

# Guidance and tutorials

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## 1. Browse

Multi-omics association of Arabidopsis can be viewed on “Browse” page.

### 1.1 eQTL

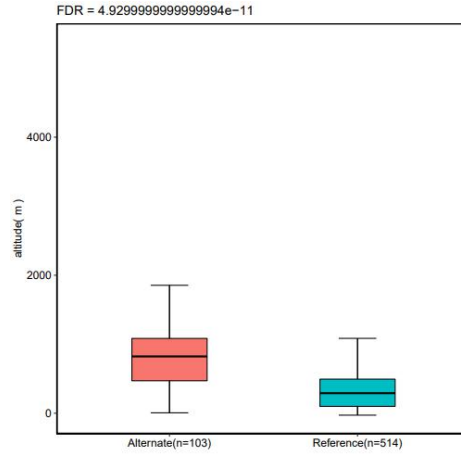
Users can browse eQTLs by clicking the cis-eQTL or trans-eQTL and searching the SNP or Gene of interest. When clicking the Box plot, a Box plot of differential gene expression caused by variant alleles will be displayed.



### 1.2 Environment-related eQTL

Display all eQTL-Environment associations. When clicking the Box plot, a Box plot of differential environmental gradient caused by variant alleles will be displayed.

eQTL	Alleles	Alteration	Environment	Beta	Pvalue	FDR	Type	Display
chr2_16719948	T_A	73	Longitude	8.781E-1	5.290E-20	2.400E-14	trans	Box plot
chr2_16715074	C_T	69	Longitude	8.936E-1	9.960E-20	2.400E-14	trans	Box plot
chr2_16720715	C_T	70	Longitude	8.709E-1	5.450E-19	6.990E-14	trans	Box plot
chr2_16719809	A_T	71	Longitude	8.649E-1	5.800E-19	6.990E-14	trans	Box plot
chr2_16708221	A_T	75	Longitude	8.387E-1	1.050E-18	1.010E-13	cis	Box plot



### 1.3 GWAS-related eQTL

Display all associations between eQTL and GWAS loci.

[SHOW IN TABLES](#)

10 records Search:

eQTL loci	eQTL alleles	eQTL alteration	GWAS loci	GWAS alleles	GWAS alteration	LD	GWAS phenotype	Type
chr4_16921058	C_T	7	chr5_9336708	T	G	0.525650402	clim-pet12	trans/cis
chr4_16921058	C_T	7	chr5_9336708	T	G	0.525650402	clim-pet1	trans/cis
chr4_16921058	C_T	7	chr5_9336708	T	G	0.525650402	clim-pet11	trans/cis
chr4_16921058	C_T	7	chr5_9336708	T	G	0.525650402	clim-aet12	trans/cis
chr4_16921058	C_T	7	chr5_9336708	T	G	0.525650402	clim-bio15	trans/cis
chr4_16921087	G_A	7	chr5_9336708	T	G	0.525650402	clim-pet12	trans/cis
chr4_16921087	G_A	7	chr5_9336708	T	G	0.525650402	clim-pet1	trans/cis

### 1.4 GWAS

Display all associations between phenotypes of AraPheno and variants.

10 records Search:

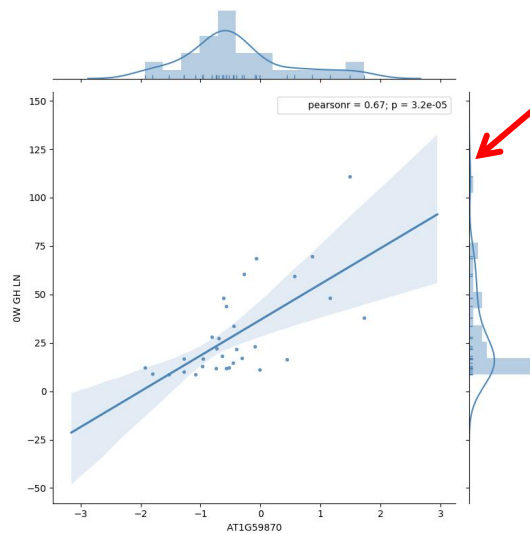
SNP	Chr	Position	Score,(-log10(p-value))	MAF	Study	Phenotype	Phenotype Ontology	Reference	Alteration	Gene
chr4_1269036	chr4	1269036	119.643133	0.219753086	144	M216T665	metabolite content trait	T	A	AT4G02
chr4_1267038	chr4	1267038	116.7682252	0.204938272	144	M216T665	metabolite content trait	C	T	AT4G02
chr4_1266038	chr4	1266038	116.7682252	0.204938272	144	M216T665	metabolite content trait	G	C	AT4G02
chr4_1269179	chr4	1269179	116.3759197	0.197530864	144	M216T665	metabolite content trait	T	G	AT4G02
chr4_1266038	chr4	1266038	113.2387985	0.204938272	146	M172T666	metabolite content trait	G	C	AT4G02
chr4_1267038	chr4	1267038	113.2387985	0.204938272	146	M172T666	metabolite content trait	C	T	AT4G02
chr4_1269163	chr4	1269163	113.0653471	0.192592593	144	M216T665	metabolite content trait	A	C	AT4G02
chr4_1269036	chr4	1269036	111.6742356	0.219753086	146	M172T666	metabolite content trait	T	A	AT4G02

## 1.5 TWAS

Display all associations between phenotypes and genes. When clicking the “Scatter plot”, a scatter plot for describing the association between gene expression and phenotype value will be displayed.

10 records Search:

Gene	Pearson	Pvalue_Pearson	FDR_Pearson	Spearman	Pvalue_Spearman	FDR_Spearman	Study	Display
AT2G17120	0.686030017	3.870E-6	4.399E-2	0.739118297	2.630E-7	1.589E-3	study1	Scatter plot
AT2G29730	0.670998904	7.510E-6	4.399E-2	0.637039436	2.950E-5	3.957E-2	study1	Scatter plot
AT3G57230	-0.663195815	1.040E-5	4.399E-2	-0.726781933	5.190E-7	2.509E-3	study1	Scatter plot
AT1G14370	0.684521313	2.170E-5	2.279E-2	0.700413464	1.150E-5	3.539E-2	study1	Scatter plot
AT1G25390	0.656812967	5.990E-5	3.367E-2	0.672380791	3.430E-5	3.624E-2	study1	Scatter plot
AT1G34420	0.715979129	5.940E-6	1.408E-2	0.662733236	4.860E-5	3.624E-2	study1	Scatter plot
AT1G59870	0.674533095	3.160E-5	2.558E-2	0.660280357	5.300E-5	3.624E-2	study1	Scatter plot

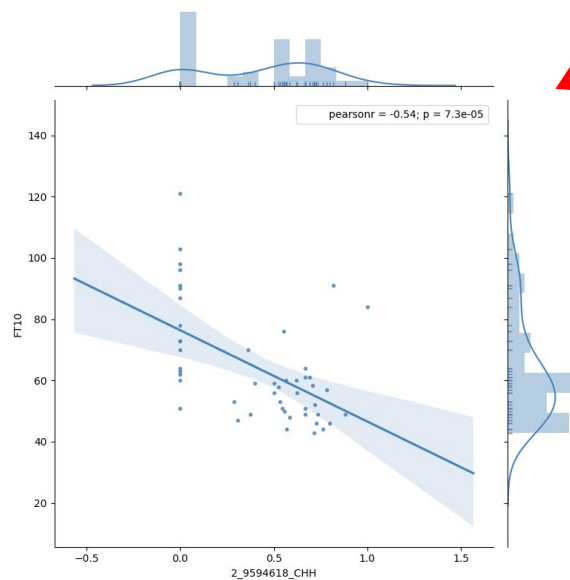


## 1.6 EWAS

Display all associations between phenotypes and methylations. When clicking the “Scatter plot” button, a scatter plot for describing the association of methylation level and phenotype value will be displayed.

10 records Search:

Methylation	Pearson	Pvalue_Pearson	FDR_Pearson	Spearman	Pvalue_Spearman	FDR_Spearman	Study	Display
<a href="#">1_19714699_CG</a>	-0.31647	9.500E-16	1.620E-11	-0.303298568683948	1.569E-14	1.551E-10	study12	Scatter
<a href="#">2_9455171_CHH</a>	-0.315309	1.220E-15	1.880E-11	-0.338339236060814	6.568E-18	5.517E-13	study12	Scatter
<a href="#">2_9456162_CG</a>	-0.300713	2.680E-14	2.030E-10	-0.312239004589087	2.374E-15	3.902E-11	study12	Scatter
<a href="#">2_9456163_CG</a>	-0.303787	1.420E-14	1.220E-10	-0.316046392653939	1.041E-15	2.140E-11	study12	Scatter
<a href="#">2_9592064_CG</a>	-0.30708	7.110E-15	7.340E-11	-0.320632295251279	3.800E-16	1.041E-11	study12	Scatter
<a href="#">2_9592064_CG</a>	-0.534682	7.570E-5	3.813E-2	-0.320632295251279	3.800E-16	1.041E-11	study1	Scatter
<a href="#">2_9594612_CHH</a>	-0.307756	6.170E-15	6.690E-11	-0.309458360867812	4.300E-15	5.667E-11	study12	Scatter
<a href="#">2_9594618_CHH</a>	-0.345445	1.200E-18	1.360E-13	-0.337935290803135	7.226E-18	5.669E-13	study12	Scatter
<a href="#">2_9594618_CHH</a>	-0.535606	7.320E-5	3.766E-2	-0.337935290803135	7.226E-18	5.669E-13	study1	Scatter



## 1.7 Pathway-mQTL

Display all associations between pathway activities and methylations.

10 records Search:

Pathway	Methylation	Pearson	Pvalue_Pearson	FDR_Pearson	Spearman	Pvalue_Spearman	FDR_Spearman
ARGASEDEG-PWY	4_5647239_CG	-0.234935717	3.200E-9	7.884E-4	-0.399561283	3.630E-25	6.260E-19
ARGASEDEG-PWY	4_5647642_CG	-0.243366813	8.250E-10	4.744E-4	-0.340227941	2.890E-18	1.660E-12
ARGASEDEG-PWY	4_5650372_CHH	0.236181764	2.630E-9	7.552E-4	0.363005787	9.540E-21	8.230E-15
ARGASEDEG-PWY	4_5650408_CHH	0.207445342	1.870E-7	1.113E-2	0.309189686	3.350E-15	4.900E-10
ARGASEDEG-PWY	4_5650410_CHH	0.216907343	4.890E-8	4.968E-3	0.329879089	3.320E-17	1.150E-11
ARGASEDEG-PWY	4_5650413_CHH	0.228465536	8.740E-9	1.596E-3	0.322903181	1.640E-16	4.710E-11
ARGASEDEG-PWY	4_5650417_CHH	0.218598808	3.830E-8	4.126E-3	0.310043461	2.790E-15	4.820E-10
ARGASEDEG-PWY	4_5650418_CHH	0.214659902	6.770E-8	5.113E-3	0.300994112	1.890E-14	2.180E-9
ARGASEDEG-PWY	5_6159887_CG	-0.21082054	1.170E-7	7.764E-3	-0.208353462	1.650E-7	4.744E-3

## 1.8 Phenotype-pathway

Display all associations between pathway activities and phenotypes.

10 records Search:

Phenotype	Phenotype Ontology	Pathway	Pearson	Pvalue_Pearson	FDR_Pearson	Spearman	Pvalue_Spearman	FDR_Spearman
2W	days to flowering trait	PWY-1081	0.555824619	1.327E-4	4.178E-2	0.585457602	4.650E-5	2.723E-2
As	bacterial disease resistance	GLYCOLYSIS	0.516852177	4.575E-4	3.605E-2	0.515736821	4.730E-4	4.899E-2
As	bacterial disease resistance	PWY-1042	0.510398168	5.537E-4	3.605E-2	0.496025584	8.359E-4	4.899E-2
As	bacterial disease resistance	PWY-3841	0.525325182	3.540E-4	3.605E-2	0.523523977	3.740E-4	4.899E-2
As	bacterial disease resistance	PWY-5484	0.515697019	4.735E-4	3.605E-2	0.507462969	6.032E-4	4.899E-2
As	bacterial disease resistance	PWY-621	0.533732724	2.726E-4	3.605E-2	0.502352648	6.989E-4	4.899E-2
As	bacterial disease resistance	PWY66-399	0.513279455	5.087E-4	3.605E-2	0.506895155	6.132E-4	4.899E-2

## 1.9 emQTL

Display all associations between gene expressions and methylations.

10 records Search:

Gene	Methylation	Pearson	Pvalue	FDR
AT1G01040	1_107_CHG	-0.329742906	3.430E-17	7.050E-12
AT1G01040	1_108_CG	-0.340326722	2.820E-18	7.720E-13
AT1G01040	1_109_CG	-0.343682723	1.250E-18	5.140E-13
AT1G01040	1_114_CG	-0.35227063	1.490E-19	1.230E-13
AT1G01040	1_115_CG	-0.304853669	8.430E-15	7.700E-10
AT1G01040	1_122_CHG	-0.312349511	1.700E-15	2.790E-10
AT1G01040	1_161_CG	-0.301094416	1.850E-14	1.380E-9
AT1G01040	1_17833_CHG	-0.302284481	1.450E-14	1.190E-9
AT1G01040	1_18445_CG	-0.309004429	3.490E-15	4.100E-10

## 2. Search database

1) Users only need to input a gene symbol or gene id. Then all information for the queried gene in AtMAD will be shown.

2) Users can also search the phenotype of interest. Plant tissues, organs or specific phenotypes can be input objects, all phenotypes were obtained from AraPheno database (<https://arapheno.1001genomes.org/>). Then all information for the corresponding phenotype in AtMAD will be displayed.

3) Users can also search the pathway of interest. Pathway ID (from AraCyc) or metabolite can be input objects. Then all information for the corresponding pathway in AtMAD will be shown.

4) Users can search a genomic region (Position). All variants and methylations in a set genomic region will be displayed. Considering the speed of our web server to retrieve the corresponding data, the recommended range is  $< 100000\text{bp}$ .

Search

Home • Search

SEARCH CONDITION

Datatype:

Gene  
Phenotype  
Pathway  
Position

SEARCH CONDITION

Datatype:

Recommended input range < 100000bp

### 3. Information for variant, gene, methylation, phenotype and pathway

#### 3.1 Variant information

Summary information of searched variants.

SNP:	chr1_4009520
Chrom:	1
Posotion:	4009520
Reference:	C
Alteration:	T
Type:	upstream_gene_variant
Gene:	AT1G11890
Network:	<a href="#">Build Network</a> ↻

Associations of GWAS, cis-eQTL, trans-eQTL, Environment-eQTL are also displayed

#### 3.2 Gene information

Summary information of searched genes.

Gene name:	AT5G10140;FLOWERING LOCUS C (FLC)
Type:	protein_coding
Short_description:	K-box region and MADS-box transcription factor family protein
Summary:	MADS-box protein encoded by FLOWERING LOCUS C - transcription factor that functions as a repressor of floral transition and contributes to temperature compensation of the circadian clock. Expression is downregulated during cold treatment. Vernalization. FRI and the autonomous pathway all influence the state of FLC chromatin. Both maternal and paternal alleles are reset by vernalization. but their earliest activation differs in timing and location. Histone H3 trimethylation at lysine 4 and histone acetylation are associated with active FLC expression. whereas histone deacetylation and histone H3 dimethylation at lysines 9 and 27 are involved in FLC repression. Expression is also repressed by two small RNAs (30- and 24-nt) complementary to the FLC sense strand 3 to the polyA site. The small RNAs are most likely derived from an antisense transcript of FLC. Interacts with SOC1 and FT chromatin in vivo. Member of a protein complex.
Araport11_description:	K-box region and MADS-box transcription factor family protein,(source:Araport11)
Computational_description:	FLOWERING LOCUS C (FLC); CONTAINS InterPro DOMAIN/s: Transcription factor. MADS-box (InterPro:IPR002100). Transcription factor. K-box (InterPro:IPR002487); BEST Arabidopsis thaliana protein match is: K-box region and MADS-box transcription factor family protein (TAIR:AT1G77080.4); Has 1807 Blast hits to 1807 proteins in 277 species: Archae - 0; Bacteria - 0; Metazoa - 736; Fungi - 347; Plants - 385; Viruses - 0; Other Eukaryotes - 339 (source: NCBI BLINK).
Network:	<a href="#">Build Network</a> ↻

Associations of Protein-Protein Interaction, Related Mutant, cis-eQTL, trans-eQTL,



Pathway, GWAS-loci in CDS region, TWAS, Phenotype-CNV and Methylation are shown in order. All URL links can be clicked to find the source of data.

Protein-Protein Interaction			
Protein	Protein name	Methods	PubMed
AT2G22540	SVP	affinity capture in vitro reconstitution assay with recombinant protein	18606145
AT4G00650	FRI	NULL	15505218
AT2G22540	SVP	Reconstituted Complex	18606145
AT1G54440	AT1G54440	Affinity Capture-RNA	25211139
AT5G60410	SIZ1	Biochemical Activity	24218331
AT2G22540	SVP	Reconstituted Complex	18606145
AT3G57230	AGL16	FRET	24876250
AT1G25540	PFT1	FRET	25150167

Related Mutant							
Mutant	Gene	Method	PO	Description	Link	Source	Image
M0313	AT5G10140	NULL		NULL	<a href="http://119.3.41.28:8080/atpid/webfile/simple_detail.php?pro=AT5G10140">http://119.3.41.28:8080/atpid/webfile/simple_detail.php?pro=AT5G10140</a>	NASC	

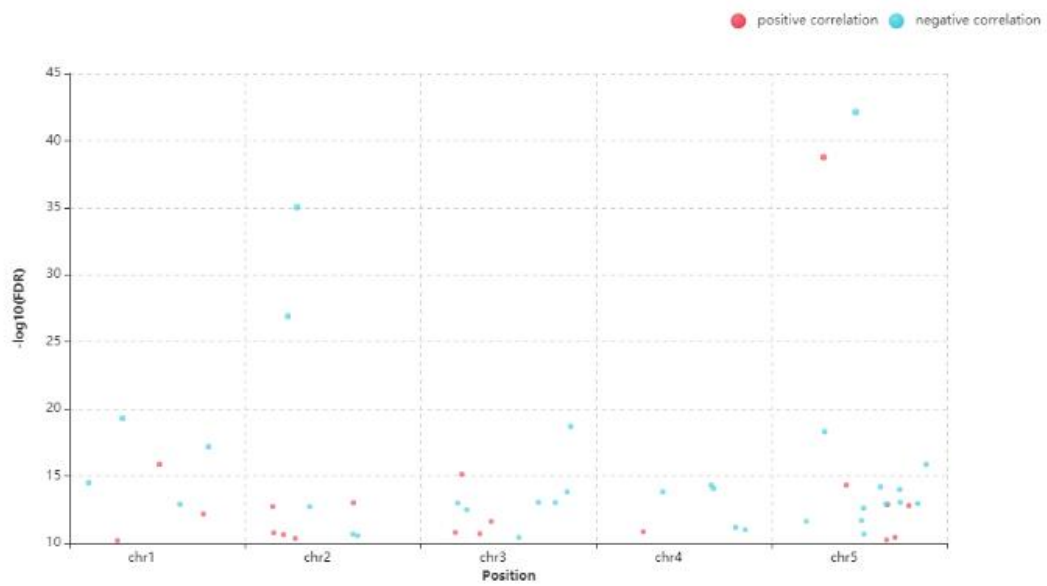
If users want to view or download the mutant image, please click on the image.

### 3.3 Phenotype information

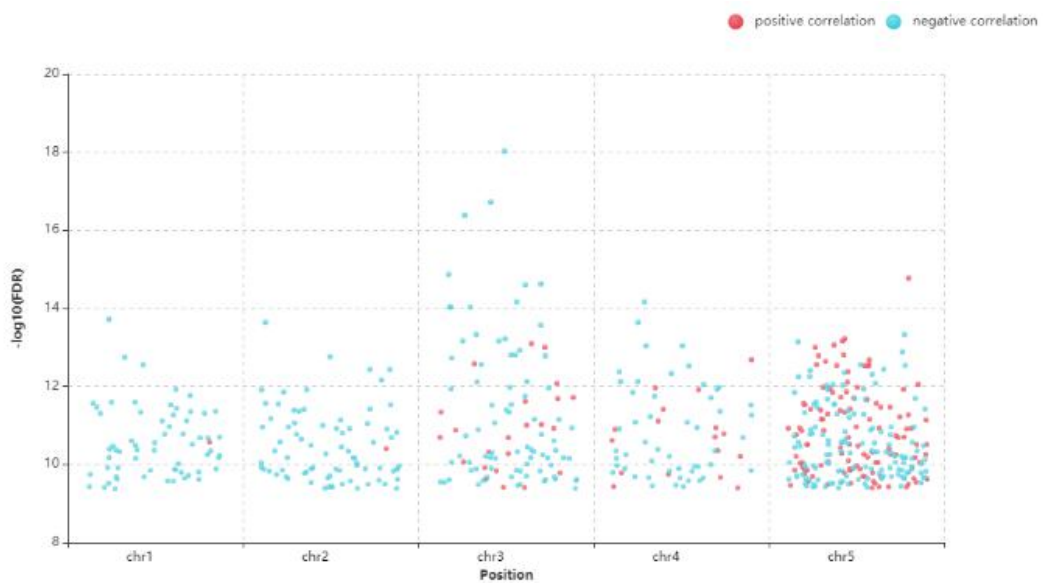
Summary information of searched phenotype.

Summary	
Arapheno Name:	DTF2
Species:	Arabidopsis thaliana (NCBI: 3702)
Phenotype ID:	701
Doi:	10.21958/phenotype:701
Study:	1001 Genomes & easyGWAS
Phenotype Scoring:	Days Until the Inflorescence Stem Elongated to 1cm
Growth_conditions:	Seeds for 1135 Arabidopsis accessions (1001 Genomes Consortium, 2016) were surface-sterilized in 95% ethanol for 5 min and allowed to air-dry. After 6 d of stratification in the dark at 4°C in 0.1% agarose, seeds were distributed across 4800 pots as four replicates in a randomized block design, with each replicate corresponding to one block. Plants were grown in controlled growth chambers with the following settings: 16 h light/8 h darkness, 16°C constant temperature, 65% humidity. All trays within a block were moved to a new shelf and rotated 180°C every other day to minimize position effects.
Integration_date:	2019-06-26T10:43:32.917000Z
TO_term:	TO:0000344
TO_name:	days to flowering trait
TO_definition:	A flowering time trait (TO:0002616) which is the number of days required for an individual flower (PO:0009046) a whole plant (PO:0000003) or a plant population to reach flowering stage (PO:0007616) from a predetermined time point (e.g. the date of seed sowing seedling transplant or seedling emergence). [GR:pj TO:cooper]
TO_source_name:	Plant Trait Ontology
Studytype:	growth chamber study
Network:	<a href="#">Build Network</a>

Manhattan for TWAS, each point can be clicked to view the related gene information.



Manhattan for EWAS, each point can be clicked to view the related methylation information.



Tables for EWAS, TWAS, GWAS, Phenotype-Pathway and CNV-Gene are also displayed in order.

### 3.4 Pathway information

Summary information of searched pathways.

Summary	
Pathway ID:	PWY-5272
Pathway name:	abscisic acid degradation by glucosylation
Reaction ID:	RXN-11469
EC:	EC-2.4.1.263, EC-3.2.1.175
Proteinid:	AT3G21780-MONOMER, AT2G23260-MONOMER, AT2G23250-MONOMER, AT4G34138-MONOMER, AT1G05560-MONOMER, AT1G05530-MONOMER, AT2G23210-MONOMER, AT3G21760-MONOMER, AT3G21790-MONOMER, AT4G15260-MONOMER, AT4G15550-MONOMER, AT1G52400-MONOMER
Protein name:	abscisic acid glycosyltransferase, abscisic acid glucosyltransferase, abscisate $\beta$ -glucosyltransferase, abscisic acid glucose ester $\beta$ -glucosidase
Gene ID:	AT3G21780, AT2G23260, AT2G23250, AT4G34138, AT1G05560, AT1G05530, AT2G23210, AT3G21760, AT3G21790, AT4G15260, AT4G15550, AT1G52400
Gene name:	UGT71B6, UGT84B1, UGT84B2, UGT73B1, UGT75B1, UGT75B2, AT2G23210, AT3G21760, AT3G21790, AT4G15260, AT4G15550, BG1
Links:	<a href="https://pmn.plantcyc.org/ARA/new-image?object=PWY-5272">https://pmn.plantcyc.org/ARA/new-image?object=PWY-5272</a>
Network:	<a href="#">Build Network</a>

Pathway-mQTL, Pathway-related phenotype, Pathway-related gene are listed in order.

Pathway-mQTL							
<a href="#">PDF</a> <a href="#">CSV</a> <a href="#">Excel</a> <a href="#">Print</a> <a href="#">Copy</a>							
Show	<input type="text" value="1"/>	entries	Search: <input type="text"/>				
Pathway	Methylation	Pearson	Pvalue_Pearson	FDR_Pearson	Spearman	Pvalue_Spearman	FDR_Spearman
PWY-5272	5_11651424_CG	-0.202776677	3.54E-07	0.02823259	-0.217949629	4.21E-08	0.000362423
PWY-5272	1_6455046_CG	0.20646353	2.14E-07	0.02823259	0.209014555	1.50E-07	0.000517148
PWY-5272	1_6455075_CG	0.260558814	4.43E-11	7.65E-05	0.263676532	2.55E-11	4.40E-05
PWY-5272	5_21796295_CHH	0.209368478	1.43E-07	0.02823259	0.215853148	5.70E-08	0.000398254
PWY-5272	5_11651002_CHG	-0.205649053	2.40E-07	0.02823259	-0.225688238	1.33E-08	0.000306157
PWY-5272	1_15160651_CG	-0.200742635	4.66E-07	0.031522258	-0.230722692	6.17E-09	0.000274179
PWY-5272	1_15509477_CG	0.201459974	4.23E-07	0.030443513	0.220277821	2.99E-08	0.000346419
PWY-5272	2_5207352_CG	0.204497606	2.81E-07	0.02823259	0.206036134	2.27E-07	0.000606188

Showing 1 to 8 of 8 entries

Phenotype	
No entries found in atmad.	

Gene								
<a href="#">PDF</a> <a href="#">CSV</a> <a href="#">Excel</a> <a href="#">Print</a> <a href="#">Copy</a>								
Show	<input type="text" value="1"/>	entries	Search: <input type="text"/>					
Pathway	Pathway name	Reaction ID	EC	Protein ID	Protein name	Gene ID	Gene name	Links
PWY-5272	abscisic acid degradation by glucosylation	RXN-11469	EC-3.2.1.175	AT1G52400-MONOMER	abscisic acid glucose ester $\beta$ -glucosidase	AT1G52400	BG1	<a href="https://pmn.plantcyc.org/ARA/new-image?object=PWY-5272">https://pmn.plantcyc.org/ARA/new-image?object=PWY-5272</a>
PWY-5272	abscisic acid degradation by glucosylation	RXN-8155	EC-2.4.1.263	AT4G15550-MONOMER	abscisate $\beta$ -glucosyltransferase	AT4G15550	AT4G15550	<a href="https://pmn.plantcyc.org/ARA/new-image?object=PWY-5272">https://pmn.plantcyc.org/ARA/new-image?object=PWY-5272</a>

### 3.5 Methylation information

Summary information of searched methylations.

Summary	
Site:	3_9115557_CG
Region:	CDS
Start:	9115527
Stop:	9115667
Gene:	AT3G25013
Network:	<a href="#">Build Network</a>

Corresponding information of the emQTL, Pathway-mQTL and EWAS are displayed in order.

emQTL									
					PDF	CSV	Excel	Print	Copy
Show	<input type="text"/>	entries	Search:			<input type="text"/>			
Gene	Methylation	Pearson	Pvalue	FDR					
AT3G24900	3_9115557_CG	-0.36999145	1.51E-21	2.06E-16					
AT3G24929	3_9115557_CG	-0.325846703	8.40E-17	5.31E-12					
AT3G25013	3_9115557_CG	0.410130019	1.50E-26	4.33E-21					
AT3G25020	3_9115557_CG	0.424536154	1.61E-28	3.30E-23					
Showing 1 to 4 of 4 entries						<input type="text"/> < 1 >			

Pathway-mQTL											
							PDF	CSV	Excel	Print	Copy
Show	<input type="text"/>	entries	Search:					<input type="text"/>			
Pathway	Methylation	Pearson	Pvalue_Pearson	FDR_Pearson	Spearman	Pvalue_Spearman	FDR_Spearman				
No data available in table											

EWAS											
							PDF	CSV	Excel	Print	Copy
Show	<input type="text"/>	entries	Search:					<input type="text"/>			
Phenotype	Phenotype Ontology	Methylation	Pearson	Pvalue_Pearson	FDR_Pearson	Spearman	Pvalue_Spearman				
Se82	selenium concentration	3_9115557_CG	-0.305299	5.98379679456124e-15	5.76231010246842e-14	-0.326283996202082	5.71609101529957e-17				

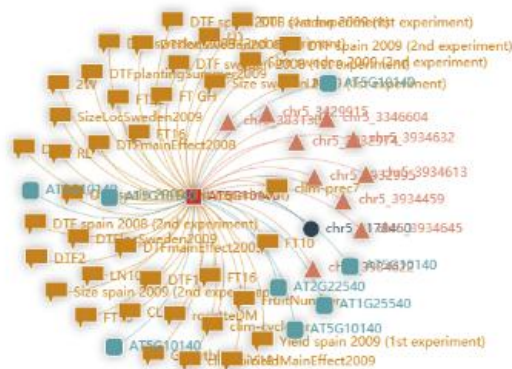
#### 4. Interactive visualization for Multi-omics Associated Networks

In AtMAD, users can build multi-omics association networks for genes, variants, methylations, pathways and phenotypes of interest. When clicking a ‘Build Network’

button, a Multi-omics Associated Network with interactive visualization will be constructed and displayed.

Summary	
Gene ID:	AT5G10140
Type:	protein_coding
Short description:	K-box region and MADS-box transcription factor family protein
Summary:	MADS-box protein encoded by FLOWERING LOCUS C - transcription factor that functions as a repressor of floral transition and contributes to temperature compensation of the circadian clock. Expression is downregulated during cold treatment. Vernalization. FRI and the autonomous pathway all influence the state of FLC chromatin. Both maternal and paternal alleles are reset by vernalization, but their earliest activation differs in timing and location. Histone H3 trimethylation at lysine 4 and histone acetylation are associated with active FLC expression, whereas histone deacetylation and histone H3 dimethylation at lysines 9 and 27 are involved in FLC repression. Expression is also repressed by two small RNAs (30- and 24-nt) complementary to the FLC sense strand 3' to the polyA site. The small RNAs are most likely derived from an antisense transcript of FLC. Interacts with SOC1 and FT chromatin in vivo. Member of a protein complex.
Computational description:	FLOWERING LOCUS C (FLC); CONTAINS InterPro DOMAIN/s: Transcription factor, MADS-box (InterPro:IPR002100), Transcription factor, K-box (InterPro:IPR002487); BEST Arabidopsis thaliana protein match is: K-box region and MADS-box transcription factor family protein (TAIR:AT1G77080.4); Has 1807 Blast hits to 1807 proteins in 277 species: Archae - 0; Bacteria - 0; Metazoa - 736; Fungi - 347; Plants - 385; Viruses - 0; Other Eukaryotes - 339 (source: NCBI BLINK).
Network:	<a href="#">Build Network</a>

Legend for network visualization:  
■ Inquired Gene    ● GWAS-Loci    ■ Protein    ▲ cis-eQTL    ◆ Pathway    ● trans-eQTL    ■ TWAS-Phenotype    ✕ CNV-Phenotype    ■ Methylation



Different data types are represented by different colors or shapes, as illustrated above.

If users are interested in gene/variant/methylation/pathway/phenotype information in the network, please click to see a detailed summary information.

## 5. Usage and case study

**Usage:**

AtMAD is a public repository for large-scale measurements of genome × transcriptome × methylome × pathway × phenotype associations in Arabidopsis, designed for facilitating identification of eQTL, emQTL, pathway-mQTL, pathway-phenotype, GWAS, TWAS and EWAS. AtMAD identifies candidate variants/methylations/genes for specific phenotypes or biological processes, and provides many associations that are novel identified in exploring biological mechanisms. All raw data comes from public free databases, including 1001 Genomes, TAIR, AraPheno, AraGWAS Catalog, AraCyc, AtPID and text mining from PubMed, etc.

In AtMAD, users can browse, search and download multi-omics associations of Arabidopsis.

1) Browse: browse module includes “Browse by datatype”, “Browse by Gene”, “Browse by Variant”. Users can click “Browse” to view all multi-omics associations. More summary information can be displayed through hyperlinks in each table.

## AtMAD: *Arabidopsis thaliana* Multi-omics Association Database

Home Browse Search Download FAQ

**Browse** Browse by datatype

eQTL Environment-eQTL GWAS-eQTL GWAS TWAS EWAS Pathway-mQTL Phenotype-pathway emQTL

cis-eQTL trans-eQTL

For more info about cis-eQTL, please click here.

10 records Search:

SNP	Alleles	Alteration number	Gene	Beta	tstat	Pvalue	FDR	Display
chr4_16921004	G_A	8	AT4G34410	1.521871419	10.85175201	3.660E-25	2.220E-16	Box plot
chr4_16921058	C_T	7	AT4G34410	1.522741867	10.07585134	3.710E-22	5.630E-14	Box plot
chr4_16921082	G_A	7	AT4G34410	1.522741867	10.07585134	3.710E-22	5.630E-14	Box plot

### Browse by datatype

**Browse** Browse by Gene

10 records Search:

Gene ID	Gene name	Protein-protein interaction	Mutant	cis-eQTL
AT5G24780	vegetative storage protein 1 (VSP1)	AT4G18960;AT5G24780;AT1G18080;AT4G09000;AT1G22300	M1804	chr5_071
AT1G09420	glucose-6-phosphate dehydrogenase 4 (G6PD4)	AT5G35790;AT1G09420;AT4G03520	M2553	
AT1G11680	CYTOCHROME P450 51G1 (CYP51G1)	AT3G53510;AT1G11680	M4016;M4015	
AT1G12130	Flavin-binding monooxygenase family protein		M3608	chr1_401

### Browse by Gene

**Browse** Browse by Variant

10 records Search:

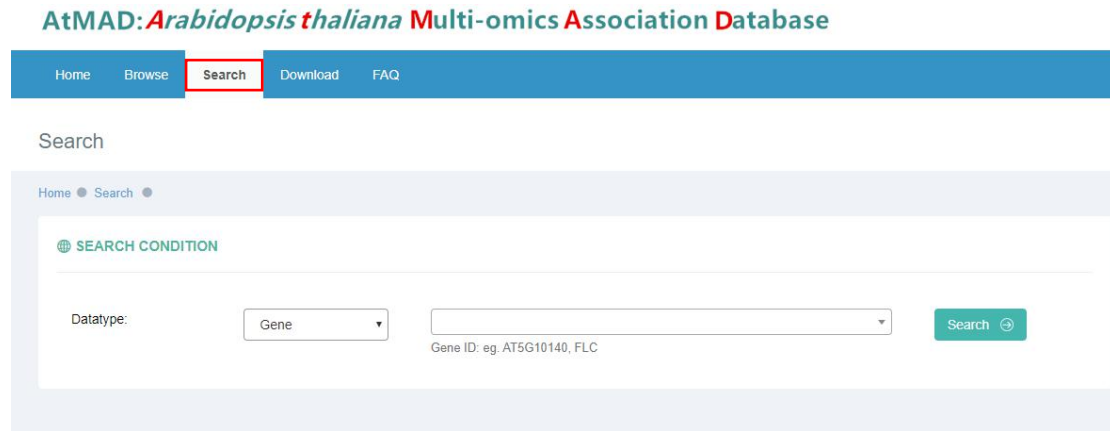
SNP	Reference	Alteration	Type	Gene	cis-eQTL	trans-eQTL	Environment-eQTL
chr2_6320961	C	T	downstream_gene_variant	AT2G14760	AT2G14610	AT3G32092	Longitude;bio9;bio7;bio6;
chr2_6321143	T	A	downstream_gene_variant	AT2G14760	AT2G14610	AT3G32092	Longitude;Elevation;bio9;
chr2_6324246	T	A	upstream_gene_variant	AT2G14760	AT2G14610	AT3G32092	Longitude;bio9;bio7;bio6;
chr2_6331762	C	G	intron_variant	AT2G14770	AT2G14610	AT3G32092	Longitude;bio9;bio7;bio6;
chr2_7974772	C	G	upstream_gene_variant	AT2G18350	AT2G18660	AT1G47920;AT1G29715	Longitude;bio9;bio8;bio7;
chr2_7977474	G	A	intron_variant	AT2G18360	AT2G19190;AT2G18660	AT2G14610;AT2G02430;AT3G57240	Longitude;bio9;bio8;bio7;

### Browse by Variant

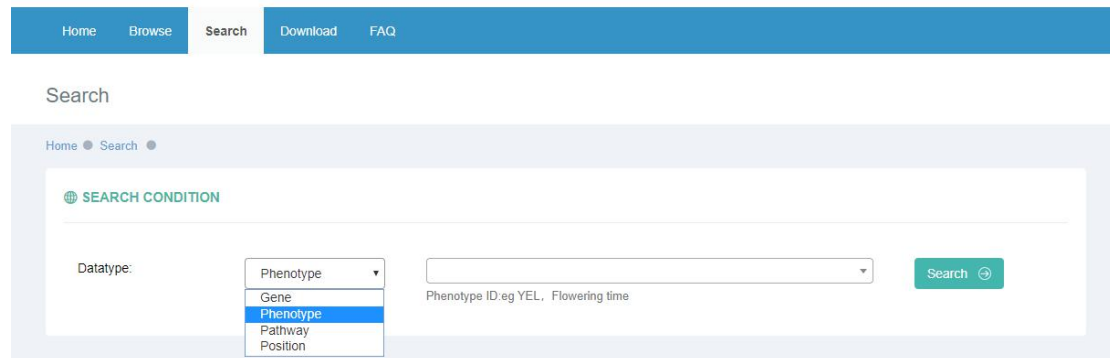
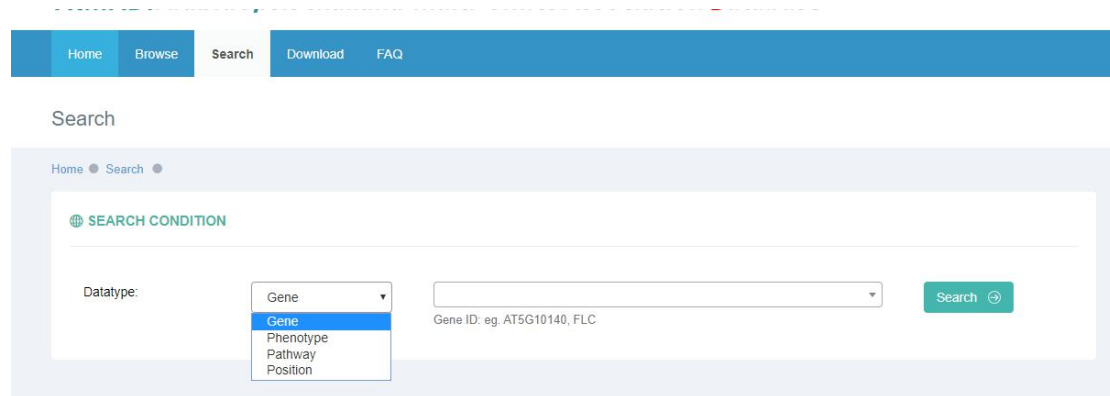
2) Search: Search module includes four functions, users can query their interested

information by searching gene, phenotype, pathway or chromosome regions.

First, users need to click the “Search” Page.



Second, select the search content.





Search

Home ● Search ●

SEARCH CONDITION

Datatype:   
 Position   
 Gene   
 Phenotype   
 Pathway   
 Position

chr\_1 start end

Recommended input range<100000bp

Search

The search module uses intelligent recognition method, users are also allowed to search AtMAD by inputting vague information, for example users can input “flower” in “phenotype module” to find flower-related phenotypes.

Then, after click “Search” button, users can query gene, phenotype, pathway or variant of interest, summary information has been described in the previous section.

### 3) Download:

Home Browse Search Download FAQ

Download

Home ● Download ●

DATA SUMMARY FOR THE ATMAD DATA REPOSITORY IN JUNE 2020

Data type	Details	Total number of associations
cis-eQTL	eQTLs were defined if the SNP was within 1 Mb from the gene transcriptional start site (TSS)	11,796
trans-eQTL	eQTLs were defined if the SNP was beyond the region of 1 Mb from the gene transcriptional start site (TSS)	10,119
Environment-related eQTL	eQTLs that associated with at least one environmental factor	68,837
GWAS-related eQTL	eQTLs that related with known GWAS loci (collected from ArabGWAS)	149,622

Users can download all associations from AtMAD by clicking the hyperlink in “Data type” column.

### Case 1: Search gene “SCPL12”

If users are interested in gene SCPL12 (AT2G22920) which has been reported to be responsible for the production of saiginols and confer greater UV light tolerance in

plants, They can input the corresponding gene name on “Search” page.

The screenshot shows a search interface with a navigation bar containing 'Home', 'Browse', 'Search', 'Download', and 'FAQ'. Below the navigation bar, there is a 'Search' section with a breadcrumb 'Home > Search >'. The main search area is titled 'SEARCH CONDITION' and includes a 'Datatype:' dropdown menu set to 'Gene'. To the right of the dropdown is a search input field containing the text 'SCPL12'. A dropdown menu is open below the input field, showing a suggestion: 'AT2G22920 (serine carboxypeptidase-like 12 (SCPL12))'. A 'Search' button is located to the right of the input field.

On summary page, users can view “Protein-Protein Interaction”, “Related Mutant”, “cis-eQTL”, “trans-eQTL”, “Pathway”, “GWAS-loci in CDS region”, “TWAS” and “Methylation”.

The screenshot shows the 'Summary' page for the gene AT2G22920. The page has a teal header with a 'Summary' tab. Below the header is a table with the following rows:

Gene name:	AT2G22920;serine carboxypeptidase-like 12 (SCPL12)
Type:	protein_coding
Short_description:	serine carboxypeptidase-like 12
Summary:	
Araport11_description:	serine carboxypeptidase-like 12;(source:Araport11)
Computational_description:	serine carboxypeptidase-like 12 (SCPL12); FUNCTIONS IN: serine-type c arboxypeptidase activity; INVOLVED IN: proteolysis; LOCATED IN: plant-t ype cell wall; EXPRESSED IN: stem. inflorescence meristem. hypocotyl. r oot. flower; EXPRESSED DURING: petal differentiation and expansion st age; CONTAINS InterPro DOMAIN/s: Peptidase S10. serine carboxypepti dase (InterPro:IPR001563); BEST Arabidopsis thaliana protein match is: s erine carboxypeptidase-like 11 (TAIR:AT2G22970.3); Has 3940 Blast hits t o 3855 proteins in 454 species: Archae - 0; Bacteria - 499; Metazoa - 627; Fungi - 829; Plants - 1550; Viruses - 0; Other Eukaryotes - 435 (source: N CBI BLink).
Network:	<a href="#">Build Network</a>

Below the summary table, there are three sections, each with a teal header and a white content area:

- Protein-Protein Interaction**: No entries found in atmad.
- Related Mutant**: No entries found in atmad.
- cis-eQTL**: (The content area is currently empty in the screenshot).

trans-eQTL

PDF CSV Excel Print Copy

Pathway

PDF CSV Excel Print Copy

TWAS

Methylation

In cis-eQTL table, all top associations (such as chr2\_10009736, chr2\_9830811, chr2\_9821946...) are found to be associated with “Elevation” when clicking on these SNPs.

cis-eQTL

PDF CSV Excel Print Copy

Show  entries Search:

SNP	Alleles	Alteration number	Gene	Beta	tstat	Pvalue	FDR
chr2_10009736	T_A	64	AT2G22920	0.615167981	7.757468423	3.77E-14	5.32E-07
chr2_9830811	T_A	46	AT2G22920	0.655156474	7.139006632	2.74E-12	1.17E-05
chr2_9821946	T_C/T_A	50/1	AT2G22920	0.61209333	7.062699927	4.56E-12	1.69E-05
chr2_9809837	A_C/A_T	41/2	AT2G22920	0.656688187	7.013816819	6.31E-12	2.18E-05
chr2_10009735	T_G/T_A	64/4	AT2G22920	0.543409066	7.006833605	6.60E-12	2.24E-05
chr2_9841226	A_T	49	AT2G22920	0.596510698	6.855566586	1.78E-11	4.78E-05
chr2_9840880	T_G	50	AT2G22920	0.605651142	6.841740739	1.94E-11	5.14E-05
chr2_9832212	C_G	45	AT2G22920	0.631370892	6.82055234	2.23E-11	5.38E-05
chr2_9819109	A_T	47	AT2G22920	0.621683627	6.817065251	2.28E-11	5.41E-05
chr2_10010445	C_T	49	AT2G22920	0.617519486	6.711811935	4.48E-11	8.98E-05

Environment eQTL

PDF CSV Excel Print Copy

Show  entries Search:

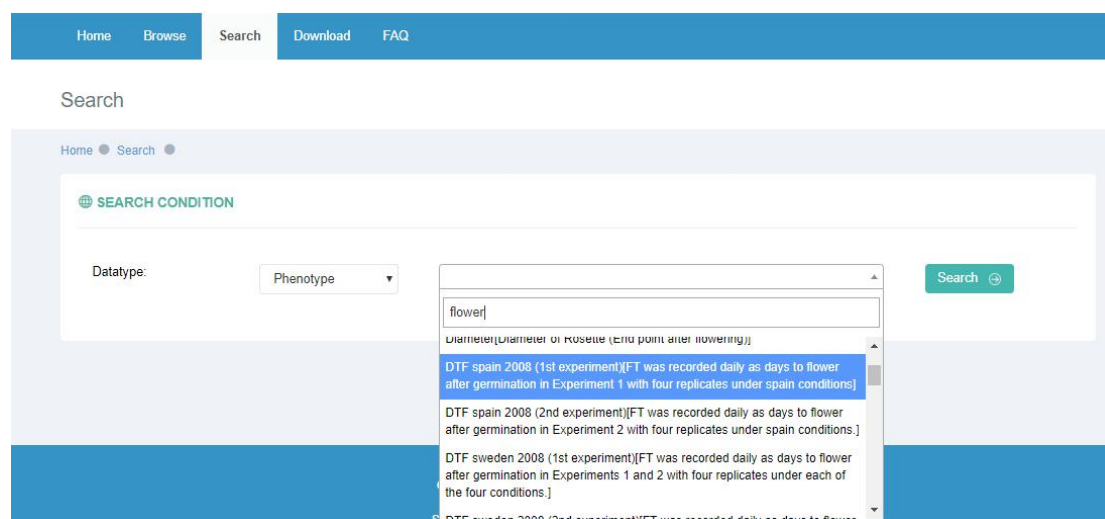
eQTL	Alleles	Alteration	Environment	Beta	Pvalue	FDR	Type
chr2_9841226	A_T	49	Latitude	-0.432278976	0.002273895	0.017189474	cis
chr2_9841226	A_T	49	Elevation	0.326584015	0.005385207	0.032741392	cis
chr2_9841226	A_T	49	bio3	0.39456386	0.006590568	0.037713341	cis
chr2_9841226	A_T	49	bio11	0.348222533	0.008143315	0.044077705	cis
chr2_9841226	A_T	49	bio9	0.384931282	0.00903865	0.047146965	cis

After integrating all the above information, we can draw a conclusion that upstream

eQTLs of AT2G22920 (SCPL12) are highly connected to elevation of habitats, and these eQTLs (such as chr2\_10009736, chr2\_9830811, chr2\_9821946 and chr2-9752742-G-to-T...) are likely to influence the ultraviolet response of individuals by changing gene expression of SCPL12, and allow individuals to adapt to different elevations. These eQTLs will provide the potential genetic basis for the research of UV tolerance in future.

### Case 2: Search phenotype “DTF spain 2008 (1st experiment)”

If users are interested in flowering-related phenotype, just input “flower” or “DTF” (days to flowering) in phenotype module.

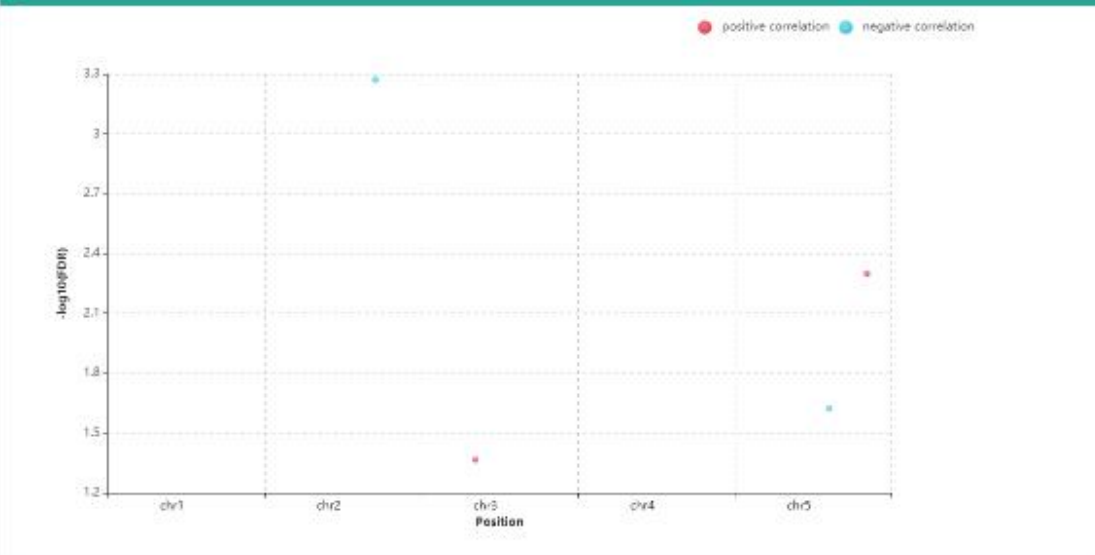


“Summary”, “Manhattan for TWAS”, “EWAS”, “TWAS”, “GWAS” and “Phenotype-Pathway” are displayed in order.

## Summary

Arapheno Name:	DTF spain 2008 (1st experiment)
Species:	Arabidopsis thaliana (NCBI: 3702)
Phenotype ID:	132
Doi:	<a href="https://doi.org/10.21958/phenotype:132">10.21958/phenotype:132</a>
Study:	Flowering time in simulated seasons
Phenotype Scoring:	FT was recorded daily as days to flower after germination in Experiment 1 with four replicates under spain conditions
Growth_conditions:	
Integration_date:	2016-07-04T11:16:56.385000Z
TO_term:	TO:0000344
TO_name:	days to flowering trait
TO_definition:	A flowering time trait (TO:0002616)which is the number of days required for an individual flower (PO:0009046) a whole plant (PO:0000003) or a plant population to reach flowering stage (PO:0007616) from a predetermined time point (e.g. the date of seed sowing seedling transplant or seedling emergence). [GR:p] TO:cooperl]
TO_source_name:	Plant Trait Ontology
Studytype:	NA
Network:	<a href="#">Build Network</a>

## Manhattan for TWAS



## EWAS

## TWAS

## GWAS

In TWAS table, four genes are discovered to be associated with “DTF spain 2008 (1st experiment)”.

Phenotype	Phenotype Ontology	Gene	Pearson	Pvalue_Pearson	FDR_Pearson
DTF spain 2008 (1st experiment)	days to flowering trait	AT2G20440	-0.670015149	2.210E-8	5.346E-4
DTF spain 2008 (1st experiment)	days to flowering trait	AT3G10010	0.564642653	7.110E-6	4.297E-2
DTF spain 2008 (1st experiment)	days to flowering trait	AT5G10140	0.621307588	4.160E-7	5.024E-3
DTF spain 2008 (1st experiment)	days to flowering trait	AT5G63120	-0.58338401	2.950E-6	2.376E-2

Showing 1 to 4 of 4 entries

A total of four genes (AT2G20440, AT5G10140, AT5G63120 and AT3G10010) are assigned to DTF spain 2008 (1st experiment), two of them AT5G10140 (FLC, pearson=0.6213, FDR=0.005) and AT5G63120 (RH30, pearson=-0.5833, FDR=0.023) have been inferred to be involved in flower development process with experimental supports.

Summary

Gene name:	AT5G10140;FLOWERING LOCUS C (FLC)	<b>Summary of FLC</b>
Type:	protein_coding	
Short_description:	K-box region and MADS-box transcription factor family protein	
Summary:	MADS-box protein encoded by FLOWERING LOCUS C - transcription factor that functions as a repressor of floral transition and contributes to temperature compensation of the circadian clock. Expression is downregulated during cold treatment. Vernalization, FRI and the autonomous pathway all influence the state of FLC chromatin. Both maternal and paternal alleles are reset by vernalization, but their earliest activation differs in timing and location. Histone H3 trimethylation at lysine 4 and histone acetylation are associated with active FLC expression, whereas histone deacetylation and histone H3 dimethylation at lysines 9 and 27 are involved in FLC repression. Expression is also repressed by two small RNAs (30- and 24-nt) complementary to the FLC sense strand 3' to the polyA site. The small RNAs are most likely derived from an antisense transcript of FLC. Interacts with SOC1 and FT chromatin in vivo. Member of a protein complex.	
Araport11_description:	K-box region and MADS-box transcription factor family protein.(source:Araport11)	
Computational_description:	FLOWERING LOCUS C (FLC); CONTAINS InterPro DOMAIN/s: Transcription factor, MADS-box (InterPro:IPR002100). Transcription factor, K-box (InterPro:IPR002487); BEST Arabidopsis thaliana protein match is: K-box region and MADS-box transcription factor family protein (TAIR:AT1G77080.4); Has 1807 Blast hits to 1807 proteins in 277 species: Archae - 0; Bacteria - 0; Metazoa - 736; Fungi - 347; Plants - 385; Viruses - 0; Other Eukaryotes - 339 (source: NCBI BLINK).	

The remaining AT2G20440&AT3G10010 are identified as flowering-related genes for the first time in AtMAD. After clicking gene “AT2G20440”, more summary information can be retrieved. Most TWAS associations are DTF-related (flowering-related).

DTF spain 2008 (1st experiment)	days to flowering trait	AT2G20440	-0.670015149	2.21e-08	0.000534559	-0.743770188
DTF spain 2008 (2nd experiment)	days to flowering trait	AT2G20440	-0.590844082	2.05e-06	0.018829966	-0.668711546
DTF spain 2009 (1st experiment)	days to flowering trait	AT2G20440	-0.565285428	6.97e-08	0.000421018	-0.658628977
DTF spain 2009 (2nd experiment)	days to flowering trait	AT2G20440	-0.567066624	6.2e-08	0.000500012	-0.687136777
DTF sweden 2008 (1st experiment)	days to flowering trait	AT2G20440	-0.614129793	6.14e-07	0.004949826	-0.684318785
DTF sweden 2008 (2nd experiment)	days to flowering trait	AT2G20440	-0.572800609	4.88e-06	0.039290905	-0.616811304
DTF sweden 2009 (1st experiment)	days to flowering trait	AT2G20440	-0.549407715	1.9e-07	0.000417065	-0.703283986
DTF sweden 2009 (2nd experiment)	days to flowering trait	AT2G20440	-0.545843181	2.36e-07	0.000725283	-0.641025479
DTF1	days to flowering trait	AT2G20440	-0.516772406	2.97e-41	2.39e-37	-0.583173177
DTF2	days to flowering trait	AT2G20440	-0.508593295	1.12e-39	9.04e-36	-0.579757619
DTF3	days to flowering trait	AT2G20440	-0.507657282	3.45e-39	2.78e-35	-0.578060584
DTFlocSweden2009	days to flowering trait	AT2G20440	-0.431764391	7.91e-05	0.024242175	-0.508236738

The same is true for AT3G10010. Most TWAS associations are DTF-related (flowering-related).

TWAS						
PDF CSV Excel Print Copy						
Show <input type="text"/> entries Search: <input type="text"/>						
Phenotype	Phenotype Ontology	Gene	Pearson	Pvalue_Pearson	FDR_Pearson	Spe
DTF spain 2008 (1st experiment)	days to flowering trait	AT3G10010	0.564642653	7.11e-06	0.042971238	0.50
DTF spain 2008 (2nd experiment)	days to flowering trait	AT3G10010	0.563355891	7.54e-06	0.031974299	0.49
DTF spain 2009 (1st experiment)	days to flowering trait	AT3G10010	0.476103769	1.05e-05	0.005312099	0.47
DTF spain 2009 (2nd experiment)	days to flowering trait	AT3G10010	0.467235316	1.61e-05	0.008797102	0.49
DTF sweden 2009 (1st experiment)	days to flowering trait	AT3G10010	0.470572937	1.38e-05	0.004892553	0.49
DTF sweden 2009 (2nd experiment)	days to flowering trait	AT3G10010	0.48855701	5.68e-06	0.003432519	0.53
DTFmainEffect2008	days to flowering trait	AT3G10010	0.566316692	6.59e-06	0.039809307	0.50
DTFmainEffect2009	days to flowering trait	AT3G10010	0.474622483	1.13e-05	0.005444937	0.47
DTFplantingSummer2009	days to flowering trait	AT3G10010	0.417910533	0.000140619	0.039528664	0.45
Size sweden 2009 (1st experiment)		AT3G10010	0.460112995	3.28e-05	0.00600417	0.46

After integrating the above information, we discovered two potential flowering-related genes (AT2G20440&AT3G10010) that were not reported before, for their significant correlations with DTF in different TWASs.

The usage of AtMAD is not limited to above two cases, more information (such as discovering pathway-related methylations, expression-methylation associations and phenotype-methylation associations) can also be mined in the AtMAD. Compared to the information at single-omics level, the multi-omics association network can convey more information for specific phenotype or biomolecule. AtMAD can not only help us to accurately identify functional biomolecules, but also provide potential genetic mechanisms for interpreting the functional associations.

## 6. Contact us

### Scientific Problems



We welcome any suggestions regarding how to improve our database, please feel free to contact us with feedback. Tieliu Shi: [tieliushi@yahoo.com](mailto:tieliushi@yahoo.com)

#### Technical Problems

If you have any questions about the usage of AtMAD, please contact Jian Ouyang: [ouyangjian12@163.com](mailto:ouyangjian12@163.com)