

# HACER

## Browse

Browse enhancers by cell line

## Query

**SNP:** Search a GWAS risk SNP or eQTL variant to find cell-type-specific enhancers harboring the SNP/variant, and show TF-enhancer-gene interactions.

**Gene:** Search a gene to find cell-type-specific enhancers targeting this gene.

**Coordinate:** Search a genomic region to find cell-type-specific enhancers overlapping this region.

**Batch:** Search a set of genomic regions to obtain an annotation summary on cell-type-specific enhancers, TF-enhancer-target interactions and associated GWAS phenotypes, and to prioritize them based on their annotations.

## Download

Download enhancers by cell line

## Contact

Report new dataset

Submit feed back

**Supplementary Figure S1. Functionality of HACER.** Functionality of HACER includes browse, query, download and contact. The query function provides four ways: SNP-centric, gene-centric, coordinate-centric, and batch query.

**A** Select the cell type(s) you want to browse

**B** Show 10 entries

Search:

Enhancer_ID	Chr	Start	End	Closest_Gene	Distance	Technique	CellType	Support
AE_hg19_A549_148	chr10	105001817	105002606	OBFC1	675439	GRO-seq	A549	ENCODE ChromMM
AE_hg19_A549_149	chr10	12375284	12376150	LOC439949	5752897	GRO-seq	A549	ENCODE ChromMM
AE_hg19_A549_150	chr10	21816756	21817957	ANKRD26	5571470	GRO-seq	A549	ENCODE ChromMM
AE_hg19_A549_151	chr10	30810921	30812280	MAP3K8	87971	GRO-seq	A549	ENCODE ChromMM
AE_hg19_A549_152	chr10	32258351	32259136	ZNF438	937485	GRO-seq	A549	ENCODE ChromMM
AE_hg19_A549_153	chr10	33268114	33273526	NRP1	350307	GRO-seq	A549	ENCODE ChromMM
AE_hg19_A549_154	chr10	33293368	33295381	NRP1	328452	GRO-seq	A549	ENCODE ChromMM
AE_hg19_A549_155	chr10	36707052	36707369	FZD8	776690	GRO-seq	A549	ENCODE ChromMM
AE_hg19_A549_156	chr10	37384531	37385441	FZD8	1454169	GRO-seq	A549	ENCODE ChromMM
AE_hg19_A549_157	chr10	37782187	37782680	FZD8	1851825	GRO-seq	A549	ENCODE ChromMM

Showing 31 to 40 of 4,232 entries

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**C** Basic TF binding Target genes GWAS eQTL

Name: AE\_hg19\_A549\_154

Cell type: A549

Genome: hg19

Location: chr10:33293368-33295381

Sequence: [Show](#)

Closest active gene (distance): NRP1 (328452bp)

Active gene(s) within 50kb: NA

Source: GSE52935

Support:

VISTA Ensembl Regulatory Build ENCODE Enhancer

**D** Basic TF binding Target genes GWAS eQTL

TFs bound to AE\_hg19\_A549\_154:

Show 10 entries

Search:

TF	c_distance	c_score	-log10 c_pvalue	h_distance	h_score	-log10 h_pvalue	CellType
ATF3	0	589	3.17580163204829	0	589	3.17580163204829	A549
BCL3	44	760	3.93130528142167	44	760	3.93130528142167	A549
BHLHE40	18	291	2.15992092031485	18	291	2.15992092031485	A549
CEBPB	129	1000	4.63583546331164	129	1000	4.63583546331164	A549
CREB1	60	801	3.09292890235521	60	801	3.09292890235521	A549
EP300	0	1000	4.39352255832354	0	1000	4.39352255832354	A549
ETS1	0	289	3.33931891322614	0	289	3.33931891322614	A549
FOXP2	5	1000	4.32190887354751	5	1000	4.32190887354751	A549
GABPA	0	219	2.2504750351821	0	418	3.60927417237851	A549
NR3C1	73	366	2.70407248251456	97	1000	4.22336612643996	A549

Showing 1 to 10 of 18 entries

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**E** Basic TF binding Target genes GWAS eQTL

Expression:

Super enhancer(s) (dbSuper):

dbSUPER_ID	S_chr	S_start
SE_28190	chr10	33226424
SE_29371	chr10	33245690
SE_34909	chr10	33268518
SE_36090	chr10	33268491

**F** Basic TF binding Target genes GWAS eQTL

GWAS SNPs in AE\_hg19\_A549\_154:

Show 10 entries

SNPs	Chr	Position	PMID	DISEASE/TRAIT	Region	p-value	OR/Beta
rs11009175	chr10	33294775	20800221	Depression (quantitative trait)	10p11.22	5E-6	0.16

**G** Basic TF binding Target genes GWAS eQTL

eQTLs in AE\_hg19\_A549\_154:

Show 10 entries

Search:

gene_ID	gene_Name	variant_ID	rs_id_SNP147_GRCh37p13	tss_Distance	p-value	Beta	Tissue/CellType
ENSG00000216937.7	CCDC7	10_33294775_G_A_b37	rs11009175	559707	8.17831e-07	0.326073	Esophagus_Mucosa
ENSG00000216937.7	CCDC7	10_33294775_G_A_b37	rs11009175	559707	7.75013e-05	0.222961	Nerve_Tibial
ENSG00000228816.1	AK3P5	10_33293588_C_T_b37	rs149310852	60179	4.55801e-05	0.899772	Cells_Transformed_Fibroblasts
ENSG00000273038.1	RP11-479G22.8	10_33294775_G_A_b37	rs11009175	115536	8.13464e-06	-0.585437	Pituitary
ENSG00000273038.1	RP11-479G22.8	10_33294775_G_A_b37	rs11009175	115536	1.06391e-05	-0.303228	Artery_Aorta
ENSG00000273038.1	RP11-479G22.8	10_33293588_C_T_b37	rs149310852	115349	2.35594e-05	-0.510712	Adipose_Visceral_Omentum
ENSG00000273038.1	RP11-479G22.8	10_33294775_G_A_b37	rs11009175	115536	5.73217e-06	-0.312524	Thyroid
ENSG00000273038.1	RP11-479G22.8	10_33294775_G_A_b37	rs11009175	115536	2.17036e-05	-0.323242	Cells_Transformed_Fibroblasts
ENSG00000273038.1	RP11-479G22.8	10_33294786_C_G_b37	rs111743079	115547	1.62351e-06	-0.669272	Heart_Left_Ventricle
ENSG00000273038.1	RP11-479G22.8	10_33293841_C_A_b37	rs143448150	115602	6.88349e-06	-0.505891	Heart_Left_Ventricle

Showing 1 to 10 of 15 entries

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**E** Basic TF binding Target genes GWAS eQTL

AE\_hg19\_A549\_154's target genes:

Show 10 entries

Search:

Gene	Cell/Tissue	Detection Method	PMID
C10orf68	IMR90	4DGenome: Hi-C	24141950
ITGB1	IMR90	4DGenome: Hi-C	24141950

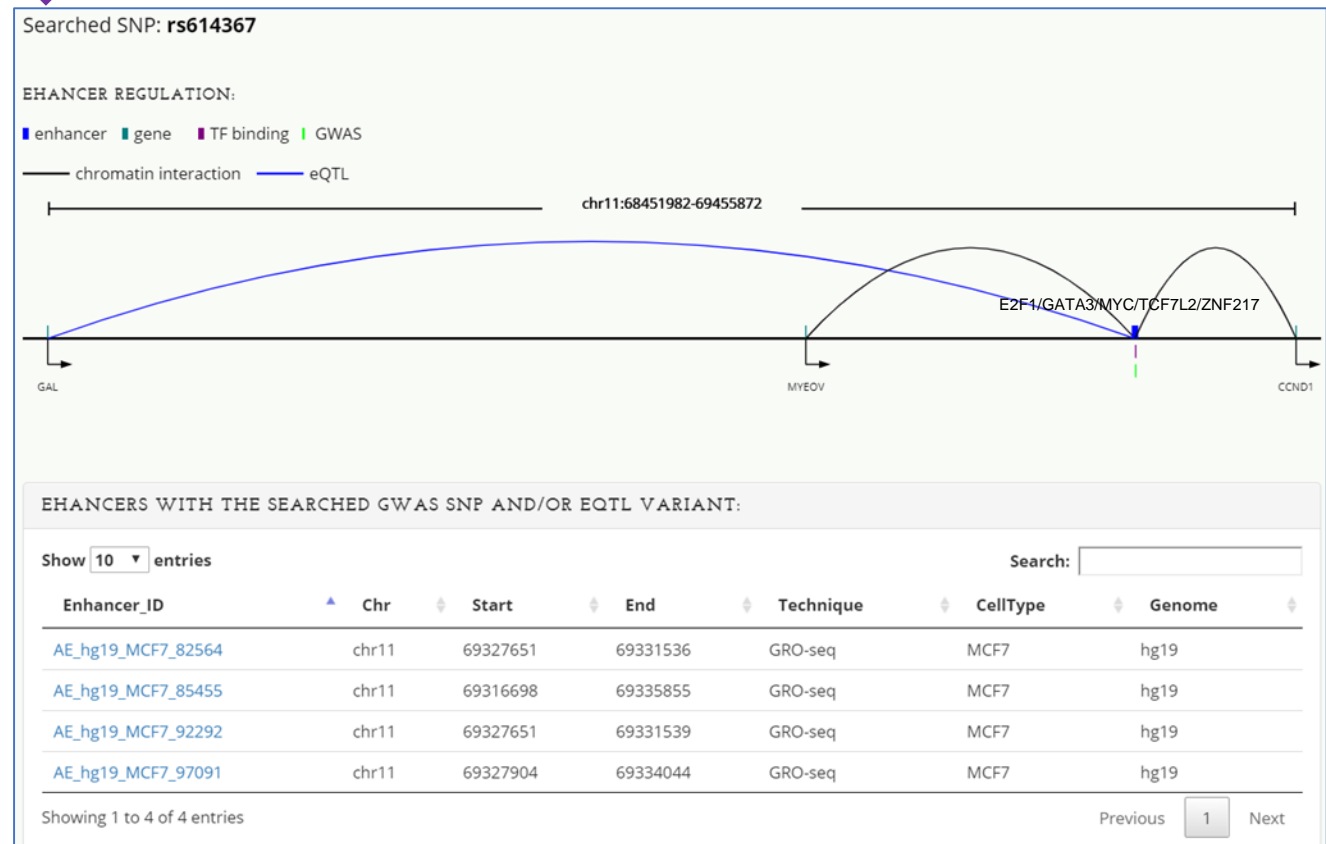
**Supplementary Figure S2. Screenshot of browsing HACER.** (A) Select the cell type for browsing. (B) List of enhancers in the cell type. (C-G) Detailed information of a selected enhancer, including basic information (C), TF binding (D), target genes (E), NHGRI-EBI GWAS SNP hits (F), and GTEx eQTL traits (G).

SNP Gene Coordinate Batch

Interpret GWAS risk SNPs or eQTL variants by exploring enhancer function:

SNP (rsID):  e.g.: rs614367 Type:

Active in Cell:  e.g.: MCF7 Chromatin Interaction in Cell/Tissue:  e.g.: MCF7



**Supplementary Figure S3. An example of interpreting the association of SNP rs614367 with breast cancer risk.** (A) Query HACER by SNP rs614367 in MCF7 cell line. (B) Enhancer-mediated regulatory network, which shows enhancers (blue) harbouring the SNP (lime), their upstream TF binding (purple) and downstream targeted genes (teal). Enhancer-gene interactions are denoted by black lines if experimentally validated or blue lines if predicted from eQTL analysis.

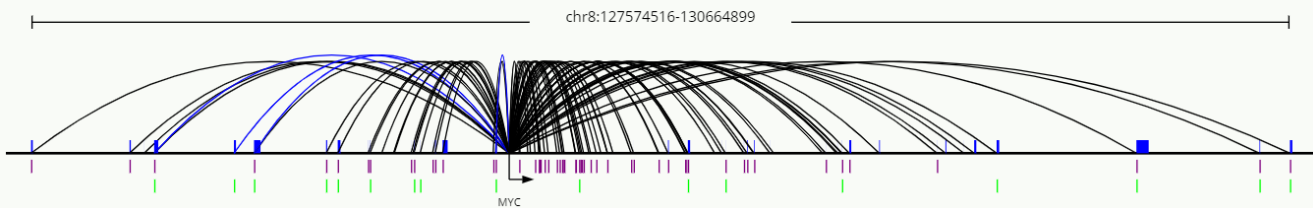
Searched gene: **MYC**

**A**

EHANCER REGULATION:

■ searched gene ■ enhancer ■ enhancer longer than 12.5kb ■ TF binding ■ GWAS

— chromatin interaction — eQTL



Searched gene: **MYC**

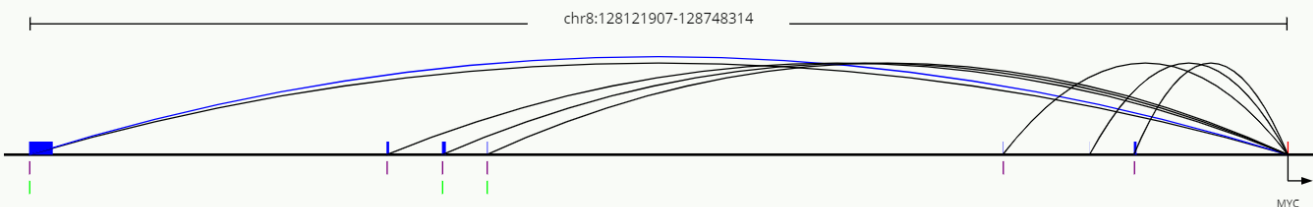
**HCT116**

**B**

EHANCER REGULATION:

■ searched gene ■ enhancer ■ enhancer longer than 12.5kb ■ TF binding ■ GWAS

— chromatin interaction — eQTL



Searched gene: **MYC**

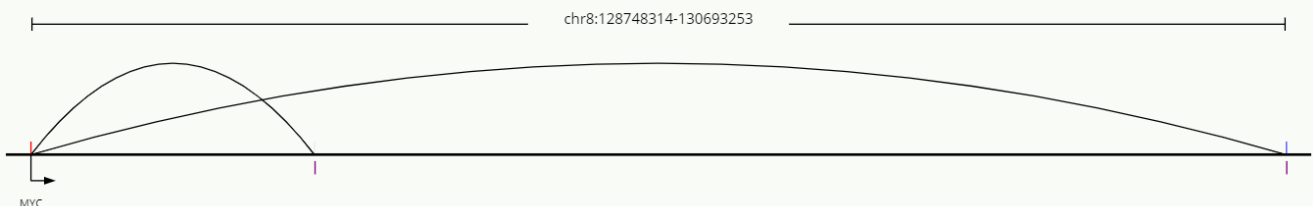
**K562**

**C**

EHANCER REGULATION:

■ searched gene ■ enhancer ■ enhancer longer than 12.5kb ■ TF binding ■ GWAS

— chromatin interaction — eQTL



**Supplementary Figure S4. An example of exploring tumor-specific enhancers targeting MYC.** Query HACER by MYC gene in all cells (A), only in HCT116 cell (B) or in K562 cell (C). Enhancers (light blue or blue boxes) targeting MYC, along with their upstream TF binding (purple) and GWAS risk SNP (lime) are shown. Enhancer-MYC interactions are denoted by black lines if experimentally validated or blue lines if predicted from eQTL analysis.

**A**

**SNP Gene Coordinate Batch**

Enter a set of coordinates.

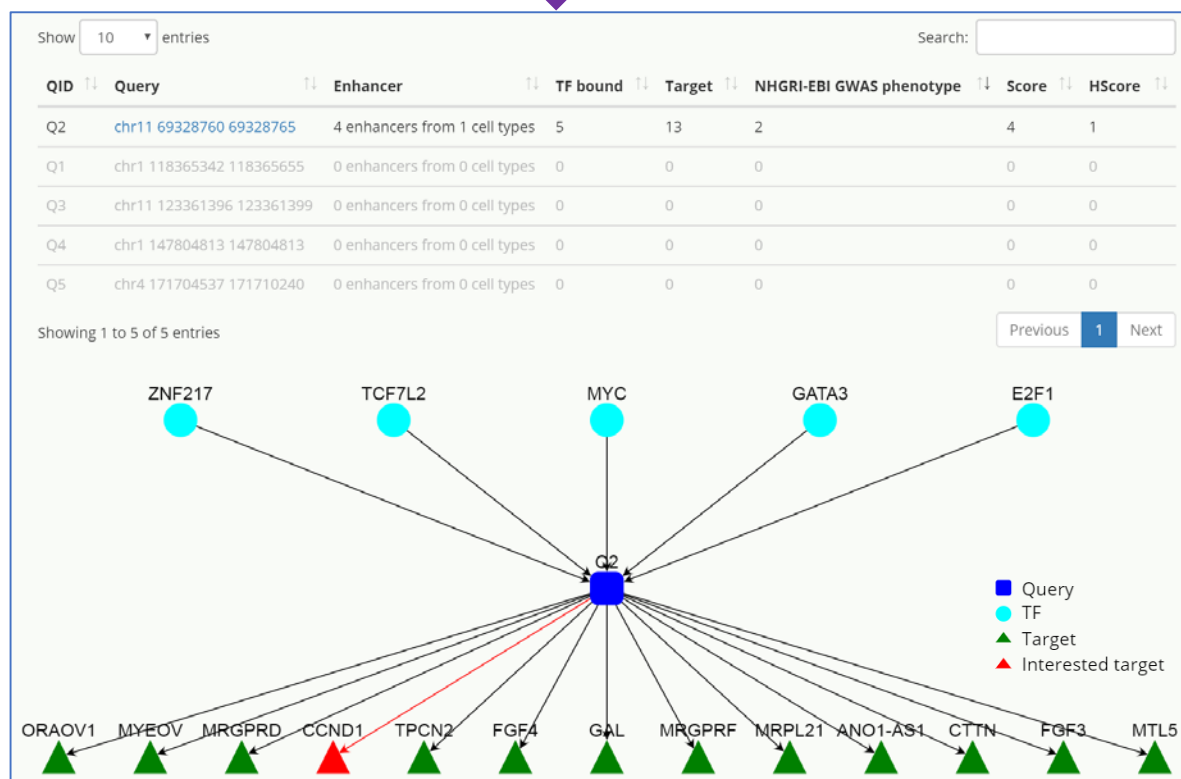
Paste/type coordinates here in bed format: [Example](#)

```
chr1 118365342 118365655
chr11 69328760 69328765
chr11 123361396 123361399
chr1 147804813 147804813
chr4 171704537 171710240
```

Enter a set of target genes to limit query results (optional).

Paste/type gene names here (one gene per line): [Example](#)

```
CCND1
```

**B**

**Supplementary Figure S5. An example for prioritizing/annotating non-coding variants/enhancers.**

(A) Query HACER by a set of coordinates (locations of enhancer or non-coding variants) and a set of target genes. (B) Queries can be ranked by the number of available functional evidence (Score) or by the number of target genes of interest (HScore) (top panel). A network is provided to show upstream TFs (cyan circle) and downstream targets (green triangle) of queries (blue rectangle) with interactions and genes of interest highlighted in red.(bottom panel).