QTL Viewer User Guide

The QTL Viewer is an interactive QTL mapping webtool developed by the Churchill Lab at The Jackson Laboratory (Bar Harbor, ME, USA). It provides a web interface for analyzing and visualizing QTL mapping data for the Diversity Outbred (DO) mice. Most of the analysis is performed utilizing the R package R/qtl2 (https://kbroman.org/qtl2/). This document contains instructions on how to navigate the data and the main functions of the webtool, using the JAX Center for Aging Research DO data from the heart as an example (https://churchilllab.jax.org/qtlviewer/JAC/DOHeart).

Section 1: Selecting a Dataset

All QTL Viewer projects contain at least one dataset. For the JAX Aging DO heart project, both proteome and transcriptome data are available. To switch datasets, click the selection box arrow next to the text "Current Data Set".

| JAC DO Heart QTL Viewer Current Data Se → DO H | eart Transcriptomics | |
|--|--|--------|
| Q Search III LOD Peaks | | |
| Please type a term to search for | JAC DO Heart QTL Viewer Please search for a term of interest. | |
| | | |
| Created by The Churchill Lab. | 🖥 Download Data | v0.5.1 |

Section 2: Searching the Dataset

To search for a term of interest, type in your search text into the Search input box and press "Enter". The search algorithm recognizes gene symbols, names, and Ensembl identifiers. All elements that match the search criteria will be displayed in a table below, but only elements that are in the dataset will be displayed in blue and clickable.



For phenotypes such as transcripts and proteins, a "LOD Peaks" tab is available next to the "Search" tab. When selecting this option, a genomic grid is displayed with LOD scores from each gene or protein. This is the easiest way to look for genomic hotspots in the data.



The number of elements in the grid can be filtered by sliding the blue dot left and right (decreasing and increasing) to increase the LOD threshold. Different types of mappings for the

LOD peaks (for example, age-interactive QTL mapping, or sex-interactive QTL mapping) can be selected by clicking the "Plot type" select box. The dots in the grid provide information on hover and are clickable.

Section 3: LOD Plot

After searching, clicking on either an element from the "LOD Peaks" grid or an element in the search will generate a genome wide LOD plot. Information about each LOD score may be contained upon hovering over that area. Clicking on the most interesting areas reveal additional information in the tabs below.



The "Plots" select box will switch between additive and interactive models.

Section 4: Effect Plot

The Effect Plot shows the estimated allele effects for the chromosome selected from the LOD Plot above. The LOD Plot from above can be used to check the allele effects at the position of the QTL (highest LOD score). In order to generate an Effect Plot, make sure the "Effect Plot" tab is selected and click on a location in the "LOD Plot" above.



In the example above, alleles A/J, C57BL/6J, 129S1/SvImJ, NZO/HiLtJ have a strong positive effect on the expression of Mrap2, while NOD/ShiLtJ, PWK/PhJ and WSB/EiJ have an opposite effect on the expression of the gene.

There is also an option to change the computation of the allele effects to the Best Linear Unbiased Predictors (BLUPs) method, in which allele effects are handled as random variables resulting in a more precise estimation.

Section 5: Mediation

The Mediation analysis is used to identify possible candidate mediators. This function runs a mediation analysis which is based on conditioning the QTL into the genotype probabilities of each gene, so the most promisor candidates are the ones that cause a higher drop of the QTL LOD score when using the conditioned model. In order to generate a Mediation Plot, make sure the "Mediation" tab is selected and click on a location in the "LOD Plot" above.



Mediation can be performed against different datasets by changing the data set in the "Mediate Against" select box.

Section 6: SNP Analysis

A SNP association analysis will show the SNP LOD scores on top and the genes located on the corresponding genomic positions on the bottom. This function is useful to highlight SNP allele patterns and where they are located in terms of gene positions. Hovering over each SNP will show information such as allele pattern, consequence, etc. In order to generate a SNP Association Plot, make sure the "SNP Association" tab is selected and click on a location in the "LOD Plot" above.



Section 7: Expression Profile Plot and Correlation

The Expression Profile Plot is generated upon when an element is first selected (as with the LOD Plot). The plot can change based upon the covariates (such as age or sex) in the experiment. Clicking on the "Select your factors" select box will turn factors on or off (include or exclude).



The "Correlation" tab will display the correlation of the selected element with any other element in the data. Select another element in the Correlation grid will display a correlation scatter plot.

Section 8: Download Data

The data for the experiment can be downloaded an R Data object by clicking the "Download Data" button in the lower right of the screen.



The underlying data is stored in an R Data object with a defined format described below.

Section 9: RData Object

The R object will be a list containing multiple items as follow:



For instructions on creating this R Data object and how to deploy the QTL Viewer, please see ... (some other document).