

# Roadmap Epigenomics Workshop

## WASHU EPIGENOME BROWSER

The First International Epigenomics Conference

*October 19<sup>th</sup>-20<sup>th</sup>, 2015 – Shanghai, China*

Presenters: Nicole Rockweiler, Renee Sears, & Ting Wang

Tutorial Overview:

0. Tutorial Key.....	2
1. Getting started with the EpiGenome Browser.....	3
2. Loading data on the EpiGenome Browser.....	4
3. Navigating the EpiGenome Browser.....	5
4. Sessions: saving and retrieving browsing sessions.....	13
5. Using Apps on the EpiGenome Browser.....	15
6. Creating Custom Tracks on the WashU Epigenome Browser.....	21
7. Using the Roadmap EpiGenome Browser.....	23
8. Additional information.....	41

WashU EpiGenome Browser:

<http://epigenomegateway.wustl.edu/browser>

Roadmap EpiGenome Browser:

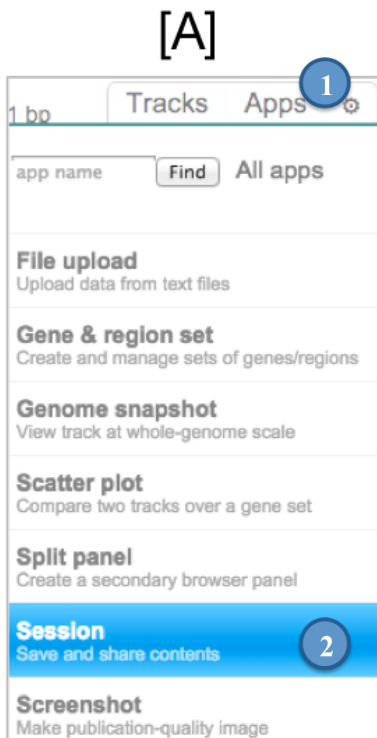
<http://epigenomegateway.wustl.edu/browser/roadmap/>

## 0. Notes

- To follow along with this tutorial, use instructions marked by ➤. We have provided screenshots for guidance (ordered by bracketed alphabets: [A], [B], ...)
- Click in the order of the numbered-circles on the screenshots to follow this tutorial.



- To catch up with any section of the *WashU EpiGenome Browser tutorial*, use the provided **session ID** and the **session name**, listed at the end of that section. For this, follow these steps:
  - [A] Click the **Apps** button to display the Apps menu. Then click **Session**.
  - [B] Under the **Retrieve** button, enter the **session ID** and then click the **Retrieve** button.
  - This will generate a list of **session names**. Click the session of interest.



- To catch up with any section of the *Roadmap EpiGenome Browser tutorial*, go to the provided **session link**, listed at the end of that section.

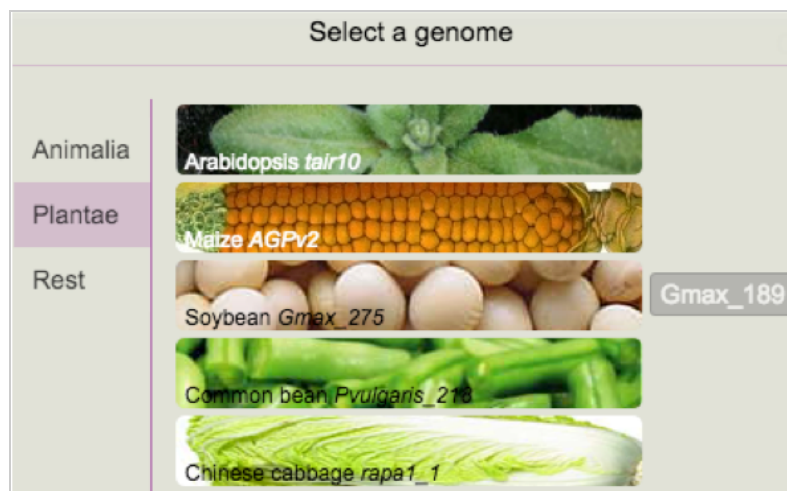
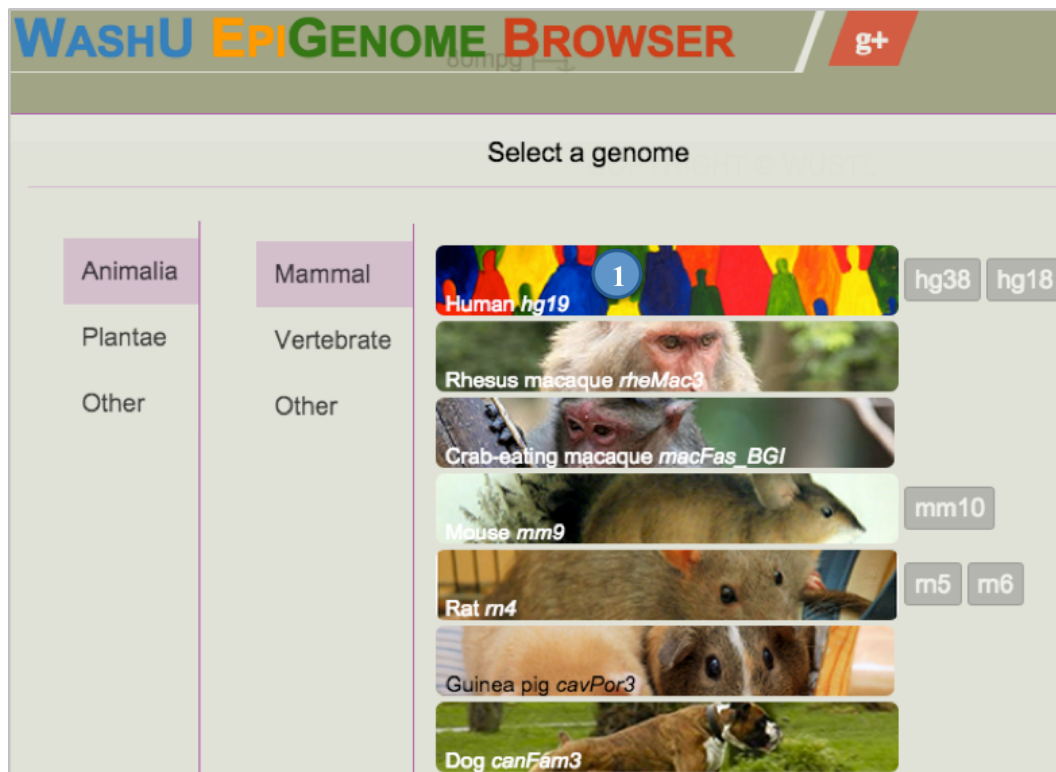
# 1. Getting started with the EpiGenome Browser

## 1.1. Loading the browser

- Access the browser at <http://epigenomegateway.wustl.edu/browser>

## 1.2. Selecting the genome assembly of interest

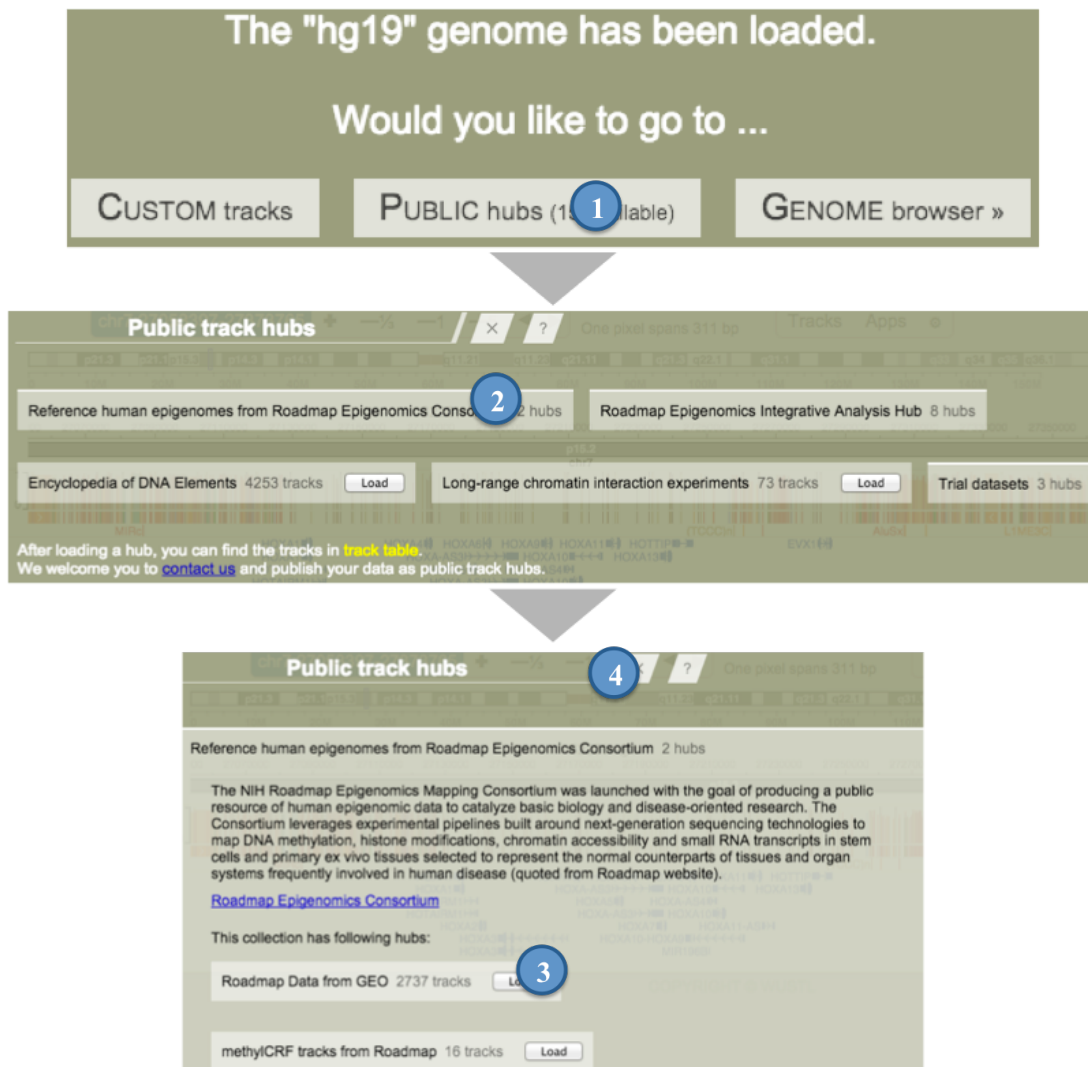
- For the purpose of this tutorial, please select **Human hg19**.
- However, you can see that many other genomes are also available.



## 2. Loading data on the EpiGenome Browser

2.1. **Data hubs:** A data hub is a collection of datasets (also called **tracks**) that can be viewed on the browser.

- [A] Click the **PUBLIC hubs (15 available)** button to view all the available public datasets on the EpiGenome Browser.
- [B] Click the **Reference human epigenomes from Roadmap Epigenomics Consortium (2 hubs)** button.
- [C] This will generate a list of available data hubs. Click the **Load** button on Roadmap Data from GEO (2737 tracks) box. Once the datasets are loaded, exit the data hub menu by clicking the **X** at the top-right of the panel or pressing **Esc**.





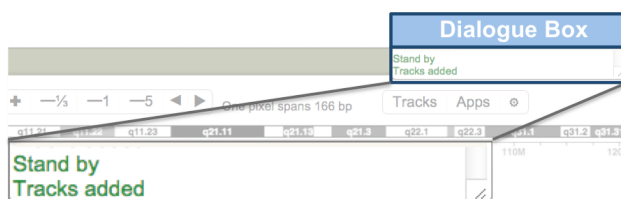
### 3. Navigating the EpiGenome Browser

### 3.1. Layout of the EpiGenome Browser



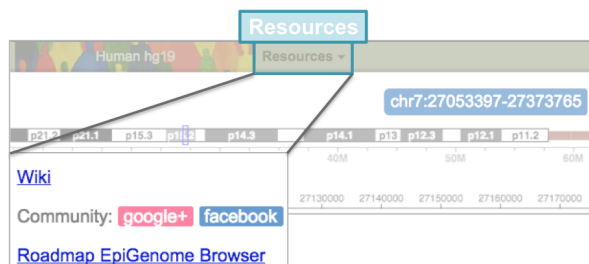
### 3.1.1. Dialogue box

- This box logs all the actions performed by the EpiGenome browser. Any errors the browser encounters are displayed.



### 3.1.2. Resources

- This window contains links to the documentation on the browser ([Wiki](#)); social-media discussion forums (on [Google+](#) and [Facebook](#)) for the browser; and the [Roadmap EpiGenome Browser](#), a companion browser for visualizing and analyzing data from the Roadmap Epigenomics Consortium.



### 3.1.3. WashU EpiGenome Browser

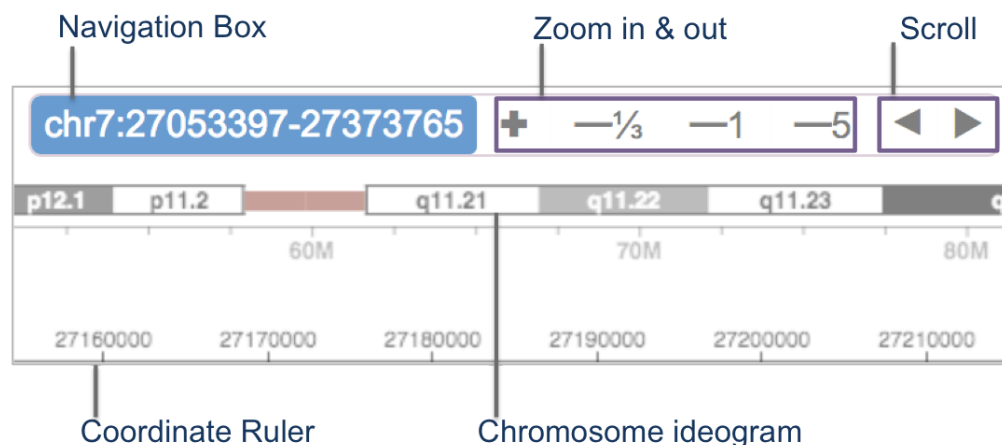
- This region contains the data tracks aligned to the genome along with reference genes and a chromosome ideogram. Additional public track hubs, annotation tracks, and custom tracks can be added by the user.



### 3.2. Navigating the genome on the EpiGenome Browser

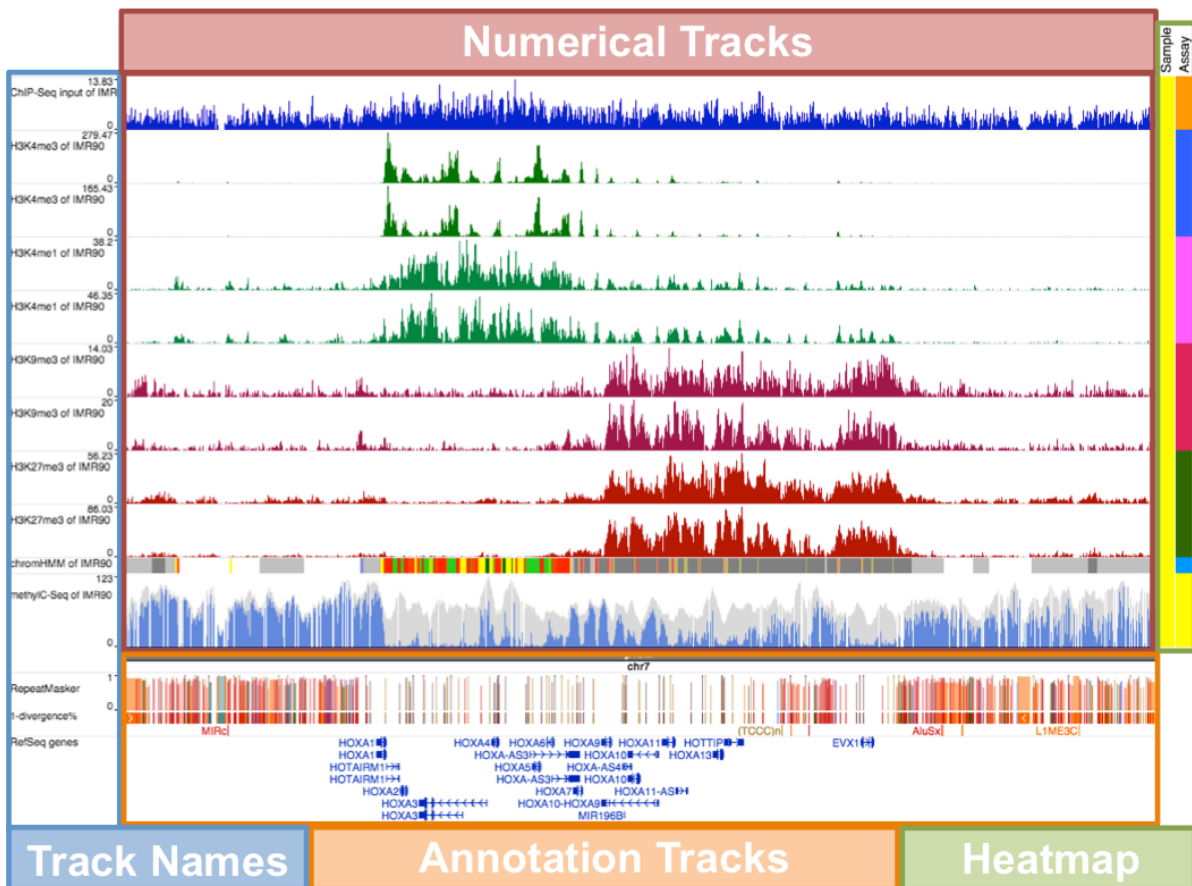
### 3.2.1. Genome navigation controls

- The controls enable exploration across the genome using the **zoom in**, **zoom out**, and **scroll** buttons.
- Alternatively, click the **navigation box** to enter the genomic coordinates of a region of interest. Click **Go** to move to the new region.



### 3.2.2. Data visualization

- **Numerical tracks** represent the density of reads from sequencing experiments aligned to the genome.
- **Track names** for each track are listed on the left-hand side of the track.
- On the right-hand side of the tracks is a **heatmap**, which represents the **metadata** for the tracks. Metadata are terms used for annotating tracks with experimental and sample information.
- Below the numerical tracks are **annotation tracks**, including annotations of genes and transposable elements.



### 3.3. Adding datasets on the EpiGenome Browser

- ### 3.3.1. Facet table:
- The facet table organizes all the loaded datasets into a table to allow the user to search for datasets using metadata terms. **Rows** represent samples and **columns** represent assay types. **Cells** with numbers represent the number of datasets for a particular sample and assay combination. For example, in the cell with numbers **11/130**, **11** represents the number of datasets currently loaded on the browser, while **130** represents the total number of datasets available.
- [A] To display the facet table, click the **Tracks** button near the top of the browser to display the Tracks menu. Click the teal box at the top of the menu to display the facet table.

- [B] To search for datasets, click on **Fetal Cells/Tissues** and then select **Fetal Brain**. Click the cell corresponding to the **Epigenetic Mark** column and the **Fetal Brain** row to list the datasets in this category.
- [C] To add the datasets, first select the datasets **H3K9me3 of Fetal Brain** and **H3K4me3 of Fetal Brain**. Then, click the **Add 2 tracks** button.
- To exit this window, click the **X** at the top-right of the panel or press **Esc**.

**[A]**

1 Tracks

2737 TOTAL / 11 SHOWN

CLICK FOR TRACK TABLE

track name Find ?

PUBLIC track hubs

ANNOTATION tracks

CUSTOM tracks

**[B]**

Experimental assay tracks

Row Sample Column Assay

Epigenetic Mark Expression Long Range Interaction Other Assays Transcription Regulator

0/1225 0/80 n/a n/a n/a Adult Cells/Tissues

0/4 n/a n/a n/a n/a Cancer Cells

0/703 0/30 n/a n/a n/a ES/iPS Cells

0/14 n/a n/a n/a n/a Fetal Cells/Tissues

0/32 0/4 n/a n/a n/a Fetal Brain

0/4 n/a n/a n/a n/a brain, fetal day122 U

0/1 n/a n/a n/a n/a brain, fetal day112 U

0/1 n/a n/a n/a n/a brain, fetal day117 F

0/3 n/a n/a n/a n/a brain, fetal day122 M

0/2 n/a n/a n/a n/a brain, fetal day85 F

0/3 n/a n/a n/a n/a brain, fetal day96 F

0/1 n/a n/a n/a n/a brain, fetal day142 F

0/3 n/a n/a n/a n/a brain, dorsal neocortex, fetal

0/30 n/a n/a n/a n/a Fetal Heart

0/27 n/a n/a n/a n/a Fetal Intestine, Large

0/23 n/a n/a n/a n/a Fetal Intestine, Small

0/73 n/a n/a n/a n/a Fetal Kidney

n/a n/a n/a n/a Fetal Liver

11/130 0/12 n/a n/a n/a Fetal Lung

n/a n/a n/a n/a Fetal Membrane

0/72 0/31 n/a n/a n/a Fetal Muscle

0/1 0/1 n/a n/a n/a Fetal Ovary

0/14 n/a n/a n/a n/a Fetal Placenta

0/120 0/18 n/a n/a n/a Fetal Skin

0/5 0/2 n/a n/a n/a Fetal Spinal Cord

0/1 n/a n/a n/a n/a Fetal Spleen

0/22 n/a n/a n/a n/a Fetal Stomach

0/2 n/a n/a n/a n/a Fetal Testes

0/21 n/a n/a n/a n/a Fetal Thymus

0/14 0/8 n/a n/a n/a Placenta

Remove all

To get additional tracks, load public track hubs.

**[C]**

6 H3K9me3 of Fetal Brain bigwig i

DNase hypersensitivity of Feta... bigwig i

7 H3K4me3 of Fetal Brain bigwig i

H3K27me3 of Fetal Brain bigwig i

ChIP-Seq input of Fetal Brain bigwig i

DNase hypersensitivity of Feta... bigwig i

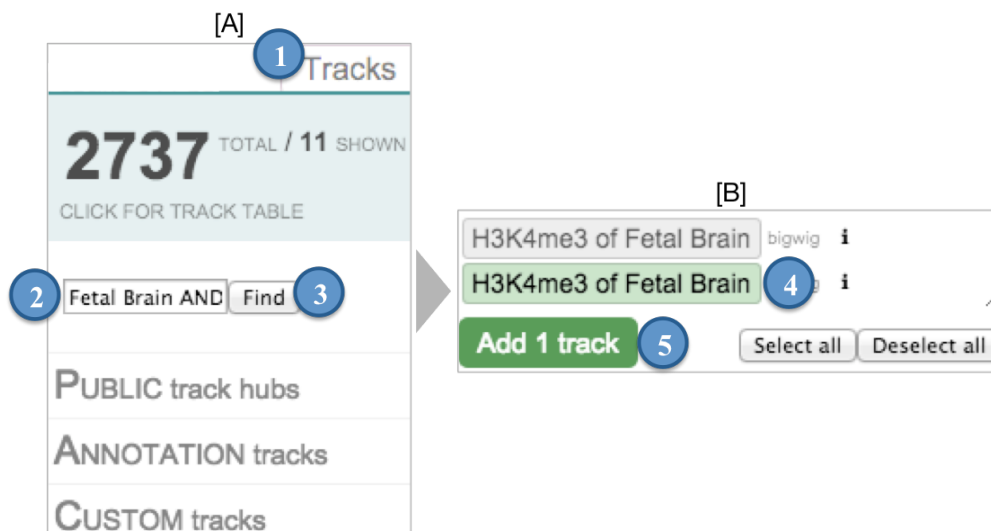
DNase hypersensitivity of Feta... bigwig i

DNase hypersensitivity of Feta... bigwig i

8 Add 2 tracks Select all Deselect all

### 3.3.2. Searching for datasets using the track search box


- [A] Click the **Tracks** button. In the search box, type **Fetal Brain AND H3K4me3**, and then click **Find**.
- [B] This will list all replicates for this sample and assay type. Only one of the two boxes listed can be selected since the other replicate has already been loaded (see section 3.3.1). Click the second **H3K4me3 and Fetal Brain** and then click **Add 1 track**.

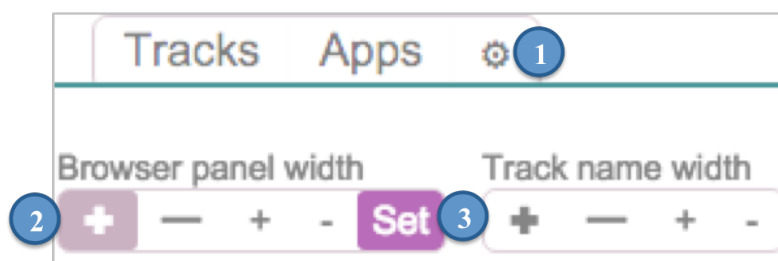


- Repeat this process to add one more replicate track for **Fetal Brain AND H3K9me3** and click outside the floating window to get back to the browser.

To catch up to this point in the workshop, enter the session ID **IECworkshop** and click the session named **Add datasets**.

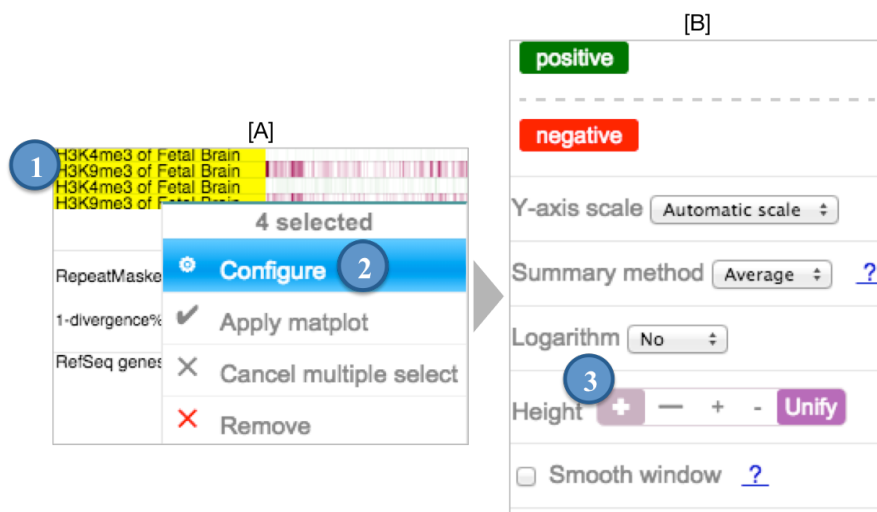
### 3.3.3. Formatting the view range

- To adjust the **browser width**, click the  button near the top of the browser. The + and - buttons increase or decrease the browser width. Click **+** then **Set** to change the browser width.
- Similarly, the **width of the track names** can be changed using the + and - buttons.



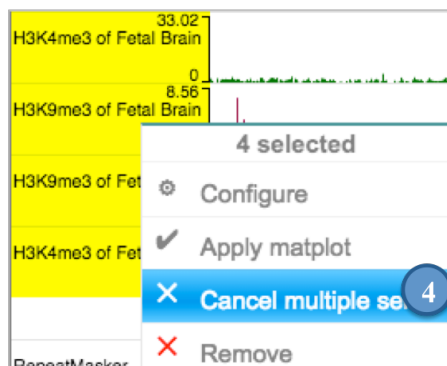
### 3.3.4. Changing the height of tracks

- [A] To select multiple tracks, hold down the **shift key** and click the names of the **four Fetal Brain tracks** that were just added. Right-click the yellow-highlighted tracks then click **Configure**.
- [B] Click the **+** sign repeatedly to increase the height of the tracks. This does not change the y-axis scale.
- Click outside the configuration menu to get back to the browser.



To catch up to this point in the workshop, enter the session ID **IECworkshop** and click the session named **Configure browser 1**.

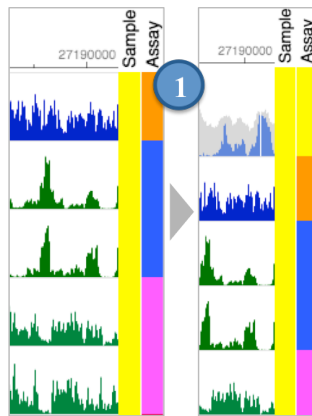
- To deselect the four tracks, right-click the yellow-highlighted track names and select **Cancel multiple select**.



### 3.3.5. Reordering tracks

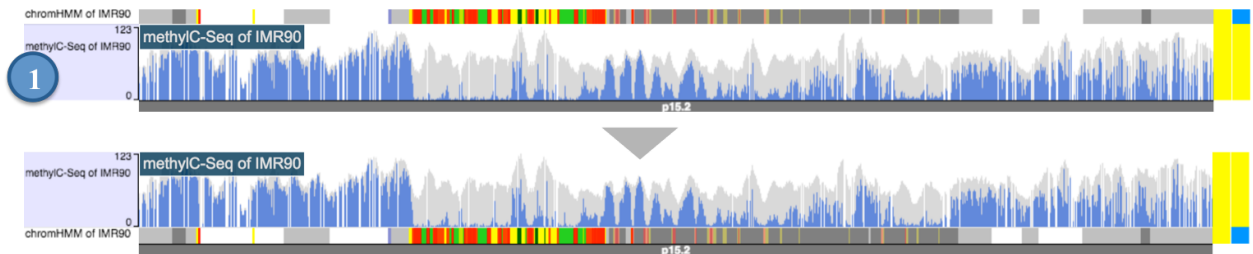
#### 3.3.5.1 Reordering by metadata terms

- To reorder the tracks based on assay type, click the **Assay** term above the heatmap.



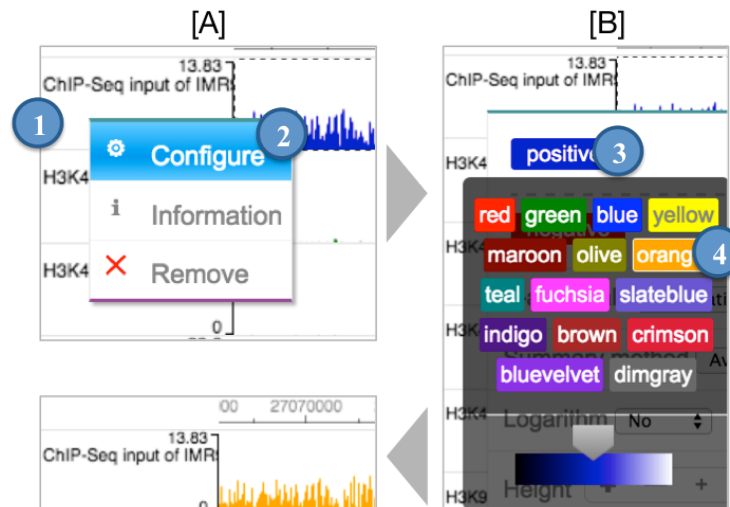
### 3.3.5.1 Reordering by click-and-drag

- Alternatively, clicking on a track name and moving that track to a new position can reorder tracks.
- Select the **methylC-Seq of IMR90** track and move the track above the **chromHMM** track.



### 3.3.6. Changing the color of tracks

- [A] Select the **ChIP-Seq input of IMR90** tracks by right-clicking on the track name and then click **Configure**.
- [B] In the configuration menu, click the **positive** button and then select the **color** of your choice to change the color of the track.





- Click outside the configuration menu to get back to the browser.

To catch up to this point in the workshop, enter the session ID **IECworkshop** and click the session named **Configure browser 2**.

### 3.3.7. Changing the y-axis scale for tracks

- [A] To select the four H3K4me3 tracks, right-click the **blue rectangle** in the heatmap (under the Assay metadata term column) and click **Configure**.
- [B] To change the height of the selected tracks, click the **y-axis scale** drop-down menu and then select **Fixed**. This will generate textboxes in which a y-axis range can be entered. Type **150** in the max textbox. Click **apply** to change the y-axis scale.
- [C] To color data beyond the range of the current y-axis, click the **beyond threshold** button. This will generate a window with color options; select the **color** of your choice



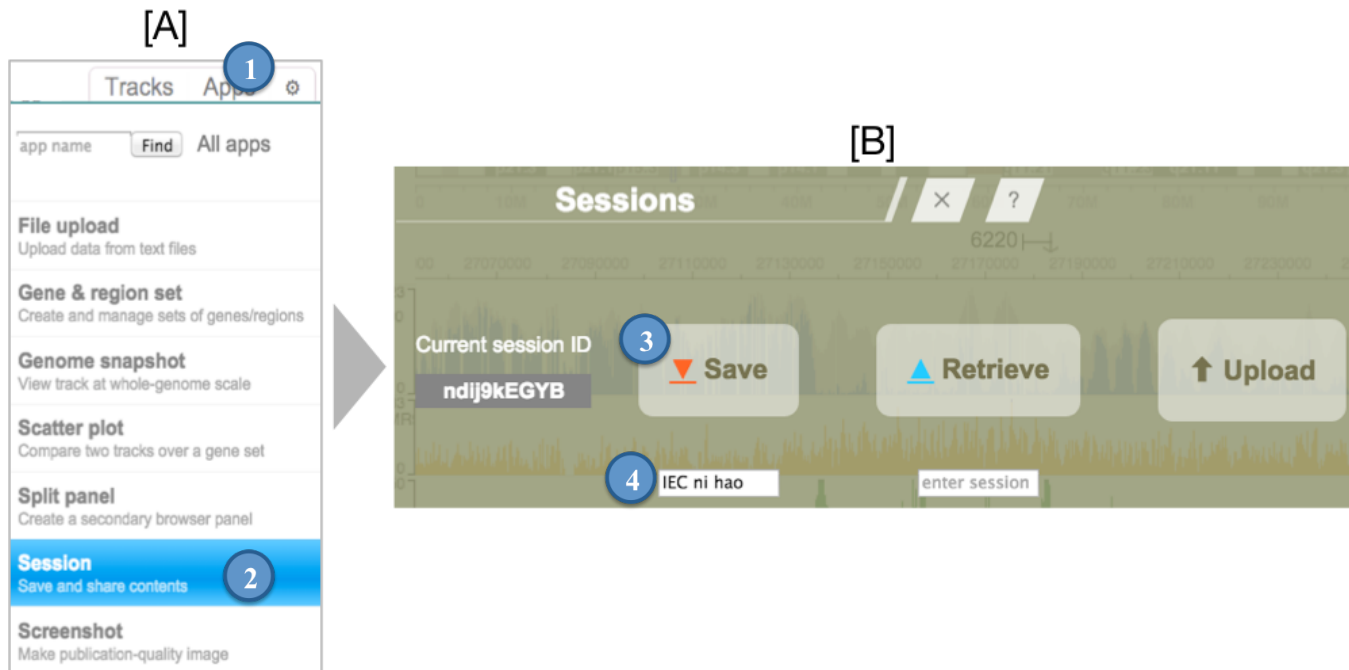
- Click anywhere outside the **Configure** box to get back to the browser.

To catch up to this point in the workshop, enter the session ID **IECworkshop** and click the session named **Configure browser 3**.

## 4. Sessions: saving and retrieving browsing sessions

### 4.1. Saving sessions

- [A] Click the **Apps** button and then select **Session**.
- [B] Type **IEC browsing** in the dialogue box under the Save button and then click **Save**. Click the **X** at the top-right of the panel to get back to the browser.



### 4.2 Sharing links for collaboration

- To generate the link for this session, click the **Link** button next to the session name. This will create a floating window with a **URL** that can be shared.



### 4.3 Retrieving Sessions

- Launch a new instance of the EpiGenome browser in a new window by going to <http://epigenomegateway.wustl.edu/browser>. Select the **Human hg19** genome assembly. Click the **GENOME Browser »** button to proceed to the browser.
- [A] Click the **Apps** button, and then select **Sessions**.
- [B] Enter the session ID **IECdemo** in the search box under the Retrieve button, and then click **Retrieve**. This will list all the available sessions under this session ID.

Click on **Start**. This will retrieve a new session that will be used for the last section of this tutorial.

Figure 1: Overview of the IEC browser interface. (A) The left sidebar menu with options: Tracks, App, File upload, Gene & region set, Genome snapshot, Scatter plot, Split panel, Session (highlighted), and Screenshot. (B) The main interface showing a genomic track with a 'Sessions' panel. The 'Current session ID' is '5UoQ6ZNU0o'. Buttons for 'Save', 'Retrieve', and 'Upload' are visible. A 'make a note' field and a session name 'IECdemo' are also shown.

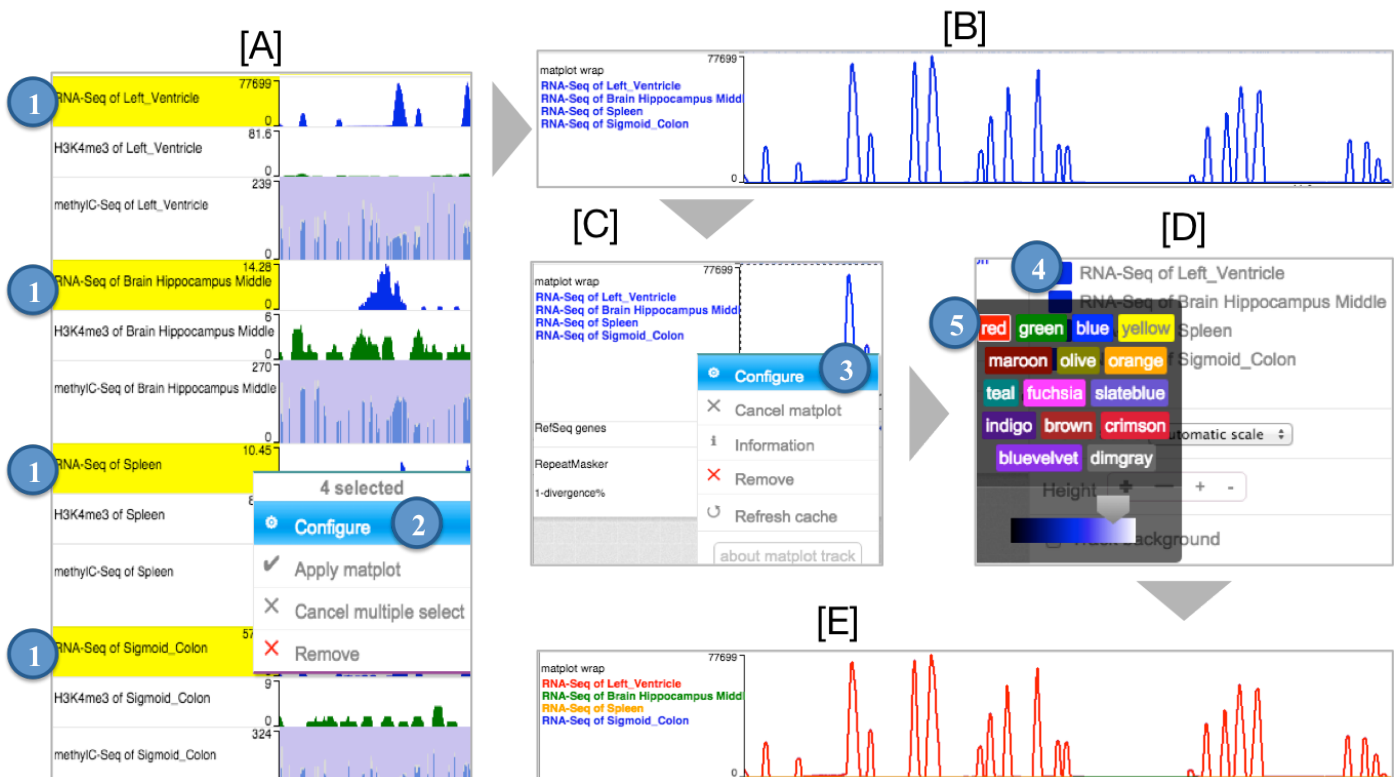
- Click the **X** at the top-right of the panel or press **Esc** to get back to the browser.
- In this session, we will be using Roadmap datasets to analyze tissue specificity of RNA Expression and H3K4me3.
- The **Start** session contains pre-loaded RNA-Seq, H3K4me3, and methylC-Seq data for the left ventricle (heart), hippocampus (brain), spleen, small intestine, and sigmoid colon.



## 5. Using Apps on the EpiGenome Browser

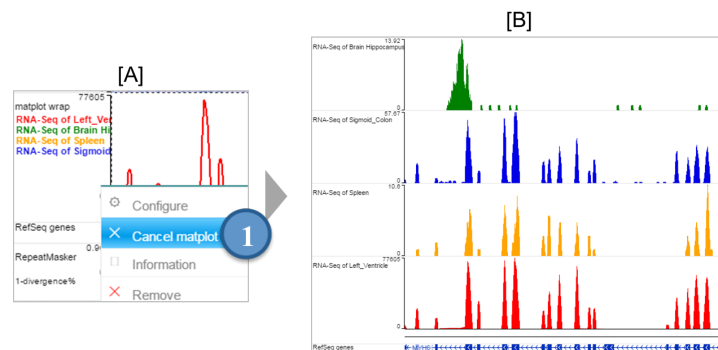
**5.1 Matplot:** A matplot (line plot) is used to compare two or more data tracks by plotting datasets on the same X and Y axes. Move to gene MYH6 in the browser.

- [A] Hold down the **shift key** and click the names of all the **RNA-SEQ** tracks. **Right-click** any of the tracks' names. Click **Apply matplot**.
- [B] This will generate a matplot track.
- [C] To change the color of the numerical tracks, **right-click** the name of the matplot track and click **Configure**.
- [D] Click the **blue-box** beside the Left Ventricle. Select **red** to change the color of the RNA-Seq Left\_Ventricle from blue to red. Colors can be changed for all subsequent tracks in the same manner.
- [E] This results in a track where the RNA-Seq data from the four tissues share the same y-axis and can be easily compared. It is evident from this view that there is high expression of MYH6 in heart as compared to other tissues.



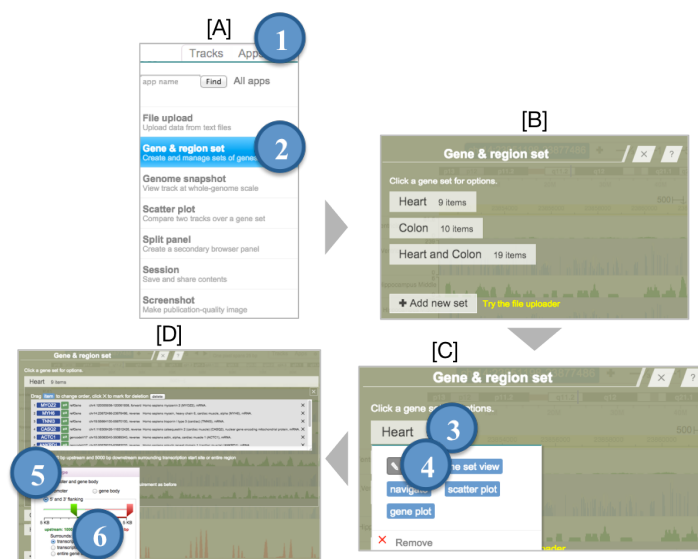
To catch up to this point in the workshop, enter the session ID **IECdemo** and click the session named **Matplot**.

- [A] To exit from the matplot view, **right-click** the matplot track name and click **Cancel matplot**.
- [B] This ungroups the tracks, but keeps their new colors. These tracks can then be moved back to the original order.

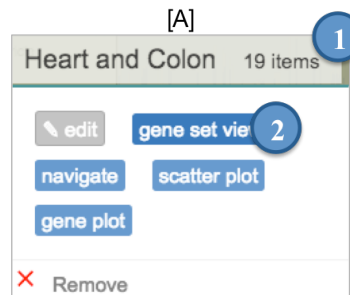


**5.2 Gene & region set:** The Gene & region set app is used to visualize multiple genomic regions in parallel. The app enables track data to be displayed over nonadjacent regions on a chromosome or even regions on different chromosomes.

- Enter the session ID **IECdemo** and click the session named **Gene Sets**. This session includes three gene sets: “Heart”, “Colon”, and “Heart and Colon”.
- [A] Click the **Apps** button and then select **Gene & region set**.
- [B] Three genes sets are available. To add a set of genes click **+ Add new set**.
- [C] Select the **Heart** button and click **edit**.
- [D] Under the list of regions, click the **change »** button to modify the view range. First select the radio button for **5' and 3' flanking** and then select the radio button for **entire gene or interval**. Adjust the **green** slider to 1 KB and the **red** to 5 KB. Click **anywhere outside the window** to exit this window and repeat for the other two sets.



- [A] To view the “Heart and Colon” gene set go to apps Gene & region set, select the **Heart and Colon** button, and then click **gene set view**.



- Change the **Y-axis scale** on all RNA-Seq tracks to a fixed scale with a max of 150.
- Change the **Y-axis scale** of all H3K4me3 tracks to a fixed scale with a max of 40.
- Adjust the **height** of the RNA-Seq tracks and then sort the metadata by sample.
- This results in a tiled-view of 19 genes arranged beside each other. By setting the same y-axis scale for all RNA-Seq data the tissue specific expression of each gene in the set can be appreciated. Additionally, looking closely at each gene reveals that many have strong H3K4me3 peaks over the TSS and promoter region in the tissue where the gene is highly expressed (indicated in **red** for left ventricle and **black** for sigmoid colon).



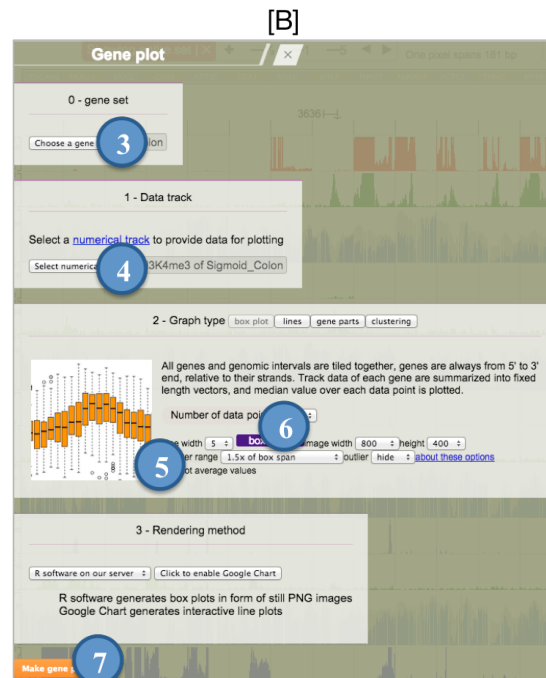
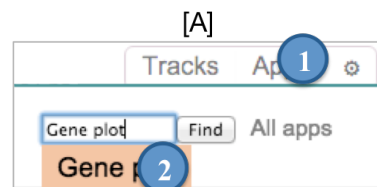
To catch up to this point in the workshop, enter the session ID **IECdemo** and click the session named **Gene Set View**.

- To exit the gene set view, click **Showing entire set | X** near the top left side of the browser.

Showing entire set | X <sup>1</sup> +

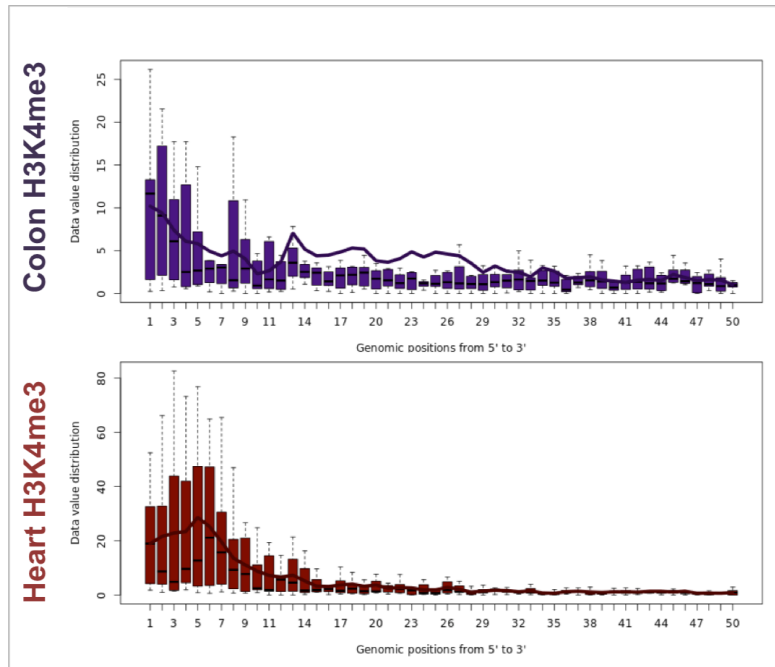
**5.3 Gene plot:** The Gene plot app summarizes the data distribution across multiple regions by splitting the regions into bins. Change the gene view area in each Gene & region set to gene body only. This app can also be accessed by clicking on any gene set.

- [A] Click the **Apps** button. In the search box, type **Gene plot** and select the **Gene plot** app.
- [B] To make a gene plot, follow these steps:
  - In the 0 – Gene set section, click the **Choose a gene set** button. Select the **Colon** gene set for this analysis.
  - In the 1 – Data track section, click the **Select numerical track »** button and then click **H3K4me3 of Sigmoid Colon**.
  - In the 2 – Graph type section, use the default graph type, a box plot. Click the **plot average values** check-box. To change the box color, click the **box color** button and then select the color of your choice.
  - Click the **Make gene plot** button to create the gene plot.



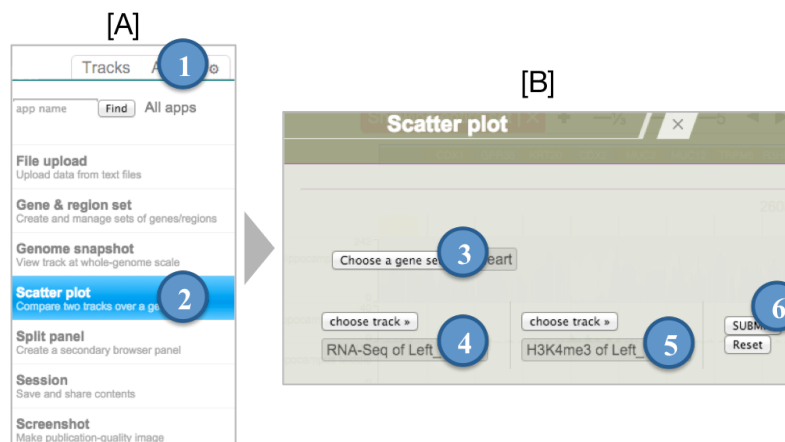


- Repeat these steps with the Heart gene set and the **H3K4me3 of Left Ventricle** dataset. Use a different box color.
- Comparing the two gene-plots reveals that the H3K4me3 signal is the strongest in the 5' upstream region of the gene with an appreciable depletion when moving towards the 3' end when pairing a preferentially expressed tissue-specific gene set with its corresponding H3K4me3 track.

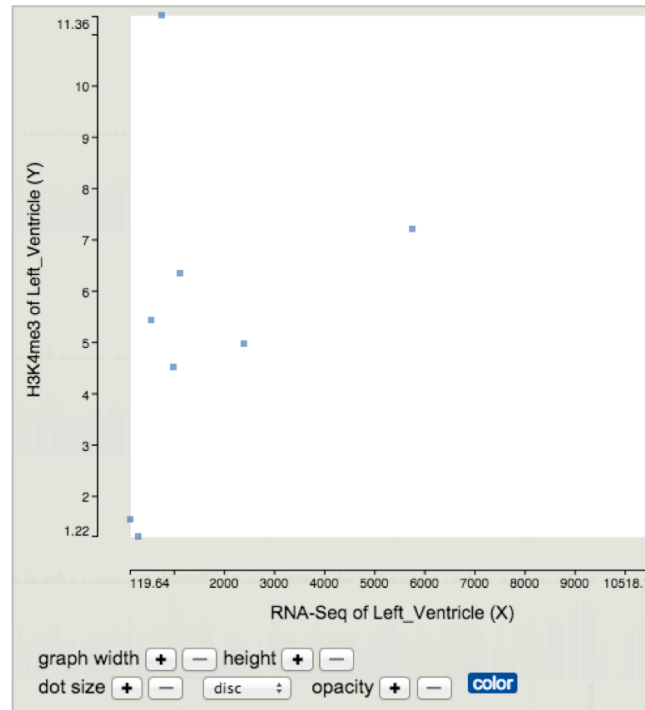


**5.4 Scatter plot:** The Scatter plot app is used to assess the relationship between two different datasets across multiple genomic regions.

- [A] Click the **Apps** button and then select **Scatter plot**.
- [B] To select the genomic regions to plot, click the **Choose a gene set** button and then click the gene set **Heart**. This gene set contains genes known to be expressed in a tissue-specific manner in the heart. To select the numerical track to plot on the x-axis, first click the **Choose track »** button above the “for X axis” button then select **RNA-Seq of Left\_Ventricle** track. To select the numerical track to plot on the y-axis, first click the **Choose track »** button above the “for Y axis button” then select the **H3K4me3 of Left\_Ventricle** track. Click **SUBMIT** to create the plot.



- The resulting scatter plot shows the correlation between gene expression and H3K4me3 for the left ventricle across the gene set. H3K4me3 is associated with active promoters, so the correlation is expected for this set of nine genes that are expressed in the heart.



- To exit the app click the **X** at the top-right of the panel or press **Esc**.

## 6. Creating Custom Tracks on the WashU Epigenome Browser

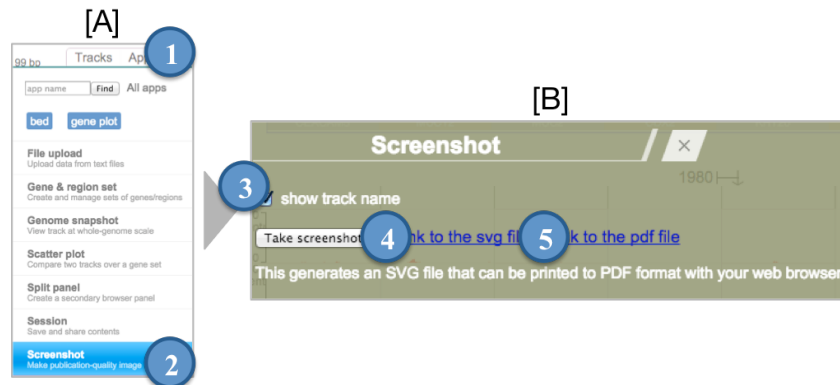
Now that you know the ins and outs of the WashU Epigenome Browser it is time to explore your data.

- [A] Click the **Tracks** button then click **Custom Tracks**.
- [B] Click on **+ Add new tracks**.
- [C] There are many supported formats that can be uploaded readily to the browser. Data must be hosted on a web server accessible to the browser. Click **BED** to create your first custom track.
- [D] Click **Use example** and then **SUBMIT**. The track now appears in the browser window, click **X** to return to the browser window.

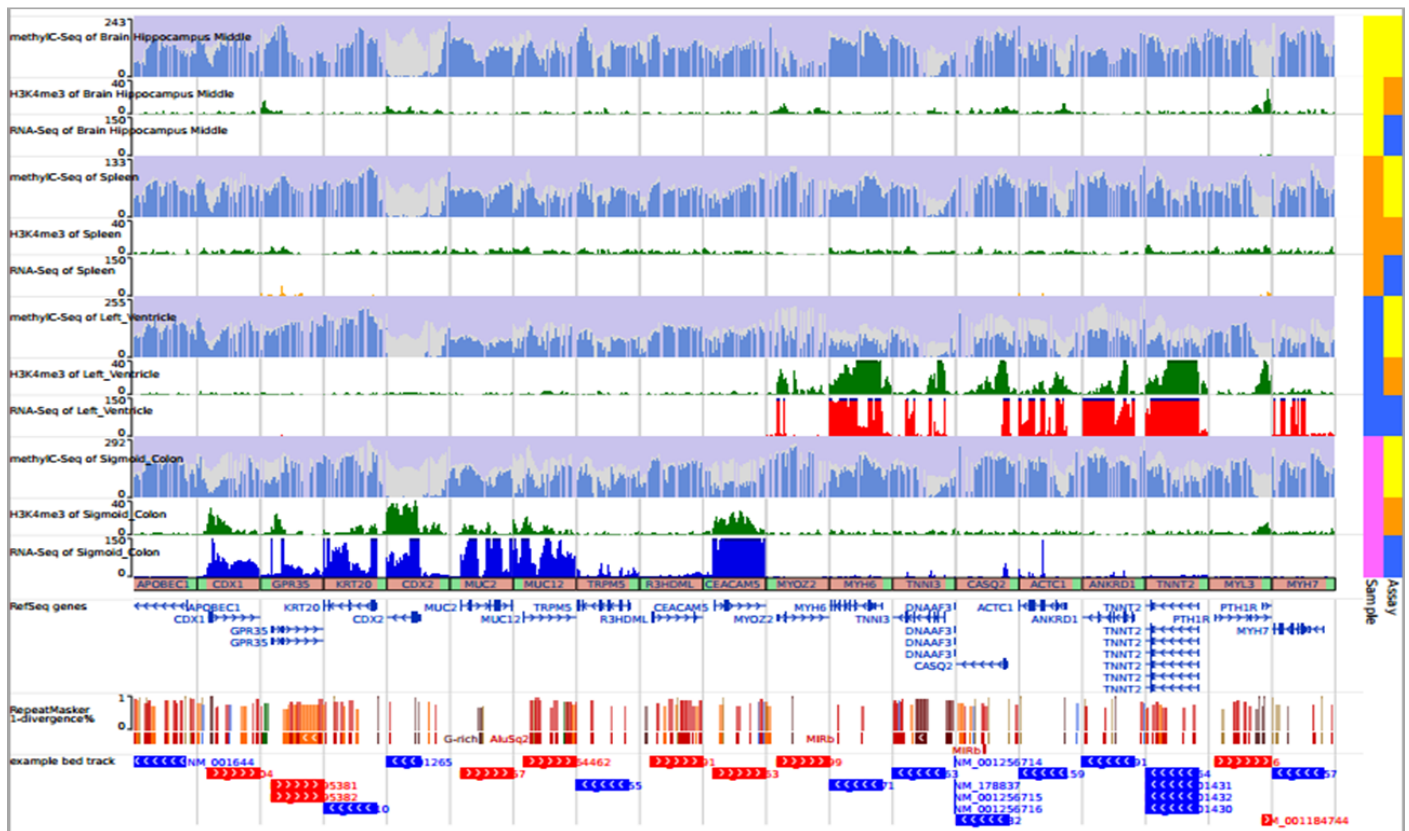


To repeat this section of the tutorial, enter the session ID **IECdemo** and click the session named **Custom Track**.

- [A] Finally you may want to take a screenshot of your final tracks, a gene of interest, or a gene set. Click the **Apps** button then click **Screenshot**.
- [B] Click the **show track name** button then click **Take Screenshot**.



- Click either the **Link to the svg file** button or the **Link to the pdf file** button to save a high quality screenshot.



## 7. Using the Roadmap EpiGenome Browser

The **Roadmap EpiGenome Browser** 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 and ENCODE projects (>20k datasets). The Browser performs real-time data clustering analyses to reveal cell type-specificity of epigenetic marks.

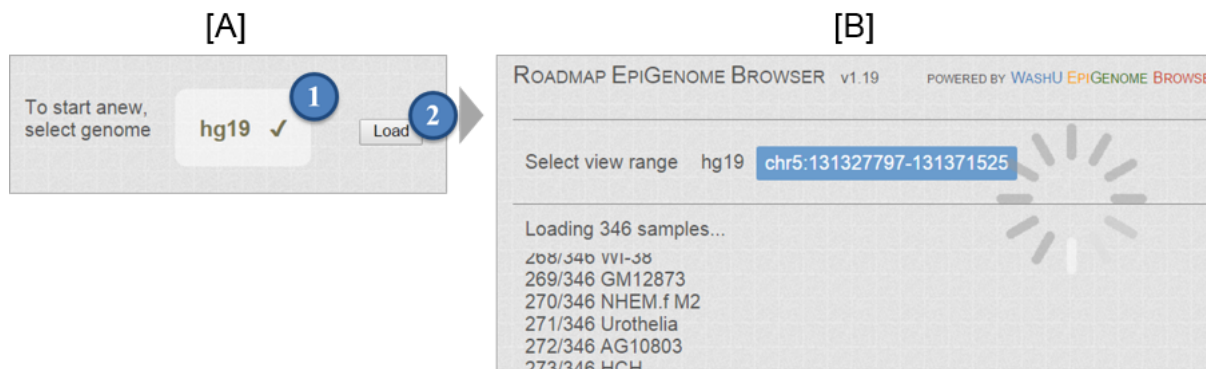
In this section of the workshop, we will demonstrate how to annotate non-coding genetic variants with epigenetic data using the Roadmap EpiGenome Browser.

### 7.1. Launching the browser

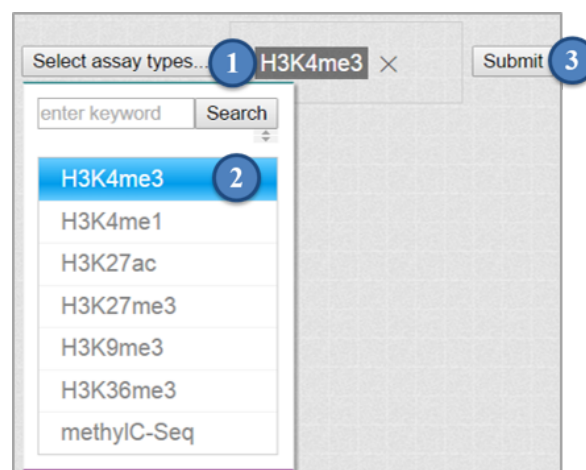
- Access the browser at <http://epigenomegateway.wustl.edu/browser/roadmap/>

### 7.2. Loading data on the Roadmap EpiGenome Browser

- [A] Click the **hg19** button then click **Load**.
- [B] The browser will load all of the Roadmap Epigenomics and ENCODE reference epigenomes.



- To display tracks for a specific epigenetic mark, click the **Select assay types...** button. Select **H3K4me3**. H3K4me3 is associated with actively transcribed promoters. Click **Submit**. The browser will display the H3K4me3 tracks for all samples.



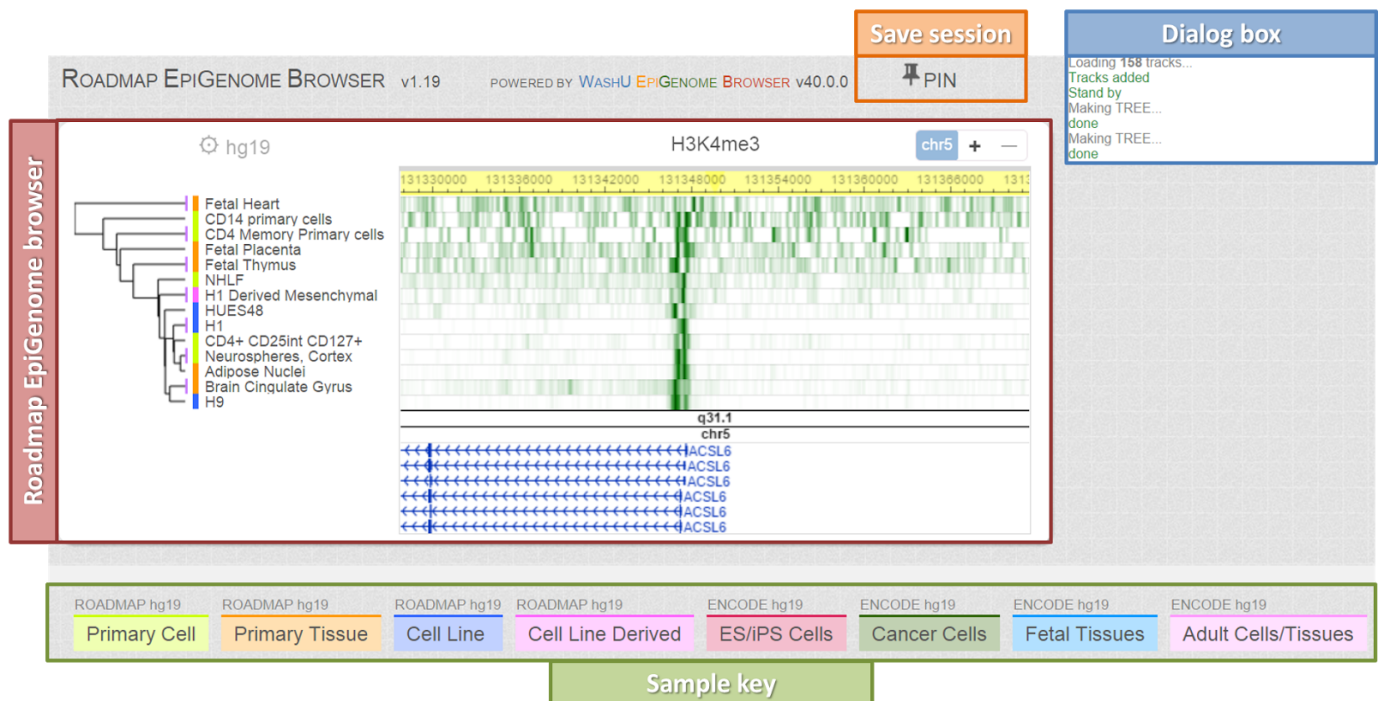


To catch up to this point in the workshop, go to

<http://epigenomegateway.wustl.edu/browser/roadmap/?pin=http://epigenomegateway.wustl.edu/browser/roadmap/t/673535216.json>.

## 7.3. Navigating the Roadmap EpiGenome Browser

### 7.3.1. Layout of the Roadmap EpiGenome Browser



#### 7.3.2. Dialog box

- This box logs all actions performed by the Roadmap EpiGenome Browser. Any errors the browser encounters are displayed.

#### 7.3.3. Save session

- Users can save their current browsing status for future reference or sharing.

#### 7.3.4. Roadmap EpiGenome Browser

- This region contains the data tracks aligned to the genome along with reference genes and a chromosome ideogram. Additional public track hubs, annotation tracks, and custom tracks can be added by the user.

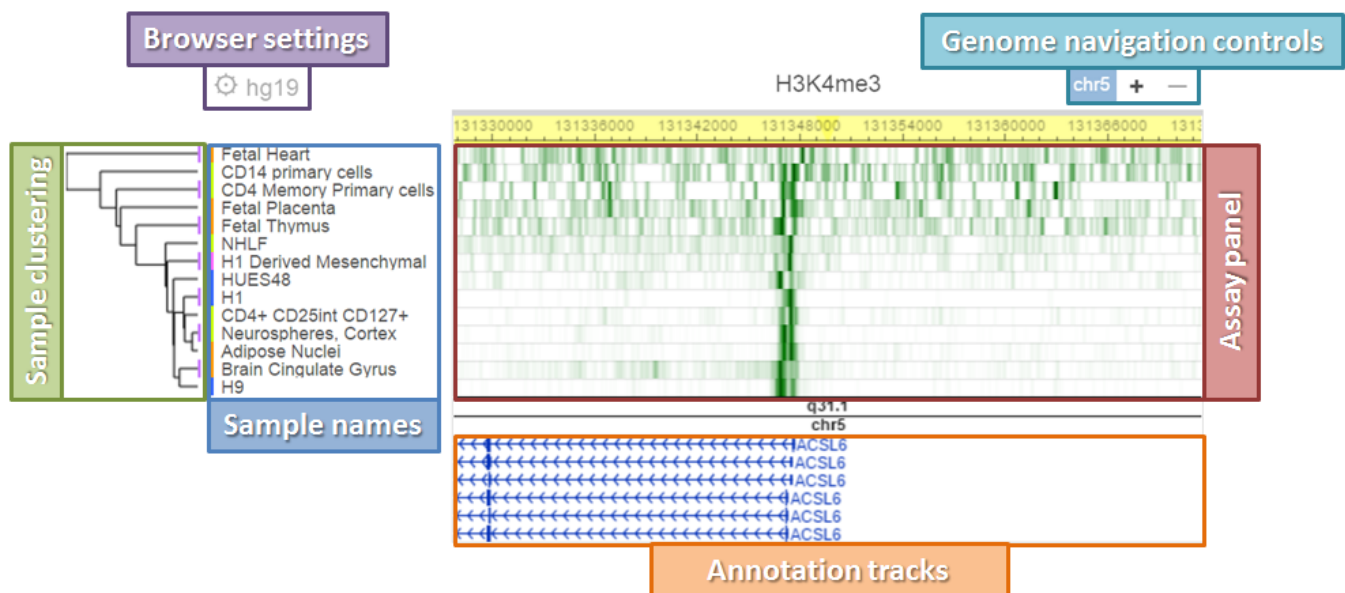
#### 7.3.5. Sample key

- This region contains the key for mapping the sample type and origin of each sample.

## 7.4. Navigating the genome on the Roadmap EpiGenome Browser

### 7.4.1. Data visualization

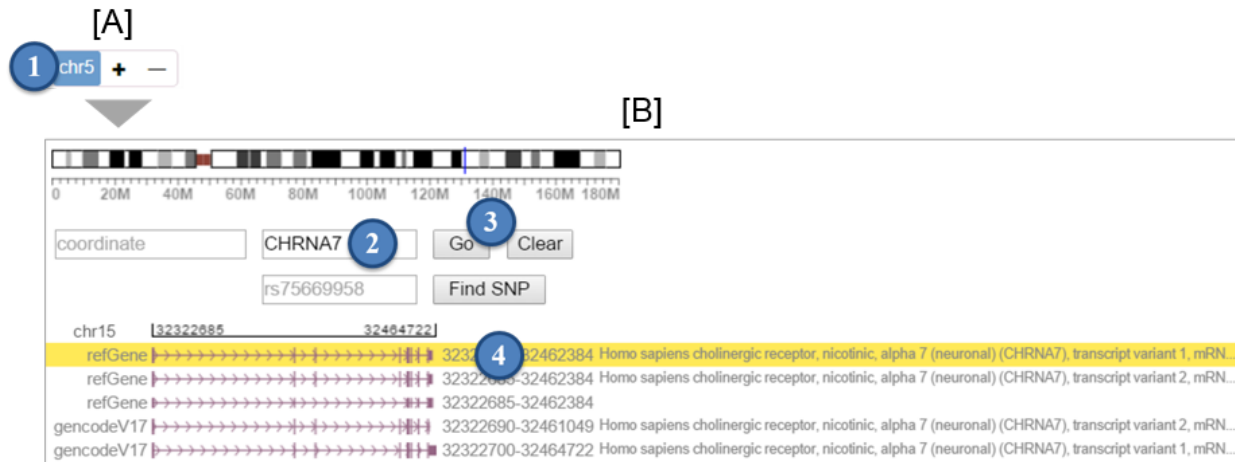
- **Browser settings** contain options to change which genomic regions, assay types, and samples are displayed as well as the **view range**.
- **Assay panel** contains the numerical tracks for each sample. All tracks are of the same assay type, for example, H3K4me3 ChIP-seq.
- **Sample names** for each track are listed on the left-hand side of the track. The colored bars indicate the sample type and origin of each sample.
- The dendrogram shows **hierarchical clustering** of the samples based on the track data in the current view range. Whenever the assay panels are updated, for example by scrolling, the hierarchical clustering analysis is automatically rerun to reflect the new sample relationships within the updated view range.
- Below the numerical tracks are **annotation tracks**, including annotations of genes.
- The **genome navigation controls** enable exploration across the genome.



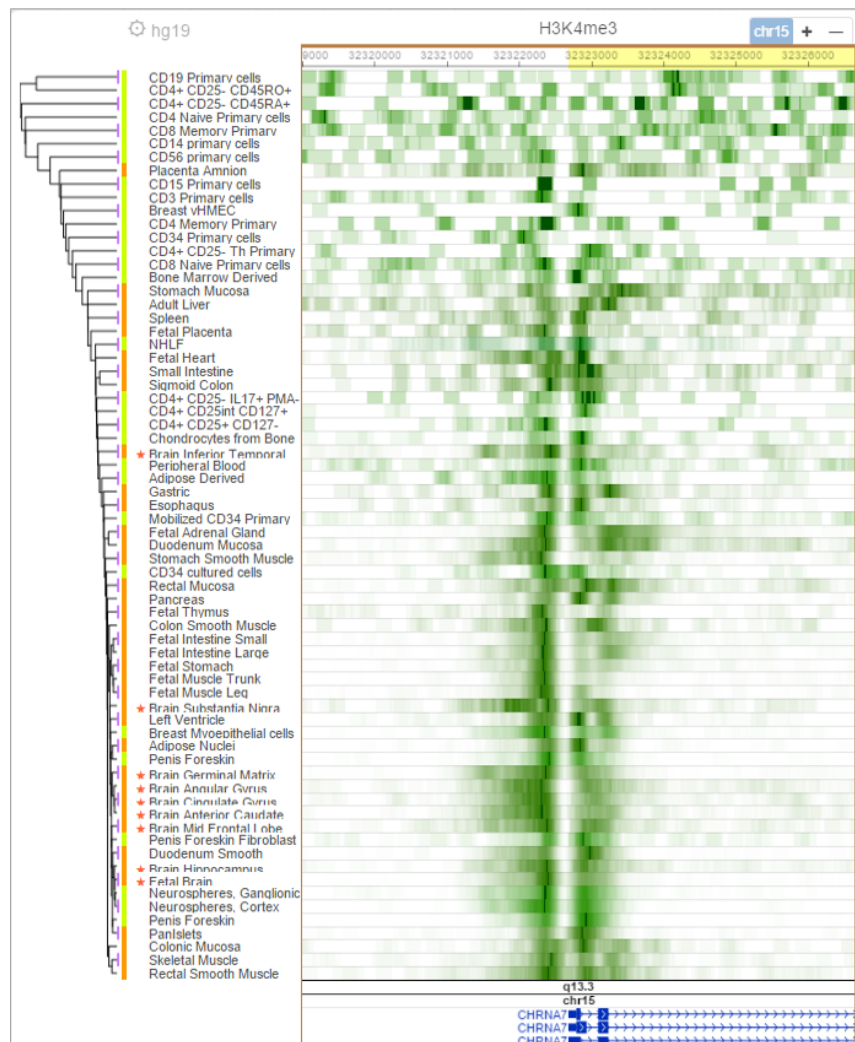
### 7.4.2. Genome navigation controls

- To zoom in or out, click on the **+** or **-** buttons. Alternatively, **select a region in the coordinate ruler** to zoom in on a region of interest.
- [A] Click the blue **navigation box** to move to a region of interest.
- [B] The region can be specified by a genomic coordinate, a gene name, or a SNP rsID. In the gene name textbox, type **CHRNA7** and click **Go**. Multiple gene models are shown for the gene. Select the **first gene model** to move to its location.





- To move the view range to the promoter of *CHRNA7*, click on the Assay Panel and drag the mouse. To zoom in on the promoter, click upstream of the transcription start site in the annotation track and drag the mouse.
- Many of the brain samples have a strong H3K4me3 signal over the *CHRNA7* promoter while the blood samples do not.





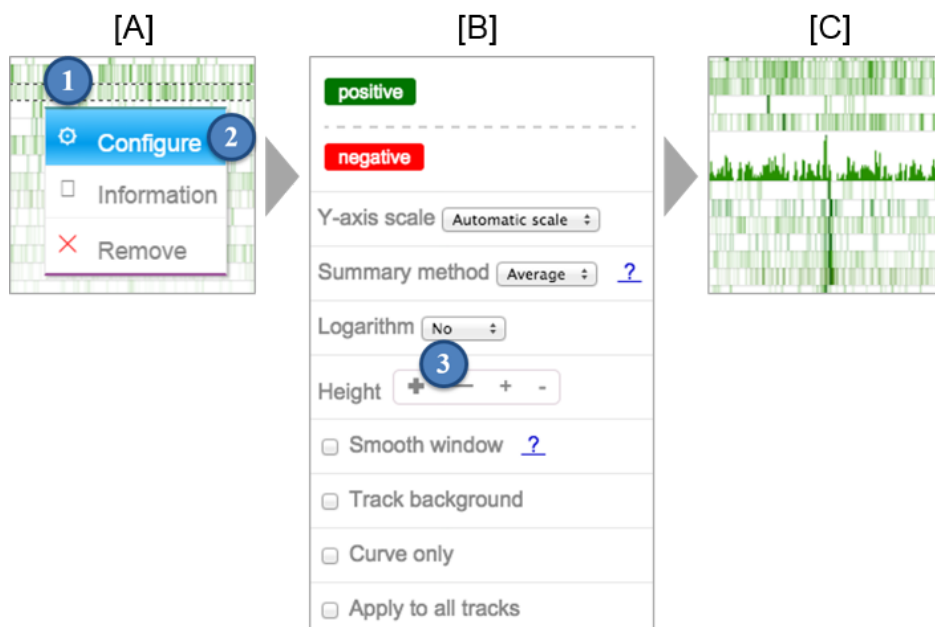
To catch up to this point in the workshop, go to

<http://epigenomegateway.wustl.edu/browser/roadmap/?pin=http://epigenomegateway.wustl.edu/browser/roadmap/t/778209644.json>.

## 7.5. Configuring the Roadmap EpiGenome Browser

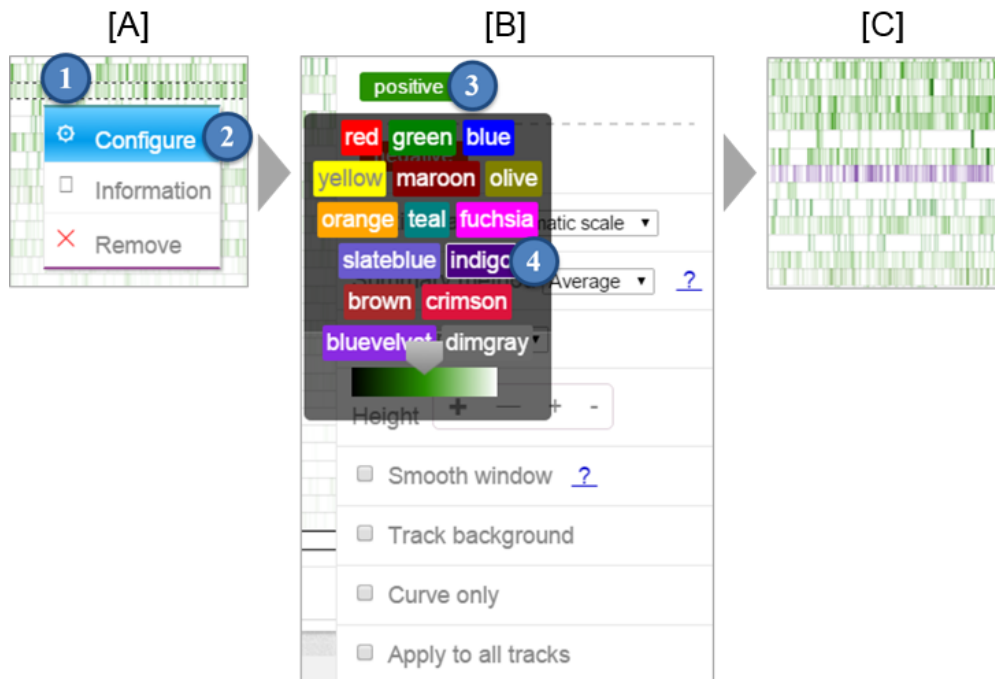
### 7.5.1. Changing the height of tracks

- [A] Right-click a track and select **Configure**.
- [B] Click the **+** sign repeatedly to increase the height of the track to your preference.
- Click outside the configuration menu to get back to the browser.



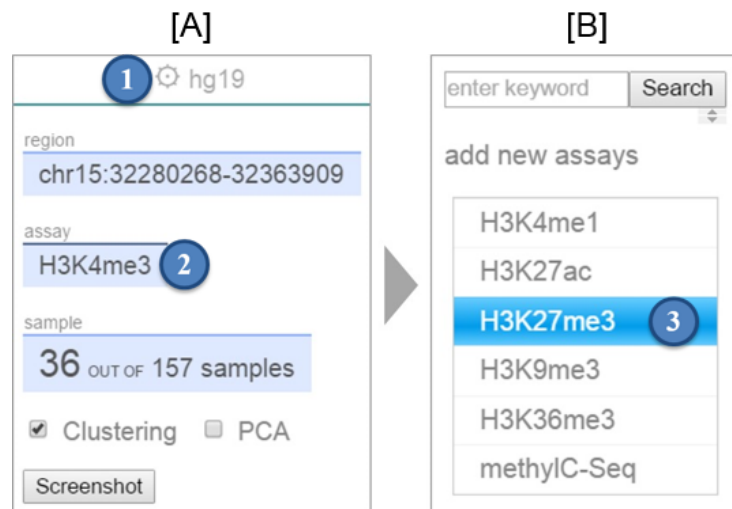
### 7.5.2. Changing the color of tracks

- [A] Right-click a track and select **Configure**.
- [B] In the configuration menu, click the **positive** button and then select the **color** of your choice to change the color of the track.
- Click outside the configuration menu to get back to the browser.

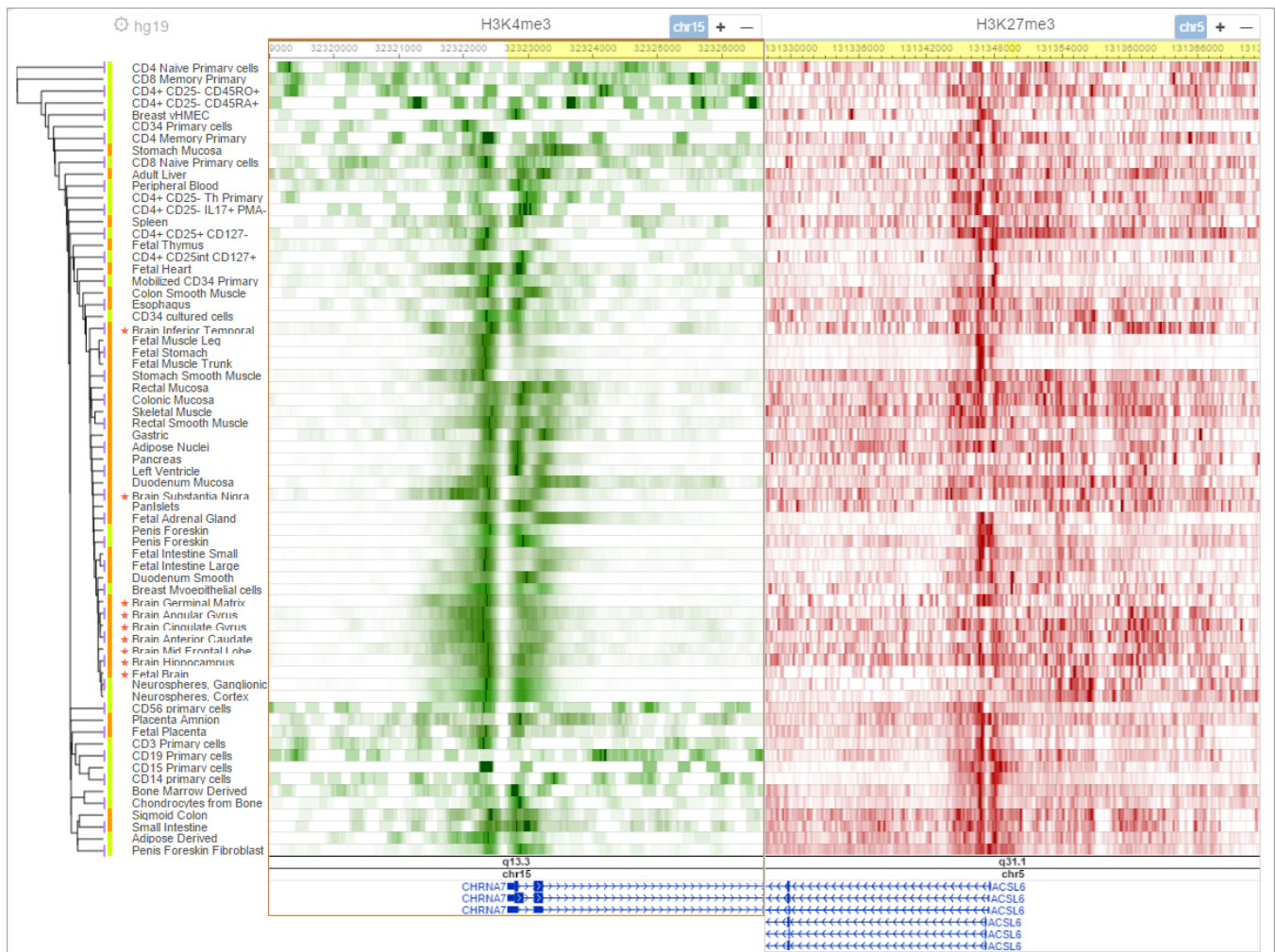


## 7.6. Adding assays on the Roadmap EpiGenome Browser

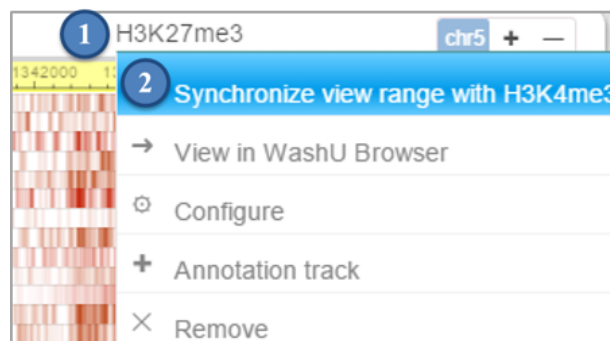
- [A] To add H3K27me3 tracks, click the button near the top of the browser and then click **assay**.
- [B] Select **H3K27me3**. H3K27me3 marks polycomb repressive chromatin.



- The H3K27me3 data is shown in a new panel. Each row now contains H3K4me3 and H3K27me3 for a particular sample. The samples are clustered using the data in *both* panels.



- The new assay panel is over the default genomic region. By default, the view range of each assay panel is independent of the others. To synchronize the view range of the panels, click the banner of the H3K27me3 assay panel and select **Synchronize view range with H3K4me3**.



- In the brain samples, H3K4me3 is high and H3K27me3 is low over the transcription start site while in the blood samples, H3K4me3 is low and H3K27me3 is high. The browser makes it easy to see the covariation of epigenetic marks within a region.

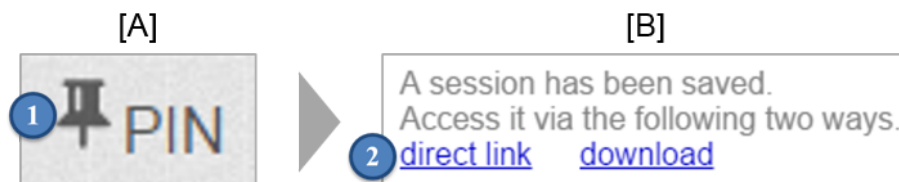


To catch up to this point in the workshop, go to

<http://epigenomegateway.wustl.edu/browser/roadmap/?pin=http://epigenomegateway.wustl.edu/browser/roadmap/t/373364002.json>.


## 7.7. Saving and retrieving browsing sessions

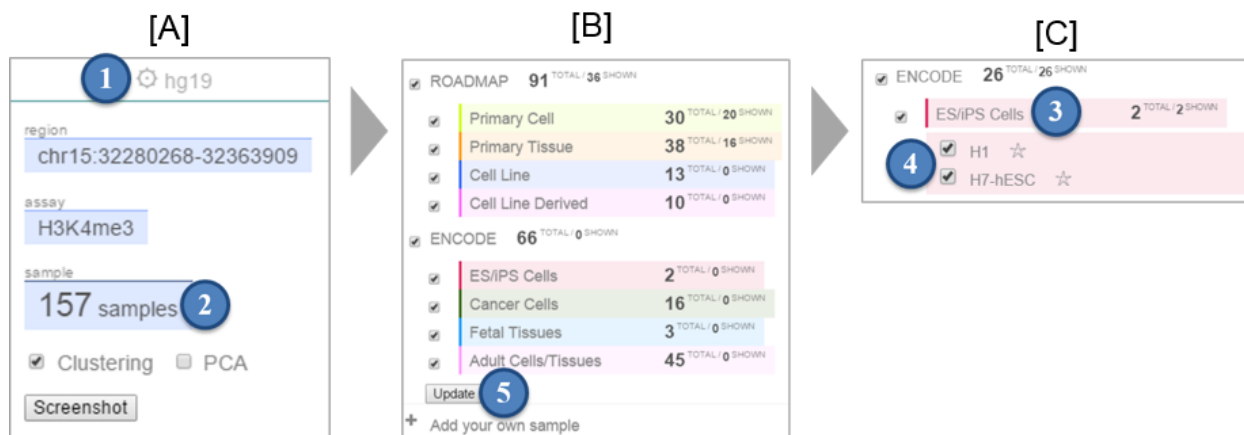
- [A] To save a session, click the **pin icon** at the top of the browser.
- [B] Save the **direct link** URL.
- To restore a session, paste the URL in a web browser.




## 7.8. Adding and removing samples

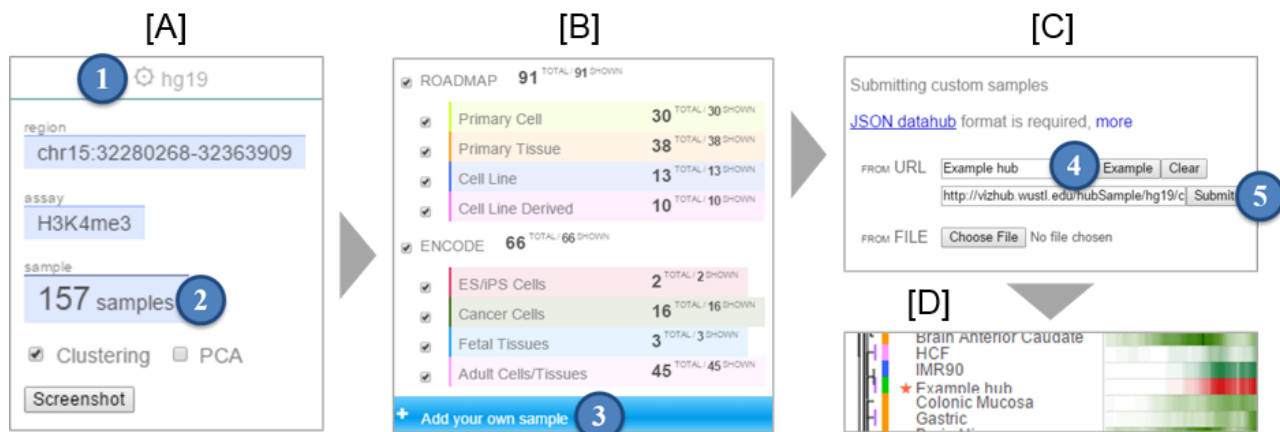
### 7.8.1. Adding and removing samples

- [A] To add a sample, click the  button and click **sample**.
- [B] The number of available samples in each category is listed.
- [C] Click on a **sample type** to list the sample names for that particular sample type. To add or remove samples, **check** or **uncheck** the checkboxes. To apply the changes, click the **Update** button.



### 7.8.2. Adding custom samples

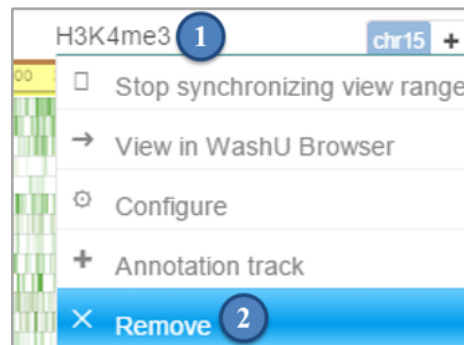
- Users can submit their own datasets to analyze them in the context of public samples from the Browser.
- [A] To add a custom sample, click the  button and click **sample**.
- [B] Select **Add your own sample**.
- [C] In the pop-up window, the user can enter the **URL** of the data in JSON datahub format and enter a sample name. In this workshop, we'll use the example custom sample. Click **Example** and click **Submit**. Alternatively, users can upload a datahub file.
- [D] The custom sample is shown as a **red** heatmap and is marked by a star.




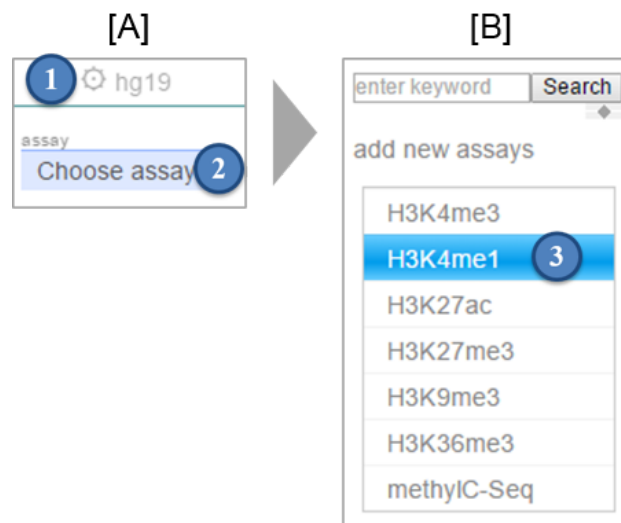
## 7.9. Annotating non-coding variants with epigenomic data

### 7.9.1. Viewing a non-coding SNP in the context of H3K4me1 data

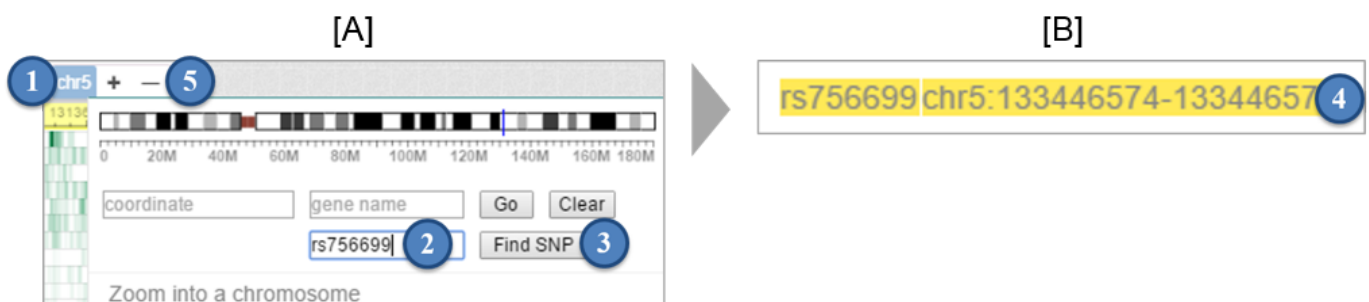
- A genome-wide association study by Sawcer et al. found SNP rs756699 to be associated with multiple sclerosis (MS). In this section, we will investigate if this SNP is associated with any regulatory elements. First, remove the current assay panels by clicking each of the **banners** and selecting **Remove**.



- To add H3K4me1 tracks, click the  button and then click **assay**. Select **H3K4me1**. H3K4me1 marks active enhancers.

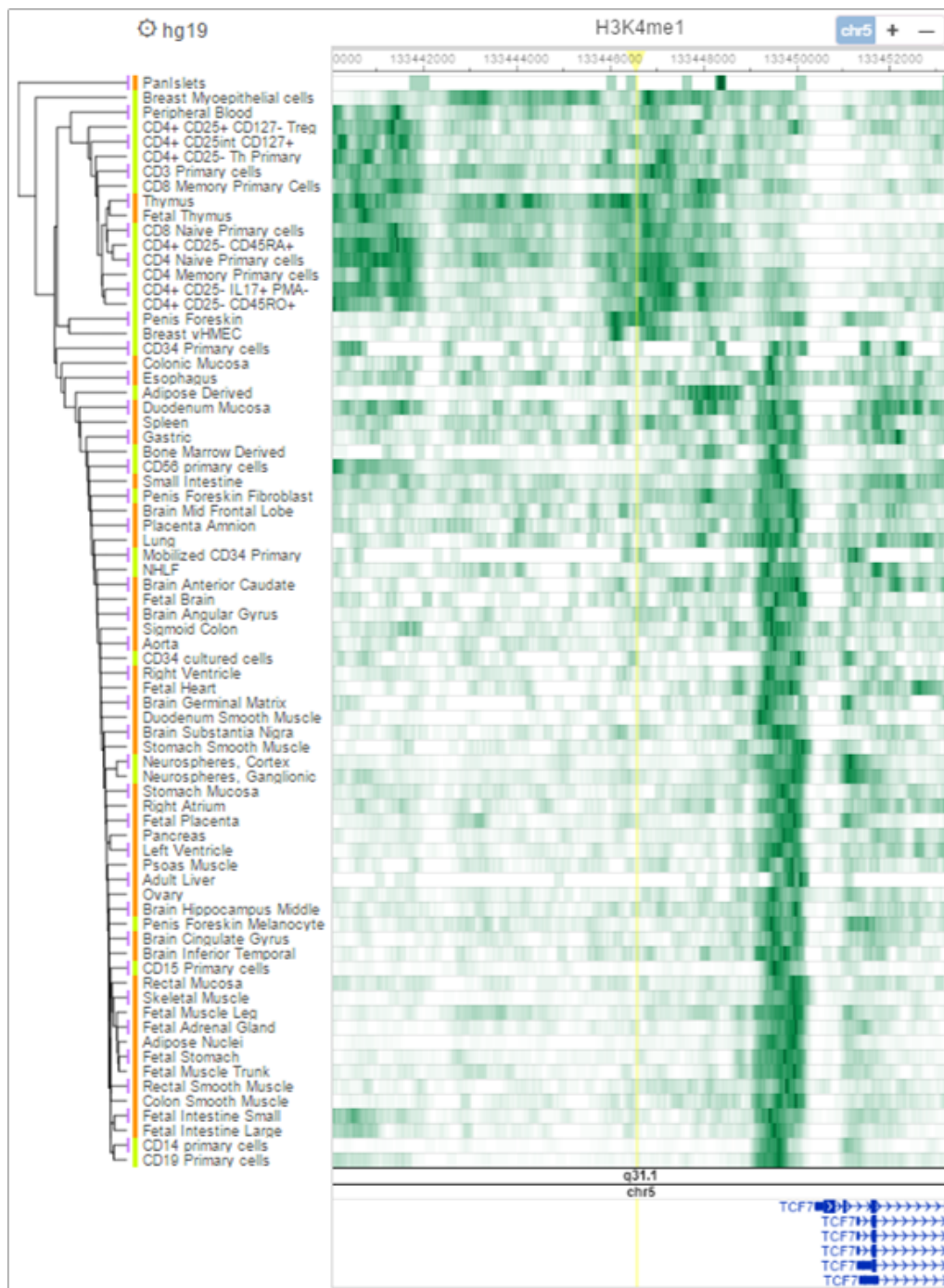


- [A] To go to the SNP location, click the blue **navigation box**. Enter **rs756699** in the SNP textbox. Then click **Find SNP**.
- [B] Select **rs756699 chr5:133446574-133446575**. The SNP is marked by a yellow rectangle. Zoom out by clicking the **-** button multiple times.





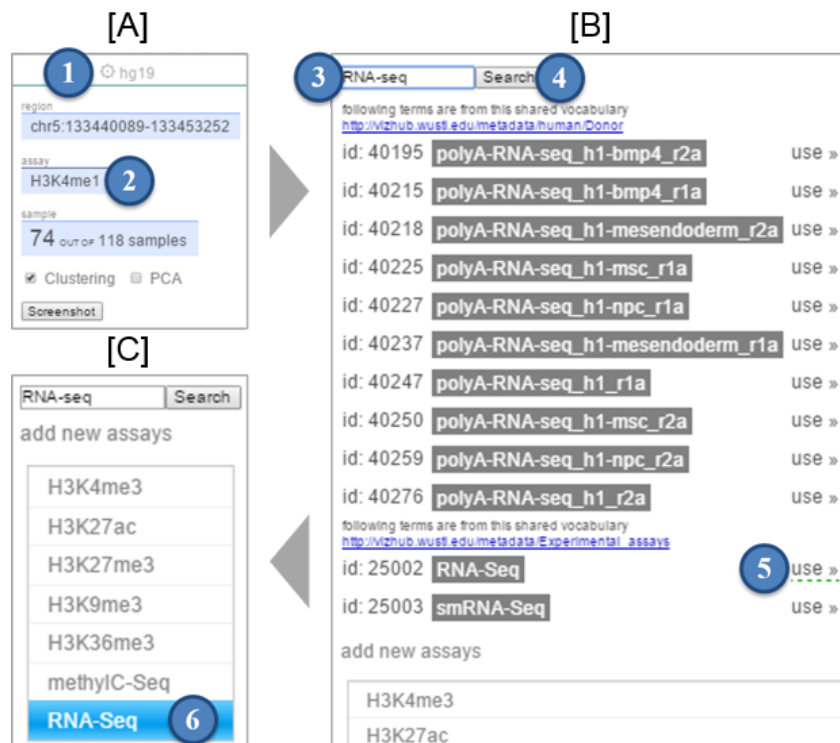
- The SNP lies in a putative blood-specific enhancer upstream of the *TCF7* transcription start site.



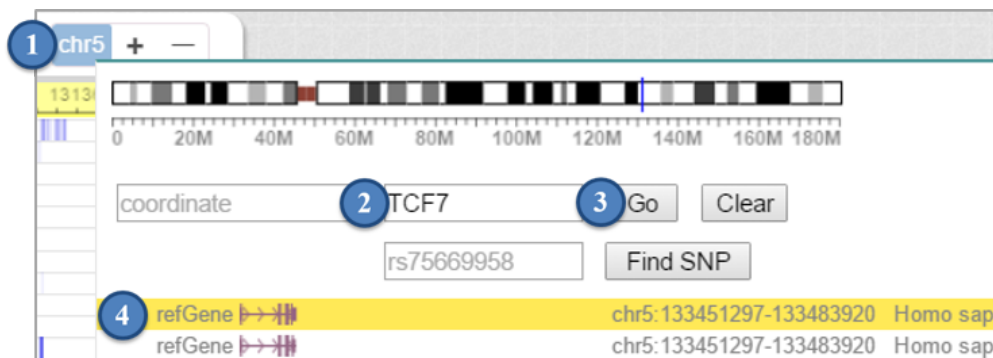
### 7.9.2. Viewing a non-coding SNP in the context of H3K4me1 and expression data

- [A] Next, we want to determine if the putative blood-specific enhancer regulates *TCF7* expression in a blood-specific fashion. To add the RNA-seq assay, click the button and then click [assay](#).

- [B] In the search textbox, type **RNA-seq** and click **Search**. In the search results, click the **use »** link next to the RNA-seq assay. The RNA-seq list has now been added to the list of assays.
- [C] Select **RNA-seq**.



- In the RNA-seq panel (not the H3K4me31 panel), click the blue **navigation box**. In the gene name textbox, type **TCF7** and click **Go**. Multiple gene models are shown for the gene. Select the **first gene model** to go to its location.



- [A] To set all of the RNA-seq tracks to the same scale, right-click on an **RNA-seq track** and select **Configure**.
- [B] Check the **Apply to all tracks checkbox**. Change the Y-axis scale drop-down menu to **Fixed**, set the max to **100**, and click **apply**.





To catch up to this point in the workshop, go to

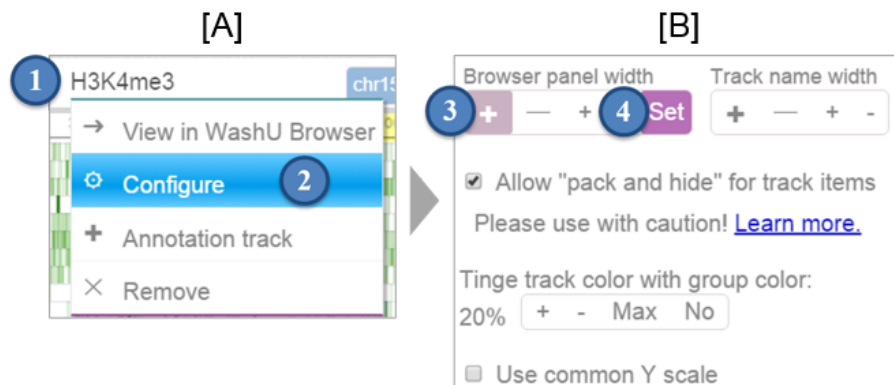
<http://epigenomegateway.wustl.edu/browser/roadmap/?pin=http://epigenomegateway.wustl.edu/browser/roadmap/t/1792526056.json>.

### 7.9.3. Viewing multiple non-coding SNPs simultaneously


- The **Gene Set View** allows users to look at data from multiple locations in the genome within the same browser panel.

#### 7.9.3.1. Formatting the view range

- [A] To view multiple locations in the genome in one browser window more easily, increase the browser width. To adjust the **browser panel width**, click the **banner** containing the assay name near the top of the browser. Select **Configure**.
- [B] The + and - buttons increase or decrease the browser width. (The smaller + and - buttons increase or decrease the browser width by a smaller amount.) Click + then **Set** to change the browser width.
- Similarly, the **width of the track names** can be changed using the + and - buttons.

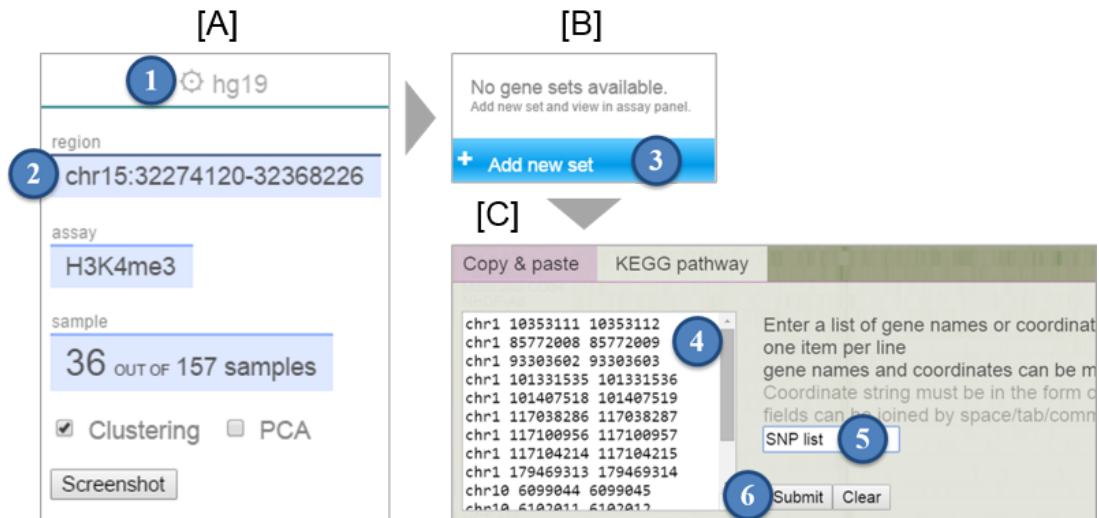


#### 7.9.3.2. Creating a gene set

- [A] To visualize a set of SNPs associated with multiple sclerosis, click the  button and then click **region**.
- [B] Click **Add new set**.
- [C] Paste the list of SNP coordinates (listed below) in the textbox, enter a **name**, and click **Submit**.

```
chr1 10353111 10353112
chr1 85772008 85772009
chr1 93303602 93303603
chr1 101331535 101331536
chr1 101407518 101407519
chr1 117038286 117038287
```

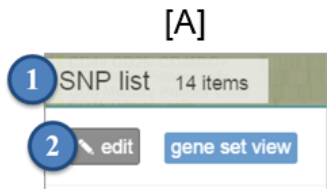
```
chr1 117100956 117100957
chr1 117104214 117104215
chr1 179469313 179469314
chr10 6099044 6099045
chr10 6102011 6102012
chr10 6110828 6110829
chr10 43814048 43814049
chr10 81036006 81036007
```



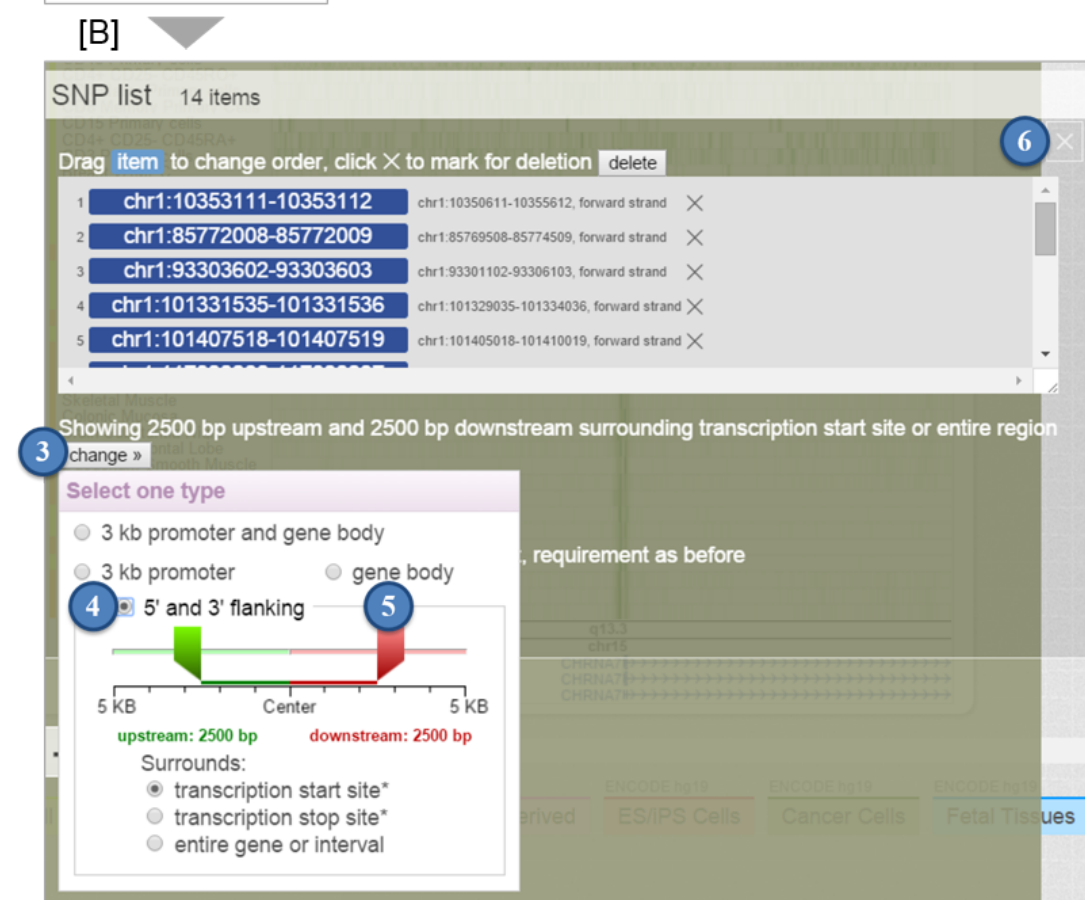
### 7.9.3.3. Editing a gene set

- [A] To focus on a 5kb window surrounding each of the SNPs, click on the **gene set banner** and then click **edit**.
- [B] Click **change**, and then select **5' and 3' flanking**. Move the **red slider** to 2.5 KB. Click the Adjust the red slider to 2.5 KB. Click the **X** button in the edit window to exit.

[A]



[B]



SNP list 14 items

Drag item to change order, click X to mark for deletion delete

1	chr1:10353111-10353112	chr1:10350611-10355612, forward strand	X
2	chr1:85772008-85772009	chr1:85769508-85774509, forward strand	X
3	chr1:93303602-93303603	chr1:93301102-93306103, forward strand	X
4	chr1:101331535-101331536	chr1:101329035-101334036, forward strand	X
5	chr1:101407518-101407519	chr1:101405018-101410019, forward strand	X

Showing 2500 bp upstream and 2500 bp downstream surrounding transcription start site or entire region

Select one type

☐ 3 kb promoter and gene body  
☐ 3 kb promoter ☐ gene body  
☒ 5' and 3' flanking

5 KB Center 5 KB

upstream: 2500 bp downstream: 2500 bp

Surrounds:

☒ transcription start site\*  
☐ transcription stop site\*  
☐ entire gene or interval

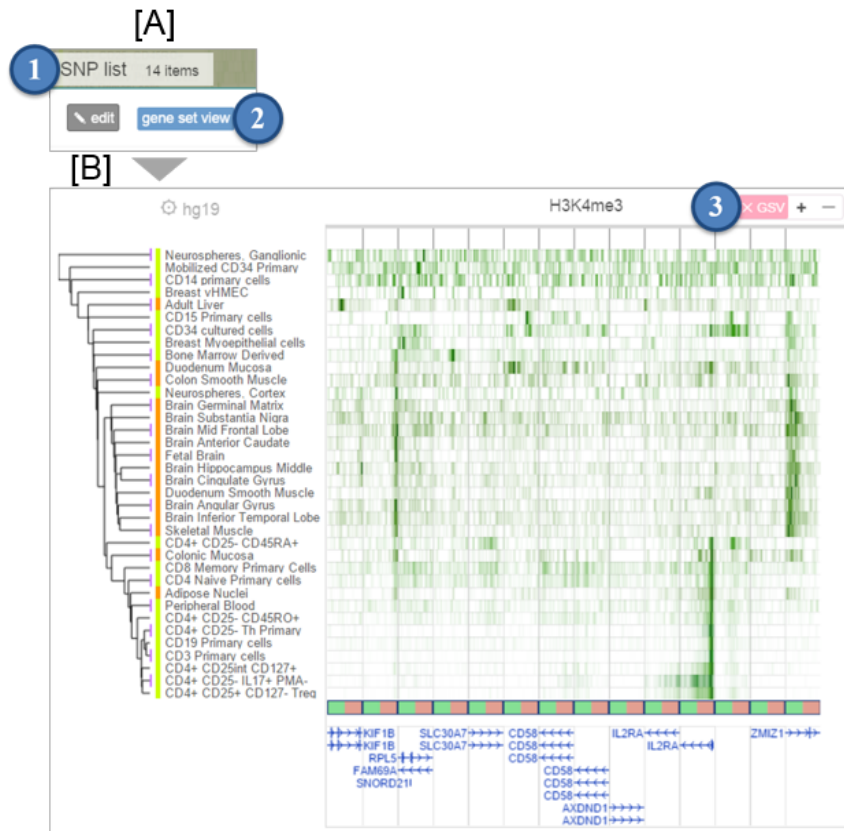
q13.3 chr15

CHRNA1 CHRNAT1 CHRNAT2

ENCODE hg19 ES/iPS Cells Cancer Cells Fetal Tissues

#### 7.9.3.4. Viewing a gene set

- [A] Click on the **gene set banner** and then click **gene set view**.
- [B] The browser shows the H3K4me1 profile over a 5 KB window centered on each of the SNPs. Several of the SNPs have tissue-specific H3K4me1. To exit the gene set view, click the **X GSV** button.



To catch up to this point in the workshop, go to

<http://epigenomegateway.wustl.edu/browser/roadmap/?pin=http://epigenomegateway.wustl.edu/browser/roadmap/t/1808443390.json>.

## 7.10. Viewing complete epigenomic profiles

- [A] To view all of the datasets for a particular sample in the WashU EpiGenome Browser, click on the sample name **CD4 Memory Primary cells** and then select **View in WashU Browser**.
- [B] A WashU EpiGenome Browser window will be opened. All of the available datasets for CD4 Memory Primary cells will loaded over the default view range.





## 8. Training and support

- For more documentation and tutorials, visit:  
<http://epigenomegateway.wustl.edu/support/index.html>
- Follow the WashU EpiGenome Browser on

 <http://epigenomegateway.wustl.edu/+>

 <http://epigenomegateway.wustl.edu/fb>

 @wuepgg