ENCODE Element Browser

Goal: to navigate the candidate DNA elements predicted by the ENCODE consortium, including gene expression, DNase I hypersensitive sites, TF binding sites, and candidate enhancers/promoters.

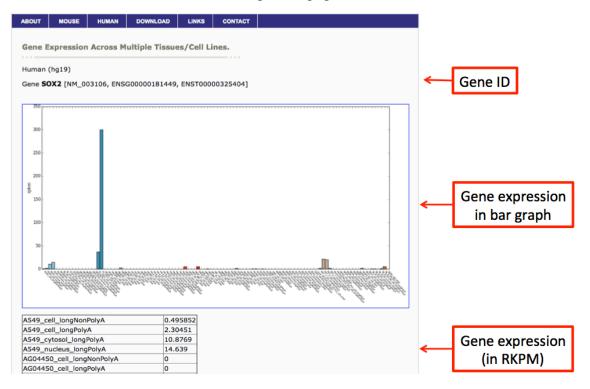
Link: http://promoter.bx.psu.edu/ENCODE

Option 1: Search Gene expression by gene, across all cell types:

Click HUMAN or MOUSE in the navigation bar to choose the right species; type in the official gene name (for example, sox2) and click submit.

uery human ENCODE data! ption 1: Search gene expression across ~ 60 human cell types (total 108 datasets) Human (hg19) ÷ Gene name(Sox2, Nanog) submit! ption 2: Search cis-elements in a given genomic region human (hg19) ÷ chr1 ÷ start: end: submit! ption 3: search cis-elements surrounding a gene Human (hg19) ÷ Gene name(Sox2, Nanog) ctended region (default +/- 100kb) kb submit! ption 4: search cis-elements LINKED to a gene based on DNaseI HSS specificity Human (hg19) ÷ Gene name(Sox2, Nanog)	HOME	MOUSE	HUMAN	DOWNLOAD	LINKS	CONTACT		
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ktended region (default +/- 100kb) kb submit	Optior	3: search	cis-elemer	nts surroundin	g a gene			
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	Extend	ed region (o	lefault +/- 1	00kb)		kb subn	nit!	
luman (hg19) Gene name(Sox2, Nanog) submit!	Option	4: search	cis-elemer	ts LINKED to	a gene ba	sed on DNa	seI HSS specific	ity
	Humar	(hg19) 🗘 🕻	Gene name(S	Sox2, Nanog)			submit!	

You will be re-directed to the following result page.



In the upper panel of the result page, we plotted gene expression in a bar graph that you can directly use in your publication. In the table below the bar graph, we listed the RPKM values across all the tissue/cell types for the queried gene.

Option 2: Search cis-elements in a given genomic region:

Under option 2, first choose chromosome from the dropdown menu and then type in the start and the end position (for example, chr3, 181000000, 182000000); click submit.

HOME	MOUSE	HUMAN	DOWNLOAD	LINKS	CONTACT		
Ouerv	human E	NCODE da	al				
query							
Option	1: Search	gene expr	ession across	~ 60 hun	nan cell ty	oes (total 108	datasets)
Human	(hg19) 🛟 🕻	Gene name(S	Sox2, Nanog			submit!	
Option	2: Search	cis-elemer	nts in a given	genomic	region		
human	(hg19) ‡	chr3 🗘 sta	art: 181000000		end: 181	2000000	submit!
Option	3: search	cis-elemer	ts surroundin	g a gene			
Human	(hg19) 🗘 🤇	Gene name(S	Sox2, Nanog	SOX2			
Extende	ed region (c	lefault +/- 1	00kb) 20		kb su	bmit!	
Option	4: search	cis-elemer	ts LINKED to	a gene ba	ased on DN	laseI HSS spec	ificity
Human	(hg19) 🗘 🤇	Gene name(S	Sox2, Nanog)		submit!	

First, we can see the experimentally determined DNase I Hypersensitive sites (DHS). The first column is the coordinates of DHS and the second column lists the tissue/cell type where the DHS is present. <u>Note:</u> at this time, the queried DHS sites only include 14 cell types where we have both DHS and H3K27ac ChIP-Seq data: *GM12878, H1-hESC, HeLa-S3, HepG2, HMEC, HSMM, HSMMtube, HUVEC, K562, NH-A, NHDF-Ad, NHEK, NHLF, Osteob*l. The list will be expanded soon to incorporate more cell types. For more information, please visit: <u>https://www.encodeproject.org/data/annotations/</u>

НОМЕ	MOUSE	HUMAN	DOWNLOAD	LINKS	CONTACT						
Candidate cis-elements in your queried region.											
Crocier	Species: human_hg19 chr3:181000000-1812000000										
species	s. numan_n	g19 cill3:10	100000-18120	00000							
DNase	I Hyperser	nsitive Site	s:								
Coordi	nate	٦	issue/cell type								
chr3:18	81010880-1	81011030	NH-A,HSMM,HSI	1Mtube,Hl	JVEC,NHLF,NH	EK,HMEC,GM12878					
chr3:18	81011740-1	81011890	IMEC								
chr3:18	81016320-1	81016470	IMEC								
chr3:1	81018360-1	81018510	NH-A								
chr3:1	81034320-1	81034470	NH-A,HUVEC,He	La-S3,NHL	F,HSMMtube,	HMEC,NHEK					
chr3:1	81042360-1	81042510	11-hESC								
chr3:1	81042880-1	81043030	11-hESC								
chr3:1	81044545-1	81044695	11-hESC,HSMM,	HUVEC,He	pG2,NHEK,G	112878,HeLa-S3,HSMMtube,NHLF,HMEC					
chr3:1	81045285-1	81045435	11-hESC								
	81048640-1										

Scrolling down in the same page, we also listed the TF binding sites in this region. This table has three columns. The first column lists the coordinates of the TF binding sites. The second column list the transcription factor and the third column list in which tissue/cell types the TF binding sites are located.

Coordinate	TF	tissue
chr3:181010880- 181011030	multiple	ATF2(GM12878), BATF(GM12878), EP300(GM12878), FOS(HUVEC), FOS(MCF10A-Er-Src), IRF4(GM12878), JUN(HUVEC), NFIC(GM12878), RUNX3(GM12878), STAT3(MCF10A-Er-Src)
chr3:181016320- 181016470	CTCF, FOS, STAT3	CTCF(BE2_C), FOS(MCF10A-Er-Src), STAT3(MCF10A-Er-Src)
chr3:181034320- 181034470	CEBPB, GATA3, REST, SP2, TCF7L2	CEBPB(HeLa-S3), GATA3(T-47D), REST(A549), REST(GM12878), REST(H1- hESC), REST(HeLa-S3), REST(HepG2), REST(K562), REST(PANC-1), REST(PFSK- 1), REST(SK-N-SH), REST(U87), SP2(HepG2), TCF7L2(HCT-116)
chr3:181042360- 181042510	CTCF, RAD21	CTCF(A549), CTCF(BE2_C), CTCF(Caco-2), CTCF(GM12892), CTCF(GM19240), CTCF(H1-hESC), CTCF(HEEpiC), CTCF(HMEC), CTCF(HepG2), CTCF(MCF-7), CTCF(NHEK), CTCF(RPTEC), CTCF(SAEC), CTCF(SK-N-SH_RA), CTCF(T-47D), CTCF(WERI-Rb-1), RAD21(H1-hESC), RAD21(HepG2), RAD21(SK-N-SH_RA)

Option 3: Search cis-elements surrounding a gene:

This option is similar to option 2, but it searches by gene names rather than a given genomic locus. Therefore, the users can conveniently type in the gene name of interest and specify the extended region around the gene TSS. The DHS sites and TF binding sites will be displayed in a similar pattern as in option 2. For example, please type in sox2 and 20 kb for the extended region.

HOME	MOUSE	HUMAN	DOWNLOAD	LINKS	CONTACT		
Query	human E	NCODE da	ta!				
Option	1: Search	gene expr	ession across	~ 60 hum	nan cell type	s (total 108 data	asets)
Human	(hg19) ‡ G	Gene name(Sox2, Nanog))		submit!	
Ontion	2. Search	cis-eleme	nts in a given	nenomic i	region		
			_	genomic	_		1
human	(hg19) ‡	chr1 ‡ st	art:		end:		submit!
Option	3: search	cis-eleme	nts surroundin	g a gene			
Human	(hg19) ‡ G	Gene name(Sox2, Nanog)) sox2 ┥	<u> </u>		
					• 	_	
Extend	ed region (c	lefault +/- 1	.00kb) 20 🗲		kb subm	nit!	
Option	4: search	cis-eleme	nts LINKED to	a gene ba	ased on DNa	seI HSS specific	ity
Human	(hq19) ‡ G	Gene name(Sox2, Nanog))		submit!	

Option 4: Search cis-elements linked to a gene based on DHS:

This option will help users predict the linkage between distal regulatory elements with their target genes. The prediction is based the tissue specificity of DHS across 129 cell types. Users can type in the gene name under option 4 and then click submit (sox2). Below is the result:

ABOUT	MOUSE	HUMAN L	INKS CONT	ACT						
Cis-elements linked to your queried gene.										
Species:	Species: human_hg19									
	me: SOX2	-								
Cis-elen	nent lined b	y DNaseI Hy	persensitive	Sites I	linkage:					
Proxima	I DHS (TSS)	start	end	Gene	Distal DHS	start	end	correlation		
chr3		181429540	181429690	SOX2	chr3	181051260	181051410	0.739482		
chr3		181429540	181429690	SOX2	chr3	181422060	181422210	0.74818		
chr3		181429540	181429690	SOX2	chr3	181430060	181430210	0.757448		
chr3		181429540	181429690	SOX2	chr3	181430620	181430770	0.735273		
1.0		181429540	181429690	SOX2	chr3	181444460	181444610	0.900111		
chr3			101100000	COVO	chr3	181634020	181634170	0.761618		
		181429540	181429690	150X2	CIIIS	101034020	1010011/0	0.701010		
chr3 chr3 chr3		181429540 181429540		SOX2		181753200	181753350	0.74952		

Columns 1-3 are the loci for the proximal DHS near the queried gene. Column 4 is the gene name. Columns 5-7 are the distal DHS that are associated with the queried gene. The last column is the Pearson correlation between the distal and proximal DHS (for more details, please refer to Thurman, et al, Science 2012)

Data: All the human data used in this query website is from:

https://www.encodeproject.org/data/annotations/. All the mouse data can be downloaded from: http://mouseencode.org.

3D genome browser

Goal: To develop user-friendly browser to visualize Hi-C and Chia-PET data.

Main features:

- 1. Easy navigation functions such as zooming in/out, moving to left/right.
- 2. The ability to incorporate customized UCSC genome browser session.
- 3. Gene centric view: allow users to predict linkage between enhancers and their target genes, based on integrated views of Hi-C/ChIA-PET data and the linkage based on correlation of distal and proximal DHS sites.
- 4. Allow query human trait and disease-associate SNPs and find regions interact with them through chromatin looping.
- 5. Use your own Hi-C data.

Link: <u>http://3dgenome.org</u>

Generate Hi-C Interaction heatmap

НОМЕ	HI-C INTERACTIONS	VIRTUAL 4C	DOWNLOAD	TUTORIAL	CITATION	CONTACT					
	elcome to the Interactive Hi-C Data Browser!										
Welcom	e to the Interactive	Hi-C Data Brov	wser!								
Step 1. C	hoose the assembly of I	li-C data:									
Species	numan + Assembly hg19	• •									
	hoose the source of the										
	Available Hi-C Data	uuu.									
_	M12878 + Resolution 2										
	MI2878 + Resolution 2:	SKD Ŧ									
OR											
Use You	ır Own Data										
Data URL					Resolut	tion (in kb)					
	cify the URL of the data, e the data must be in binary elv.					are set					
	hoose the region to sho	w Hi-C interactio	ns:								
	Option 1: Search by Ge	ne Name		Option 2: Searc	ch by Location						
				Chromosome	chr1 ‡						
	Gene name (Sox2, Nar	nog)									
				Start							
				End							
	Show Interaction			Show Inte	eraction						

- 1. Click "HI-C INTERACTIONS" tab;
- 2. Using dropdown menu to choose species and assembly.
- 3. Choose the source of Hi-C data:

Option 1. Use dropdown menu to choose the published Hi-C data;

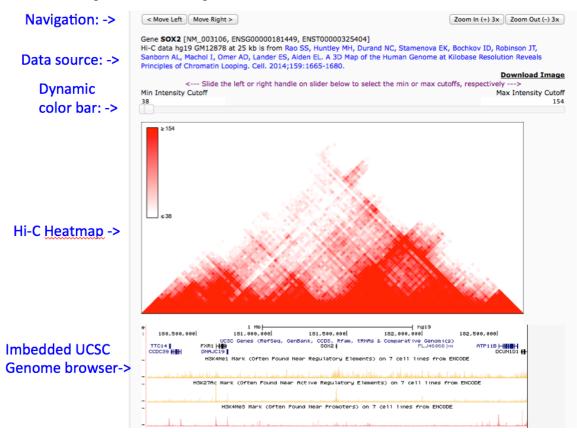
<u>Option 2</u>. Specify the location of your own Hi-C data. Note: it needs to be converted to a binary file using our provided script.

4. Choose genomic region to show Hi-C interaction

<u>Option 1</u>: Search by Gene Name(RefSeq ID or Uniprot ID). By default, this regions will be \pm 50 bins, with each bin size = matrix resolution;

Option 2: Search by genomic locus.

Example: 1) Choose human, hg19; 2) choose "Browse available Hi-C data", GM12878, 25kb 3) type sox2 in the under Option 1 and click "show Interaction". Below is the Hi-C interaction map around sox2 region.



Navigate Hi-C data:

1. The "<u>Move Left</u>" and "<u>Move Right</u>" buttons allow users traversing the current genomic regions in the upstream or downstream directions, respectively.

2. The "Zoom In" and "Zoom Out" buttons allow users zoom in or zoom out from the current genomic region by three times. In order to not overload the server, we only support a maximum region of 1500 bins currently.

3. <u>Adjusting color scale</u>: The minimum and maximum intensity cutoff values are important in determining the colors of Hi-C heatmaps. As the values inside the bins of the contact matrix reflect the number of interactions, any values below the minimum cutoff value would be shown as white and any values above the maximum cutoff value would be shown as red.

Download Image: To save the image, right click this link and select "Save Link As" (this might be different depending on the web browser). In the resulting dialog box, enter an appropriate name and click "Save" to save the heatmap as a jpeg.

Use your own UCSC genome browser session

Users can locate your UCSC genome browser session and copy and paste the session ID in the 3D genome browser, so that they can overlay the Hi-C data with other genomics/epigenomics data. The UCSC genome browser session ID is the string after "hgsid=".

genome.ucsc.ed			
s	ep 1. Choose the assembly of Hi-C data:		
S	Decles mouse + Assembly mm9 +		
S	ep 2. Choose the source of the data:		
	Browse Available Hi-C Data ssue ESC + Resolution 40kb +		
0	R		
	"C" Your Data ata URL		Resolution (in
N	asse specify the URL of the data, e.g. http://promoter.bi ote that the data must be in binary format. Ensure that t propriately.		ns are set
N a;	the provided and the set of the data, e.g. http://promoter.bu the that the data must be in binary format. Ensure that the propriately. The 3. Choose the region to show Hi-C interactions :	he server supports HTTP and that the permission	
N a;	ease specify the URL of the data, e.g. http://promoter.bu te that the data must be in binary format. Ensure that t propriately.	he server supports HTTP and that the permission	
N a;	the provided and the set of the data, e.g. http://promoter.bu the that the data must be in binary format. Ensure that the propriately. The 3. Choose the region to show Hi-C interactions :	he server supports HTTP and that the permission	
N a;	the provided and the set of the data, e.g. http://promoter.bu the that the data must be in binary format. Ensure that the propriately. The 3. Choose the region to show Hi-C interactions :	be server supports HTTP and that the permission Option 2: Search by Location	
N a;	Sease specify the URL of the data, e.g. http://promoter.bu te that the data must be in binary format. Ensure that t opropriately. Sep 3. Choose the region to show Hi-C interactions: Option 1: Search by Gene Name	be server supports HTTP and that the permission Option 2: Search by Location Chromosome chr1 ==	
N a;	Sease specify the URL of the data, e.g. http://promoter.bu te that the data must be in binary format. Ensure that t opropriately. Sep 3. Choose the region to show Hi-C interactions: Option 1: Search by Gene Name	be server supports HTTP and that the permission Option 2: Search by Location Chromosome chr1 : Start 172600000	
N a;	Gene name (Sox2, Nanog) Show Interaction	Option 2: Search by Location Chromosome chr1 Start 172600000 End 190275000	
N a;	Gene name (Sox2, Nanog) Show Interaction	Option 2: Search by Location Chromosome Chromosome	

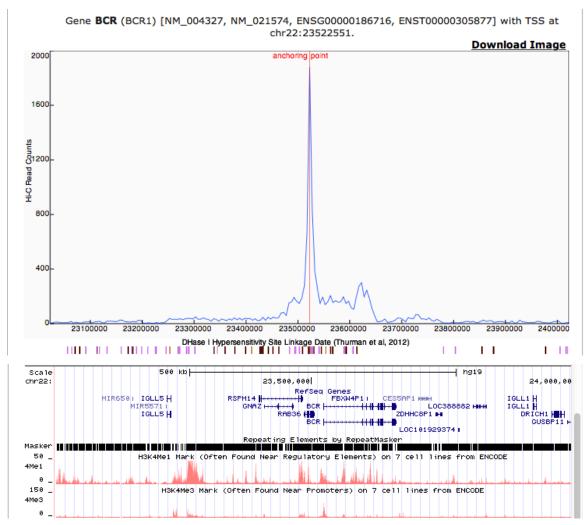
User your own Hi-C data

A useful feature for our 3D genome browser is that you can visualize your own Hi-C data. This feature is important to work with unpublished data, as only the users can know and specify the location of their Hi-C data. However, users need to convert the standard Hi-C interaction matrix to binary format, using a script that we provide. Next, a user can put the binary Hi-C data in an internet accessible place and copy the link in our browser.

Potential pitfall: Please make sure the genome assembly and bin size is set correctly.

HOME	HI-C INTERACTIONS	VIRTUAL 4C	DOWNLOAD	TUTORIAL	CITATION	CONTACT
Welsem	e to the Interactive	Ui C Data Brea	waard			
weicom	le to the Interactive	HI-C Data Brow	wser!			
Step 1. C	hoose the assembly of	Hi-C data:				
Species	mouse + Assembly mm	9 \$				
Step 2. C	hoose the source of the	data:				
	e Available Hi-C Data					
Tissue E		\$				
OR						
⊖"C" Yo	ur Data					
Data URL						Resolution (i
kb)						
	ecify the URL of the data,					
Note that appropria	the data must be in binary tely.	y format. Ensure th	at the server suppo	orts HTTP and tha	it the permission	s are set

Virtual 4C



Rather than visualizing **all** the interactions in a given region, some users are more interested to see the chromatin interactions with one anchor point, for example, a gene

promoter region. This information might be useful to predict the enhancers that regulate their genes of interests. To address this request, we can extract a row of data from a Hi-C interaction matrix, centered at the queried gene, and plot it in the follow figure. This figure is termed "virtual 4C", as the way the data is presented is the same as 4C (Circularized Chromosome Conformation Capture), but we use Hi-C instead.

Example: In the above example, click virtual 4C, choose human, hg19 and type in BRC1. The vertical red line is the promoter of BRC1. Be default, we display +-500kb around the anchor point. The value in y-axis is the interaction frequencies measured by Hi-C. For this feature, you can either use gene name or a SNP ID.

Immediately below the virtual 4C track, the color bars indicate the distal DHS sites that are correlated to the proximal DHS near the queried gene.

On the lower panel of the result page, we show the histone modification in the same cell type, which can be used to predict candidate enhancers.

Therefore, by visualizing the virtual 4C, linkage by DHS and Epigenomics data generated by ENCODE, the query provide a powerful tool to predict the linkage between target genes and their distal regulatory elements.