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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	1) Passport data of wheat accessions were collected from the websites (https://npgsweb.ars-grin.gov/gringlobal/search; http://wgb.cimmyt.org/gringlobal/search.aspx; http://wheatpedigree.net/; https://www.cgris.net/query/croplist.php#; https://www.ipk-gatersleben.de/en/gbisipk-gaterslebendegbis-i/). 2) Disease scores were recorded manually. 3) The newly sequencing was performed using BGISEQ500 on the DNBSEQ platform. 4) Publicly available data were downloaded and used. 5) The initial mutation information of EMS mutants was collected from the Wheat JING411 TILLING Database (http://jing411.molbreeding.com) and WheatOmics v1.0 (http://wheatomics.sdau.edu.cn). 6) Functional domains in different TaEDR2-B proteins were predicted by SMART v9 web-tool (https://smart.embl.de). 7) The images of yellow rust responses of the gene-silenced plants were recorded at 14 days post inoculation (dpi) using fluorescence microscope (Olympus BX-63, Japan).
Data analysis	1) From raw sequencing reads to VCF files conversion a series of softwares were used: BWA-MEM (v0.7.17), SAMtools (v1.11), GATK (v.4.1.8.0), snpEff (v.5.1d), VCFtools (v.0.1.17). 2) The lme4 package in R 3.5.3 was used for best linear unbiased estimations (BLUEs), variance components and broad-sense heritability. 3) Additional softwares: ADMIXTURE (v1.3.0) for population structure; plink (v1.90) for linkage disequilibrium computation and PCA; FastTree (v 2.1.11) for the unrooted neighbour-joining phylogenetic tree; rMVP for GWAS; Beagle v.5.4 for 660K SNP array marker imputation; MEGA7.0 for phylogenetic tree of START protein family.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The raw sequence data of 349 newly sequenced accessions and RNA-seq were deposited in the Genome Sequence Archive (https://ngdc.cncb.ac.cn/gsa/) under the accession number (GSA: CRA004322, CRA014998, CRA005878 and CRA021484). The SNP matrix was also uploaded to the Genome Variation Map (GVM) in the National Genomics Data Center, Beijing Institute of Genomics, Chinese Academy of Sciences and China National Center for Bioinformation (https://bigd.big.ac.cn/gvm) under accession number GVM000830. The sequence data of the remaining 1,228 accessions were downloaded from the Sequence Read Archive (https://www.ncbi.nlm.nih.gov/sra) under accession numbers PRJNA663409, PRJNA476679, PRJNA596843, and PRJNA439156. Additionally, raw sequence data have also been deposited in the European Nucleotide Archive (https://www.ebi.ac.uk/ena/) under the following Project IDs: PRJEB41976 (GBS), PRJEB48988 (WGS), and PRJEB48738 (WGS).

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	N/A
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	N/A

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Our sample of 14,688 common wheat accessions cover most of the yellow rust epidemics regions, 1,629 of 14,688 wheat accessions were carefully chosen to cover most of the diversity of worldwide wheat according to their growth habitat, status (i.e. landraces or cultivars), geographical origin, and diversity of genetics and phenotype. Five hundred and sixty-two among 768 genotyped common wheat accessions by WGS from German national genebank were also integrated into this study to generate a high-density genome variation map and validate the frequencies of favorable haplotypes. Additionally, 280 K SNP genotyping data for 4,506 wheat accessions in the INRAE global collection were also used in evaluating genetic diversity. The entire panel of 1,629 accessions was used for GWAS analyses at different levels.
Data exclusions	No data were exclude from the analyses.
Replication	1) From raw sequencing reads to VCF files conversion a series of softwares were used: BWA-MEM (v0.7.17), SAMtools (v1.11), GATK (v.4.1.8.0), snpEff (v.5.1d), VCFtools (v.0.1.17). 2) The lme4 package in R 3.5.3 was used for best linear unbiased estimations (BLUEs), variance components and broad-sense heritability. 3) Additional softwares: ADMIXTURE (v1.3.0) for population structure; plink (v1.90) for linkage disequilibrium computation and PCA; FastTree (v 2.1.11) for the unrooted neighbour-joining phylogenetic tree; rMVP for GWAS; Beagle v.5.4 for 660K SNP array marker imputation; MEGA7.0 for phylogenetic tree of START protein family.
Randomization	A randomized complete block design (RCBD) was used for phenotypic data collection. Random shuffling of samples was performed using the "sample()" function in R.
Blinding	Blinding is not necessary for sampling accessions for genome sequencing. The samples for genome sequencing were selected based on their

Blinding	geographic distribution and phylogenetic tree to cover the geographic distribution and genetic diversity of the species. The investigators were blinded to the population structure or origin of accessions when collecting trait data in the field.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☐	☒ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Dual use research of concern

Policy information about dual use research of concern

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes
☒	☐ Public health
☒	☐ National security
☒	☐ Crops and/or livestock
☒	☐ Ecosystems
☒	☐ Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes
☒	☐ Demonstrate how to render a vaccine ineffective
☒	☐ Confer resistance to therapeutically useful antibiotics or antiviral agents
☒	☐ Enhance the virulence of a pathogen or render a nonpathogen virulent
☒	☐ Increase transmissibility of a pathogen
☒	☐ Alter the host range of a pathogen
☒	☐ Enable evasion of diagnostic/detection modalities
☒	☐ Enable the weaponization of a biological agent or toxin
☒	☐ Any other potentially harmful combination of experiments and agents

Plants

Seed stocks	The wheat accessions are available at CGRIS, NSGC, IPK genebank, ICARDA genebank, and CIMMYT Wheat Germplasm Bank. More details are listed in Supplementary Table 1.
Novel plant genotypes	1)The 11 T2 independent transgenic lines for TaEDR2-B and 9 T1 transgenic lines for Yr5x were generated by agrobacterium-mediated transformation. 2) The EMS mutants of Jing 411 for TaEDR2-B was collected from http://jing411.molbreeding.com. 3)The CRISPR-Cas9 genome editing system were used to knock out Yr6/Pm5 and generate yr6 mutant lines. The target sequences for the single guide RNA (sgRNA) are listed in Table S24.
Authentication	1) Each seed stock is assigned a unique identifier and accompanied by detailed records of its origin, collection methods, storage conditions, and any relevant genetic or phenotypic information. 2) Molecular marker techniques, such as DNA sequencing or genotyping by SNP array, are employed to generate a unique genetic fingerprint for each seed stock. 2) For CRISPR-Cas9 mutants and transgenic lines, we can perform molecular marker detection using the primers. The primers sequences are listed in Table S24.