Semidwarfing genes have greatly increased wheat yields globally, yet the widely used gibberellin (GA)-insensitive genes *Rht-B1b* and *Rht-D1b* have disadvantages for seedling emergence. Use of the GA-sensitive semidwarfing gene *Rht13* avoids this pleiotropic effect. Here, we show that *Rht13* encodes a *nucleotide-binding site/leucine-rich repeat (NB-LRR)* gene. A point mutation in the semidwarf *Rht-B13b* allele autoactivates the NB-LRR gene and causes a height reduction comparable with *Rht-B1b* and *Rht-D1b* in diverse genetic backgrounds. The autoactive *Rht-B13b* allele leads to transcriptional up-regulation of pathogenesis-related genes including class III peroxidases associated with cell wall remodeling. *Rht13* represents a new class of reduced height (*Rht*) gene, unlike other *Rht* genes, which encode components of the GA signaling or metabolic pathways. This discovery opens avenues to use autoactive NB-LRR genes as semidwarfing genes in a range of crop species, and to apply *Rht13* in wheat breeding programs using a perfect genetic marker.

**Significance**

Conventional dwarfing genes increased wheat yields by disrupting plant hormone (gibberellin) signaling. Alternative wheat-dwarfing genes, suitable for use in additional environmental conditions, have been shown to encode components of gibberellin metabolism. Here, we found that the alternative dwarfing gene *Rht13* encodes an autoactive NB-LRR gene rather than a component of gibberellin signaling or metabolism. The autoactive *Rht13* allele (Rht-B13b) causes up-regulation of pathogenesis-related genes and affects cell wall properties. *Rht-B13b* reduces height to a comparable degree as conventional dwarfing genes and offers an additional benefit of increased stem strength. This discovery reveals an unexpected class of reduced height gene in wheat and opens up opportunities to use autoactive NB-LRR genes to reduce height in a range of crop species.
Results

Characterization of the Rht13 Phenotype in Magnif. The Rht13 semidwarfing gene was originally identified as an induced mutant in the Magnif background (22). We carried out a detailed characterization and found that Rht13 caused a 30 to 35% height reduction in both greenhouse and field conditions (birdcage) (Fig. 1). A comparison of internode lengths showed that most of the height reduction occurred in the peduncle, and this effect was confirmed in field-grown plants that were measured for height from early stem elongation to maturity (Fig. 1 C and D). Height differences were apparent after Zadoks growth stage 50, with reduced peduncle length accounting for most of the effect.

Fine Genetic Mapping of Rht13 to a Region on Chromosome 7B. Previously, Rht13 was mapped to the long arm of chromosome 7B and genetically linked to simple sequence repeats (SSR) marker gwm577 (21). An F3 population from a cross between parental lines ML45-S carrying Rht13 and tall line ML80-T was developed for fine mapping. Approximately 2,400 F3 gametes were screened with SSR markers gwm577 and wmc276 that were previously shown to flank the locus. The screen identified 21 recombinants that corresponded to less than 1 cM of genetic distance between flanking markers (Fig. 2A and SI Appendix, Table S2). Additional DNA markers were added to the genetic interval after parental lines were screened with the 9K and 90K wheat single nucleotide polymorphism (SNP) arrays (23, 24). In addition, the project was given early access in 2013 to the emerging physical map of chromosome 7B, which was part of the international initiative to generate maps of individual Chinese Spring chromosomes led by the IWGSC and Norwegian University of Life Sciences. Several BAC clones were assigned to the region, and markers that were developed from BAC sequences were added to the interval (SI Appendix, Table S2). In total, 33 DNA markers were added to the genetic interval. BAC sequence-derived markers 7J15.144I10.2_2 and 127M17.134P08.3 flanked the Rht13 locus on the proximal and the distal sides, respectively, and defined a genetic interval of approx. 0.1 cM (Fig. 2).

Next-Generation Sequencing Approaches Revealed a Single Amino Acid Change Between Expressed Genes in the Region on Chromosome 7B. The Rht13 region defined by flanking markers 7J15.144I10.2_2 and 127M17.134P08.3 corresponded to a 1.93-Mb interval on chromosome 7B in Chinese Spring RefSeqv1.0. To identify candidate SNPs in the interval, we generated an additional population from a Magnif x Magnif M cross and selected four short and two tall F3:F4 lines that were homozygous at Rht13. For each of these lines, we isolated chromosome 7B by flow sorting and then sequenced the chromosome using Illumina short-reads. We attempted to identify SNPs within the mapping interval by mapping this chrom-seq data to the RefSeqv1.0 genome sequence (25), but we found that over half of the 1.93-Mb interval had few reads mapping (1.07/1.93 Mb), which suggested haplotype divergence between Chinese Spring and Magnif. We then examined the alignment of chromosome 7B between Chinese Spring and several cultivars whose genome sequences were available from the 10+ Wheat Genomes Project (26). We found that CDC Stanley had significant haplotype divergence from Chinese Spring in the Rht13 interval on chromosome 7B (SI Appendix, Fig. S3); therefore, we tested whether CDC Stanley would be a more appropriate reference sequence. Using CDC Stanley as the reference, the flanking markers spanned 1.86 Mb on chromosome 7B (Fig. 2B). Within this interval, a 0.49-Mb region had more SNPs between all samples (four short and two tall F3:F4 lines derived from Magnif x Magnif M cross) and the reference sequence, suggesting some divergence between CDC Stanley and Magnif.

We identified 12 SNPs and 1 INDEL between the tall and short fixed lines in the mapping interval (Fig. 2C). To identify potential causal genes for Rht13, we carried out RNA-seq on developing peduncle tissues from four fixed short and four fixed tall F3:F4 lines from the same Magnif x Magnif M population that was used for chrom-seq. We found that one transcript within the interval from our de novo annotation was more highly expressed in Magnif M than Magnif samples (2.5-fold change, padj < 0.001; indicated by * in Fig. 2D). However, this transcript did not translate to a protein longer than 76 amino acids in any frame, suggesting that pseudogenization might have occurred. Since there were no obvious changes in expression levels of genes within the interval, except the putative pseudogene, we examined whether the SNP’s detected by chrom-seq were contained within any of the de novo assembled transcripts. We found that only 1 SNP (G to A at chr7B:714,391,008) was located within a transcript (Fig. 2E), and this SNP was predicted to cause...
an amino acid change within the conserved RNBS-A motif of the predicted protein sequence (Fig. 2F). A Kompetitive allele specific PCR (KASP) marker developed for the SNP cosegregated with the height phenotype in the Magnif x Magnif M population (SI Appendix, Fig. S4).

**The Amino Acid Change S240F Reduces Plant Height.** The expressed transcript with an amino acid change was predicted to encode an NB-LRR protein (Fig. 2F). The mutation was predicted to cause an amino acid substitution of the serine at position 240 to phenylalanine (S240F) in the RNBS-A motif (27). To test whether this amino acid change caused the reduced height phenotype observed in Magnif M, we searched the Cadenza TILLING population for mutations within closely related genes (28). Line Cadenza0453 was identified as carrying a gene that was 100% identical at the nucleotide level to the mutant NB-LRR gene at the Rht13 locus, resulting in the same amino acid change (S240F) as found in Magnif M. Examination of mega base-scale haplotypes (29) did not indicate a conserved haplotype across this region between Cadenza and CDC Stanley, instead only a small region encompassing Rht13 (10,377 bp) was 100% identical between these cultivars before Ns in the contig interrupted the alignment at both ends. The KASP marker developed for the mutation segregated within progeny derived from Cadenza0453.

Homozygous mutant plants (Rht-B13b) were on average 16.7 cm shorter than homozygous wild-type plants (Rht-B13a) at maturity in the Cadenza0453 background (Fig. 3A and B; P < 0.001, Student's t test). This difference in height was reflected in shorter peduncle and internode lengths, except for the first internode (SI Appendix, Table S5).

**Characterization of the Rht13 Reduced Height Phenotype in Different Genetic Backgrounds.** To assess the potential for use of Rht-B13b in breeding programs, we generated sister lines for Rht13 in three Australian elite backgrounds, alongside Rht-B1b (in EGA Gregory) or Rht-D1b (in Espada and Magenta) dwarfing alleles for comparison. We found that Rht-B13b stems elongated earlier than Rht-B1b or Rht-D1b stems, but final lengths were shorter.
than the tall sister lines due to an earlier arrest in growth (Fig. 4 A–C). This lower final length is largely due to the peduncle being shorter in Rht-B13b than in Rht-B1b or Rht-D1b plants (Fig. 4 D–F). No differences in spike length were observed. We found some differences in the effect between cultivars. In Magenta, Rht13 is a stronger dwarfing gene than Rht-D1b (shorter peduncle, no difference in lower internodes; 33.2% and 23.0% stem length reduction, respectively, compared with tall at Zadoks 77.0; P < 0.001, ANOVA with the post hoc Tukey test; Fig. 4 C and F). In Espada and EGA Gregory, the effect of Rht-B13b on height is comparable with Rht-D1b and Rht-B1b (Fig. 4 A, B, D, and E; reduction in stem length compared with tall at Zadoks 77.0 for Espada Rht-B13b 16.8%, Espada Rht-D1b 18.3%, EGA Gregory Rht-B13b 27.6%, EGA Gregory Rht-B1b 28.5%; P < 0.001 compared with tall, ANOVA with the post hoc Tukey test). Comparing Rht-B13b with tall plants lacking conventional dwarfing genes, the reductions in heights are larger in Magenta and EGA Gregory than Espada. Taken together, our results (Figs. 1, 3 and 4) show that Rht-B13b is effective at reducing height in a range of genetic backgrounds including lines from the United Kingdom (Cadenza), Australia (Espada, EGA Gregory, and Magenta), Argentina (Magnif), and the United States (Fielder).

**Fig. 3.** Validation that the S240F mutation in Rht-B13b causes a reduction in height. (A) Cadenza0453 segregates for plants homozygous for the wild-type allele Rht-B13a (Left) and mutant allele Rht-B13b (Right) and (B) Cadenza0453 height quantification, the black bars represent the mean, *** P < 0.001, Student’s t test. (C) Height of T1 progeny of two transgenic events (families 2 and 6) in Fielder background transformed with Rht-B13b allele, stunted plants are represented by points immediately above the X-axis (details in SI Appendix, Table S6). (D) and (E) show families 2 and 6, respectively. Null segregants (−) are on the left of each image.

**Rht-B13b is Autoactive and Causes a Cell Death Response in Nicotiana benthamiana.** The mutation causing the reduction in height (S240F; Fig. 2F) occurred in the RNBS-A domain of the NB-LRR protein at the same position as a mutation observed in the tomato (Lycopersicon esculentum) NB-LRR protein I-2 (Fig. 5A). In I-2, the mutation converting the serine (S) residue to a phenylalanine (F) caused autoactivation of the protein (31).
Therefore, we hypothesized that the S240F mutation in Rht13 would also result in autoactivation of the NB-LRR protein, up-regulating defense responses and reducing plant growth. We first tested this through heterologous expression of the wild-type (Rht-B13a) and mutant Rht13 gene (Rht-B13b) in tobacco leaves. We found that the Rht-B13b allele induced more cell death 5 d post inoculation than the Rht-B13a allele (Fig. 5B), which is a typical defense response to pathogen invasion.

No visible signs of cell death were observed in any of the wheat backgrounds containing Rht-B13b. It is possible that autoactivation of Rht13 in wheat might nevertheless enhance defense responses leading to a reduction in growth, without leading to cell death.

Fig. 4. Effect of Rht-B13b and conventional dwarfing alleles Rht-B1b and Rht-D1b on stem and peduncle length in different wheat backgrounds in the field. (A–C) stem length, (D–F) peduncle length, (A and D) EGA Gregory, (B and E) Espada and (C and F) Magenta. Letters indicate significant differences at maturity determined by a one-way ANOVA followed by the Tukey post hoc test (P < 0.05). Data points combine measurements from 5–20 individual field-grown plants. The error bars represent the SEM.

Fig. 5. Rht-B13b induces defense gene responses in N. benthamiana and wheat. (A) Alignment of the RNBS-A motif from Rht-B13a and Rht-B13b protein with the tomato I-2 protein and the I-2 mutant (S233F) that induces autoactivation. (B) Infiltration of Rht-B13b into N. benthamiana induces significantly more cell death (right side of leaf) than Rht-B13a (left side of leaf, no cell death observed). Black arrows indicate the infiltrated region. The experiment was repeated twice, on six plants each time, a representative result is shown 6 d post inoculation. Expression of PR genes PR3 (C–E) and PR4 (F–H) were measured in wheat basal peduncle (C, F), apical peduncle (D, G), and flag leaf blade (E, H). PR gene expression was normalized to actin. For each graph, the expression level is normalized to be 1 in Rht-B13a, error bars represent the SE (n = 3–4). Significant differences were calculated using a t test on log transformed values, *P < 0.05, **P < 0.01, ***P < 0.001.
death. We found that the expression level of PR genes PR3 and PR4 were >20-fold up-regulated in the basal peduncle in the Rht-B13b mutant compared with the Rht-B13a wild-type sibling Cadenza0453 (Fig. 5 C–F), suggesting that autoactivation of defense responses occurred in the Rht13 mutant plants in rapidly expanding tissue. PR4 was 15-fold up-regulated in the apical peduncle, but no significant difference was observed in PR3 expression (Fig. 5 D–G). No differences were observed in PR gene expression between Rht-B13b and Rht-B13a in the flag leaf blade (Fig. 5 E–H).

RNA-seq Analysis Reveals that Class III Peroxidases are Up-Regulated by Autoactive Rht13. To further explore the pathways through which Rht13 reduces height, we used the same RNA-seq data from peduncle samples of fixed lines from the Magnif x Magnif M population, which was previously used to identify the causal gene (see Fig. 2). We confirmed that PR genes were up-regulated in Magnif M (Rht-B13b) compared with Magnif (Rht-B13a) (SI Appendix, Fig. S6), similar to observations in Cadenza (Fig. 5 C–H). The fold changes observed were higher in the RNA-seq data (SI Appendix, Fig. S6) than the qPCR data (Fig. 5 C–H); however, PR4 up-regulation was only borderline significant (P = 0.05). The up-regulation of PR genes was consistent with up-regulation of defense response-associated genes in the Magnif M plants compared with Magnif, identified by gene ontology (GO) term enrichment (SI Appendix, Fig. S7). Overall, we found that more genes were up-regulated (1,560 genes) than down-regulated (726 genes) in Magnif M compared with Magnif (>two-fold, padj < 0.001). Up-regulated genes were enriched for GO terms including defense responses, cell wall organization, regulation of hydrogen peroxide metabolic processes, and salicylic acid biosynthetic processes. We did not detect any enrichment for genes related to GA signaling or biosynthesis. Down-regulated genes were associated with flavonoid biosynthetic processes, responses to cytokinin and photosynthesis (SI Appendix, Fig. S7).

We further hypothesized that the autoactivation of defense responses in the mutant line will cause the production of reactive oxygen species, which can promote cross-linking and cell wall stiffening leading to less growth (32, 33). To investigate this, we examined the expression of class III peroxidases that can use hydrogen peroxide in cross-linking reactions during cell wall organization and pathogen defense (34). We identified 218 class III peroxidases that were expressed in Magnif or Magnif M peduncle samples. Of these, 28 were significantly up-regulated in Magnif M (Rht-B13b) compared with Magnif (Rht-B13a) in the peduncle (padj < 0.001, >two-fold, Fig. 6A), which is a significantly greater proportion than would be expected for a set of 218 random genes (12.8% vs. 2.6%, chi-squared test, P < 0.001). Furthermore, many of the class III peroxidase genes were very strongly up-regulated (11/28 are up-regulated >10-fold).

We found that Magnif M (Rht-B13b) peduncles had lower hydrogen peroxide content than Magnif (Rht-B13a) (Fig. 6B, P < 0.05, Student’s t test), consistent with the up-regulation of class III peroxidases in the mutant (Fig. 6A). Expression levels of other families of enzymes that affect hydrogen peroxide levels in cell walls were not substantially different between Magnif M (Rht-B13b) and Magnif (Rht-B13a) peduncles (1/23 NADPH oxidase genes was up-regulated padj < 0.001, >two-fold, none were down-regulated, 0/4 oxalate oxidases (germin-like proteins), and 0/15 Ca/Zn superoxide dismutase genes were differentially expressed, P > 0.05). To test whether the changes to class III peroxidase gene expression and hydrogen peroxide content influence cell wall mechanical properties, we used a three-point bend test to measure peduncle strength and rigidity. We found that the Magnif M (Rht-B13b) peduncles were stronger and more rigid than Magnif (Rht-B13a) peduncles (Fig. 6C and D, P = 0.02 and P = 0.003 respectively, Student’s t test). The Magnif M (Rht-B13b) peduncles had shorter cell lengths in their epidermis, with cell lengths of approximately 2/3 of wild type, suggesting a lower level of cell expansion (Fig. 6E). To investigate whether these mechanical changes are mediated by changes to lignification, we examined cross-sections of the peduncle taken from the apical part of the peduncle immediately under the ear, the midpoint of the peduncle, and the basal part of the peduncle just above the node. Using toluidine blue, we did not observe any obvious morphological changes (Fig. 6F), and no significant differences in lignification were observed between Magnif and Magnif M in the apical or middle peduncle (Fig. 6G). However, the basal sections of Magnif M (Rht-B13b) peduncles had much lower staining of lignin in and around vascular bundles than the Magnif (Rht-B13a) (Fig. 6G).

Discussion

Novel Mechanism for a Wheat Rht Gene. A striking difference to other reported Rht genes in wheat is that Rht13 is not directly involved in GA signaling or metabolism, as is the case for conventional dwarfing genes Rht-B1b and Rht-D1b (2) and the cloned alternative dwarfing genes Rht12 (11), Rht18 (8), and Rht24 (13). Instead, Rht13 is an NB-LRR gene with a point mutation that induces autoactivation. The amino acid change in Rht13 is the same mutation as previously characterized in the tomato protein I-2, which impeded ATP hydrolysis and promoted an ATP-bound active form of the protein (31). Due to the high conservation between the RNBS-A motif between I-2 and Rht13, we hypothesize that the mutation in Rht13 has the same biochemical function to impede ATP hydrolysis, consistent with the hypersensitive response (HR) we observed upon expressing Rht-B13b in N. benthamiana leaves.

Autoactive NB-LRR genes have been reported to reduce growth in several plant species (35–37), including causing reduced internode length in flax (38). However, autoactive NB-LRRs are often associated with negative pleiotropic effects including a spontaneous HR resulting in necrotic lesions. We did not observe any spontaneous HR or necrosis in any of the wheat genetic backgrounds tested. Similarly, transgenic flax lines expressing specific autoactive alleles of the L6 NB-LRR gene showed a reduction in height without necrosis (38), suggesting that it may be possible to identify autoactive alleles to alter growth without negative pleiotropic effects in a range of plant species. Rht-B13b behaves differently from known autoactive NB-LRR genes in cereals that reduce height, such as Rp1-D21 in maize which induces a spontaneous HR in a range of genetic backgrounds, although to differing degrees of severity (35). Nevertheless, Rht-B13b induced a HR in tobacco, which could be a result of high transient expression in tobacco, although overexpression of Rht-B13b in wheat did not cause a HR despite severe stunting. One possibility is that the cell death response in wheat is suppressed by the presence of homologous genes, as was observed for the Pm8 resistance gene to powdery mildew, which was suppressed by its homolog Pm3 (39). It is also possible that tissue-specific expression of Rht13 in wheat or differences in signaling pathway thresholds between tobacco and wheat may explain these differences. This is supported by our finding that PR genes were up-regulated only in peduncle tissues, and not in the flag leaves of Cadenza Rht-B13b. The up-regulation of PR genes in Rht-B13b containing wheat raises the question whether Rht-B13b could also enhance resistance response to certain pathogens. Autoactive mutants in flax, potato,
and tomato were shown to gain additional specificities to strains of the same pathogen or became effective against other pathogen species (38, 40, 41), but further research will be required to determine any association between 

Among the PR genes up-regulated by Rht-B13b are class III peroxidases which are known to act in a wide range of physiological processes, including cross-linking of cell wall components, formation of lignin, and metabolism of reactive oxygen species such as hydrogen peroxide (34). The up-regulation of class III peroxidases is associated with reduction in peduncle growth. Therefore, the gene is well suited to water-limiting environments that require deeper planting to access available moisture and rapid leaf area development to lower evaporative losses from the soil surface.

Applications in Agriculture. Rht13 is effective in multiple genetic backgrounds and provides a height reduction similar to conventional dwarfing genes Rht-B1b and Rht-D1b. Rht13 dwarfism is not associated with reduced seedling growth or coleoptile length, and most of the height-reducing effect occurs later in development (after Zadoks stage 50), which is mainly associated with reduction in peduncle growth. Therefore, the gene is well suited to water-limiting environments that require deeper planting to access available moisture and rapid leaf area development to lower evaporative losses from the soil surface. We found that Rht-B13b increased bending strength, which may further decrease lodging and reduce yield losses compared with...
in breeding programs. It is possible that Rht-B13b mutation is already circulating in some breeding materials, for example, in the WM-800 eight-way MAGIC population of European winter wheat cultivars, a significant quantitative trait locus (QTL) was identified on chromosome 7B, for which the peak SNP marker maps only 10 Mb away from the location of Rht13 (42). However, no height QTL was identified on chromosome 7B in other MAGIC populations including a diverse UK 16 founder MAGIC population (43) and an Australian four-way MAGIC population (44).

In conclusion, the identification of an NB-LRR gene underlying an alternative dwarfing gene in wheat has provided insight into an alternative pathway, where GA biosynthesis or signaling is not directly affected. This discovery will open up opportunities to alter height, potentially through engineering of autoactive NB-LRR genes and cell wall enzymes. More knowledge will be needed to establish whether the activation of defense responses by Rht-B13b could influence disease resistance.

Methods

All methodological information is available in SI Appendix, Materials and Methods. This includes details about plant materials, genetic mapping, chromosome-seq, RNA-seq, candidate gene identification and validation (transgenics and TILLING), heterologous N. benthamiana expression, qPCR, hydrogen peroxide, cell size, and stem property measurements.

Data, Materials, and Software Availability. The data that support the findings of this study are available in the SI Appendix of this article, and raw reads for the chromosome-seq and RNA-seq are deposited as PRJEB51492 (45) in the European Nucleotide Archive. BAC sequences have been deposited with NCBI under accessions OP009266 (46) and OP009267 (47).

Acknowledgments. We thank Zbigniew Stachurski for assistance with stem physical property measurements and Bujie Zhan for assistance with BAC libraries. We thank Jan Vrána, Zdeňka Dubska, Romana Šperková, and Jitka Weiserová for assistance with chromosome sorting and DNA amplification. This research was supported by the Norwegian BioSciences Institutes Research Computing group through high performance computing resources. This work was supported by the UK Biotechnology and Biological Science Research Council (BBSRC) through the Designing Future Wheat Institute Strategic Programme (BB/P016855/1). P.B. acknowledges funding from the Rank Prize New Lecturer Award and a Royal Society Research Grant (RG1311191163). I.M. was supported from Marie Curie Fellowship grant award “AEGILWHEAT” (H2020-MSCA-IF-2016-746253). J.D. was supported from European Regional Development Fund project “Plants as a tool for sustainable global development” (No. CZ.02.1.01/0.0/0.0/16_019/0000827). O.A.O. thanks Graminor AS and the Norwegian Research Council (NFR) for financial support for NFR project 199387 at the Norwegian University of Life Sciences.

Author affiliations: aJohn Innes Centre, Norwich Research Park, Norwich, NR4 7UH, UK; bCommonwealth Scientific and Industrial Research Organisation (CSIRO) Agriculture and Food, Canberra, ACT 2601, Australia; cInstitute of Molecular, Cell and Systems Biology, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow G12 8QQ, UK; dGrains Research and Development Corporation, Canberra, ACT2600, Australia; eResearch School of Biology, The Australian National University, Canberra, ACT 2601, Australia; fInstitute of Experimental Botany of the Czech Academy of Sciences, Centre of the Region Hana for Biotechnological and Agricultural Research, Olomouc, 783 71 Czech Republic; gGrain Research Laboratory, Canadian Grain Commission, Winnipeg, MBR3C 3G8, Canada; hUniversity of Saskatchewan, Saskatoon, SK S7N 5A8 Canada; iUniversity of Ottawa, Ottawa, ON, Canada; and jNorwegian University of Life Sciences, As, 1432, Norway.

1. P. Hedden, The genes of the Green Revolution. Trends Genet. 19, 5–9 (2003).
2. J. Peng et al., ‘Green revolution’ genes encode mutant gibberellin response modulators. Nature 400, 25–26 (1999).
3. S. S. Thomas, Novel Rht-1 dwarfing genes: Tools for wheat breeding and dissecting the function of DELLA proteins. J. Exp. Bot. 68, 2417–2424 (2017).
4. R. E. Allan, Influence of semidwarfism and genetic background on stand establishment of wheat. Crop Sci. 20, 634–638 (1980).
5. Sinivasachary et al., Semi-dwarfing Rht-B1 and Rht-D1 loci of wheat differ significantly in their influence on resistance to Fusarium head blight. Theor. Appl. Genet. 118, 695–702 (2009).
6. R. A. Richards et al., Breeding for improved water productivity in temperate cereals: Phenotyping, quantitative trait loci, markers and the selection environment. Funct. Plant Biol. 37, 85–97 (2010).
7. R. A. McIntosh, J. Dubcovsky, W. J. Rogers, X. C. Xia, W. J. Raupp, Catalogue of Gene Symbols for Wheat. https://wheat.pw.usda.gov/GG3/WGC (2020). Accessed 10 January 2022.
8. B. A. Ford et al., Rht8 semidwarfism in wheat is due to increased GA2-oxidaseA9 expression and reduced GA content. Plant Physiol. 177, 168–180 (2018).

9. M. Haque, F. Martinek, N. Watanabe, I. Kuboyama, Genetic mapping of gibberellic acid-sensitive genes for semi-dwarfism in durum wheat. Cereal Res. Commun. 39, 177–178 (2011).

10. T. Tang, Physiological and Genetic Studies of an Alternative Semi-Dwarfing Gene Rht18 in Wheat (University of Texas, 2016).

11. W. Buss et al., Overgrowth mutants determine the causal role of gibberellin GA2oxidaseA73 in Rht12 dwarfism of wheat. J. Exp. Bot 71, 7171–7178 (2020).

12. L. Sun et al., A wheat dominant dwarfing line with Rht12, which reduces stem cell length and affects gibberellic acid synthesis, is a 5AL terminal deletion line. Plant J. 97, 887–900 (2019).

13. X. Tian et al., Rht24b, an ancient variation of TaGA2oxA9, reduces plant height without yield penalty in wheat. New Phytol. 233, 739–750 (2022).

14. S. Pearce et al., Heterologous expression and transcript analysis of gibberellin biosynthetic genes of grasses reveals novel functionality in the GA4ox family. BMC Plant Biol 15, 130 (2015).

15. M. H. Ellis et al., The effect of different height reducing genes on the early growth of wheat. Funct. Plant Biol. 31, 583–589 (2004).

16. G. J. Rebetzke et al., The Rht13 dwarfing gene reduces peduncle length and plant height to increase grain number and yield of wheat. Field Crops Res. 124, 323–331 (2011).

17. G. J. Rebetzke et al., Height reduction and agronomic performance for selected gibberellin-responsive dwarfing genes in bread wheat (Triticum aestivum L.). Field Crops Res. 126, 87–96 (2012).

18. Y. Wang et al., Genetic effect of dwarfing gene Rht13 compared with Rht12 on plant height and some agronomic traits in common wheat (Triticum aestivum L.). Field Crops Res. 162, 39–47 (2014).

19. Y. Wang et al., Comparing the effects of GA-responsive dwarfing genes Rht13 and Rht8 on plant height and some agronomic traits in common wheat. Field Crops Res. 179, 35–43 (2015).

20. M. G. Drayshuk et al., Effect of gibberellin-responsive reduced height allele Rht13 on agronomic traits in spring bread wheat in field experiment in non-black soil zone. Agronomy 10, 927 (2020).

21. M. H. Ellis, G. J. Rebetzke, F. Avanza, R. A. Richards, W. Spielmeyer, Molecular mapping of gibberellin-responsive dwarfing genes in bread wheat. Theor. Appl. Genet. 111, 423–430 (2005).

22. C. Konzak, ‘Evaluation and genetic analysis of semi-dwarf mutants of wheat in Semi-Dwarf Wheat Mutants and Their Use in Cross-Breeding’. Research Coordination Meeting 1981 (International Atomic Energy Agency, Vienna, Austria, 1982), pp. 25–37.

23. C. R. Cavanagh et al., Genome-wide comparative diversity uncovers multiple targets of selection for improvement in hexaploid wheat landraces and cultivars. Proc. Natl. Acad. Sci. U.S.A. 110, 8057–8062 (2013).

24. S. Wang et al., Characterization of polyploid wheat genomic diversity using a high-density 90,000 single nucleotide polymorphism array. Plant Biotechnol. J. 12, 787–796 (2014).

25. MGIC et al., Shifted limits in ‘Arabidopsis’ research and breeding using a fully annotated reference genome. Science 361, eaar7191, (2018).

26. S. Walkowski et al., Multiple wheat genomes reveal global variation in modern breeding. Nature 588, 277–283 (2020).

27. B. C. Meyer, A. Kozai, A. Greigco, H. Kuang, R. W. Michelmore, Genome-wide analysis of NBS-LRR-encoding genes in Arabidopsis. Plant Cell 15, 809–834 (2003).

28. K. V. Krasilova et al., Uncovering hidden variation in polyploid wheat. Proc. Natl. Acad. Sci. U.S.A 114, E1913–E1921 (2017).

29. J. Brinton et al., A haplotype-led approach to increase the precision of wheat breeding. Commun. Biol. 3, 712 (2020).

30. K. Sato et al., Chromosome-scale genome assembly of the transformation-amenable common wheat cultivar ‘Fielder’. DNA Res. 28, dial008 (2021).

31. W. I. L. Tameling et al., Mutations in the NB-ARC domain of I-2 that impair ATP hydrolysis cause autoactivation. Plant Physiol. 140, 1233–1245 (2006).

32. V. Schopfer et al., Hydrogen peroxide-mediated cell-wall stiffening in vitro in maize coleoptiles. Planta 199, 43–49 (1996).

33. R. Schmidt et al., A. B. Kunkowska, J. H. M. Schippers, Role of reactive oxygen species during cell expansion in leaves. Plant Physiol. 172, 2098–2106 (2016).

34. N. Smirnoff et al., Hydrogen peroxide metabolism and functions in plants. New Phytol. 221, 1197–1214 (2019).

35. S. Chimatanan et al., S. H. Hubert et al., P. J. Balint-Kurti, Identification of a gene that modulates the hypersensitive defense response, using mutant-assisted gene identification and characterization. Genetics 184, 813–825 (2010).

36. S. Yang et al., A haplotype-specific resistance gene regulated by BONZAI1 mediates temperature-dependent growth control in Arabidopsis. Plant Cell 16, 1060–1071 (2004).

37. M. Roberts et al., S. Tang, A. Stallmann, J. L. Dangl, V. Bonardi, Genetic requirements for signaling from an autoactive plant NB-LRR intracellular innate immune receptor. PLOS Genet. 9, e1003465. (2013).

38. P. Howles et al., Autoactive alleles of the flax Le rust resistance gene induce non-race-specific rust resistance associated with the hypersensitive response. Mol. Plant Microbe Interact. 18, 570–582 (2005).

39. S. Hurni et al., The powdery mildew resistance gene Pm8 derived from rye is suppressed by its wheat ortholog Pm3. Plant J. 79, 904–913 (2014).

40. G. Farnham et al., Artificial evolution extends the spectrum of viruses that are targeted by a disease-resistance gene from potato. Proc. Natl. Acad. Sci. U.S.A. 103, 18828–18833 (2006).

41. A. Giannakopoulou et al., Tomato I2 immune receptor can be engineered to confer partial resistance to the oomycete Phytophthora infestans in addition to the fungus Fusarium avenaceum. Mol. Plant-Microbe Interact. 28, 1316–1329 (2015).

42. W. Sennemann et al., Adaptive selection of founder segments and epistatic control of plant height in the MAGIC winter wheat population WM-800. BMC Genomics 19, 559 (2018).

43. M. F. Scott et al., Limited haplotype diversity underlies polygenic trait architecture across 70 years of wheat breeding. Genome Biol. 22, 1–30 (2021).

44. B. E. Huang et al., A multiparent advanced generation inter-crop population for genetic analysis in wheat. Plant Biotechnol. J. 10, 826–839 (2012).

45. P. Borrelli et al., Spielmeyer, Triticum aestivum clone BAC 7J15.144010_2 sequence. National Centre for Biotechnology Information. https://www.ncbi.nlm.nih.gov/nuccore/OP095266.1. Deposited 27 July 2022.

46. P. Borrelli et al., Spielmeyer, Triticum aestivum clone BAC 127M17.134PD08_3 sequence. National Centre for Biotechnology Information. https://www.ncbi.nlm.nih.gov/nuccore/op095267. Deposited 27 July 2022.