chong, K., Xu, Z., Tan, K., et al. (2003). Vernalization-induced flowering in wheat is mediated by a lectin-like gene *VER2*. Planta 217, 261–270.
Yu, G., Matny, O., Champouret, N., Steuernagel, B., Moscou, M.J., Hernández-Pinzón, I., Green, P., Hayta, S., Smedley, M., Harwood, W., et al. (2022). *Aegilops sharonensis* genome-assisted identification of stem rust resistance gene *Sr62*. Nat Commun 13, 1607.
Yu, J., Wang, K., and Beckles, D.M. (2021). Starch branching enzymes as putative determinants of postharvest quality in horticultural crops. BMC Plant Biol 21, 479.
Yu, K., Liu, D., Chen, Y., Wang, D., Yang, W., Yang, W., Yin, L., Zhang, C., Zhao, S., Sun, J., et al. (2019). Unraveling the genetic architecture of grain size in einkorn wheat through linkage and homology mapping and transcriptomic profiling. J Exp Bot 70, 4671–4688.
Yu, S., Wu, J., Wang, M., Shi, W., Xia, G., Jia, J., Kang, Z., and Han, D. (2020). Haplotype variations in QTL for salt tolerance in Chinese wheat accessions identified by marker-based and pedigree-based kinship analyses. Crop J 8, 1011–1024.
Yuan, J., Sun, H., Wang, Y., Li, L., Chen, S., Jiao, W., Jia, G., Wang, L., Mao, J., Ni, Z., et al. (2022). Open chromatin interaction maps reveal functional regulatory elements and chromatin architecture variations

during wheat evolution. Genome Biol 23, 34.
Zachara, N.E., and Hart, G.W. (2004). *O*-GlcNAc a sensor of cellular state: the role of nucleocytoplasmic glycosylation in modulating cellular function in response to nutrition and stress. Biochim Biophys Acta (BBA)-Gen Subj 1673, 13–28.
Zadoks, J.C., Chang, T.T., and Konzak, C.F. (1974). A decimal code for the growth stages of cereals. Weed Res 14, 415–421.
Zang, X., Geng, X., Wang, F., Liu, Z., Zhang, L., Zhao, Y., Tian, X., Ni, Z., Yao, Y., Xin, M., et al. (2017). Overexpression of wheat ferritin gene *TaFER-5B* enhances tolerance to heat stress and other abiotic stresses associated with the ROS scavenging. BMC Plant Biol 17, 14.
Zeng, X.Y., Zhang, Z.Y., Du, L., Xin, Z.Y., and Chen, X. (2005). Development of wheat germplasms with multi-resistance to powdery mildew, stripe rust and yellow dwarf virus by molecular marker-assisted selection (in Chinese). Sci Agric Sin 38, 2380–2386.
Zhang, B., Liu, X., Xu, W., Chang, J., Li, A., Mao, X., Zhang, X., and Jing, R. (2015). Novel function of a putative *MOC1* ortholog associated with spikelet number per spike in common wheat. Sci Rep 5, 12211.
Zhang, C., Huang, L., Zhang, H., Hao, Q., Lyu, B., Wang, M., Epstein, L., Liu, M., Kou, C., Qi, J., et al. (2019a). An ancestral NB-LRR with duplicated 3′UTRs confers stripe rust resistance in wheat and barley. Nat Commun 10, 4023.
Zhang, D., Zhu, K., Dong, L., Liang, Y., Li, G., Fang, T., Guo, G., Wu, Q., Xie, J., Chen, Y., et al. (2019b). Wheat powdery mildew resistance gene *Pm64* derived from wild emmer (*Triticum turgidum* var. *dicoccoides*) is tightly linked in repulsion with stripe rust resistance gene *Yr5*. Crop J 7, 761–770.
Zhang, J., Li, B., Yang, Y., Mu, P., Qian, W., Dong, L., Zhang, K., Liu, X., Qin, H., Ling, H., et al. (2016a). A novel allele of L-galactono-1,4-lactone dehydrogenase is associated with enhanced drought tolerance through affecting stomatal aperture in common wheat. Sci Rep 6, 30177.
Zhang, J., Li, X.M., Lin, H.X., and Chong, K. (2019c). Crop improvement through temperature resilience. Annu Rev Plant Biol 70, 753–780.
Zhang, J., Wu, J., Liu, W., Lu, X., Yang, X., Gao, A., Li, X., Lu, Y., and Li, L. (2013). Genetic mapping of a fertile tiller inhibition gene, *ftin*, in wheat. Mol Breeding 31, 441–449.
Zhang, L., He, G., Li, Y., Yang, Z., Liu, T., Xie, X., Kong, X., and Sun, J. (2021a). PIL transcription factors directly interact with SPLs and repress tillering/branching in plants. New Phytol 233, 1414–1425.
Zhang, L., Dong, C., Chen, Z., Gui, L., Chen, C., Li, D., Xie, Z., Zhang, Q., Zhang, X., Xia, C., et al. (2021b). WheatGmap: a comprehensive platform for wheat gene mapping and genomic studies. Mol Plant 14, 187–190.
Zhang, L., Geng, M., Zhang, Z., Zhang, Y., Yan, G., Wen, S., Liu, G., and Wang, R. (2020). Molecular mapping of major QTL conferring resistance to orange wheat blossom midge (*Sitodiplosis mosellana*) in Chinese wheat varieties with selective populations. Theor Appl Genet 133, 491–502.
Zhang, L.J., Ju, X.T., Gao, X., and Zhang, F.S. (2005). Recovery of labeled nitrate-N in different soil layers by two kind of crops. Sci Agric Sin 36, 333–340.
Zhang, N., Yin, Y., Liu, X., Tong, S., Xing, J., Zhang, Y., Pudake, R.N., Izquierdo, E.M., Peng, H., Xin, M., et al. (2017a). The E3 ligase TaSAP5 alters drought stress responses by promoting the degradation of DRIP proteins. Plant Physiol 175, 1878–1892.
Zhang, P., Guo, G., Wu, Q., Chen, Y., Xie, J., Lu, P., Li, B., Dong, L., Li, M., Wang, R., et al. (2020). Identification and fine mapping of spot blotch (*Bipolaris sorokiniana*) resistance gene *Sb4* in wheat. Theor Appl Genet 133, 2451–2459.
Zhang, R., Fan, Y., Kong, L., Wang, Z., Wu, J., Xing, L., Cao, A., and Feng, Y. (2018a). *Pm62*, an adult-plant powdery mildew resistance gene introgressed from *Dasypyrum villosum* chromosome arm 2VL into wheat. Theor Appl Genet 131, 2613–2620.
Zhang, R., Sun, B., Chen, J., Cao, A., Xing, L., Feng, Y., Lan, C., and Chen, P. (2016b). *Pm55*, a developmental-stage and tissue-specific powdery mildew resistance gene introgressed from *Dasypyrum villosum* into common wheat. Theor Appl Genet 129, 1975–1984.
Zhang, R., Xiong, C., Mu, H., Yao, R., Meng, X., Kong, L., Xing, L., Wu, J., Feng, Y., and Cao, A. (2021c). *Pm67*, a new powdery mildew resistance gene transferred from *Dasypyrum villosum* chromosome 1V to common wheat (*Triticum aestivum* L.). Crop J 9, 882–888.
Zhang, R., Feng, Y., Li, H., Yuan, H., Dai, J., Cao, A., Xing, L., and Li, H. (2016). Cereal cyst nematode resistance gene *CreV* effective against *Heterodera filipjevi* transferred from chromosome 6VL of *Dasypyrum villosum* to bread wheat. Mol Breeding 36, 122.
Zhang, W., Chen, S., Abate, Z., Nirmala, J., Rouse, M.N., and Dubcovsky, J. (2017b). Identification and characterization of *Sr13*, a tetraploid wheat gene that confers resistance to the Ug99 stem rust race group. Proc Natl Acad Sci USA 114, E9483–E9492.
Zhang, X., Gao, M., Wang, S., Chen, F., and Cui, D. (2015). Allelic variation at the vernalization and photoperiod sensitivity loci in Chinese winter wheat cultivars (*Triticum aestivum* L.). Front Plant Sci 6, 470.
Zhang, X.K., Xiao, Y.G., Zhang, Y., Xia, X.C., Dubcovsky, J., and He, Z.H. (2008). Allelic variation at the vernalization genes *Vrn-A1*, *Vrn-B1*, *Vrn-D1*, and *Vrn-B3* in Chinese wheat cultivars and their association with growth habit. Crop Sci 48, 458–470.
Zhang, Y., Li, D., Zhang, D., Zhao, X., Cao, X., Dong, L., Liu, J., Chen, K., Zhang, H., Gao, C., et al. (2018b). Analysis of the functions of *TaGW2* homoeologs in wheat grain weight and protein content traits. Plant J 94, 857–866.
Zhang, Y., Li, Z., Zhang, Y., Lin, K., Peng, Y., Ye, L., Zhuang, Y., Wang, M., Xie, Y., Guo, J., et al. (2021d). Evolutionary rewiring of the wheat transcriptional regulatory network by lineage-specific transposable elements. Genome Res 31, 2276–2289.
Zhang, Y., Yang, Z., Ma, H., Huang, L., Ding, F., Du, Y., Jia, H., Li, G., Kong, Z., Ran, C., et al. (2021e). Pyramiding of Fusarium head blight resistance quantitative trait loci, *Fhb1*, *Fhb4*, and *Fhb5*, in modern Chinese wheat cultivars. Front Plant Sci 12, 694023.
Zhang, Z., Han, H., Liu, W., Song, L., Zhang, J., Zhou, S., Yang, X., Li, X., and Li, L. (2019d). Deletion mapping and verification of an enhanced-grain number per spike locus from the 6PL chromosome arm of *Agropyron cristatum* in common wheat. Theor Appl Genet 132, 2815–2827.
Zhang, Z., Running, K.L.D., Seneviratne, S., Peters Haugrud, A.R., Szabo-Hever, A., Shi, G., Brueggeman, R., Xu, S.S., Friesen, T.L., and Faris, J. D. (2021f). A protein kinase-major sperm protein gene hijacked by a necrotrophic fungal pathogen triggers disease susceptibility in wheat. Plant J 106, 720–732.
Zhang, Z.G., Lv, G., Li, B., Wang, J.J., Zhao, Y., Kong, F.M., Guo, Y., and Li, S.S. (2017c). Isolation and characterization of the *TaSnRK2.10* gene and its association with agronomic traits in wheat (*Triticum aestivum* L.). PLoS ONE 12, e0174425.
Zhao, G., Zou, C., Li, K., Wang, K., Li, T., Gao, L., Zhang, X., Wang, H., Yang, Z., Liu, X., et al. (2017). The *Aegilops tauschii* genome reveals multiple impacts of transposons. Nat Plants 3, 946–955.
Zhao, K.J., and Bao, W.K. (1995). A probable mechanism on the origin of salt-tolerant somaclonal variation in octoploid triticale. In: Li, Z.S., and Xin, Z.Y., ed. Proceedings of the Eighth International Wheat Genetics Symposium. Beijing: China Agricultural Scientech Press. 1043–1046.
Zhao, K.J., and Li, X.M. (1994). Octoploid triticale 40 years in China. In: Abstracts of the Third International Symposium on Triticale (Portugal). pF29.
Zhao, K., Xiao, J., Liu, Y., Chen, S., Yuan, C., Cao, A., You, F.M., Yang, D., An, S., Wang, H., et al. (2018). *Rht23* (*5Dq′*) likely encodes a *Q* homeologue with pleiotropic effects on plant height and spike compactness. Theor Appl Genet 131, 1825–1834.
Zhao, L., Lin, X., Yang, Y., Bie, X., Zhang, H., Chen, J., Liu, X., Wang, H., Jiang, J., et al. (2022). Chromatin reprogramming and transcriptional regulation orchestrate embryogenesis in hexaploid wheat. BioRxiv: 101101/20220121477188.
Zhao, R., Wang, H., Xiao, J., Bie, T., Cheng, S., Jia, Q., Yuan, C., Zhang,

R., Cao, A., Chen, P., et al. (2013). Induction of 4VS chromosome recombinants using the CS *ph1b* mutant and mapping of the wheat yellow mosaic virus resistance gene from *Haynaldia villosa*. Theor Appl Genet 126, 2921–2930.

Zhao, X., Fu, X., Yin, C., and Lu, F. (2021). Wheat speciation and adaptation: perspectives from reticulate evolution. aBIOTECH 2, 386–402.

Zhao, X., Guo, Y., Kang, L., Bi, A., Xu, D., Zhang, Z., Zhang, J., Yang, X., Xu, J., Xu, S., et al. (2022) Population genomics unravels the Holocene history of *Triticum-Aegilops* species. BioRxiv: 10.1101/2022.04.07.487499.

Zhao, Y., Ai, X., Wang, M., Xiao, L., and Xia, G. (2016). A putative pyruvate transporter TaBASS2 positively regulates salinity tolerance in wheat via modulation of *ABI4* expression. BMC Plant Biol 16, 109.

Zhao, Y., Dong, W., Zhang, N., Ai, X., Wang, M., Huang, Z., Xiao, L., and Xia, G. (2014). A wheat allene oxide cyclase gene enhances salinity tolerance via jasmonate signaling. Plant Physiol 164, 1068–1076.

Zheng, J., Liu, H., Wang, Y., Wang, L., Chang, X., Jing, R., Hao, C., and Zhang, X. (2014). *TEF-7A*, a transcript elongation factor gene, influences yield-related traits in bread wheat (*Triticum aestivum* L.). J Exp Bot 65, 5351–5365.

Zheng, L., Karim, M.R., Hu, Y.G., Shen, R., and Lan, P. (2021). Greater morphological and primary metabolic adaptations in roots contribute to phosphate-deficiency tolerance in the bread wheat cultivar Kenong199. BMC Plant Biol 21, 381.

Zheng, X., Liu, C., Qiao, L., Zhao, J., Han, R., Wang, X., Ge, C., Zhang, W., Zhang, S., Qiao, L., et al. (2020). The MYB transcription factor *TaPHR3-A1* is involved in phosphate signaling and governs yield-related traits in bread wheat. J Exp Bot 71, 5808–5822.

Zhou, J., Gu, B., Schlesinger, W.H., and Ju, X. (2016). Significant accumulation of nitrate in Chinese semi-humid croplands. Sci Rep 6, 25088.

Zhou, Y., Bai, S., Li, H., Sun, G., Zhang, D., Ma, F., Zhao, X., Nie, F., Li, J., Chen, L., et al. (2021). Introgressing the *Aegilops tauschii* genome into wheat as a basis for cereal improvement. Nat Plants 7, 774–786.

Zhou, Y., Zhao, X., Li, Y., Xu, J., Bi, A., Kang, L., Xu, D., Chen, H., Wang, Y., Wang, Y.G., et al. (2020). *Triticum* population sequencing provides insights into wheat adaptation. Nat Genet 52, 1412–1422.

Zhou, Y., Conway, B., Miller, D., Marshall, D., Cooper, A., Murphy, P., Chao, S., Brown-Guedira, G., and Costa, J. (2017). Quantitative trait loci mapping for spike characteristics in hexaploid wheat. Plant Genome 10, plantgenome2016.10.0101.

Zhu, H., Li, C., and Gao, C. (2020). Applications of CRISPR-Cas in agriculture and plant biotechnology. Nat Rev Mol Cell Biol 21, 661–677.

Zhu, J., Fang, L., Yu, J., Zhao, Y., Chen, F., and Xia, G. (2018). 5-Azacytidine treatment and *TaPBF-D* over-expression increases glutenin accumulation within the wheat grain by hypomethylating the *Glu-1* promoters. Theor Appl Genet 131, 735–746.

Zhu, J., Pearce, S., Burke, A., See, D.R., Skinner, D.Z., Dubcovsky, J., and Garland-Campbell, K. (2014). Copy number and haplotype variation at the *VRN-A1* and central *FR-A2* loci are associated with frost tolerance in hexaploid wheat. Theor Appl Genet 127, 1183–1197.

Zhu, X., Rong, W., Wang, K., Guo, W., Zhou, M., Wu, J., Ye, X., Wei, X., and Zhang, Z. (2022). Overexpression of *TaSTT3b-2B* improves resistance to sharp eyespot and increases grain weight in wheat. Plant Biotechnol J 20, 777–793.

Zou, S., Wang, H., Li, Y., Kong, Z., and Tang, D. (2018). The NB-LRR gene *Pm60* confers powdery mildew resistance in wheat. New Phytol 218, 298–309.