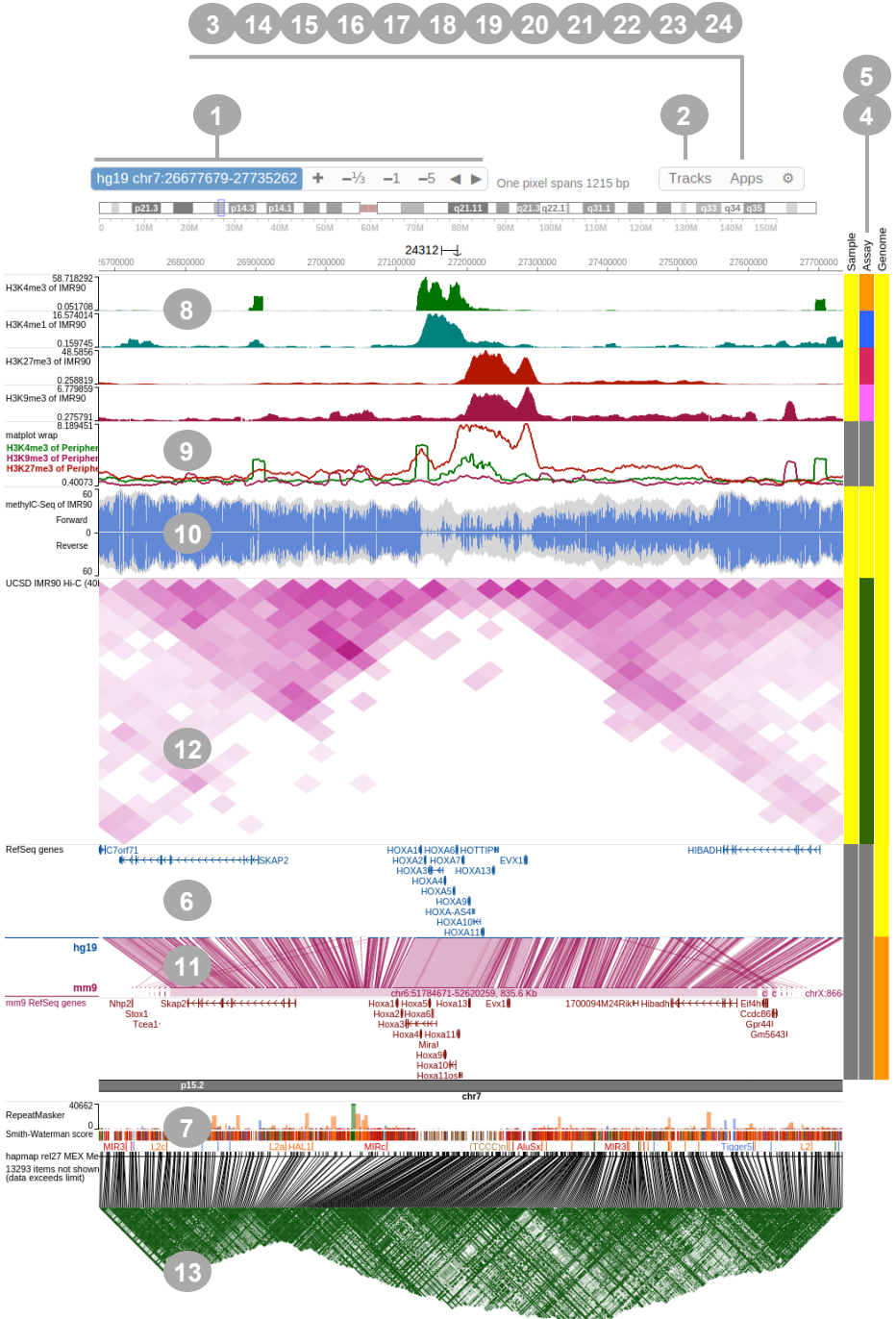


WASHU EPIGENOME BROWSER

2018

epigenomegateway.wustl.edu

BROWSER MAP



Key

1 = Go to this page number to learn about the browser feature

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BROWSER TRACKS

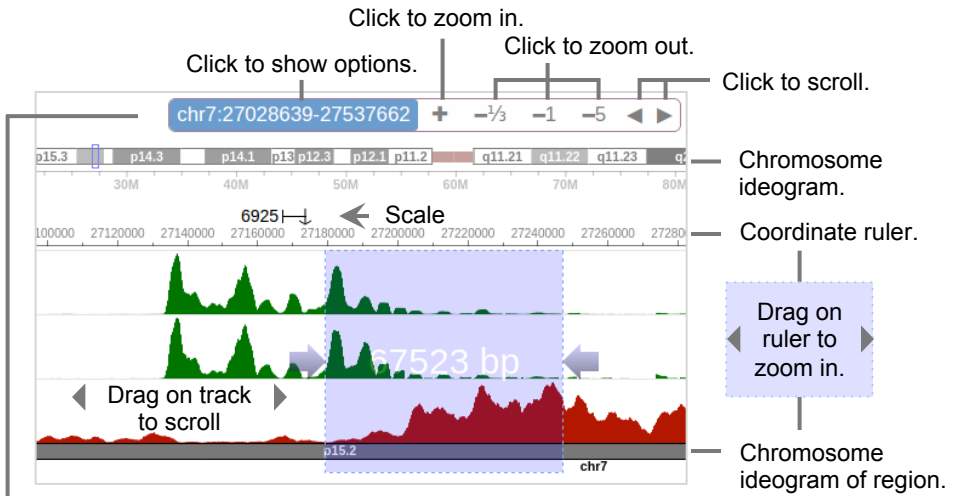
6. Genes
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18. Gene & Region Set View
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Enter coordinates to jump to a region.

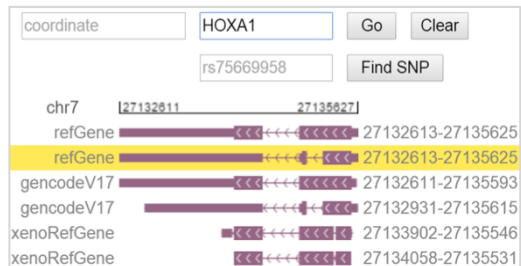
Coordinate string can be one of:

1. chr9:1234-5678 a region.
2. chr9:123456 a single base.
3. chr9 a chromosome to jump to the middle of that chromosome.
4. 1234-5678 coordinates without a chromosome name to jump to this region on the current chromosome.

Enter the reference SNP cluster ID (rsID) to jump to a specific SNP.

Enter a gene name to jump to a gene.

Multiple gene models may be shown for a gene. Choose one gene model to jump to its location.



At fine resolution, the chromosome ideogram is replaced by the DNA sequence.



A browser **app** is a self-contained program for executing a specific task. Examples of browser apps include uploading files and taking screenshots.

Apps

Click to find browser apps.

Tracks Apps

Find apps by name. Apps will appear as you type.

app name Find All apps

Show all apps.

find ortholog

validate hub & refresh cache

Recently used apps.

14

18

21

23

Frequently used apps.

19

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16

Apps usually appear as transparent panels on top of the browser and are used in the context of browser visualization. You never have to leave the browser to use an app.

Drag the app name banner to move the panel.

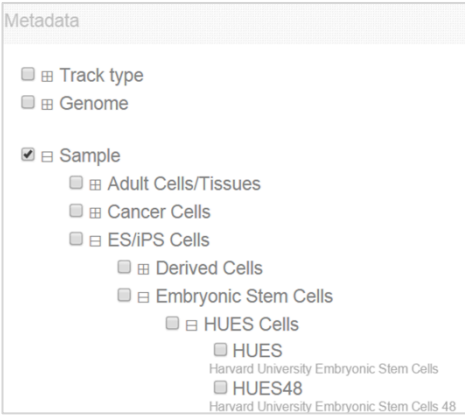
Close this app. Get help on this app.

Gene & region set

Close this app. Get help on this app.

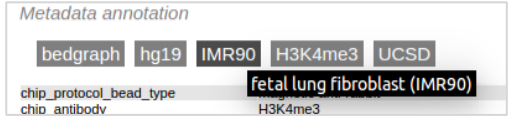
You don't have any gene sets yet.

+ Add new set Try the file uploader



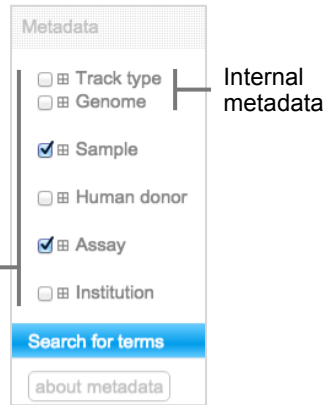
Metadata are vocabularies for annotating tracks with experimental and sample information. Terms in a vocabulary are organized in a hierarchical structure. The same vocabulary can be used across datasets to facilitate data integration.

To load metadata vocabularies available for the human genome, load the public datahub for the Roadmap Epigenomics Project. The metadata annotation for a track can be viewed by right-clicking a track and selecting "Information."

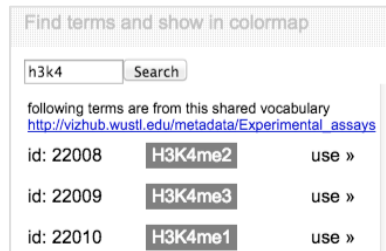


To view loaded metadata vocabularies, right-click on the metadata heatmap header, then select "Add metadata terms".

5 Metadata vocabularies.

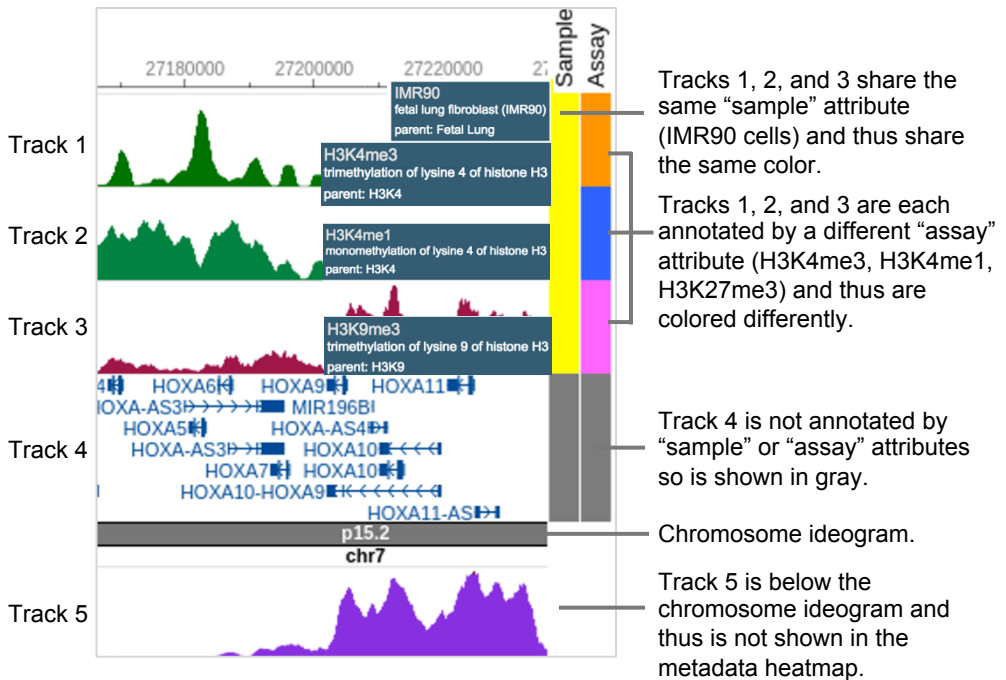


Once a metadata vocabulary has been loaded, its terms can be searched by keyword. Results include the term id for each found term. The term id can be used to annotate tracks in a datahub.



Learn more about how to define metadata vocabularies and annotate tracks at <http://wiki.wubrowse.org/Metadata>.

A metadata heatmap with two metadata terms.



To add or remove a track from the metadata heatmap, drag the track name above or below the chromosome ideogram.

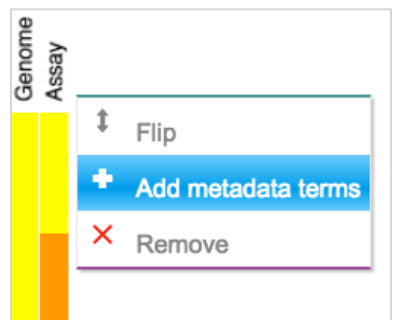
To search for new terms to be added to the metadata heatmap, right-click the term name and then open the **Metadata term finder** app by clicking "Add metadata terms."

Find terms and show in colormap

h3k4 Search

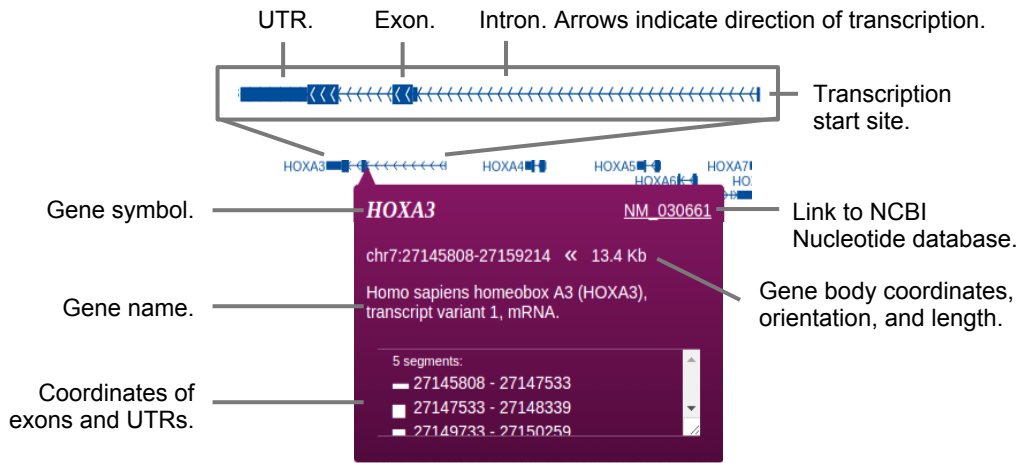
following terms are from this shared vocabulary
http://vizhub.wustl.edu/metadata/Experimental_assays

id: 22008	H3K4me2	use »
id: 22009	H3K4me3	use »
id: 22010	H3K4me1	use »
id: 22011	H3K4ac	use »



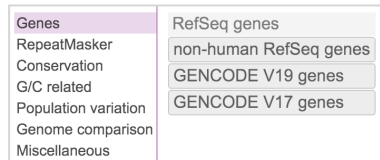
The source metadata vocabulary. 4

Click to show this term in the heatmap.

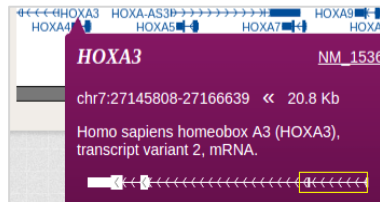


The human **RefSeq gene track** for *HOXA3* is shown above. The tooltip bubble displays information on the *HOXA3* gene.

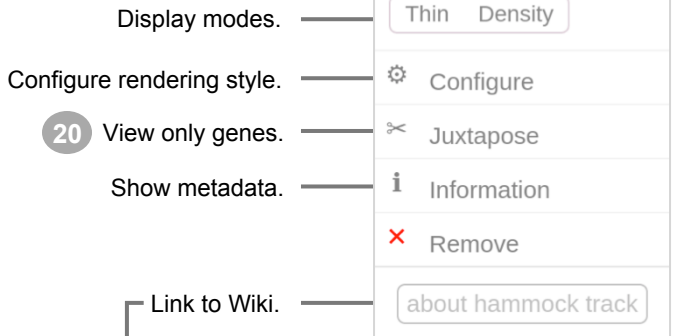
Multiple gene tracks are usually available for a genome. To find other gene tracks, go to “Tracks” > “Annotation tracks” > “Genes” or search by keyword “gene” in “Tracks.”



When a gene is partially visible in the browser, click this gene to display the entire gene model in the tooltip bubble. The visible section is marked by a yellow box.



Right-click on the gene track (and any other tracks) for the **configuration menu**.



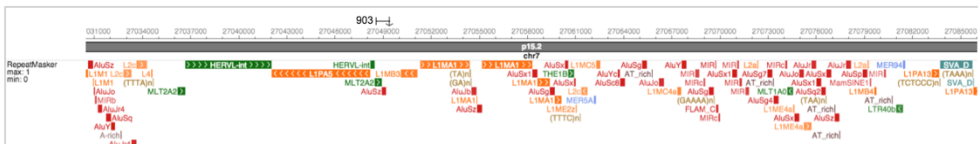
The gene track is based on the “hammock” track format, which can be displayed as a custom track.

Learn more at <http://wiki.wubrowse.org/Hammock>.

The **RepeatMasker** and RepeatMasker slim tracks show all repetitive elements in the genome. Repetitive elements and transposons are predicted by the RepeatMasker software (<http://www.repeatmasker.org/>).

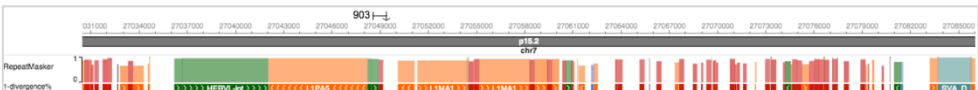
To add the RepeatMasker track, go to “Tracks” > “Annotation tracks” > “RepeatMasker” > “RepeatMasker”. The track is also available as RepeatMasker slim, a simplified version of the RepeatMasker track.

Genes	All Repeats	RepeatMasker
RepeatMasker	Transposable Elements	RepeatMasker slim
Conservation	DNA class	
G/C related	LTR class	
Population variation	LINE class	
Genome comparison	SINE class	



Full mode

Elements are shown as boxes, transparency reflects the 1-divergence% score of each element. More transparent elements have greater divergence.



Bar plot mode

Elements are packed tightly into a single row with bars on top indicating 1-divergence% scores.

The elements are colored by class. To view the list of classes, right-click the RepeatMasker track and click “Configure.”

■	SINE - short interspersed nuclear element
■	LINE - long interspersed nuclear element
■	LTR - long terminal repeat element
■	DNA transposon
■	Simple repeat, micro-satellite
■	Satellite repeat
■	Low complexity repeat
■	RNA repeat
■	Other repeats
■	Unknown

Hover over a specific element to display the element’s score, class, name, and genomic position.

The user can choose which type of score to show for the repetitive elements using the configuration menu.

Apply score

do not use score

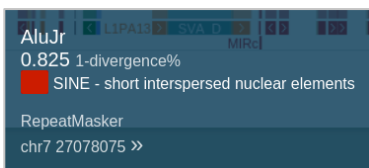
Smith-Waterman score

SW score normalized by length

1-divergence%

automatic scale ▼

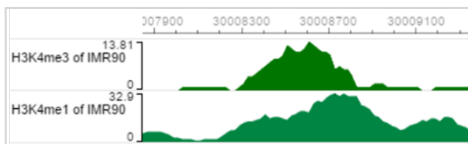
The user can also choose to show elements from a specific class or family in the Annotation tracks menu.



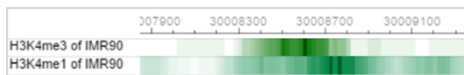
Genes	All Repeats	ERV
RepeatMasker	Transposable Elements	ERV1
Conservation	DNA class	ERVK
G/C related	LTR class	ERVL?
Population variation	LINE class	
Genome comparison	SINE class	

A **numerical track** displays a series of quantitative values along the genome as a highly customizable graph. When the track height is small, the track is shown as a heatmap, otherwise it is shown as a bar plot.

Bar plot (track height ≥ 20 pixels)



Heatmap (track height < 20 pixels)



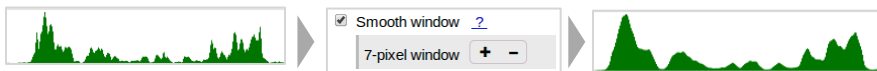
Positive and negative values are rendered using different colors.



The default y-axis scale is an automatic scale which can be changed into a fixed or percentile scale using the configuration menu. Bars with values beyond a set threshold are indicated with a different color on the peaks.

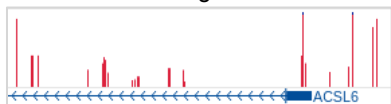


Bar plot shape can be smoothed using the configuration menu.

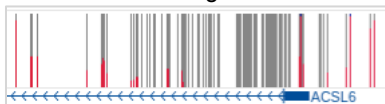


A background can be applied to bar plots to distinguish regions with no data from those with low data values.

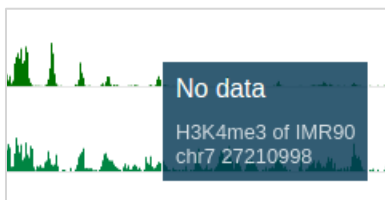
No background



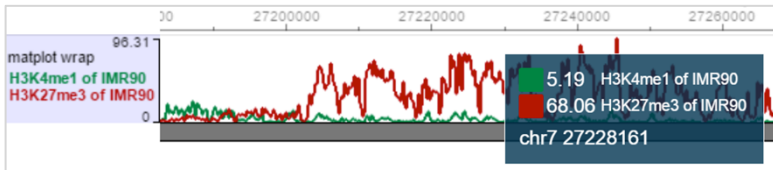
With background



Missing values are labelled as “No data” on the tooltip for bedGraph format tracks (not applicable for bigWig format tracks).



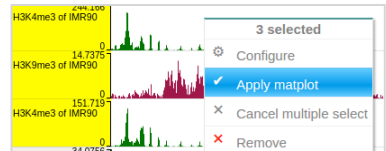
A **matplot** (also called a line plot) displays multiple numerical tracks on the same X and Y axes to easily compare datasets. Data is plotted as curves instead of bar plots.



Matplots can be created while browsing:

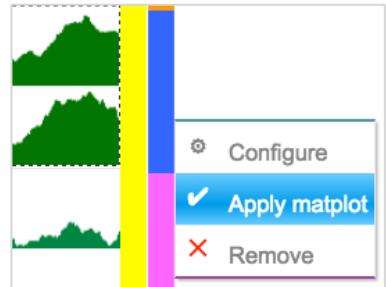
Method 1:

1. Hold shift and click on track names to select multiple numerical tracks. (Track names will be highlighted in yellow.)
2. Right-click on the selected tracks and select "Apply matplot."



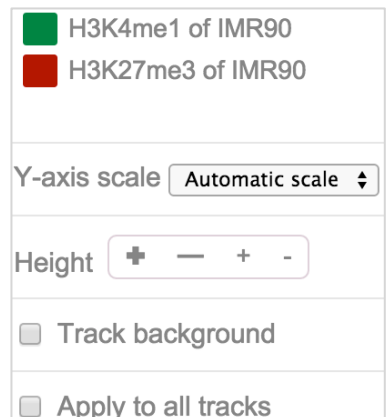
Method 2:

Right-click on a colored box in the metadata heatmap to convert a group of tracks sharing the same metadata attributes into a matplot.

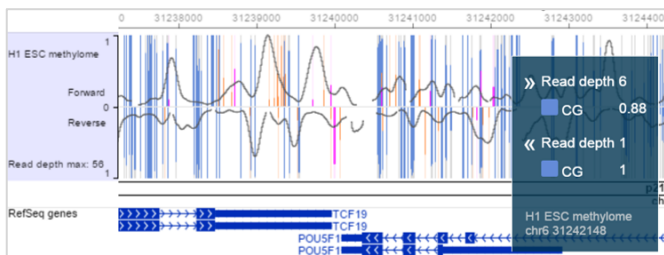


Colors of member tracks in a matplot can be individually configured using the configuration menu.

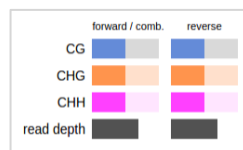
To cancel a matplot, right-click on the track and select "Cancel matplot." The matplot will be replaced by individually displayed member tracks.



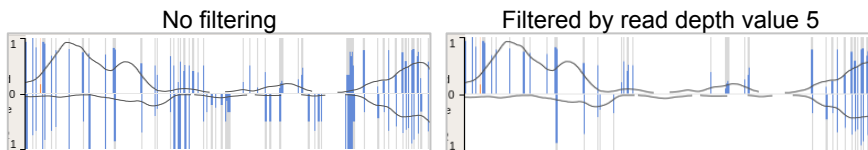
The **methylC track**¹ is designed to display DNA methylation data from whole-genome bisulfite sequencing experiments. It distinguishes cytosine methylation levels (as bar plots) on separate strands and in different sequence contexts and integrates sequencing read depth (as curves) as a measure of confidence.



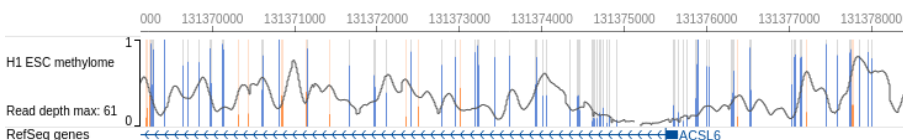
The color legend for a methylC track can be viewed using its configuration menu. All colors are configurable by clicking on the color boxes.



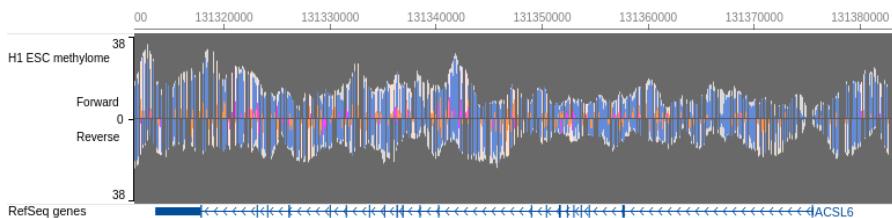
To filter methylation data by read depth, in the configuration menu, select "Filter by read depth," enter a threshold, and click "Apply."



To combine the forward and reverse strands, in the configuration menu, select "Combine two strands."



To scale the methylation level bar plots by read depth, in the configuration menu, select "Scale bar height by read depth." The y-axis value will now represent the read depth.



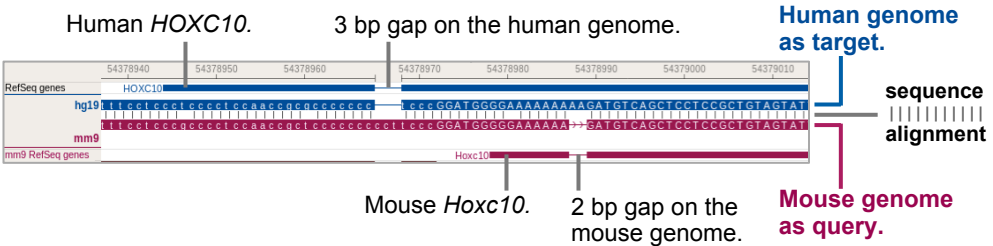
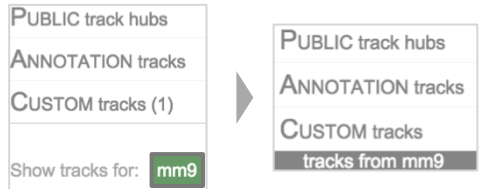
The **genome comparison track** visualizes pairwise alignments of two genomes allowing for comparison at fine (base pair) or large (megabase) scale. Alignment is unbiased with gaps in both the query and target genomes.

To add the genome comparison track, go to "Tracks" > "Annotation tracks" > "Genome comparison."

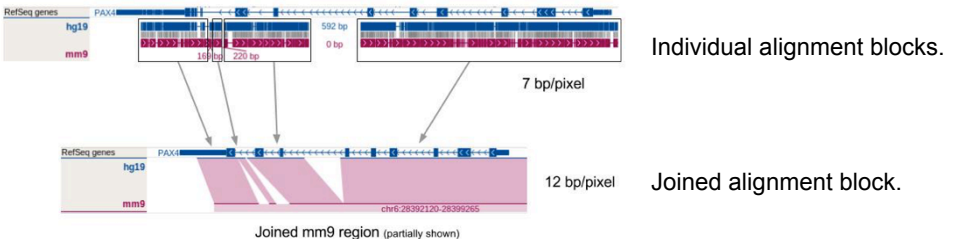
Many pre-built genome comparison tracks are available.

Genes	Mouse mm9 to hg19 blastz
RepeatMasker	Mouse mm10 to hg19 blastz
Conservation	Rat rn4 to hg19 blastz
G/C related	Rat rn5 to hg19 blastz
Population variation	Rhesus macaque rheMac3 to hg19...
Genome comparison	Guinea pig cavPor3 to hg19 blastz
Miscellaneous	Zebrafish danRer7 to hg19 blastz

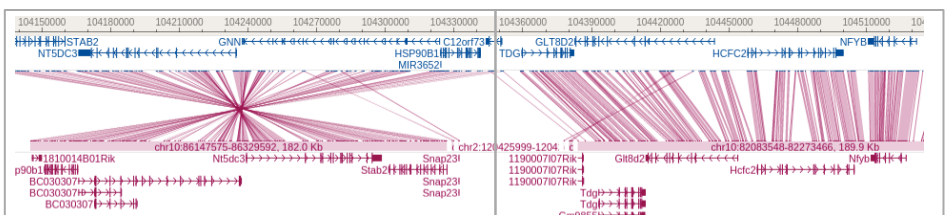
Annotation tracks for either species can now be loaded using the tracks panel.



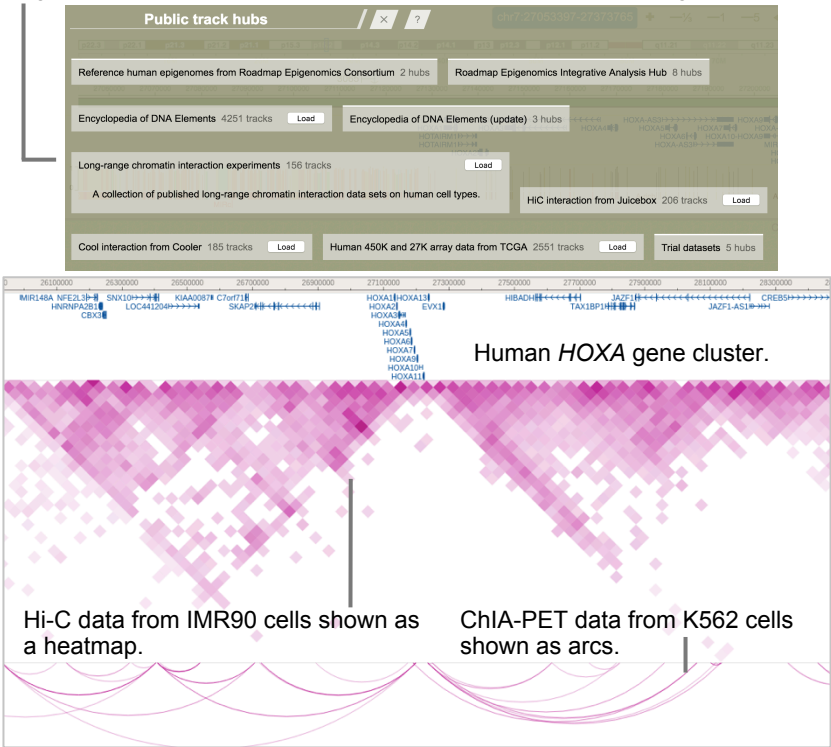
At 10 bp/pixel resolution, the browser will transition from individual alignment blocks to a joined alignment block.



Complex genome rearrangements can be visualized by observing synteny blocks.



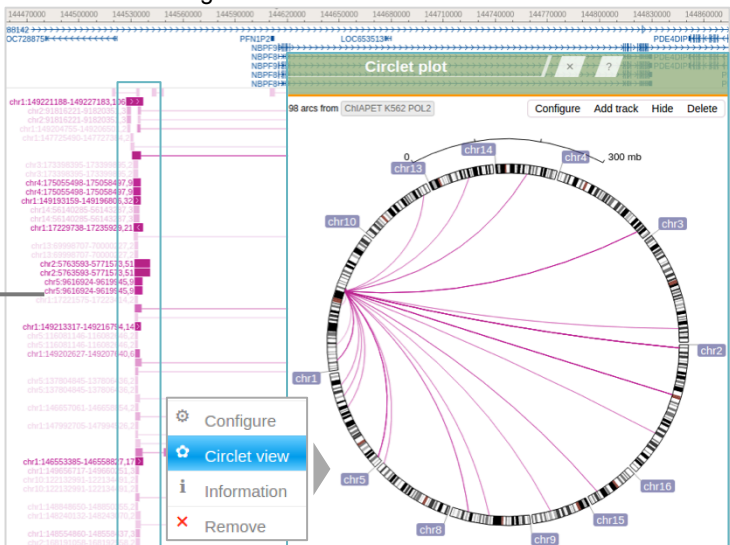
Long-range chromatin interaction experiments can be accessed through public track hubs¹.



Highlights:

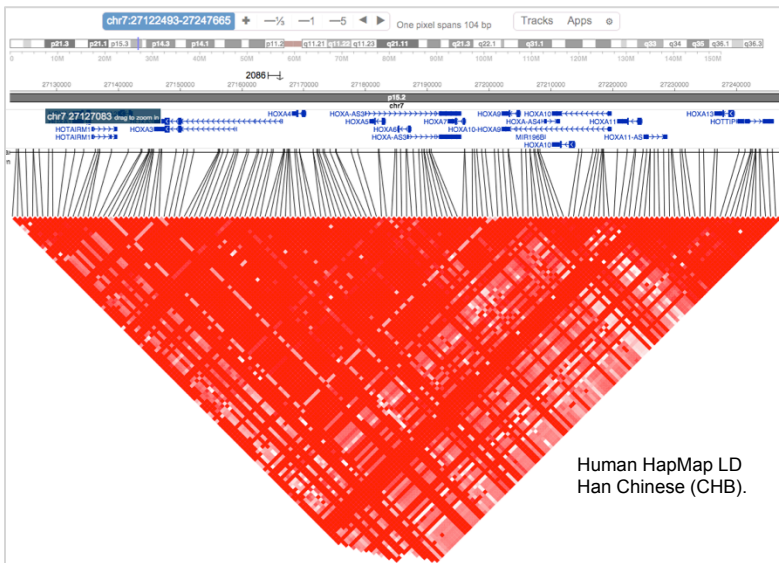
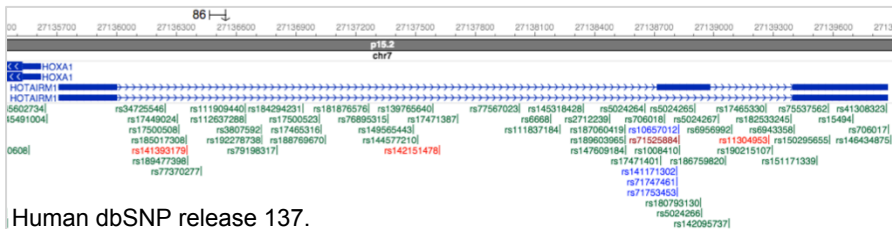
1. Supports pairwise chromatin interaction results from Hi-C, 5C, and ChIA-PET.
2. Multiple display modes: heatmaps, arcs, and joined-boxes (full display).
3. Visualizes interactions from distant regions and different chromosomes.
4. The **Circllet view** visualizes global interactions.

Hi-C data from IMR90 cells shown as joined-boxes.



Learn more at <http://wiki.wubrowse.org/Long-range>.

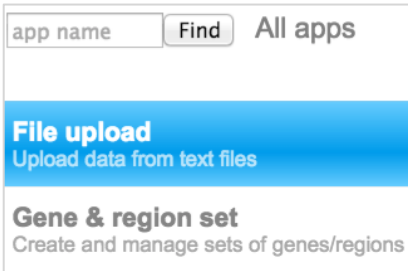
¹Zhou X, et al., Nature Methods 10, 375-376 (2013)



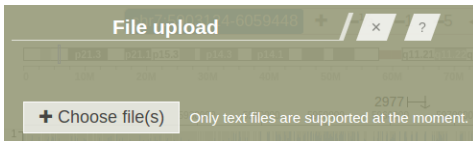
SNP and LD annotation tracks are available for human genomes. By default, the LD scoring system is D' . The correlation coefficient (R square) or LOD can be displayed using the configuration menu.

These tracks can be found in the “Population variation” group of the annotation track panel. To search for a SNP, type the reference SNP cluster ID (rsID) into the search bar and click “Find SNP.” SNPs are colored by class.

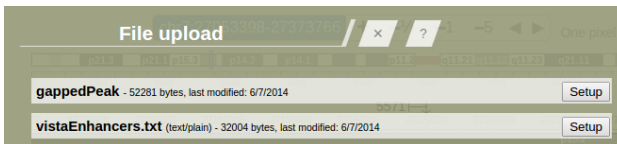
Genes	dbSNP release 137	■ single nucleotide variation
RepeatMasker	hapmap rel27 MEX Mexican ances...	■ insertion/deletion
Conservation	hapmap rel27 ASW African ances...	■ heterozygous variation
G/C related	hapmap rel27 CEU Utah resident...	■ microsatellite
Population variation	hapmap rel27 CHB Han Chinese i...	■ text name but not sequence
Genome comparison	hapmap rel27 CHD Chinese in Me...	■ a cluster of multiple classes
Miscellaneous	hapmap rel27 GIH Gujarati Indi...	■ multiple nucleotide polymorphism
	hapmap rel27 JPT Japanese in T...	■ insertion
	hapmap rel27 LWK Luhya in Webu...	■ deletion
	hapmap rel27 MKK Maasai in Kin...	
	hapmap rel27 TSI Tuscans in Italy	
	hapmap rel27 YRI Yoruba in Iba...	
		Show category id



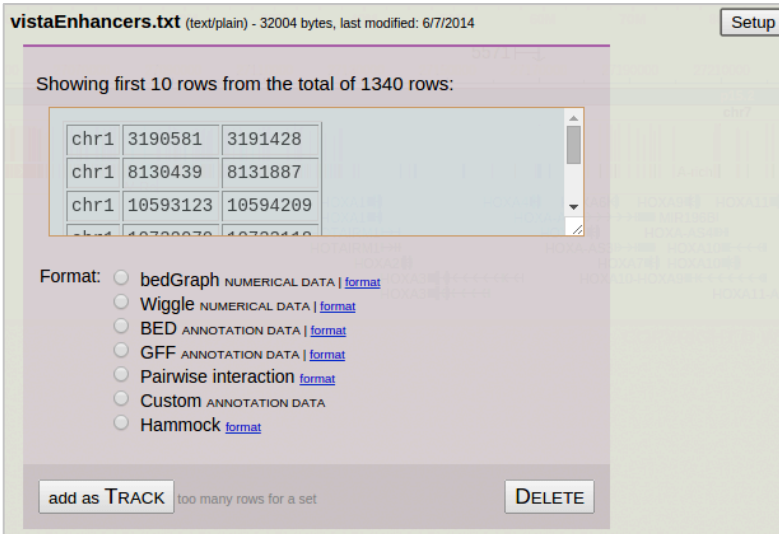
Use the **File Upload** app to upload data from a text file.



Click the “Choose file(s)” button to select one or more unzipped text files from the computer for upload.



Selected files appear as boxes.



To prepare a file for upload:

1. Click the “Setup” button.
2. Inspect the content of the first 10 lines.
3. Select the appropriate file format.
4. Click “add as Track” to load this file as a custom track or click “add as Set” to load this file as a gene set. The gene set option is limited to 100 items per set.

A **datahub** is a collection of data from multiple sources.

An example datahub.

```
[
# this hub contains only one track
{
  type:"bedgraph",
  url:"http://vizhub.wustl.edu/hubSample/hg19/GSM432686.gz",
  name:"my track",
  mode:"show",
  colorpositive:"#ff33cc",
  height:50,
},
]
```

Highlights:

1. Batch uploading of many tracks at the same time.
2. Custom track information is preserved in a datahub.
3. Tracks in a datahub can come from different servers.
4. Track rendering style can be customized.
5. Tracks can be annotated with metadata.

A datahub is written in JSON text. The JSON content of a datahub can be validated by the browser. Search for the “Validate datahub” app to run validation.

Use the datahub app to upload a datahub to the browser.

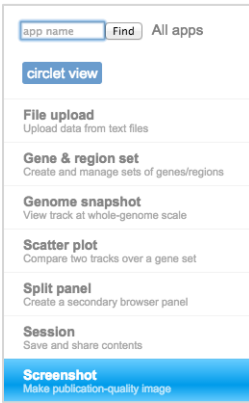
A datahub file can be either hosted on the Web or saved locally.

If the datahub is hosted on the Web, it can be referenced by the browser through the URL parameter. In this way, you can bookmark the parameterized browser link for quick reference or sharing.

<http://epigenomegateway.wustl.edu/browser/?genome=hg19&datahub=http://vizhub.wustl.edu/hubSample/hg19/hub.json>

Dissecting the browser URL parameters.

browser URL	?genome=	genome identifier	&datahub=	datahub URL
-------------	----------	-------------------	-----------	-------------

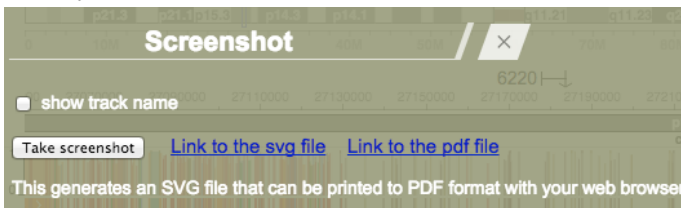


Use the **Screenshot** app in the Apps menu to save images of the current genomic view.

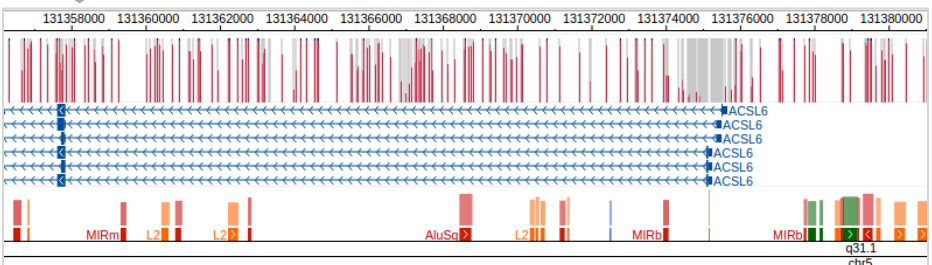


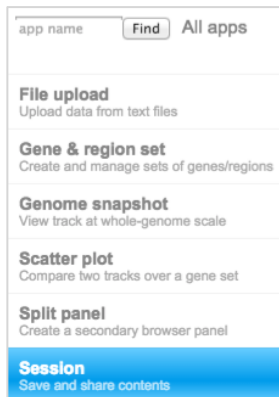
The “Screenshot” app will convert the browser contents to an SVG file. The SVG file is a high-quality vector-based graphics file. In addition, a PDF file will also be created.

To take a screenshot, click the “Take screenshot” button. Links to both the SVG and PDF files will be displayed.



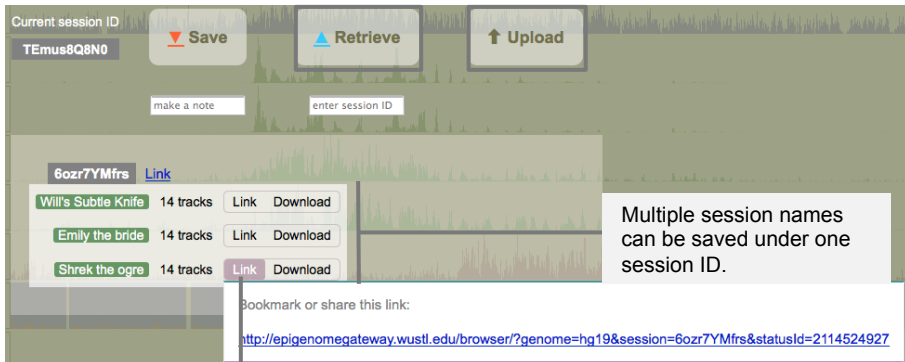
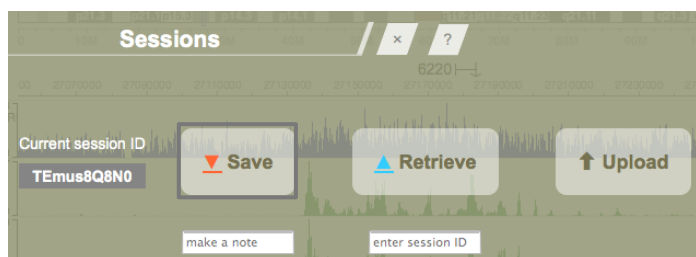
Click either link and the file will be shown on the browser. From either page you can save the file to your computer.





Use the **Session** app in the Apps menu to save the current browser status, including tracks, view range, and customization, for later viewing.

To save a session, click the “Save” button. Enter a name for this session (optional). A link to the saved session will appear. Alternatively, the user can download the session as a JSON datahub file.



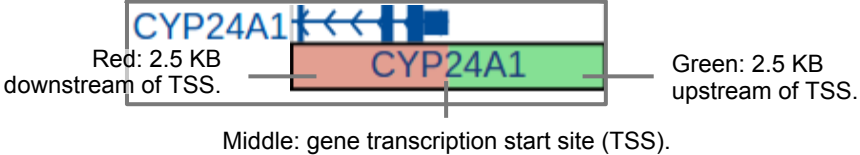
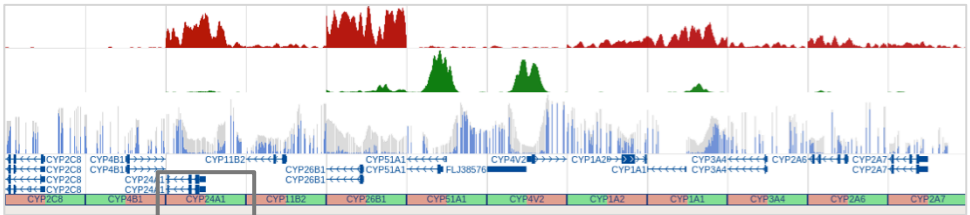
A link is generated for each session name.

A session can be recovered in three ways:

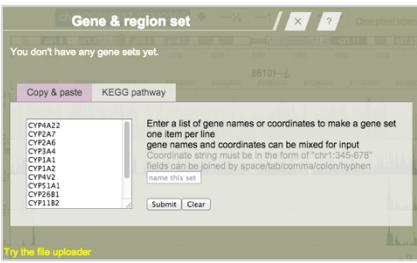
1. Save the generated link and simply use this link to reload the session.
2. Upload a saved JSON datahub file by clicking the “Upload” button in the “Sessions” app.
3. Copy the unique session ID and paste this into the “Retrieve” box in the “Sessions” app.

Sessions and datahubs only record information about tracks; they do not save actual track data. If the track file has been moved, the browser won't be able to recover that track from the session or datahub.

Use the **Gene & region set** app to show track data over a set of genes or regions. The “Gene & region set” app enables track data to be displayed over regions that are not adjacent on a chromosome or even on different chromosomes.

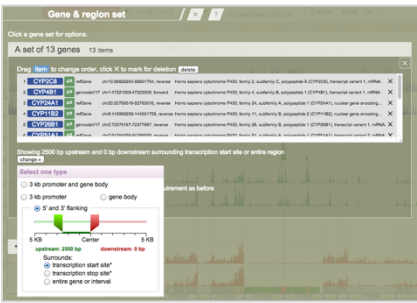


The user can create a set of genes or regions of interest.

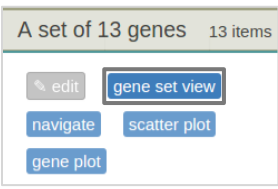


Gene and region sets can be submitted in three ways:

1. By pasting a list of gene names or genomic coordinates in the “Gene & region set” app.
2. By file upload in the “Gene & region set” app.
3. By using predefined KEGG pathways.



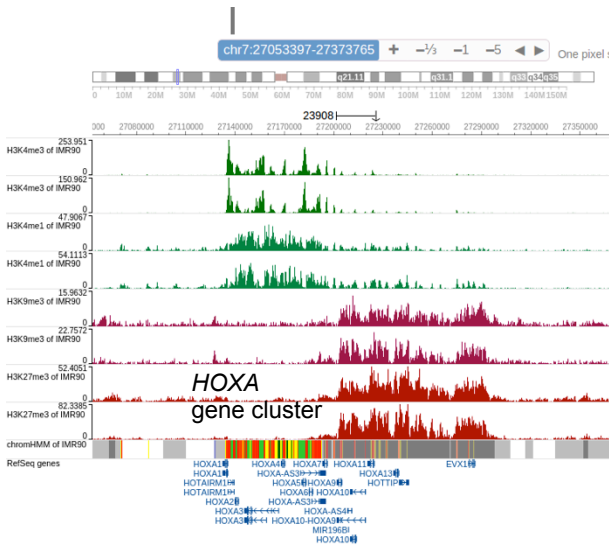
The user can specify custom flanking regions (up to 5 KB on each side) surrounding the gene transcriptional start sites to focus on the gene promoters.



“Gene set view” can be applied to see all regions in one browser view. To quit the gene set view, click the pink button next to the zoom buttons near the top of the browser.

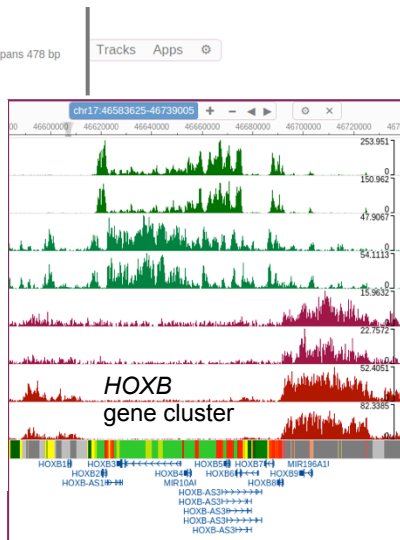
Use the **Split panel** app to “split” the browser panel in two. The order of the tracks remains the same in both of the panels, but the panels can be separately scrolled and zoomed. This allows the user to easily explore data patterns of the same set of tracks across two different genomic locations.

Main panel navigation buttons.



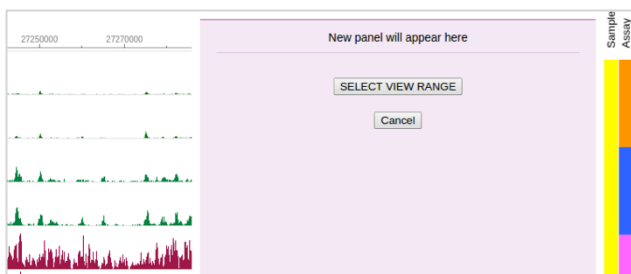
Main panel

Split panel navigation buttons.

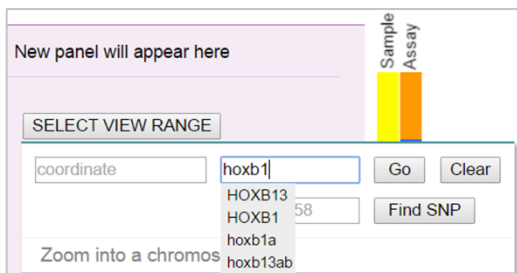


Split panel

When splitting the browser panel, the browser inserts a blank panel to the right of the existing panel.



Click the “SELECT VIEW RANGE” button to choose a view range for the new panel.



app name Find All apps

File upload
Upload data from text files

Gene & region set
Create and manage sets of genes/regions

Genome snapshot
View track at whole-genome scale

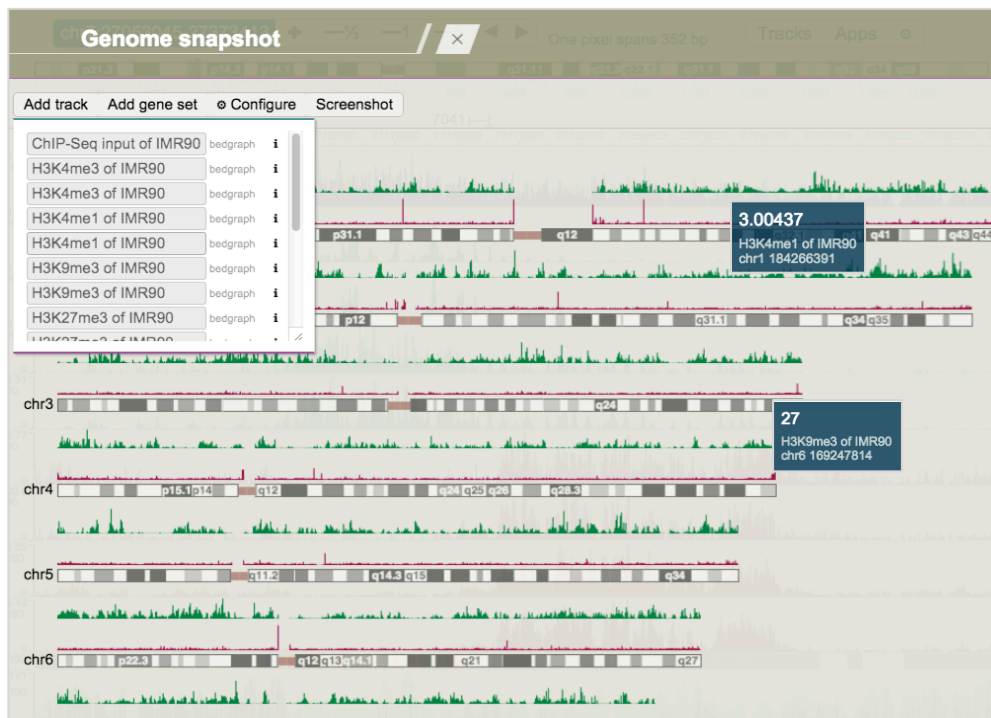
Scatter plot
Compare two tracks over a gene set

Split panel
Create a secondary browser panel

Session
Save and share contents

Screenshot
Make publication-quality image

Use the **Genome snapshot** app in the Apps menu to visualize the genome-wide profile for numerical tracks over all chromosomes.



Numerical tracks from the browser can be added to the genome snapshot using the “Add track” button. Above, H3K4me1 and H3K4me3 of IMR90 cells are shown. Just like browser tracks, track styles can be customized when the user right clicks. The global view can be changed using the “Configure” button. Lastly, a snapshot of all chromosomes can be captured and saved using the “Screenshot” button.

Use the **Find orthologs** app to identify highly similar genomic regions from the query genome for a set of target genomic regions based on the information in a genome-comparison track.

To find orthologs:

1. Display a genome-comparison track by selecting “Tracks” > “Annotation Tracks” > “Genome comparison”.
2. Create a gene set for the target genome.
3. Send this gene set to the “Find orthologs” app.
4. Click the “find orthologs” button.
5. View or export the result.

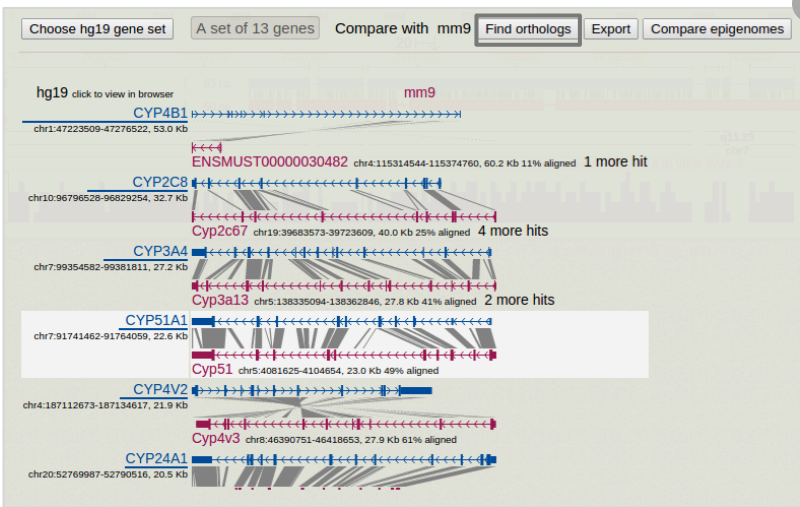
A set of 13 genes 13 items

edit
gene set view

navigate
scatter plot

gene plot
find orthologs

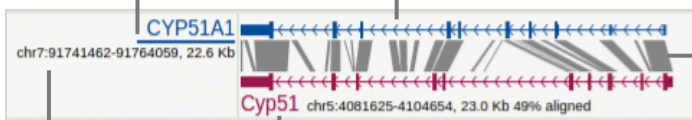
Remove



For each target region, the most similar region is found from the query genome based on the data in the genome alignment track. In the resulting output, the target genome regions are ranked by length in descending order. Each pair of aligned regions is graphically rendered.

Target gene name. Line width indicates relative region length.

Target genome gene model.



Sequence alignment.

Target genome coordinate.

Query genome gene name, gene model, and coordinate.

app name Find All apps

circlet view

File upload
Upload data from text files

Gene & region set
Create and manage sets of genes/regions

Genome snapshot
View track at whole-genome scale

Scatter plot
Compare two tracks over a gene set

Split panel
Create a secondary browser panel

Session
Save and share contents

Screenshot
Make publication-quality image

Use the **Scatter plot** app in the Apps menu to assess the relationship between two numerical tracks over a gene set.

Scatter plot [Close] [Help]

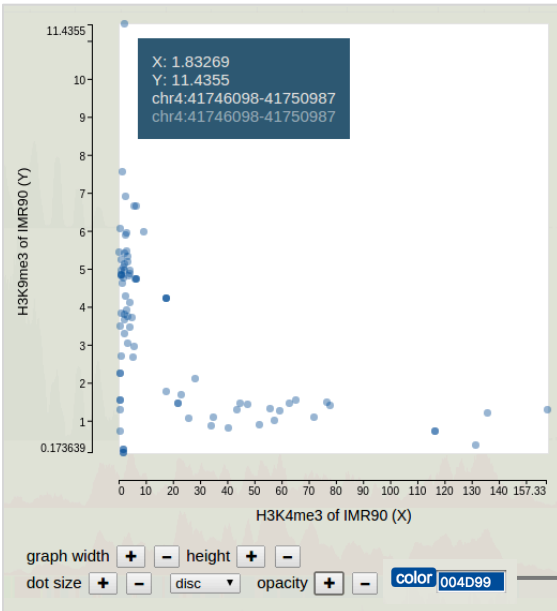
Choose a gene set No gene set selected

choose track » choose track »

for X axis for Y axis

SUBMIT
Reset

Choose a pre-made gene set. Choose two numerical tracks for the x- and y- axes and click "SUBMIT."



Anti-correlation between H3K4me3 (active mark) and H3K9me3 (repressive mark) in human IMR90 cells over a list of regions.

The plot is interactive. Mouse over each datapoint for information.

Click a datapoint to show its corresponding region in the browser.

Customization options.

In making the scatter plot, the average value over each item in the gene set is calculated for both numerical tracks.

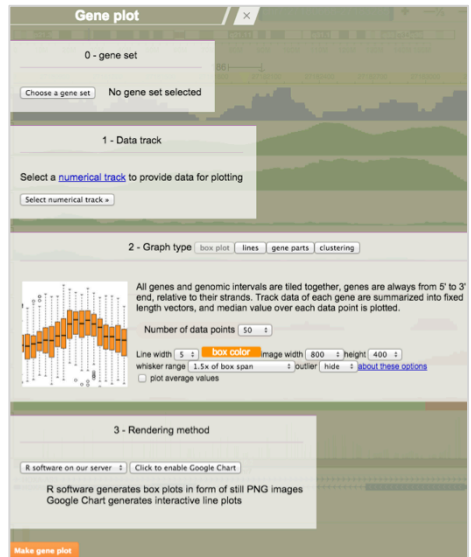
Use the **Gene plot** app to explore the data variation and distribution of a numerical track with respect to a group of genes or regions of interest. The gene set needs to be loaded using the “Gene & region set” app before using the “Gene plot” app. Search for the “Gene plot” app in the Apps menu.

Choose a gene set.

Select the data to be plotted.

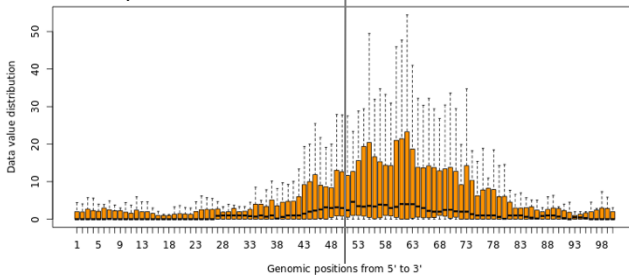
Four plots (box plot, matplot, gene part plot, and clustering) are available, and each is fully customizable.

Plots can be rendered in either R or Google Charts.

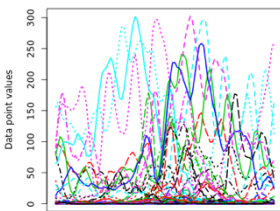


Gene transcription start sites.

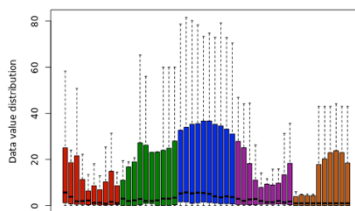
2.5 KB upstream of TSS. ◀ ▶ 2.5 KB downstream of TSS.



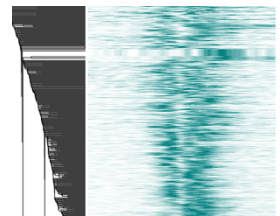
The above boxplot shows the IMR90 H3K4me3 signal distribution over 5 KB regions centered on the transcription start site of 100 random human genes. Data from each region is evenly summarized into 100 data points, and a boxplot is shown over each summary point to indicate the data distribution. Outliers are hidden in the boxplot.



Genomic positions from 5' to 3'



Genomic positions from 5' to 3'



Individual curves for each item.

Profile over gene features.

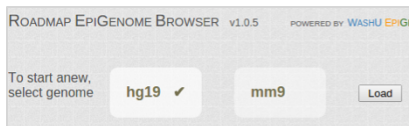
Hierarchical clustering.

The Roadmap EpiGenome Browser¹ is built on top of the WashU EpiGenome Browser to serve as a point-of-access to explore and analyze comprehensive epigenomics data generated by the Roadmap Project.

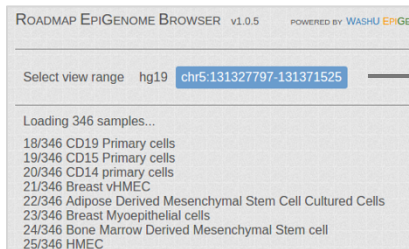
Highlights:

1. Access tens of thousands of epigenomic assays with a few clicks.
2. Applies real-time data clustering to reveal cell type-specificity of epigenetic marks.
3. Reveals covariations of epigenomic profiles and gene expression.
4. Integrates datasets from Roadmap Epigenomics and ENCODE projects.
5. Supports cross-species epigenome comparison (human and mouse).

Visit the browser at: <http://epigenomegateway.wustl.edu/browser/roadmap>

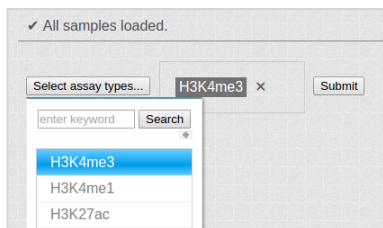


Select a genome (human hg19 and/or mouse mm9) and click “Load” to continue.



The browser starts loading information on the samples.

Click the Navigation box to choose a view range.



Select an assay type to launch the browser.

Browser options.



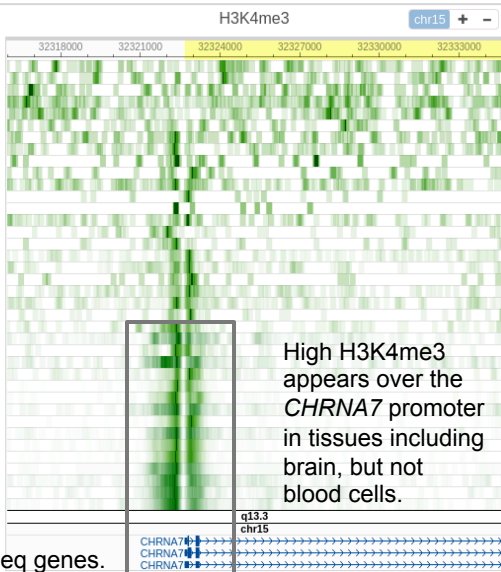
hg19

Hierarchical clustering.

Sample names.

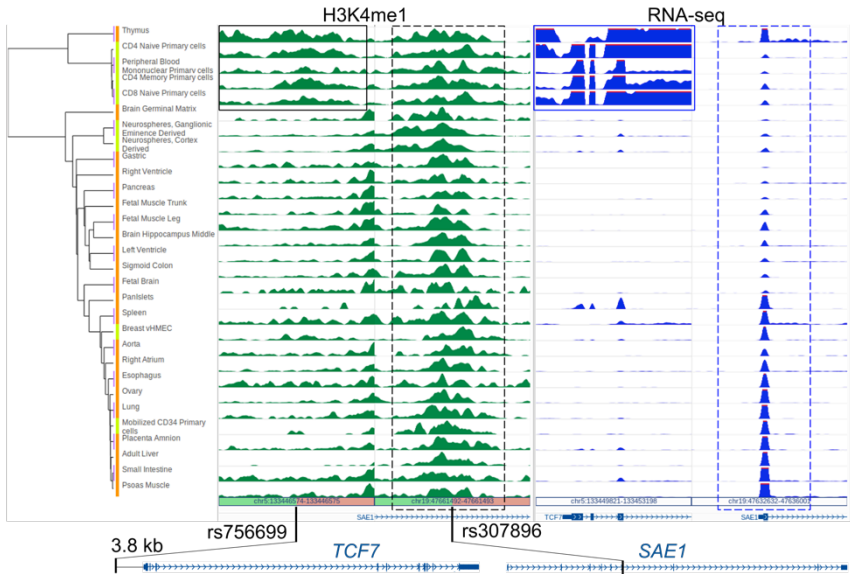
Navigation options.

RefSeq genes.



1 Epigenetic annotation of genetic variants

Multiple sclerosis-associated noncoding SNPs are annotated using epigenomic and expression data. rs307896 marks an enhancer common across all displayed samples, whereas rs756699 is located in an enhancer specific to immune cells.

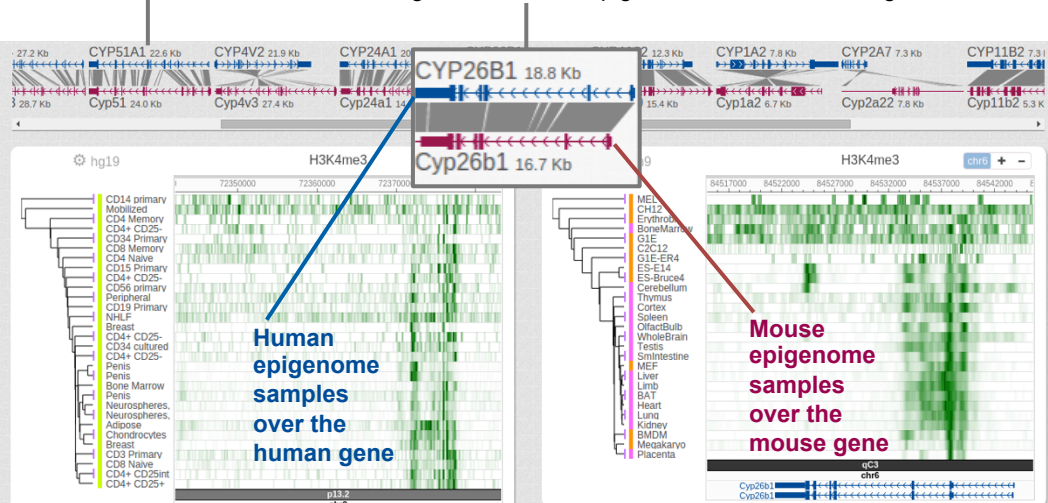


2 Cross-species epigenome comparison

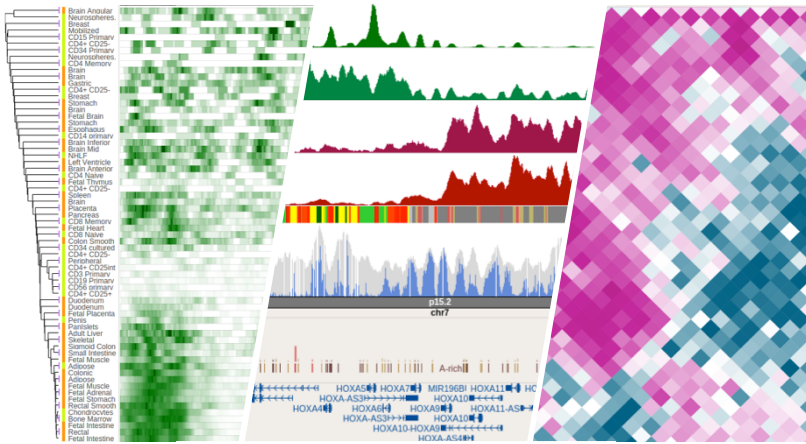
Human and mouse epigenomes can be compared over orthologous regions.

Human and **mouse** homologous genes found by the "Find orthologs" app. 22

Click an alignment to show epigenomes over the two regions.



Everything can be found at epigenomegateway.wustl.edu



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1. Zhou X, et al., Nature Methods 8, 989-990 (2011)
2. Zhou X & Wang T, Current Protocols in Bioinformatics Unit 10.10 (2012)
3. Zhou X, et al., Nature Methods 10, 375-376 (2013)
4. Zhou X, et al., Bioinformatics 30, 2206-2207 (2014)
5. Zhou X, et al., Nature Biotechnology 33, 345-346 (2015)
6. He Yu, et al., Bioinformatics 33, 3268-3275 (2017)

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Twitter: @wuepgg

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CONTACT US Lab: wang.wustl.edu

Browser Developers: Xin Zhou, Daofeng Li, Deepak Purushotham, and Silas Hsu

Booklet Authors: Renee Sears, Vasavi Sundaram, Rebecca Lowdon, Erica Pehrsson, and Nicole Rockweiler

Principal Investigators: Joseph Costello and Ting Wang

Cover art: Ting Wang