

# Climate-related naturally occurring epimutation and their roles in plant adaptation in *A. thaliana*

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## Abstract

DNA methylation has been proposed to be an important mechanism that allows plants to respond to their environments sometimes entirely uncoupled from genetic variation. To understand the genetic basis, biological functions and climatic relationships of DNA methylation at a population scale in *Arabidopsis thaliana*, we performed a genome-wide association analysis with high-quality single nucleotide polymorphisms (SNPs), and found that ~56% on average, especially in the CHH sequence context (71%), of the differentially methylated regions (DMRs) are not tagged by SNPs. Among them, a total of 3235 DMRs are significantly associated with gene expressions and potentially heritable. 655 of the 3235 DMRs are associated with climatic variables, and we experimentally verified one of them, *HEI10* (HUMAN ENHANCER OF CELL INVASION NO.10). Such epigenetic loci could be subjected to natural selection thereby affecting plant adaptation, and would be expected to be an indicator of accessions at risk. We therefore incorporated these climate-related DMRs into a gradient forest model, and found that the natural *A. thaliana* accessions in Southern Europe that may be most at risk under future climate change. Our findings highlight the importance of integrating DNA methylation that is independent of genetic variations, and climatic data to predict plants' vulnerability to future climate change.

## KEY WORDS

DNA methylation, genetic basis, global climate change, gradient forest, plants vulnerability

## 1 | INTRODUCTION

Global climate change is posing a profound threat to life on Earth and leads to a drastic decrease of the numbers and variety of plants, animals and other organisms (Dawson et al., 2011; Pacifici et al., 2015; Walther et al., 2002; Warren et al., 2013). To avoid extinction in the rapidly alternative environments, species must either migrate to other suitable locations or adapt or respond to the new conditions in current habitats through the phenotypic plasticity, genetic or epigenetic variations (Aitken et al., 2008; Bossdorf et al., 2008; Davis & Shaw, 2001). Unlike animals, migrations, in order to keep pace with climate change, may be difficult for most of the plant species (De Lafontaine et al., 2018). Therefore, understanding and quantifying the relations between the genomic variations and climate is not only relevant for understanding how species can persist in the context of climate change, but it could also benefit conservation and management strategies of the species to cope with global biodiversity loss (Browne et al., 2019; Waldvogel et al., 2020).

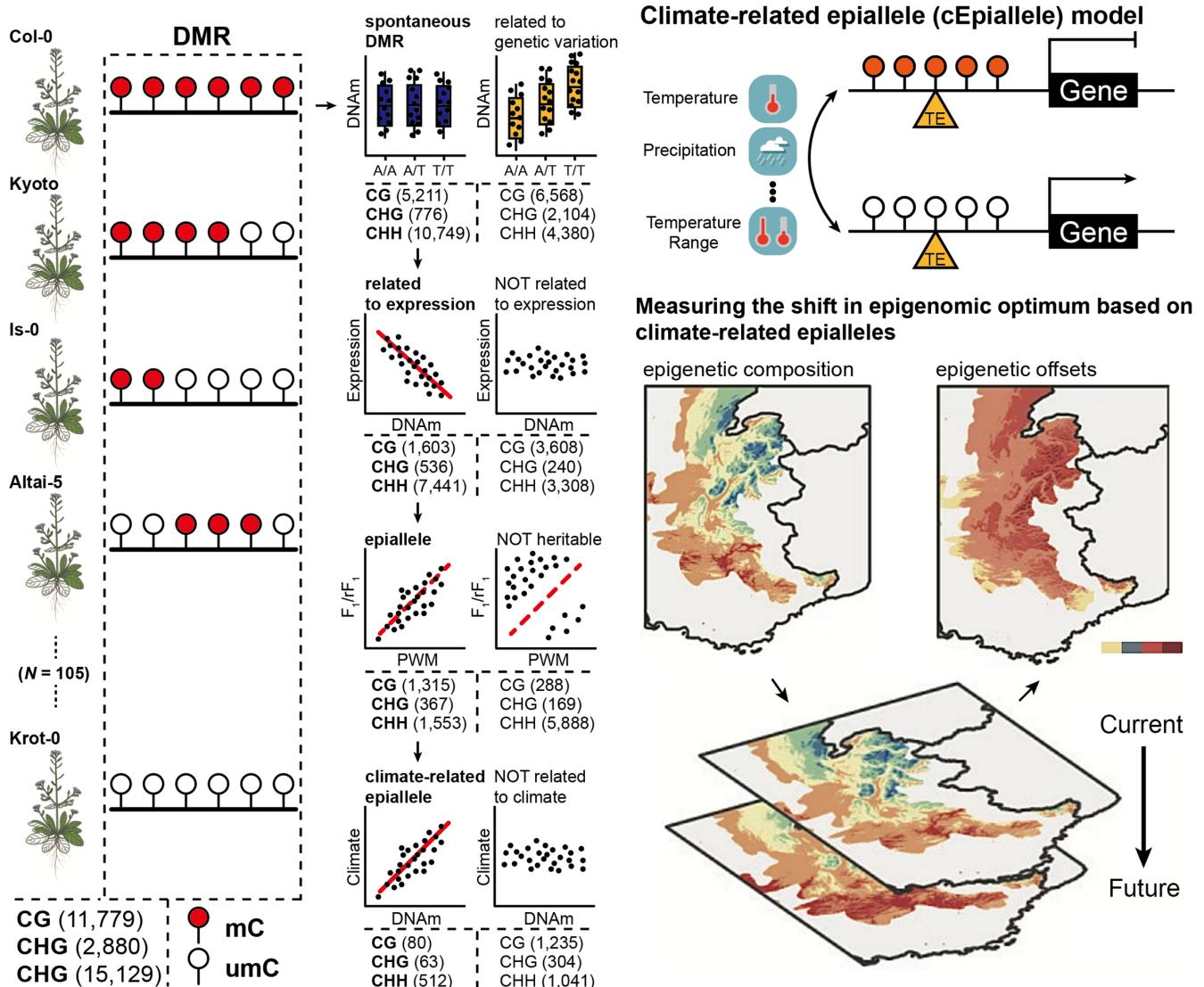
Ecological genetics has been informative about how natural selections can result in the associations of genetic structure or candidate genes with environments (Mooney et al., 2010; Yang et al., 2016). Besides, epigenetics can provide an additional mechanism to facilitate plants responses to short- or long-term environmental changes (Becker & Weigel, 2012; He et al., 2018; Richards, 2006, 2011; Verhoeven et al., 2016). Currently, the most studied and well-known epigenetic mechanism in ecology is DNA methylation (Angers et al., 2010; Bossdorf et al., 2008; Flores et al., 2013; Richards et al., 2017). It can occur in three sequence backgrounds in plants: CG, CHG and CHH ( $H=A, T, \text{ or } C$ ). DNA methylation often varies across different individuals of the same species, and some of them could be resulted from genetic variations, such as transposon insertions or rearrangements cause the changes in methylation (obligatory or facilitated epimutations) (Luff et al., 1999; Richards, 2006; Vidalis et al., 2016). However, DNA methylation variations may occur at a faster and higher rate ( $\sim 4.43 \times 10^{-4}$ ) than do DNA sequence alterations ( $\sim 7.00 \times 10^{-9}$ ) (Banta & Richards, 2018; Graaf et al., 2015; Ossowski et al., 2010), suggesting that DNA methylome patterns could be significantly shaped without presence of genetic variations. As such, excluding the effect of genetic variation on DNA methylation is an important basis for the explorations of the pure epigenetics. In general, such epigenetic variations that occurs in the absence of any causative genetic variations, are referred to as the spontaneous epimutations (Johannes & Schmitz, 2019), and those can be further able to regulate gene expressions and also be heritable, are referred to as the epialleles. However, the impact of the spontaneous epimutations and epialleles has been studied in only a few species, including *A. thaliana* (He et al., 2018), *Z. mays* (Coccilone et al., 2001), *L. vulgaris* (Cubas et al., 1999), *O. sativa* (Miura et al., 2010), *S. lycopersicum* (Manning et al., 2006) and *E. guineensis* (Ong-Abdullah et al., 2015). In addition, they have not been studied on a population-scale in a specific-context, which may have different stabilities and biological functions.

A large number of research have now pointed out that DNA methylation is significantly associated with environmental gradients and

climate change (McCaw et al., 2020). For example, genome-wide DNA methylation modifications of some representative species, including *Arabidopsis thaliana* (Kawakatsu et al., 2016), *Bruguiera gymnorhiza* (Lira-Medeiros et al., 2010), *Betula platyphylla* (Chen, Guo, et al., 2022), *Crassostrea gigas* (Gawra et al., 2023), *Fragaria vesca* (De Kort et al., 2022) and *Quercus lobata* (Gugger et al., 2016), are determined to be related with some environmental perturbations, such as temperatures, salts and drought (Sun et al., 2022). In addition, our previous research in *A. thaliana* accessions identified a leaf senescence-related epiallele, and found that it is significantly associated with the local mean temperature of driest quarter (BIO9) (He et al., 2018). Nevertheless, to what extent of the epialleles in *A. thaliana* accessions can be associated with the local climates remains unclear.

Genomic offset is a recently developed index describing mismatch between the current and required genomic compositions in a set of putatively adaptive loci under the future or changed environments, which was first presented by Fitzpatrick and Keller using the gradient forest (GF) (Fitzpatrick & Keller, 2015), a community-level transfer function based on a machine-learning regression tree approach (Ellis et al., 2012). This approach has been applied with several natural species, such as *Pinus densata* (Zhao et al., 2020), *Platycladus orientalis* (Jia et al., 2020), *Betula platyphylla* (Nocchi et al., 2022) and *Populus koreana* (Sang et al., 2022), to predict their vulnerability to future climates. As such, using this genomic tool can offer the novel insights into assessing the evolutionary adaptive potential and also predicting the disruption of the local adaptation and species mal-adaptation under the global climate change (Bay et al., 2018; Fitzpatrick & Keller, 2015; Hoffmann et al., 2021; Waldvogel et al., 2020). In addition to the genetics, DNA methylation, as the fifth base, has the similar potential to shape organism's phenotypic responses to environmental changes (Angers et al., 2010; Bossdorf et al., 2008; McCaw et al., 2020), therefore the offset of DNA methylation, especially those epialleles, can provide additional insights into evaluating the mal-adaptation. Regrettably, this forecast has not been implemented from a perspective of epigenetics so far, to our knowledge.

In this research, the main target was to identify the regions of climate mal-adaptation for *Arabidopsis thaliana* accessions based on landscape patterns of epigenomic data, which is important for assessing plants fate in future scenarios. To accomplish this goal, we performed the association analysis by using the multi-omics public data (re-sequencing, methylomes and transcriptomes) and 196 climatic variables of the 105 *A. thaliana* accessions with the diverse geographical habitats (Figure 1; Table S1), to identify the spontaneous epimutations, epialleles and those associated with climatic variables. Based on these climate-related epialleles (cEpialleles), we predicted the natural distribution of *A. thaliana* accessions with a high vulnerability under future climate conditions by using GF model. Here, we aimed to the following three questions: (1) to what extent the differentially methylated regions (DMRs) can be de-coupled with the genetic variants; (2) to what extent the epialleles can be associated with the climatic variables and (3) to quantify and map the vulnerable populations of the natural *A. thaliana* under future climates based on the cEpialleles.



**FIGURE 1** Scheme of data analysis overview. The differentially methylated regions (DMRs) between Col-0 and the remaining *A. thaliana* accessions were identified by a 200 bp sliding window algorithm across the Col-0 genome with Fisher's exact test. The genetically dependent DMRs refer to those DMRs that were significantly associated with  $\geq 1$  SNPs in GWAS, while the spontaneous DMRs are referred to those DMRs that were not associated with any SNPs. The epialleles refer to those spontaneous DMRs that were significantly associated with  $\geq 1$  gene expression and also heritable. The climate-related epialleles (cEpialleles) refer to those epialleles that were significantly associated with  $\geq 1$  climatic variable. In the top centre bar graph, the x-axis labels 'A/A', 'A/T' and 'T/T', respectively, represent the different genotypes. The label 'DNAm' indicates the 5-cytosine methylation level. The labels ' $F_1$ ' and ' $rF_1$ ' indicate where the maternal line was Col-0 and C24 accessions in crosses, respectively. The label 'PWM' indicates the parentally (Col-0 and C24 accessions) weighted methylation level. Black dots in the inheritance analysis represent the DMRs, and black dots in the other cases represent the accessions. The numbers of the DMRs are shown under each panel. The epigenetic offset was used to describe the mismatch in the epigenetic-climatic associations between the current and future climate regimes. Parts of this figure used with permission of Annual Reviews, Inc, from Genomic Prediction of (Mal)Adaptation Across Current and Future Climatic Landscapes, Capblancq, Thibaut; Fitzpatrick, Matthew C.; Bay, Rachael A.; Exposito-Alonso, Moises; Keller, Stephen R., 51:1, 2020; permission conveyed through Copyright Clearance Center, Inc. [Correction added on 31 May 2024, after first online publication: copyright line updated.] [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

## 2 | MATERIALS AND METHODS

### 2.1 | Detection of DMRs in 105 *A. thaliana* accessions

The methylomes of the 105 natural *A. thaliana* accessions with the diverse geographical origins (across Central Asia, Europe and North America) were downloaded from 1001 Arabidopsis

Genomes, Methylomes, Transcriptomes and Physical Maps to identify the landscape of the DMRs (Kawakatsu et al., 2016; Schmitz et al., 2013). Data were first filtered to retain those cytosines with  $\geq 4$  reads aligned. The initial DMRs were obtained from the comparisons between Col-0 (the reference genome accession) and the other 104 *A. thaliana* accessions using a 200-bp sliding window algorithm across the genome (Zhang, Wang, et al., 2016). The candidate DMRs were then identified based on Fisher's exact test with

a Benjamini–Hochberg (BH)-adjusted  $p \leq .01$  and a fold-change of methylation level  $\geq 2$ . These DMRs were further sorted based on genomic positions, merged in a 1-bp end-to-end manner, and classified based on their sequence contexts (CG, CHG and CHH, where H=A, T or C). Moreover, DMRs with a minor epimutation frequency  $\leq 5\%$  were filtered out according to Xu et al. (2019).

## 2.2 | Detection of spontaneous DMRs

A single nucleotide polymorphism (SNP) matrix, derived from the Arabidopsis 1001 Genome Project database (Alonso-Blanco et al., 2016), was filtered with PLINK v1.90 (Chang et al., 2015) using the parameters '--maf 0.05 --geno 0.01 --hwe 0.0001'. Non-linked variants were kept through the linkage disequilibrium (LD) analysis using PLINK with the default parameters '--indep-pairwise' (sliding window of 50 bp and step size of 10 bp to delete one of the SNP pairs with an LD  $\geq 0.2$ ).

To illustrate the genetic basis of the DMRs, the R package 'MatrixEQTL' v2.3 (Shabalin, 2012) integrated with generalised linear model (GLM) was used to perform a genome-wide association study (GWAS) between the approximately 35,000 high-quality SNP matrix screened above and the methylation levels of the DMRs matrix. The population structure was calculated with the principal component analysis (PCA, the 'FactoMineR' package in R) as the covariates in the GWAS. The genetically dependent DMRs were defined as the DMRs that were significantly associated with  $\geq 1$  SNPs (BH-adjusted  $p$ -value  $\leq .05$ ). They can be further classified into the *local*-acting and the *distal*-acting ones, based on the relative distances (1.0 Mb) from their associated SNPs, and those with both were assigned as the *both*-acting ones (Schmitz et al., 2013; Vidalis et al., 2016). The remaining DMRs that were not associated with any SNPs were defined as the spontaneous DMRs.

## 2.3 | Inheritance analysis of DMRs

DNA methylation interaction (MI) in  $F_1$  hybrids derived from crossing the Col-0 and C24 accessions was used to investigate the heritability of the DMRs. To simulate the pattern of the parental DNA methylation in the progeny, the weighted DNA methylation level of DMRs in the parental lines was defined as the parentally weighted methylation level (PWM) (Schultz et al., 2012; Zhang, Wang, et al., 2016), which is calculated with the following formula:

$$\text{PWM} = \frac{\sum_{i=1}^n (\text{MC}_i + \text{PC}_i)}{\sum_{i=1}^n (\text{MT}_i + \text{PT}_i)}$$

where  $i$  is the position of cytosine,  $n$  is the total number of cytosine positions in DMRs, MC is the maternally methylated reads, PC is the paternally methylated reads, MT is the maternal total reads, PT is the paternal total reads, and the total reads contain the methylated and the unmethylated reads. In brief, PWM was calculated by dividing the combined number of parental methylated reads by the combined

number of parental total reads in DMRs. The differences between the PWM and the methylation level of their progeny ( $F_1/rF_1$ ) were compared using Fisher's exact test. The potentially heritable DMRs were defined as the non-interaction DMRs ('NI-DMRs'), of which the DNA methylation levels calculated in both the  $F_1$  and the  $rF_1$  were not significantly distinct from the PWM (BH-adjusted  $p$ -value  $> .05$ ). Instead, the non-heritable DMRs were defined as the methylation interaction DMRs ('MI-DMRs'; BH-adjusted  $p$ -value  $\leq .05$ ).

## 2.4 | Detection of epialleles and climate-related epialleles

Epialleles are generally referred to as those spontaneous epimutations that are capable of regulating gene expression and could also be inherited in subsequent generations. In this research, the associations between spontaneous DMRs and gene expressions at the population level were assessed using the GLM of the OSCA v0.46.1 software (Zhang et al., 2019) that integrated with the population structure, and those were considered as the significant associations at a genome-wide significance level of 0.05 (BH-adjusted  $p$ -value). The normalised expression data were downloaded from the 1001 Arabidopsis Genomes, Methylomes, Transcriptomes and Physical Maps, and a total of 33,163 genes expressed in  $\geq 1$  accessions were retained for the subsequent analysis. The expression-associated spontaneous DMRs could be further referred to as *cis* if the associated genes were within 1.0 Mb and otherwise as *trans*. Those expression-associated spontaneous DMRs can be defined as the epialleles when they were additionally classified as 'NI-DMRs' in the inheritance analysis (Section 2.3). In addition, the biological functions of these epialleles were investigated based on gene ontology (GO) enrichment analysis in TAIR (Berardini et al., 2015).

To identify the climate-related epialleles, the relations of the epialleles and the climatic variables were assessed using the same approach by the OSCA software integrated with the population structure. A total of 196 local climatic variables for the habitats of these 105 *A. thaliana* accessions were derived from AraCLIM (Ferrero-Serrano & Assmann, 2019). These climatic variables included temperature and precipitation regimes from WorldClim2 (Fick & Hijmans, 2017) and CHELSA (Karger et al., 2017), the physical and chemical properties of the soils from SoilGrids (Poggio et al., 2021), and the other important climatic indicators from the NASA (<https://neo.sci.gsfc.nasa.gov/>), such as atmospheric properties, radiation and water equivalent. The climate-related epialleles were recognised when those epialleles were significantly associated with  $\geq 1$  climatic variable (BH-adjusted  $p$ -value  $\leq .05$ ), namely cEpialleles.

## 2.5 | Species distribution modelling

The natural distribution of the 105 *A. thaliana* accessions from Europe, Asia and North Africa was predicted using MaxEnt v3.4.3 (Phillips & Dudik, 2008) integrated with the maximum entropy

model, a classic species distribution model (SDM) based on machine-learning algorithms. Although we initially used 196 climatic variables from AraCLIM to identify cEpialleles (see above), only WorldClim2 provides information about future scenarios. Therefore, 19 bioclimatic variables from WorldClim2 were used in this SDM. Initially, these 19 bioclimatic variables at 2.5 min spatial resolution for each accession habitat were derived from WorldClim2. To remove the influence of the high collinearity, five variables (BIO4, BIO8, BIO11, BIO16 and BIO18) with an absolute coefficient ( $|ρ|$ )  $\leq 0.6$  were retained by the pairwise Spearman's correlation analysis, the PCA and the hierarchical cluster analysis (Figure S1, Table S2). The MaxEnt model was built based on these five climatic variables to predict the occurrence probability of the region ( $20^{\circ}\text{W}$ – $40^{\circ}\text{E}$  and  $35^{\circ}\text{N}$ – $65^{\circ}\text{N}$ ). The locations with a predicted occurrence probability  $\geq 0.3$  were considered to be the suitable regions where *A. thaliana* probably exists (Figure S2). More details about species distribution modelling can be referred to the Appendix Method S1.

## 2.6 | Assessment of vulnerability regarding climate change based on cEpialleles

To assess where epigenetic–environmental relationships regarding cEpialleles will most likely be disrupted by future climate change, the landscape epigenetic offset across the simulated regions was calculated based on the Euclidean distances between the current and predicted future epigenetic compositions (Fitzpatrick & Keller, 2015; Jia et al., 2020; Zhao et al., 2020). GF model was built to evaluate the current epigenomic compositions in terms of the identified cEpialleles (i.e. the methylation levels (methylated reads/total reads) of cEpialleles) with these five bioclimatic variables (mentioned in Section 2.5) using the R package 'gradientForest' (Ellis et al., 2012). The model was used to predict the future epigenetic compositions with the same five climatic variables in 2041–2060 and 2081–2100 respectively. The resulting multidimensional epigenomic patterns were summarised by using PCA (Ellis et al., 2012). The first three PCs were each assigned an RGB (red, green and blue) colour, and similar colours in simulated regions (mentioned in Section 2.5) correspond to the similar expected epigenetic compositions. More details about the epigenetic offset can be referred to the Appendix Method S2.

## 3 | RESULTS

### 3.1 | Genetic basis of DMRs and identification of epialleles

A substantial portion of the epimutations, especially of the CHH context, are decoupled from genetic variations in natural *A. thaliana* populations. Specifically, we identified a total of 11,779, 2880 and 15,129 DMRs of CG, CHG and CHH contexts, respectively, in the 105 *A. thaliana* accessions with diverse habitats (Figure 2; Figure S3–S6,

Table S3). Among them, we detected 6568 (~56%), 2104 (~73%) and 4380 (~29%) DMRs associated with the SNPs. However, ~56% on average, especially in the CHH sequence context (10,749, 71%), of DMRs are not associated with SNPs, that is, spontaneous DMRs (Figures 2a and 3; Figures S5, S7–S9, Table S4, Appendix Method S3). By EWAS, a total of 1315 (CG, 82%, 1315), 367 (CHG, 69%, 367) and 1553 (CHH, 21%, 1553) spontaneous DMRs were found to be associated with at least one gene expression, and potentially inherited into offspring, that is, epialleles (Figures 2a and 4a,b; Figures S5 and S10, Tables S5 and S6, Appendices S1–S4, Appendix Method S4). GO enrichment analysis showed that these epialleles were mainly involved in terms, such as 'regulation of defense response (GO:0031347)', 'response to abiotic stimulus (GO:0009628)' and 'response to water deprivation (GO:0009414)' (Figure 4c; Table S7), suggesting that the epialleles can contribute to the responses to external stimuli and environmental changes.

### 3.2 | Association of epialleles with climate variables

Hundreds (655) of the epialleles, especially of the CHH context (512), are significantly associated with at least one bio-climate variable, that is, climate-related epialleles, defined as the cEpialleles (Figure 2; Figures S5, S11 and S12, Tables S8 and S9). There are 44% (CG), 60% (CHG) and 83% (CHH) of the cEpialleles associated with the temperature and/or precipitation (Figure 5a), suggesting that these two classes of climate variables play an important role in shaping methylation patterns. GO enrichment analysis of these cEpialleles showed a similar result with that of the epialleles, that they could contribute to the response to the external stimuli and environmental changes (Figure 5b; Table S10). One (HEI10) of the cEpialleles is exemplified to demonstrate the potential effect of a DMR on the phenotype of the chromosome crossover (CO) frequencies (Figures S13–S17, Appendix S5, Appendix Method S5).

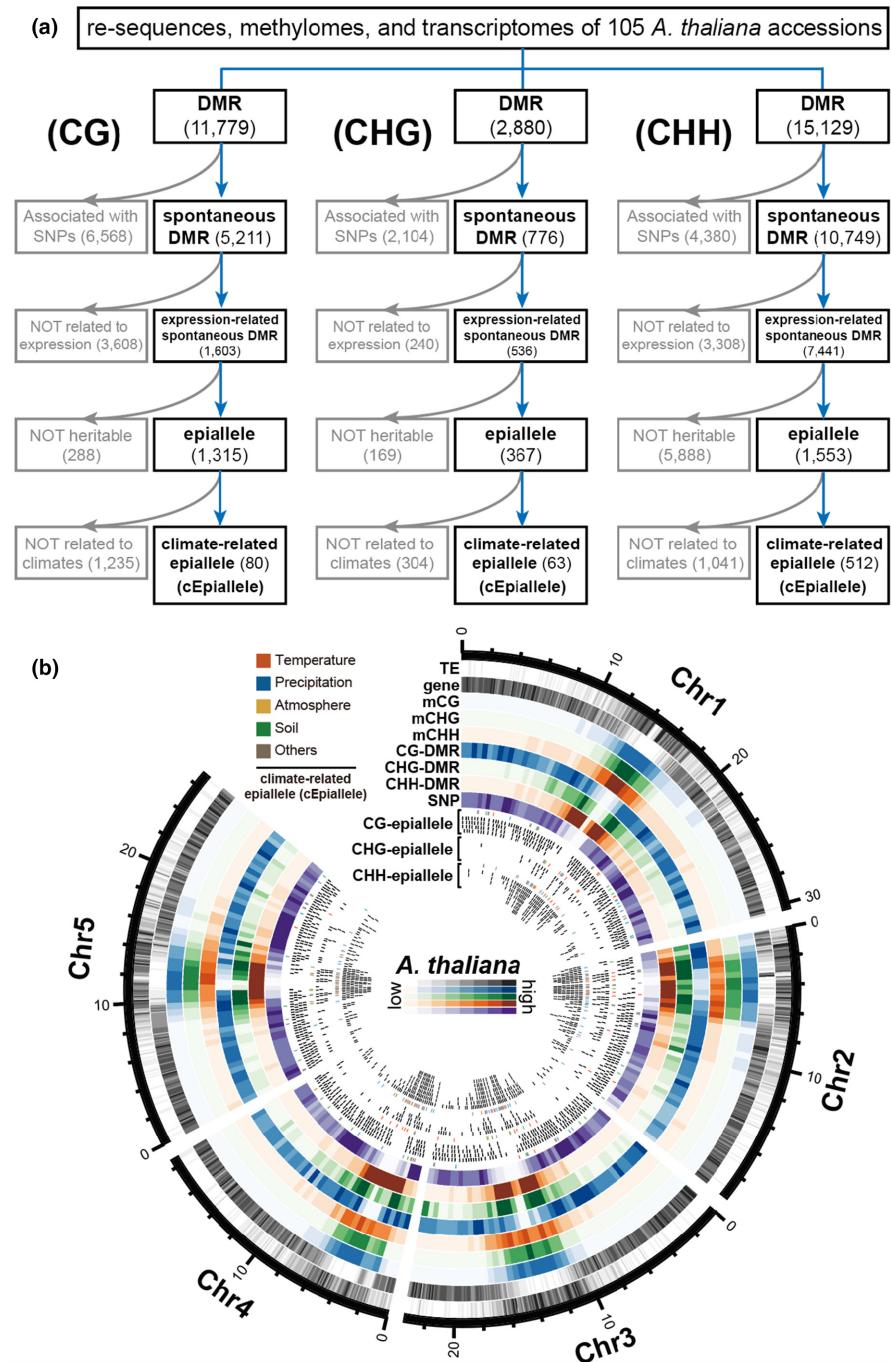
### 3.3 | Prediction of *A. thaliana* responses to climate change based on cEpialleles

Gradient forest modelling predicted higher epigenetic offset around the simulated distribution margins of *A. thaliana* under future climates (Figure 5c). To better explain the influences of epigenetic offset, we selected five representative geographical regions, that is, Southern Europe (SE,  $10.0^{\circ}\text{W}$ – $30.0^{\circ}\text{E}$ ,  $30.0^{\circ}\text{N}$ – $42.50^{\circ}\text{N}$ ), Northern Europe (NE,  $10.00^{\circ}\text{W}$ – $30.00^{\circ}\text{E}$ ,  $50.00^{\circ}\text{N}$ – $54.00^{\circ}\text{N}$ ), Western Europe (WE,  $2.31^{\circ}\text{W}$ – $2.45^{\circ}\text{E}$ ,  $46.62^{\circ}\text{N}$ – $49.57^{\circ}\text{N}$ ), Eastern Europe (EE,  $15.80^{\circ}\text{E}$ – $22.90^{\circ}\text{E}$ ,  $50.52^{\circ}\text{N}$ – $53.66^{\circ}\text{N}$ ) and the Alps ( $8.24^{\circ}\text{E}$ – $14.84^{\circ}\text{E}$ ,  $46.13^{\circ}\text{N}$ – $47.98^{\circ}\text{N}$ ) (Figure S18, Table S11). Overall, the epigenetic offset was significantly lower in NE and EE than in SE, WE and the Alps (Figure 5c,d; Figure S19, Table S12), and it will be further increased at least until the end of this century especially in the latter three regions (Table S13), suggesting that *A.*

*thaliana* accessions distributed in SE, WE and the Alps are more vulnerable to future climate change, and northern Europe may serve as the migration direction of natural *A. thaliana* accessions under future conditions.

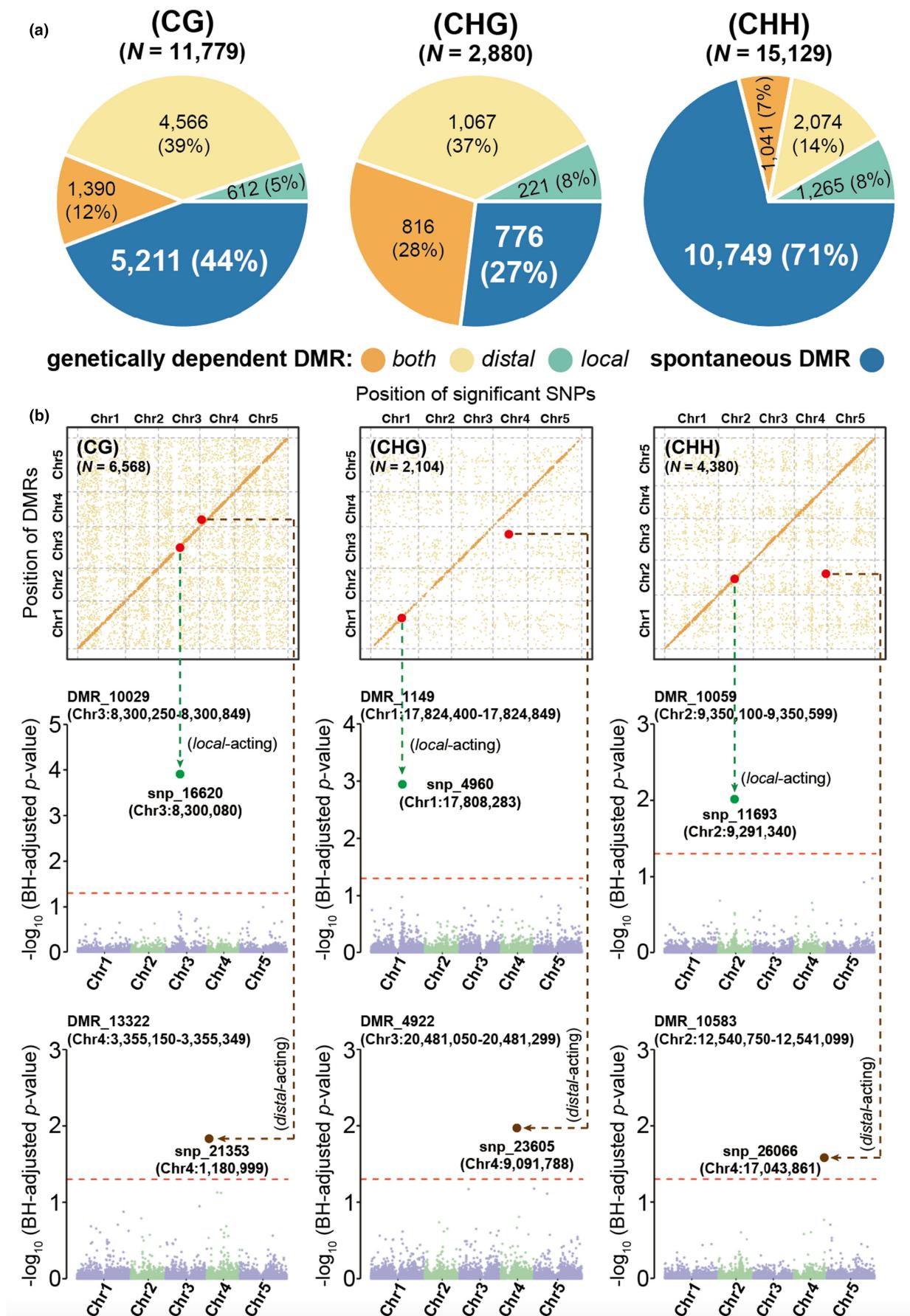
## 4 | DISCUSSION

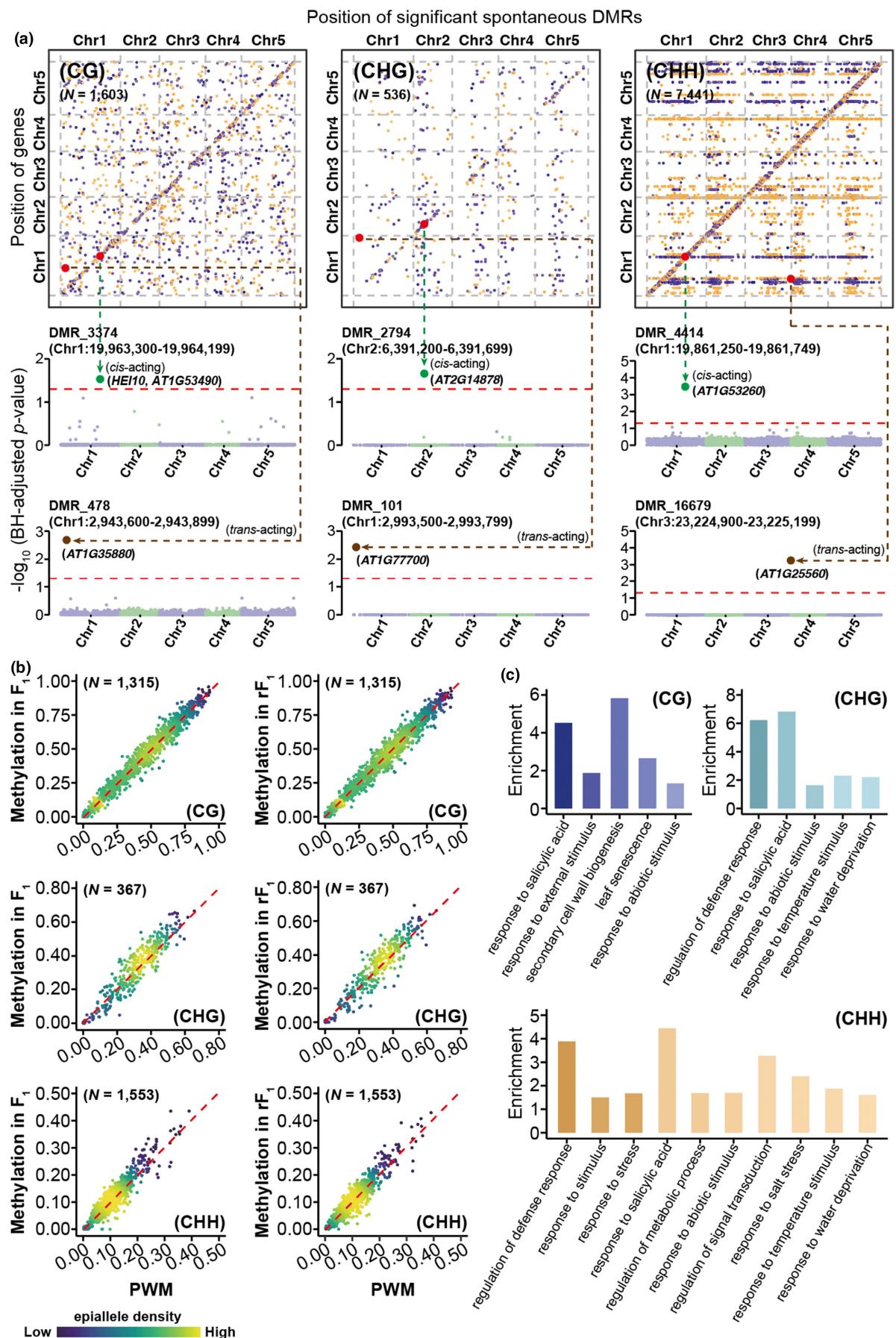
Understanding the mechanisms of plant responses to local environments has long been a central topic in ecology and biology,



**FIGURE 2** Natural variation of the DNA methylation in the 105 *A. thaliana* accessions. (a) Flowchart used to identify the climate-related epialleles (cEpialleles) in this research. More details about these concepts can be referred to the Table S1. (b) DNA methylation landscape across the five chromosomes of *A. thaliana*. TEs (transposons) and genes are indicated by grayscale in the first two circles (from the 1st to 2nd circles); the CG, CHG and CHH methylation levels of Col-0 accession are displayed in order (from the third to fifth circles), and the maximum methylation level for each sequence context was 1.0, 0.6 and 0.2 respectively; the differentially methylated regions (DMRs) were visualised in each sequence context (from the sixth to eighth circles), and the maximum DMRs threshold was set to 70 (CG), 30 (CHG) and 150 (CHH); the population single nucleotide polymorphisms (SNPs) are displayed in the ninth circle, and the maximum SNP threshold was set to 800; the epialleles and cEpialleles are shown by different coloured tiles in the innermost three circles (from the 10th to 12th circles), where the black ones indicate the epialleles and the other different coloured tiles (available from the upper left legend) indicate the epialleles associated with different climatic variables (cEpialleles). [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

**FIGURE 3** Genetic basis of differentially methylated regions (DMRs). (a) Proportion of genetically dependent DMRs and the spontaneous DMRs in each sequence context. (b) Genomic distribution of the SNPs and their associated DMRs. x-axis indicates the genomic position of the SNPs, and y-axis shows the genomic positions of the genetically dependent DMRs. When the dots are on the diagonals, it indicates that the relative distance of the association is quite near (*local*-acting), and those off the diagonals indicate that the relative distance of the association is far (*distal*-acting). Examples of the *local*-acting (green circles) and *distal*-acting (brown circles) genetically dependent DMRs are displayed in the lower panels. Red dashed lines indicate the associated threshold [ $-\log_{10}$  (BH-adjusted *p*-value)=1.3]. Dots above the threshold indicate significant associations, and vice versa. [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]





**FIGURE 4** Analysis of epialleles. (a) Genomic distribution of spontaneous differentially methylated regions (DMRs) and their associated genes. x-axis indicates genomic positions of spontaneous DMRs, and y-axis indicates genomic positions of the corresponding genes. The colour reflects the association directions between gene expressions and spontaneous DMRs, with orange for positive associations, and blue for negative associations. When the dots are on the diagonals, it indicates that relative distance of the associations is quite near (*cis*-acting), while those off diagonals indicate that relative distance of the associations is far (*trans*-acting). Examples of the *cis*-acting (green circles) and the *trans*-acting (brown circles) expression-associated spontaneous DMRs are shown in the lower panels. Red dashed lines indicate the associated threshold [ $-\log_{10}$  (BH-adjusted *p*-value) = 1.3]. Dots above the threshold indicate significant associations. (b) Inheritance of epialleles. We mapped the DNA methylation levels of the epialleles in PWM (an index describing the weighted methylation levels of both parents [Col-0 and C24 accessions]) and in  $F_1/rF_1$  onto the x and y coordinates respectively. Each dot in the figures represents an epiallele and the colour indicates the density of epialleles located there. All dots were determined near the diagonals (red dotted line), which indicates that the methylation levels of the epialleles in both  $F_1$  and  $rF_1$  is comparable to the PWM. (c) GO enrichment of the genes associated with the epialleles. The colour indicates the  $-\log_{10}$  (Bonferroni-adjusted *p*-value). Darker colours indicate higher values, and lighter colours indicate lower values. [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

and has now become an imperative due to global climate change. It has been highly debated whether DNA methylation is involved in the plant plasticity to environmental perturbations and/or climate change (Bossdorf et al., 2008; Johannes & Schmitz, 2019; Springer & Schmitz, 2017). Recently, several studies have supported the roles of DNA methylation in phenotypic responses and abiotic stress (He et al., 2018; Kawakatsu et al., 2016). However, systematic mining of epialleles and assessments of their phenotypic consequences, and relationships with climatic variables at a population level is missing. In this study, we identified 655 cEpialleles (Figure 2a; Table S9), suggesting their potential roles in plant adaptation to the future climates, which is characterised by rising temperatures and global fluctuations in rainfall regimes (IPCC, 2014). Based on these cEpialleles, we determined that the natural *A. thaliana* accessions distributed in Southern Europe, Western Europe and the Alps were more vulnerable to future climate change (Figure 5), while Northern Europe could serve as a buffer zone.

#### 4.1 | Association of DMRs with SNPs

DNA methylation variations can be associated with SNPs (Dubin et al., 2015; Eichten et al., 2013; Kawakatsu et al., 2016; Schmitz et al., 2013), providing evidence that genetic variation is one possible explanation for the occurrence of epimutations. This is true for all sequence contexts with variability in the proportion of DMRs for different sequence contexts that can be linked to SNPs. This result is further supported by the observation that a closer relatedness of the CG-DMRs and CHG-DMRs with SNPs compared to the CHH-DMRs (Figure S9). However, a substantial portion of the DMRs is not tagged by SNPs, especially of the CHH context, suggesting a unique information existing in the DNA methylomes. These findings support the concept that spontaneous DMRs could carry the unique heritable information and that this information may not be captured in current SNP-based GWAS approaches (Xu et al., 2019). However, we also should note that lack of associations with the SNPs does not necessarily mean that these DMRs are purely epigenetic, because the low frequency SNPs which by design are not considered in GWAS, and other types of structure variants, which show low LD with SNPs, have the potential to be linked with the DMRs as well.

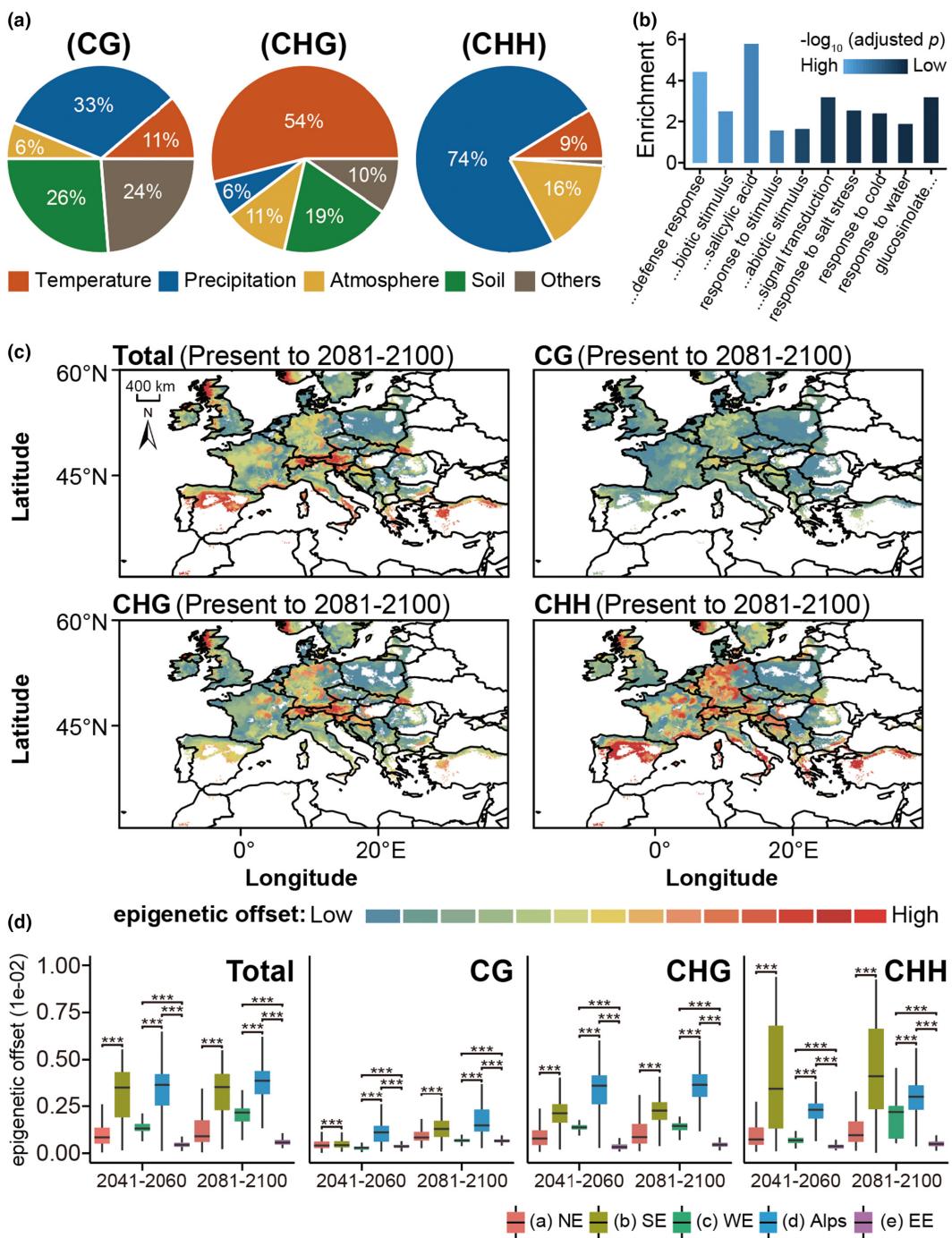
#### 4.2 | Contribution of DNA methylation to gene expression

Both positive and negative associations between DNA methylation and gene expression have been proposed (Gent et al., 2013; Li, Gent, et al., 2015; Li, Song, et al., 2015; Meng et al., 2016). We found that this relationship depends heavily on the sequence context and the position of DMRs relative to TSS of genes. In general, the symmetric DNA methylation (CG and CHG) of the DMRs located in the promoters tend to be enriched for negative associations, probably due to the fact that symmetric DNA methylation is often coupled with the histone modifications of heterochromatin (e.g. H3K9me2) (Kim et al., 2014; Zhang et al., 2018). In contrast, asymmetric DNA methylation (CHH) of these DMRs tend to show a positive association, which is likely attribute to the recruitment by DNA methylation of specific transcription factors to increase gene expressions (Harris et al., 2018).

#### 4.3 | Epialleles with phenotypic consequences

Many traits have a complex genetic basis with substantial minor effect QTLs (Kump et al., 2011; Li et al., 2013; Wang et al., 2018). In fact, only a portion of the phenotypic alterations of these traits can be explained by SNPs has led to the suggestions that other kinds of heritable information may be involved. Our research is interested in exploring the potential of methylation conveying heritable information about gene expression or even phenotypic differences that may not be present in SNP profiles. Several examples for which DNA methylation, especially epialleles, rather than the genetic variations, at specific loci are the cause of the phenotypic changes (Cortijo et al., 2014; Furci et al., 2019; Quadrana & Colot, 2016), such as the photosynthetic capacity (AK1) (Wei et al., 2017), incompatibility (HISN6B) (Blevins et al., 2017), fruit ripening (CNR) (Manning et al., 2006), leaf senescence (PPH) (He et al., 2018), flowering time (Cortijo et al., 2014) and primary root length (Cortijo et al., 2014) (see a brief list for more (Gahlaut et al., 2020)). Here, we found some of the epialleles with important phenotypic diversity.

One of the most influential epialleles was *HEI10* found in EWAS and CRISPR/dCas9-TET1cd in *A. thaliana* (Figures S13–S17). This



**FIGURE 5** Climate-related epialleles (cEpialleles) and the plants vulnerability to future climate change under scenario SSP585 in 2081-2100. (a) Proportion of the cEpialleles in each class of the climatic variables. (b) Gene ontology enrichment of genes associated with the cEpialleles involving temperature and/or precipitation regimes. (c) Predicted epigenetic offset across the simulated regions of *A. thaliana* in 2081-2100 under scenario SSP585. Red and blue represent high and low epigenetic offset respectively. Epigenetic offset signals range from 0.000 to 0.005 and are divided into 14 colour gradients. (d) Epigenetic offset among the five representative regions (Table S11) between the current and future climate conditions (2041-2060 and 2081-2100). The  $p \leq .001$  is marked as \*\*\*. [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

gene has been reported to be involved in the euchromatic CO events, which can influence genetic diversity, recombination and may, ultimately, affect how species adapt to their environments (Shang et al., 2022; Tock et al., 2021; Ziolkowski et al., 2017). Here, we demonstrated that this epiallele covering the TSS can affect the euchromatic COs by regulating the expression of *HEI10*, which

is independent of the genetic variations. Moreover, we found that several retrotransposons were recognised as the epialleles, supporting the view that changes in DNA methylation are an important component of the natural variations in retroelements (Rangwala et al., 2006). For example, a previously discovered meiotically stable natural epiallele, *Sadhu* (an *Arabidopsis* retrotransposon, AT5G27927)

(Rangwala et al., 2006), was included in our results, that is, its expression level was significantly associated with the methylation level of *cis*-acting epialleles (DMR17427 and DMR6912) (Table S6). However, probably due to the three facts that (i) small sampling size (105), (ii) lack of other types of genetic variations and (iii) the limited power of GWAS, some of known epialleles, such *PPH*, *HISNB6*, and *QQS* have not been identified in our results. Hence, more optimisations need to be considered in our future studies.

#### 4.4 | Association of epialleles with climate variables

Epigenetic variations can be linked to climate change (Bossdorf et al., 2008). Some of the studies have assessed this linkage in a few species, such as *P. lanceolata* (Gaspar et al., 2019), *A. thaliana* (Kawakatsu et al., 2016), *T. pratense* (Lehmair et al., 2022), *V. elatior* (Schulz et al., 2014), *L. racemosa* (Lira-Medeiros et al., 2010) and *Q. lobata* (Gugger et al., 2016), providing solid evidence of an association between the epigenetic variations and environmental gradients. In addition, our previous results exhibited that the DNA methylation levels of epiallele (*PPH*) were significantly negatively correlated with the local mean temperature of driest quarter (BIO9), and hypothesised that those *A. thaliana* accessions that experienced a loss of methylation modifications at this locus were acclimated to increasing local temperatures (He et al., 2018). In the present study, we found a total of 655 cEpialleles involved in the response to environmental changes (Figures 2a and 5b; Table S9). For example, we found a significant association between DNA methylation levels of epiallele (*HEI10*) and CO<sub>2</sub> emission (Figure S13), supporting the hypothesis that the plants DNA methylation could be altered by the CO<sub>2</sub> environment and can persist into next generation (Panda et al., 2023). Similarly, another epiallele (DMR7061) regulating expression of *AT1G61190*, which has been reported to be responsive to the elevated CO<sub>2</sub> (Saban et al., 2020), was significantly associated with the topsoil gravel content (derived from the HWSD database, Table S9), one of the most important limiting variables in carbon stock and concentration (De Baets et al., 2013; Leifeld et al., 2005). These findings provide a hypothesis that the plant epialleles can be involved in responses to environmental changes, such as CO<sub>2</sub>.

Many of the other climate-related epialleles that likely influence important biological functions were also illustrated (Figure S20, Table S14). Yet, this comprehensive list of climate-related epialleles were detected in silico analysis, and they still need further validation by the wet-experiments, such as the Caps-PCR, Chop-PCR, CRISPR/dCas9 system, transplanting and phenotypic validations.

#### 4.5 | Vulnerability of natural *A. thaliana* to the future climates

Natural populations at range edges tend to be more vulnerable to future climate change. Recently, several studies have been performed

with landscape genomics to assess plant vulnerability to future climates based on genetic offset, that is, the mismatch in genotype-climate associations between current and future climate regimes (Chen, Jiang, et al., 2022; Fitzpatrick & Keller, 2015; Jia et al., 2020; Martins et al., 2018; Yu et al., 2022; Zhao et al., 2020). For example, southern margins (Hengduan mountain) of widespread conifer *Platycladus orientalis* and western margins (Tibetan mountain) of *Pinus densata* were predicted with the higher genetic offset (Jia et al., 2020; Zhao et al., 2020), that is, these populations in margins have an intense selective pressure as well as decreased gene flow (Jump & Penuelas, 2005), and are thus more vulnerable to future climates. Similarly, natural *A. thaliana* accessions distributed in southern Europe will face more intense natural selection pressure due to more frequent drought events by the end of this century (Exposito-Alonso et al., 2018, 2019). Here, for the first time, to our knowledge, we assessed epigenetic offset in natural *A. thaliana* accessions based on the cEpialleles (Figure 5c,d). A big difference in assessing genetic versus epigenetic offset is the possibility that future populations will not have the same epigenetic patterns given their either non-heritability or short-term heritability unless stable epigenetic loci are used.

Based on epigenetic offset we found that *A. thaliana* accessions distributed in Southern Europe are predicted to experience the highest selection pressures from the disturbance of the precipitation of warmest quarter (BIO18) until the end of this century (Figure 5c,d; Figure S21). These results are in accordance with the findings based on genetic variations (Exposito-Alonso et al., 2018, 2019), suggesting an obvious lag in adaptation for those accessions in margins regarding both their genetic and epigenetic compositions. More importantly, we found that *A. thaliana* accessions from Northern Europe would be less challenged by future climate change (Figure 5c,d). These habitats have an overall lower CO<sub>2</sub> emission level (2362C/cm<sup>2</sup>/s vs. 3180C/cm<sup>2</sup>/s), and the DNA methylation level of *HEI10* was relatively low (CG, 0.48 vs. 0.59; CHG, 0.26 vs. 0.30 and CHH, 0.048 vs. 0.057) and expression level of *HEI10* was high (75.30 vs. 42.40) (Figure S22). This may increase genetic diversity with much more frequent CO events and thus augment molecular resources for natural selection and facilitate rapid adaptation of *A. thaliana* to changing climates.

## 5 | CONCLUSION

In this study, based on multi-omics datasets, we identified DMRs, spontaneous DMRs, epialleles and cEpialleles, and further to investigate the plant vulnerability to the future climates in the 105 *A. thaliana* accessions (Figure 1). We found that (1) substantial (over 50%) natural DNA methylation variations were not associated with any causative SNPs; (2) thousands (3235) of spontaneous DMRs can be associated with gene expressions, that is, epialleles, one (*HEI10*) of which was experimentally validated to provide evidence that DNA methylation can affect gene expressions; (3) hundreds (655) of epialleles can be associated with the climatic variables, that is, cEpialleles;

and (4) based on these cEpialleles, the *A. thaliana* accessions in southern Europe, as well as the Alps, exhibited a relatively higher risk of mal-adaptation, with the diverse sequence backgrounds showing different patterns. Specifically, epigenetic offset in the context of CG sequence is relatively lower across the continent of Europe, in the context of CHG sequence is relatively higher in the Alps of the high altitude, and in the context of CHH sequence is relatively higher in southern Europe, the Alps and central Europe. However, it should be noted that these vulnerability predictions to future climates must be used with caution, because this high epigenomic offset can be only observed if epigenetic compositions can be maintained in future generations.

Moreover, there are still some improvements that required to be further considered. For example, (1) GWAS and EWAS could integrate the multiple genomic loci (which may have co-interactions) to further improve the prediction of the epialleles and cEpialleles; (2) GF model can include some other factors, such as species migration and gene flows; and (3) the adaptive phenotypes (e.g. the leaf traits, individual sizes and flowering period) and the fitness (e.g. seed number, survival and developmental traits) could be further determined with the common gardens and/or reciprocal transplanting. Meanwhile, *A. thaliana* may not be an appropriate species to illustrate the effects of climate change. The analysis flow in this study also shows its promise for other non-model organisms, especially the forest trees. Because climate change is more likely to happen within the lifetimes of their single individuals, especially for those (e.g. valley oak) (Gugger et al., 2016) with the narrow geographical distributions and the habitat specialisation, and their long generation times constrain their ability to adapt to the rapid climatic change via genetic modifications (Brautigam et al., 2013; Holliday et al., 2017). Taken together, our research not only provides the epialleles associated with the environmental changes, but also can further aid in predicting the plants' vulnerability to climate change, and therefore to develop the broad-scale adaptation strategy for the conservation and management of ecosystem services, in light of future climate change.

## AUTHOR CONTRIBUTIONS

BC, MW and YG contribute equally to this work. BC, YG, ZZ and LC conducted the experimental design, data analysis and prepared the manuscript. MW, WZ, TZ and AS provided help in carrying out the experiments. QZ, SS, LX, YL, ZG and BC interpreted the results and modify the manuscript. All the authors contributed to the manuscript and approved the submitted version.

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## CONFLICT OF INTEREST STATEMENT

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## DATA AVAILABILITY STATEMENT

The methylomes and transcriptomes of the *A. thaliana* accessions can be derived from NCBI Sequence Read Archive (PRJNA187927 and PRJNA187928). The methylomes of *met1*, *cmt3*, *cmt2* and *nrpd1/e1* mutants together with their corresponding wild-type (Col-0 accession) can be acquired from NCBI Sequence Read Archive (PRJNA289907, PRJNA566445, PRJNA603989, PRJNA316982 and PRJNA295546). The methylomes and transcriptomes of the parents (Col-0 and C24 accessions) and their progeny ( $F_1$  and  $rF_1$ ) in the wild-type and *ddm1* background can be acquired from NCBI Sequence Read Archive (PRJNA295546 and PRJNA300685). The SNPs and the 196 climatic variables datasets of 105 *A. thaliana* accessions can be derived from the Salk Arabidopsis thaliana 1001 Genome (<https://1001genomes.org/data/GMI-MPI/releases/v3.1/>) and AraCLIM (<https://github.com/CLIMtools/AraCLIM/>) respectively. Plant material in this research is available from the corresponding author with request.

## BENEFIT-SHARING STATEMENT

All data in this study are published public data and are accessible through appropriate biological databases.

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## REFERENCES

- Aitken, S. N., Yeaman, S., Holliday, J. A., Wang, T., & Curtis-McLane, S. (2008). Adaptation, migration or extirpation: Climate change outcomes for tree populations. *Evolutionary Applications*, 1(1), 95–111. <https://doi.org/10.1111/j.1752-4571.2007.00013.x>
- Alonso-Blanco, C., Andrade, J., Becker, C., Bemm, F., Bergelson, J., Borgwardt, K. M., Cao, J., Chae, E., DeZwaan, T. M., Ding, W., Ecker, J. R., Exposito-Alonso, M., Farlow, A., Fitz, J., Gan, X., Grimm, D. G., Hancock, A. M., Henz, S. R., Holm, S., ... Genomes, C. (2016). 1,135 genomes reveal the global pattern of polymorphism in *Arabidopsis thaliana*. *Cell*, 166(2), 481–491. <https://doi.org/10.1016/j.cell.2016.05.063>
- Angers, B., Castonguay, E., & Massicotte, R. (2010). Environmentally induced phenotypes and DNA methylation: How to deal with unpredictable conditions until the next generation and after. *Molecular Ecology*, 19(7), 1283–1295. <https://doi.org/10.1111/j.1365-294X.2010.04580.x>
- Banta, J. A., & Richards, C. L. (2018). Quantitative epigenetics and evolution. *Heredity*, 121(3), 210–224. <https://doi.org/10.1038/s41437-018-0114-x>

- Bay, R. A., Harrigan, R. J., Le Underwood, V., Gibbs, H. L., Smith, T. B., & Ruegg, K. (2018). Genomic signals of selection predict climate-driven population declines in a migratory bird. *Science*, 359(6371), 83–86. <https://doi.org/10.1126/science.aan4380>
- Becker, C., & Weigel, D. (2012). Epigenetic variation: Origin and transgenerational inheritance. *Current Opinion in Plant Biology*, 15(5), 562–567. <https://doi.org/10.1016/j.pbi.2012.08.004>
- Berardini, T. Z., Reiser, L., Li, D. H., Mezheritsky, Y., Muller, R., Strait, E., & Huala, E. (2015). The *Arabidopsis* information resource: Making and mining the “gold standard” annotated reference plant genome. *Genesis*, 53(8), 474–485. <https://doi.org/10.1002/dvg.22877>
- Blevins, T., Wang, J., Pfleiger, D., Pontvianne, F., & Pikaard, C. S. (2017). Hybrid incompatibility caused by an epiallele. *Proceedings of the National Academy of Sciences of the United States of America*, 114(14), 3702–3707. <https://doi.org/10.1073/pnas.1700368114>
- Bossdorf, O., Richards, C. L., & Pigliucci, M. (2008). Epigenetics for ecologists. *Ecology Letters*, 11(2), 106–115. <https://doi.org/10.1111/j.1461-0248.2007.01130.x>
- Brautigam, K., Vining, K. J., Lafon-Placette, C., Fosdal, C. G., Mirouze, M., Marcos, J. G., Fluch, S., Fraga, M. F., Guevara, M. A., Abarca, D., Johnsen, O., Maury, S., Strauss, S. H., Campbell, M. M., Rohde, A., Diaz-Sala, C., & Cervera, M. T. (2013). Epigenetic regulation of adaptive responses of forest tree species to the environment. *Ecology and Evolution*, 3(2), 399–415. <https://doi.org/10.1002/ece3.461>
- Browne, L., Wright, J. W., Fitz-Gibbon, S., Gugger, P. F., & Sork, V. L. (2019). Adaptational lag to temperature in valley oak (*Quercus lobata*) can be mitigated by genome-informed assisted gene flow. *Proceedings of the National Academy of Sciences of the United States of America*, 116(50), 25179–25185. <https://doi.org/10.1073/pnas.1908771116>
- Capblancq, T., Fitzpatrick, M. C., Bay, R. A., Exposito-Alonso, M., & Keller, S. R. (2020). Genomic Prediction of (Mal)Adaptation Across Current and Future Climatic Landscapes. *Annual Review of Ecology, Evolution, and Systematics*, 51, 245–269. <https://doi.org/10.1146/annurev-ecolsys-020720-042553>
- Chang, C. C., Chow, C. C., Tellier, L. C. A. M., Vattikuti, S., Purcell, S. M., & Lee, J. J. (2015). Second-generation PLINK: Rising to the challenge of larger and richer datasets. *GigaScience*, 4(25), 7. <https://doi.org/10.1186/s13742-015-0047-8>
- Chen, B., Guo, Y., Zhang, X., Wang, L., Cao, L., Zhang, T., Zhang, Z., Zhou, W., Xie, L., Wang, J., Sun, S., Yang, C., & Zhang, Q. (2022). Climate-responsive DNA methylation is involved in the biosynthesis of lignin in birch. *Frontiers in Plant Science*, 13(1), 1090967. <https://doi.org/10.3389/fpls.2022.1090967>
- Chen, Y. L., Jiang, Z. Y., Fan, P., Ericson, P. G. P., Song, G., Luo, X., Lei, F. M., & Qu, Y. H. (2022). The combination of genomic offset and niche modelling provides insights into climate change-driven vulnerability. *Nature Communications*, 13(1), 4821. <https://doi.org/10.1038/s41467-022-32546-z>
- Coccilione, S. M., Chopra, S., Flint-Garcia, S. A., McMullen, M. D., & Peterson, T. (2001). Tissue-specific patterns of a maize Myb transcription factor are epigenetically regulated. *The Plant Journal*, 27(5), 467–478. <https://doi.org/10.1046/j.1365-313X.2001.01124.x>
- Cortijo, S., Wardenaar, R., Colome-Tatche, M., Gilly, A., Etcheverry, M., Labadie, K., Caillieux, E., Hospital, F., Aury, J.-M., Wincker, P., Roudier, F., Jansen, R. C., Colot, V., & Johannes, F. (2014). Mapping the epigenetic basis of complex traits. *Science*, 343(6175), 1145–1148. <https://doi.org/10.1126/science.1248127>
- Cubas, P., Vincent, C., & Coen, E. (1999). An epigenetic mutation responsible for natural variation in floral symmetry. *Nature*, 401(6749), 157–161. <https://doi.org/10.1038/43657>
- Davis, M. B., & Shaw, R. G. (2001). Range shifts and adaptive responses to quaternary climate change. *Science*, 292(5517), 673–679. <https://doi.org/10.1126/science.292.5517.673>
- Dawson, T. P., Jackson, S. T., House, J. I., Prentice, I. C., & Mace, G. M. (2011). Beyond predictions: Biodiversity conservation in a changing climate. *Science*, 332(6025), 53–58. <https://doi.org/10.1126/science.1200303>
- De Baets, S., Meersmans, J., Vanacker, V., Quine, T. A., & Van Oost, K. (2013). Spatial variability and change in soil organic carbon stocks in response to recovery following land abandonment and erosion in mountainous drylands. *Soil Use and Management*, 29(1), 65–76. <https://doi.org/10.1111/sum.12017>
- De Kort, H., Toivainen, T., Van Nieuwerburgh, F., Andres, J., Hytonen, T. P., & Honnay, O. (2022). Signatures of polygenic adaptation align with genome-wide methylation patterns in wild strawberry plants. *New Phytologist*, 235(4), 1501–1514. <https://doi.org/10.1111/nph.18225>
- De Lafontaine, G., Napier, J. D., Petit, R. J., & Hu, F. S. (2018). Invoking adaptation to decipher the genetic legacy of past climate change. *Ecology*, 99(7), 1530–1546. <https://doi.org/10.1002/ecy.2382>
- Dubin, M. J., Zhang, P., Meng, D. Z., Remigereau, M. S., Osborne, E. J., Casale, F. P., Drewe, P., Kahles, A., Jean, G., Vilhjalmsson, B., Jagoda, J., Irez, S., Voronin, V., Song, Q., Long, Q., Ratsch, G., Stegle, O., Clark, R. M., & Nordborg, M. (2015). DNA methylation in *Arabidopsis* has a genetic basis and shows evidence of local adaptation. *eLife*, 4(1), e05255. <https://doi.org/10.7554/elife.05255>
- Eichten, S. R., Briskine, R., Song, J., Li, Q., Swanson-Wagner, R., Hermanson, P. J., Waters, A. J., Starr, E., West, P. T., Tiffin, P., Myers, C. L., Vaughn, M. W., & Springer, N. M. (2013). Epigenetic and genetic influences on DNA methylation variation in maize populations. *Plant Cell*, 25(8), 2783–2797. <https://doi.org/10.1105/tpc.113.114793>
- Ellis, N., Smith, S. J., & Pitcher, C. R. (2012). Gradient forests: Calculating importance gradients on physical predictors. *Ecology*, 93(1), 156–168. <https://doi.org/10.1890/11-0252.1>
- Exposito-Alonso, M., Burbano, H. A., Bossdorf, O., Nielsen, R., Weigel, D., Exposito-Alonso, M., Gomez Rodriguez, R., Barragan, C., Capovilla, G., Chae, E., Devos, J., Dogan, E. S., Friedemann, C., Gross, C., Lang, P., Lundberg, D., Middendorf, V., Kageyama, J., Karasov, T., ... 500 Genomes Field Experiment Team. (2019). Natural selection on the *Arabidopsis thaliana* genome in present and future climates. *Nature*, 573(7772), 126–129. <https://doi.org/10.1038/s41586-019-1520-9>
- Exposito-Alonso, M., Vasseur, F., Ding, W., Wang, G., Burbano, H. A., & Weigel, D. (2018). Genomic basis and evolutionary potential for extreme drought adaptation in *Arabidopsis thaliana*. *Nature Ecology & Evolution*, 2(2), 352–358. <https://doi.org/10.1038/s41559-017-0423-0>
- Ferrero-Serrano, A., & Assmann, S. M. (2019). Phenotypic and genome-wide association with the local environment of *Arabidopsis*. *Nature Ecology & Evolution*, 3(2), 274–285. <https://doi.org/10.1038/s41559-018-0754-5>
- Fick, S. E., & Hijmans, R. J. (2017). WorldClim 2: New 1-km spatial resolution climate surfaces for global land areas. *International Journal of Climatology*, 37(12), 4302–4315. <https://doi.org/10.1002/joc.5086>
- Fitzpatrick, M. C., & Keller, S. R. (2015). Ecological genomics meets community-level modelling of biodiversity: Mapping the genomic landscape of current and future environmental adaptation. *Ecology Letters*, 18(1), 1–16. <https://doi.org/10.1111/ele.12376>
- Flores, K. B., Wolschin, F., & Amdam, G. V. (2013). The role of methylation of DNA in environmental adaptation. *Integrative and Comparative Biology*, 53(2), 359–372. <https://doi.org/10.1093/icb/ict019>
- Furci, L., Jain, R., Stassen, J., Berkowitz, O., Whelan, J., Roquis, D., Baillet, V., Colot, V., Johannes, F., & Ton, J. (2019). Identification and characterisation of hypomethylated DNA loci controlling quantitative resistance in *Arabidopsis*. *eLife*, 8(1), e40655. <https://doi.org/10.7554/eLife.40655>
- Gahlaut, V., Zinta, G., Jaiswal, V., & Kumar, S. (2020). Quantitative epigenetics: A new avenue for crop improvement. *Epigenomes*, 4(4), 25. <https://doi.org/10.3390/epigenomes4040025>

- Gaspar, B., Bossdorf, O., & Durka, W. (2019). Structure, stability and ecological significance of natural epigenetic variation: A large-scale survey in *Plantago lanceolata*. *New Phytologist*, 221(3), 1585–1596. <https://doi.org/10.1111/nph.15487>
- Gawra, J., Valdivieso, A., Roux, F., Laporte, M., de Lorgeril, J., Gueguen, Y., Saccas, M., Escoubas, J.-M., Montagnani, C., Destoumieux-Garzón, D., Lagarde, F., Leroy, M. A., Haffner, P., Petton, B., Cosseau, C., Morga, B., Degremont, L., Mitta, G., Grunau, C., & Vidal-Dupiol, J. (2023). Epigenetic variations are more substantial than genetic variations in rapid adaptation of oyster to Pacific oyster mortality syndrome. *Science Advances*, 9(36), eadh8990. <https://doi.org/10.1126/sciadv.adh8990>
- Gent, J. I., Ellis, N. A., Guo, L., Harkess, A. E., Yao, Y., Zhang, X., & Dawe, R. K. (2013). CHH islands: *de novo* DNA methylation in near-gene chromatin regulation in maize. *Genome Research*, 23(4), 628–637. <https://doi.org/10.1101/gr.146985.112>
- Graaf, A., Wardenaar, R., Neumann, D. A., Taudt, A., & Johannes, F. (2015). Rate, spectrum, and evolutionary dynamics of spontaneous epimutations. *Proceedings of the National Academy of Sciences of the United States of America*, 112(21), 6676–6681. <https://doi.org/10.1073/pnas.1424254112>
- Gugger, P. F., Fitz-Gibbon, S., Pellegrini, M., & Sork, V. L. (2016). Species-wide patterns of DNA methylation variation in *Quercus lobata* and their association with climate gradients. *Molecular Ecology*, 25(8), 1665–1680. <https://doi.org/10.1111/mec.13563>
- Harris, C. J., Scheibe, M., Wongpalee, S. P., Liu, W., Cornett, E. M., Vaughan, R. M., Li, X., Chen, W., Xue, Y., Zhong, Z., Yen, L., Barshop, W. D., Rayatpisheh, S., Gallego-Bartolome, J., Groth, M., Wang, Z., Wohlschlegel, J. A., Du, J., Rothbart, S. B., ... Jacobsen, S. E. (2018). A DNA methylation reader complex that enhances gene transcription. *Science*, 362(6419), 1182–1186. <https://doi.org/10.1126/science.aar7854>
- He, L., Wu, W., Zinta, G., Yang, L., Wang, D., Liu, R., Zhang, H., Zheng, Z., Huang, H., Zhang, Q., & Zhu, J.-K. (2018). A naturally occurring epiallele associates with leaf senescence and local climate adaptation in *Arabidopsis* accessions. *Nature Communications*, 9(1), 460. <https://doi.org/10.1038/s41467-018-02839-3>
- Hoffmann, A. A., Weeks, A. R., & Sgrò, C. M. (2021). Opportunities and challenges in assessing climate change vulnerability through genomics. *Cell*, 184(6), 1420–1425. <https://doi.org/10.1016/j.cell.2021.02.006>
- Holliday, J. A., Aitken, S. N., Cooke, J. E. K., Fady, B., Gonzalez-Martinez, S. C., Heuertz, M., Jaramillo-Correa, J. P., Lexer, C., Staton, M., Whetten, R. W., & Plomion, C. (2017). Advances in ecological genomics in forest trees and applications to genetic resources conservation and breeding. *Molecular Ecology*, 26(3), 706–717. <https://doi.org/10.1111/mec.13963>
- IPCC. (2014). Climate change 2014: Impacts, adaptation, and vulnerability. Part A: Global and sectoral aspects. In *Contribution of Working Group II to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change*. Cambridge University Press.
- Jia, K. H., Zhao, W., Maier, P. A., Hu, X. G., Jin, Y. Q., Zhou, S. S., Jiao, S. Q., El-Kassaby, Y. A., Wang, T. L., Wang, X. R., & Mao, J. F. (2020). Landscape genomics predicts climate change-related genetic offset for the widespread *Platycladus orientalis* (Cupressaceae). *Evolutionary Applications*, 13(4), 665–676. <https://doi.org/10.1111/eva.12891>
- Johannes, F., & Schmitz, R. J. (2019). Spontaneous epimutations in plants. *New Phytologist*, 221(3), 1253–1259. <https://doi.org/10.1111/nph.15434>
- Jump, A. S., & Penuelas, J. (2005). Running to stand still: Adaptation and the response of plants to rapid climate change. *Ecology Letters*, 8(9), 1010–1020. <https://doi.org/10.1111/j.1461-0248.2005.00796.x>
- Karger, D. N., Conrad, O., Boehner, J., Kawohl, T., Kreft, H., Soria-Auza, R. W., Zimmermann, N. E., Linder, H. P., & Kessler, M. (2017). Climatologies at high resolution for the earth's land surface areas. *Scientific Data*, 4(10), 170122. <https://doi.org/10.1038/sdata.2017.122>
- Kawakatsu, T., Huang, S. S. C., Jupe, F., Sasaki, E., Schmitz, R. J., Urich, M. A., Castanon, R., Nery, J. R., Barragan, C., He, Y. P., Chen, H. M., Dubin, M., Lee, C. R., Wang, C. M., Bemm, F., Becker, C., O'Neil, R., O'Malley, R. C., Quarless, D. X., ... Genomes, C. (2016). Epigenomic diversity in a global collection of *Arabidopsis thaliana* accessions. *Cell*, 166(2), 492–505. <https://doi.org/10.1016/j.cell.2016.06.044>
- Kim, J., Kim, J. H., Richards, E. J., Chung, K. M., & Woo, H. R. (2014). *Arabidopsis* VIM proteins regulate epigenetic silencing by modulating DNA methylation and histone modification in cooperation with MET1. *Molecular Plant*, 7(9), 1470–1485. <https://doi.org/10.1093/mp/ssu079>
- Kump, K. L., Bradbury, P. J., Wisser, R. J., Buckler, E. S., Belcher, A. R., Oropeza-Rosas, M. A., Zwönitzer, J. C., Kresovich, S., McMullen, M. D., Ware, D., Balint-Kurti, P. J., & Holland, J. B. (2011). Genome-wide association study of quantitative resistance to southern leaf blight in the maize nested association mapping population. *Nature Genetics*, 43(2), 163–168. <https://doi.org/10.1038/ng.747>
- Lehmair, T. A., Poschlod, P., & Reisch, C. (2022). The impact of environment on genetic and epigenetic variation in *Trifolium pratense* populations from two contrasting semi-natural grasslands. *Royal Society Open Science*, 9(5), 211406. <https://doi.org/10.1098/rsos.211406>
- Leifeld, J., Bassin, S., & Fuhrer, J. (2005). Carbon stocks in Swiss agricultural soils predicted by land-use, soil characteristics, and altitude. *Agriculture Ecosystems & Environment*, 105(1–2), 255–266. <https://doi.org/10.1016/j.agee.2004.03.006>
- Li, H., Peng, Z., Yang, X., Wang, W., Fu, J., Wang, J., Han, Y., Chai, Y., Guo, T., Yang, N., Liu, J., Warburton, M. L., Cheng, Y., Hao, X., Zhang, P., Zhao, J., Liu, Y., Wang, G., Li, J., & Yan, J. (2013). Genome-wide association study dissects the genetic architecture of oil biosynthesis in maize kernels. *Nature Genetics*, 45(1), 43–50. <https://doi.org/10.1038/ng.2484>
- Li, Q., Gent, J. I., Zynda, G., Song, J. W., Makarevitch, I., Hirsch, C. D., Hirsch, C. N., Dawe, R. K., Madzima, T. F., McGinnis, K. M., Lisch, D., Schmitz, R. J., Vaughn, M. W., & Springer, N. M. (2015). RNA-directed DNA methylation enforces boundaries between heterochromatin and euchromatin in the maize genome. *Proceedings of the National Academy of Sciences of the United States of America*, 112(47), 14728–14733. <https://doi.org/10.1073/pnas.1514680112>
- Li, Q., Song, J., West, P. T., Zynda, G., Eichten, S. R., Vaughn, M. W., & Springer, N. M. (2015). Examining the causes and consequences of context-specific differential DNA methylation in maize. *Plant Physiology*, 168(4), 1262–1274. <https://doi.org/10.1104/pp.15.00052>
- Lira-Medeiros, C. F., Parisod, C., Fernandes, R. A., Mata, C. S., Cardoso, M. A., & Gomes Ferreira, P. C. (2010). Epigenetic variation in mangrove plants occurring in contrasting natural environment. *PLoS One*, 5(4), e10326. <https://doi.org/10.1371/journal.pone.0010326>
- Luff, B., Pawlowski, L., & Bender, J. (1999). An inverted repeat triggers cytosine methylation of identical sequences in *Arabidopsis*. *Molecular Cell*, 3(4), 505–511. [https://doi.org/10.1016/s1097-2765\(00\)80478-5](https://doi.org/10.1016/s1097-2765(00)80478-5)
- Manning, K., Tor, M., Poole, M., Hong, Y., Thompson, A. J., King, G. J., Giovannoni, J. J., & Seymour, G. B. (2006). A naturally occurring epigenetic mutation in a gene encoding an SBP-box transcription factor inhibits tomato fruit ripening. *Nature Genetics*, 38(8), 948–952. <https://doi.org/10.1038/ng.1841>
- Martins, K., Gugger, P. F., Llanderal-Mendoza, J., González-Rodríguez, A., Fitz-Gibbon, S. T., Zhao, J. L., Rodríguez-Correa, H., Oyama, K., & Sork, V. L. (2018). Landscape genomics provides evidence of climate-associated genetic variation in Mexican populations of *Quercus rugosa*. *Evolutionary Applications*, 11(10), 1842–1858. <https://doi.org/10.1111/eva.12684>
- McCaw, B. A., Stevenson, T. J., & Lancaster, L. T. (2020). Epigenetic responses to temperature and climate. *Integrative and Comparative Biology*, 60(6), 1469–1480. <https://doi.org/10.1093/icb/icaa049>

- Meng, D. Z., Dubin, M., Zhang, P., Osborne, E. J., Stegle, O., Clark, R. M., & Nordborg, M. (2016). Limited contribution of DNA methylation variation to expression regulation in *Arabidopsis thaliana*. *PLoS Genetics*, 12(7), e1006141. <https://doi.org/10.1371/journal.pgen.1006141>
- Miura, K., Ikeda, M., Matsubara, A., Song, X. J., Ito, M., Asano, K., Matsuoka, M., Kitano, H., & Ashikari, M. (2010). OsSPL14 promotes panicle branching and higher grain productivity in rice. *Nature Genetics*, 42(6), 545–549. <https://doi.org/10.1038/ng.592>
- Mooney, E., Edwards, M., & Niesenbaum, R. (2010). Genetic differentiation between sun and shade habitats in populations of *Lindera benzoin* L. *Population Ecology*, 52(3), 417–425. <https://doi.org/10.1007/s10144-010-0197-6>
- Nocchi, G., Wang, J., Yang, L., Ding, J. Y., Gao, Y., Buggs, R. J. A., & Wang, N. (2022). Genomic signals of local adaptation and hybridization in Asian white birch. *Molecular Ecology*, 32(3), 595–612. <https://doi.org/10.1111/mec.16788>
- Ong-Abdullah, M., Ordway, J. M., Jiang, N., Ooi, S.-E., Kok, S.-Y., Sarpan, N., Azimi, N., Hashim, A. T., Ishak, Z., Rosli, S. K., Malike, F. A., Abu Bakar, N. A., Marjuni, M., Abdullah, N., Yaakub, Z., Amiruddin, M. D., Nookiah, R., Singh, R., Low, E.-T. L., ... Martienssen, R. A. (2015). Loss of Karma transposon methylation underlies the mantled somaclonal variant of oil palm. *Nature*, 525(7570), 533–537. <https://doi.org/10.1038/nature15365>
- Ossowski, S., Schneeberger, K., Lucas-Lledo, J. I., Warthmann, N., Clark, R. M., Shaw, R. G., Weigel, D., & Lynch, M. (2010). The rate and molecular spectrum of spontaneous mutations in *Arabidopsis thaliana*. *Science*, 327(5961), 92–94. <https://doi.org/10.1126/science.1180677>
- Pacifici, M., Foden, W. B., Visconti, P., Watson, J. E. M., Butchart, S. H. M., Kovacs, K. M., Scheffers, B. R., Hole, D. G., Martin, T. G., Akcakaya, H. R., Corlett, R. T., Huntley, B., Bickford, D., Carr, J. A., Hoffmann, A. A., Midgley, G. F., Pearce-Kelly, P., Pearson, R. G., Williams, S. E., ... Rondinini, C. (2015). Assessing species vulnerability to climate change. *Nature Climate Change*, 5(3), 215–225. <https://doi.org/10.1038/nclimate2448>
- Panda, K., Mohanasundaram, B., Gutierrez, J., McLain, L., Castillo, S. E., Sheng, H. D. Y., Casto, A., Gratacos, G., Chakrabarti, A., Fahlgren, N., Pandey, S., Gehan, M. A., & Slotkin, R. K. (2023). The plant response to high CO<sub>2</sub> levels is heritable and orchestrated by DNA methylation. *New Phytologist*, 238(6), 2427–2439. <https://doi.org/10.1111/nph.18876>
- Phillips, S. J., & Dudik, M. (2008). Modeling of species distributions with Maxent: New extensions and a comprehensive evaluation. *Ecography*, 31(2), 161–175. <https://doi.org/10.1111/j.0906-7590.2008.5203.x>
- Poggio, L., de Sousa, L. M., Batjes, N. H., Heuvelink, G. B. M., Kempen, B., Ribeiro, E., & Rossiter, D. (2021). SoilGrids 2.0: Producing soil information for the globe with quantified spatial uncertainty. *The Soil*, 7(1), 217–240. <https://doi.org/10.5194/soil-7-217-2021>
- Quadrana, L., & Colot, V. (2016). Plant transgenerational epigenetics. *Annual Review of Genetics*, 50(1), 467–491. <https://doi.org/10.1146/annurev-genet-120215-035254>
- Rangwala, S. H., Elumalai, R., Vanier, C., Ozkan, H., Galbraith, D. W., & Richards, E. J. (2006). Meiotically stable natural epialleles of Sadhu, a novel *Arabidopsis* retroposon. *PLoS Genetics*, 2(3), 270–281. <https://doi.org/10.1371/journal.pgen.0020036>
- Richards, C. L., Alonso, C., Becker, C., Bossdorf, O., Bucher, E., Colome-Tatche, M., Durka, W., Engelhardt, J., Gaspar, B., Gogol-Doring, A., Grosse, I., van Gurp, T. P., Heer, K., Kronholm, I., Lampei, C., Latzel, V., Mirouze, M., Opgenoorth, L., Paun, O., ... Verhoeven, K. J. F. (2017). Ecological plant epigenetics: Evidence from model and non-model species, and the way forward. *Ecology Letters*, 20(12), 1576–1590. <https://doi.org/10.1111/ele.12858>
- Richards, E. J. (2006). Inherited epigenetic variation - revisiting soft inheritance. *Nature Reviews Genetics*, 7(5), 395–401. <https://doi.org/10.1038/nrg1834>
- Richards, E. J. (2011). Natural epigenetic variation in plant species: A view from the field. *Current Opinion in Plant Biology*, 14(2), 204–209. <https://doi.org/10.1016/j.pbi.2011.03.009>
- Saban, J. M., Watson-Lazowski, A., Chapman, M. A., & Taylor, G. (2020). The methylome is altered for plants in a high CO<sub>2</sub> world: Insights into the response of a wild plant population to multigenerational exposure to elevated atmospheric CO<sub>2</sub>. *Global Change Biology*, 26(11), 6474–6492. <https://doi.org/10.1111/gcb.15249>
- Sang, Y., Long, Z., Dan, X., Feng, J., Shi, T., Jia, C., Zhang, X., Lai, Q., Yang, G., Zhang, H., Xu, X., Liu, H., Jiang, Y., Ingvarsson, P. K., Liu, J., Mao, K., & Wang, J. (2022). Genomic insights into local adaptation and future climate-induced vulnerability of a keystone forest tree in East Asia. *Nature Communications*, 13(1), 6541. <https://doi.org/10.1038/s41467-022-34206-8>
- Schmitz, R. J., Schultz, M. D., Urich, M. A., Nery, J. R., Pelizzola, M., Libiger, O., Alix, A., McCosh, R. B., Chen, H. M., Schork, N. J., & Ecker, J. R. (2013). Patterns of population epigenomic diversity. *Nature*, 495(7440), 193–198. <https://doi.org/10.1038/nature11968>
- Schultz, M. D., Schmitz, R. J., & Ecker, J. R. (2012). 'Leveling' the playing field for analyses of single-base resolution DNA methylomes. *Trends in Genetics*, 28(12), 583–585. <https://doi.org/10.1016/j.tig.2012.10.012>
- Schulz, B., Eckstein, R. L., & Durka, W. (2014). Epigenetic variation reflects dynamic habitat conditions in a rare floodplain herb. *Molecular Ecology*, 23(14), 3523–3537. <https://doi.org/10.1111/mec.12835>
- Shabalin, A. A. (2012). Matrix eQTL: Ultra fast eQTL analysis via large matrix operations. *Bioinformatics*, 28(10), 1353–1358. <https://doi.org/10.1093/bioinformatics/bts163>
- Shang, Y. L., Tan, T. C., Fan, C. X., Nie, H., Wang, Y., Yang, X., Zhai, B. Y., Wang, S. X., & Zhang, L. R. (2022). Meiotic chromosome organization and crossover patterns. *Biology of Reproduction*, 107(1), 275–288. <https://doi.org/10.1093/biolre/ioac040>
- Springer, N. M., & Schmitz, R. J. (2017). Exploiting induced and natural epigenetic variation for crop improvement. *Nature Reviews Genetics*, 18(9), 563–575. <https://doi.org/10.1038/nrg.2017.45>
- Sun, M. H., Yang, Z., Liu, L., & Duan, L. (2022). DNA methylation in plant responses and adaption to abiotic stresses. *International Journal of Molecular Sciences*, 23(13), 6910. <https://doi.org/10.3390/ijms23136910>
- Tock, A. J., Holland, D. M., Jiang, W., Osman, K., Sanchez-Moran, E., Higgins, J. D., Edwards, K. J., Uauy, C., Franklin, F. C. H., & Henderson, I. R. (2021). Crossover-active regions of the wheat genome are distinguished by DMCI, the chromosome axis, H3K27me3, and signatures of adaptation. *Genome Research*, 31(9), 1614–1628. <https://doi.org/10.1101/gr.273672.120>
- Verhoeven, K. J. F., Vonholdt, B. M., & Sork, V. L. (2016). Epigenetics in ecology and evolution: What we know and what we need to know. *Molecular Ecology*, 25(8), 1631–1638. <https://doi.org/10.1111/mec.13617>
- Vidalis, A., Zivkovic, D., Wardenaar, R., Roquis, D., Tellier, A., & Johannes, F. (2016). Methylome evolution in plants. *Genome Biology*, 17(12), 264. <https://doi.org/10.1186/s13059-017-1176-4>
- Waldvogel, A. M., Feldmeyer, B., Rolshausen, G., Exposito-Alonso, M., Rellstab, C., Kofler, R., Mock, T., Schmid, K., Schmitt, I., Bataillon, T., Savolainen, O., Bergland, A., Flatt, T., Guillaume, F., & Pfenninger, M. (2020). Evolutionary genomics can improve prediction of species' responses to climate change. *Evolution Letters*, 4(1), 4–18. <https://doi.org/10.1002/evl3.154>
- Walther, G.-R., Post, E., Convey, P., Menzel, A., Parmesan, C., Beebee, T. J. C., Fromentin, J.-M., Hoegh-Guldberg, O., & Bairlein, F. (2002). Ecological responses to recent climate change. *Nature*, 416(6879), 389–395. <https://doi.org/10.1038/416389a>

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- Wang, H., Xu, S., Fan, Y., Liu, N., Zhan, W., Liu, H., Xiao, Y., Li, K., Pan, Q., Li, W., Deng, M., Liu, J., Jin, M., Yang, X., Li, J., Li, Q., & Yan, J. (2018). Beyond pathways: Genetic dissection of tocopherol content in maize kernels by combining linkage and association analyses. *Plant Biotechnology Journal*, 16(8), 1464–1475. <https://doi.org/10.1111/pbi.12889>
- Warren, R., VanDerWal, J., Price, J., Welbergen, J. A., Atkinson, I., Ramirez-Villegas, J., Osborn, T. J., Jarvis, A., Shoo, L. P., Williams, S. E., & Lowe, J. (2013). Quantifying the benefit of early climate change mitigation in avoiding biodiversity loss. *Nature Climate Change*, 3(7), 678–682. <https://doi.org/10.1038/nclimate1887>
- Wei, X. J., Song, X. W., Wei, L. Y., Tang, S. Q., Sun, J., Hu, P. S., & Cao, X. F. (2017). An epiallele of rice AK1 affects photosynthetic capacity. *Journal of Integrative Plant Biology*, 59(3), 158–163. <https://doi.org/10.1111/jipb.12518>
- Xu, J., Chen, G., Hermanson, P. J., Xu, Q., Sun, C. S., Chen, W. Q., Kan, Q. X., Li, M. Q., Crisp, P. A., Yan, J. B., Li, L., Springer, N. M., & Li, Q. (2019). Population-level analysis reveals the widespread occurrence and phenotypic consequence of DNA methylation variation not tagged by genetic variation in maize. *Genome Biology*, 20(1), 243. <https://doi.org/10.1186/s13059-019-1859-0>
- Yang, A. H., Wei, N., Fritsch, P. W., & Yao, X. H. (2016). AFLP genome scanning reveals divergent selection in natural populations of *Liriodendron chinense* (magnoliaceae) along a latitudinal transect. *Frontiers in Plant Science*, 7(1), 698. <https://doi.org/10.3389/fpls.2016.00698>
- Yu, Y., Aitken, S. N., Rieseberg, L. H., & Wang, T. L. (2022). Using landscape genomics to delineate seed and breeding zones for lodgepole pine. *New Phytologist*, 235(4), 1653–1664. <https://doi.org/10.1111/nph.18223>
- Zhang, F., Chen, W., Zhu, Z., Zhang, Q., Nabais, M. F., Qi, T., Deary, I. J., Wray, N. R., Visscher, P. M., McRae, A. F., & Yang, J. (2019). OSCA: A tool for omic-data-based complex trait analysis. *Genome Biology*, 20(1), 107. <https://doi.org/10.1186/s13059-019-1718-z>
- Zhang, H. M., Lang, Z. B., & Zhu, J. K. (2018). Dynamics and function of DNA methylation in plants. *Nature Reviews Molecular Cell Biology*, 19(8), 489–506. <https://doi.org/10.1038/s41580-018-0016-z>
- Zhang, Q. Z., Wang, D., Lang, Z. B., He, L., Yang, L., Zeng, L., Li, Y. Q., Zhao, C., Huang, H., Zhang, H., Zhang, H. M., & Zhu, J. K. (2016). Methylation interactions in *Arabidopsis* hybrids require RNA-directed DNA methylation and are influenced by genetic variation. *Proceedings of the National Academy of Sciences of the United States of America*, 113(29), E4248–E4256. <https://doi.org/10.1073/pnas.1607851113>
- Zhao, W., Sun, Y. Q., Pan, J., Sullivan, A. R., Arnold, M. L., Mao, J. F., & Wang, X. R. (2020). Effects of landscapes and range expansion on population structure and local adaptation. *New Phytologist*, 228(1), 330–343. <https://doi.org/10.1111/nph.16619>
- Ziolkowski, P. A., Underwood, C. J., Lambing, C., Martinez-Garcia, M., Lawrence, E. J., Ziolkowska, L., Griffin, C., Choi, K., Franklin, F. C. H., Martienssen, R. A., & Henderson, I. R. (2017). Natural variation and dosage of the HEI10 meiotic E3 ligase control *Arabidopsis* crossover recombination. *Genes & Development*, 31(3), 306–317. <https://doi.org/10.1101/gad.295501.116>

## SUPPORTING INFORMATION

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