

NCBI GTEx eQTL Browser Tutorial

eQTL Overview:

An expression quantitative trait locus (eQTL) represents a marker (locus) in the genome in which variation between individuals is associated with a quantitative gene expression trait, often measured as mRNA abundance. Thus, the three critical components to eQTL results are 1) the genotypes at a marker (here a SNP), 2) the gene expression levels, as measured by a probe or sequence information, and 3) a measure of the statistical association between the two in a study population, such as the p-value. The eQTL browser described here provides a means to query a database of eQTL results, applying filters based on the above types of data. It should be recognized that a substantial number of tests are performed, and that the significance of p-values should be considered in this multiple testing context.

eQTLs can be described as being *cis*, where the genotyped marker is near, perhaps within 2 MB, of the expressed gene, or *trans*, in which the genotyped marker is distant from the expressed gene or even on another chromosome. Currently only the *cis*-eQTLs from the Stranger et al. paper are displayed, although in the future *trans* will be displayed as well.

eQTL Browser Tutorial:

Upon initial loading, the GTEx webpage displays two sections:

Current Dataset Information – a description of the current dataset

Search Parameters – allows a user to build complex queries

Use case 1: Display top eQTL results - To display the most significant associations within the dataset

Accept the default parameters by leaving blank the Search Parameters form.

Mouse-click on the **Display Results** buttons either above or below the search form.

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GTEx (Genotype-Tissue Expression) eQTL Browser

Search [All Databases] for [] Search

The GTEx eQTL database and browser aims to provide a central resource to archive and display association between genetic variation and high-throughput molecular-level phenotypes. This effort originated with the [NIH GTEx roadmap project](#); however the scope of this resource will be extended to include any available genotype/molecular phenotype datasets. [Click here for a tutorial.](#)

Search Parameters

[Display Results](#) [Download Text](#) [Clear Form](#) [Tutorial](#)

Analysis ID

ID	Tissue	Title	Exp. Method	Assoc. Method	Samples	Pubmed ID
<input type="checkbox"/>	1	Lymphoblastoid	Transcriptome genetics using second generation sequencing in a Caucasian population.	RNA-seq	Sperman Rank corr.	60 20220756
<input type="checkbox"/>	2	Liver	Mapping the genetic architecture of gene expression in human liver	Array	Kruskal-Wallis	427 18462017
<input type="checkbox"/>	3	Brain Cerebellum	Abundant quantitative trait Loci exist for DNA methylation and gene expression in human brain	Array	Linear Repr.	143 20485568
<input type="checkbox"/>	4	Brain Frontal Cortex	Abundant quantitative trait Loci exist for DNA methylation and gene expression in human brain	Array	Linear Repr.	143 20485568
<input type="checkbox"/>	5	Brain Temporal Cortex	Abundant quantitative trait Loci exist for DNA methylation and gene expression in human brain	Array	Linear Repr.	144 20485568
<input type="checkbox"/>	6	Brain Pons	Abundant quantitative trait Loci exist for DNA methylation and gene expression in human brain	Array	Linear Repr.	142 20485568
<input type="checkbox"/>	7	Lymphoblastoid	Population genomics of human gene expression	Array	Linear Repr.	210 17873874

[Select All](#) [Invert Selection](#)

SNP filters

RS numbers:

File containing RS numbers: [Browse...](#)

Chromosome:

Chr. Position: From: to:

Gene Expression Filters

Gene symbols, gene IDs, RefSeq IDs, and/or Probe GIs:

File containing gene symbols, gene IDs, RefSeq IDs, and/or Probe GIs: [Browse...](#)

Chromosome:

Chr. Position: From: to:

Gene Description (keywords):

Phenotype Traits

- Abdominal aortic aneurysm
- Acenocoumarol maintenance dosage
- Activated partial thromboplastin time
- Acute lymphoblastic leukemia (childhood)
- Adiponectin levels
- Adiposity
- Age-related macular degeneration
- Aging
- Aging traits
- AIDS
- AIDS progression
- Alcohol dependence

Association Test Significance Filters

P-value: $< 1 \times 10^{-5}$

R² value:

Output

Display mRNA and Description
 Compact Verbose

Sort Output:

By: P-value Ascending

Then: Ascending

Then: Ascending

Lines per page: 50

[Display Results](#) [Download Text](#) [Clear Form](#) [Tutorial](#)

The Search Results table will now be displayed; it is comprised of three primary header sections:

SNP - SNP marker name and position

Probe - Probe name, position, gene name, and mRNA splice variant list

Statistics – P-value and other test statistics related to the test of association between SNP genotype and gene expression.

The final column *Description* provides additional details of probe annotation.

The screenshot shows the GTEx (Genotype-Tissue Expression) eQTL Browser interface. The search parameters are collapsed. The search results table displays columns for SNP, Probe, Gene, mRNA, P-Value, and R². The first 23 rows are visible, showing various SNPs and their associations with genes like HLA-DQA1 and ERAP2.

#	A	P	SNP	Probe	Gene	mRNA	Statistics	Description	
			RS	Chr: Position	ID	Chr: Position	P-Value	R ²	
1	1	P	rs35367950	6: 32732638	ENSE00000617155	6: 32717065 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>
2	1	P	rs17843593	6: 32723928	ENSE00000617155	6: 32717065 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>
3	1	P	rs17843604	6: 32728261	ENSE00000617155	6: 32717065 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>
4	1	P	rs17843608	6: 32728432	ENSE00000617155	6: 32717065 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>
5	1	P	rs1063355	6: 32735692	ENSE00000617155	6: 32717065 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>
6	1	P	rs9272346	6: 32712350	ENSE00000617155	6: 32717065 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>
7	1	P	rs9273349	6: 32733847	ENSE00000617155	6: 32717065 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>
8	1		rs6871162	5: 96307418	ENSE00001083358	5: 96241024 ERAP2	n/a	0	endoplasmic reticulum am... more >>
9	1		rs3909451	5: 96320877	ENSE00001083358	5: 96241024 ERAP2	n/a	0	endoplasmic reticulum am... more >>
10	1		rs2351010	5: 96319685	ENSE00001083358	5: 96241024 ERAP2	n/a	0	endoplasmic reticulum am... more >>
11	1		rs38034	5: 96348175	ENSE00001083358	5: 96241024 ERAP2	n/a	0	endoplasmic reticulum am... more >>
12	1		rs7716222	5: 96318762	ENSE00001083358	5: 96241024 ERAP2	n/a	0	endoplasmic reticulum am... more >>
13	1		rs1363974	5: 96319572	ENSE00001083358	5: 96241024 ERAP2	n/a	0	endoplasmic reticulum am... more >>
14	1		rs27290	5: 96375844	ENSE00001083358	5: 96241024 ERAP2	n/a	0	endoplasmic reticulum am... more >>
15	1		rs27300	5: 96389163	ENSE00001083358	5: 96241024 ERAP2	n/a	0	endoplasmic reticulum am... more >>
16	1		rs10044354	5: 96346251	ENSE00001083358	5: 96241024 ERAP2	n/a	0	endoplasmic reticulum am... more >>
17	1		rs10051637	5: 96305246	ENSE00001083358	5: 96241024 ERAP2	n/a	0	endoplasmic reticulum am... more >>
18	1	P	rs35367950	6: 32732638	ENSE00001423443	6: 32717727 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>
19	1	P	rs17843608	6: 32728432	ENSE00001423443	6: 32717727 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>
20	1	P	rs17843593	6: 32723928	ENSE00001423443	6: 32717727 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>
21	1	P	rs1063355	6: 32735692	ENSE00001423443	6: 32717727 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>
22	1	P	rs9272346	6: 32712350	ENSE00001423443	6: 32717727 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>
23	1	P	rs9273349	6: 32733847	ENSE00001423443	6: 32717727 HLA-DQA1	NM_002122.3	0	major histocompatibility... more >>

Result sets can be very large: the search above resulted in 12,399 results, with only the first 1-50 displayed. Search results can be paged through using the **Next Page** and **Previous Page** buttons. The **Download Text** button will download a tab delimited results file.

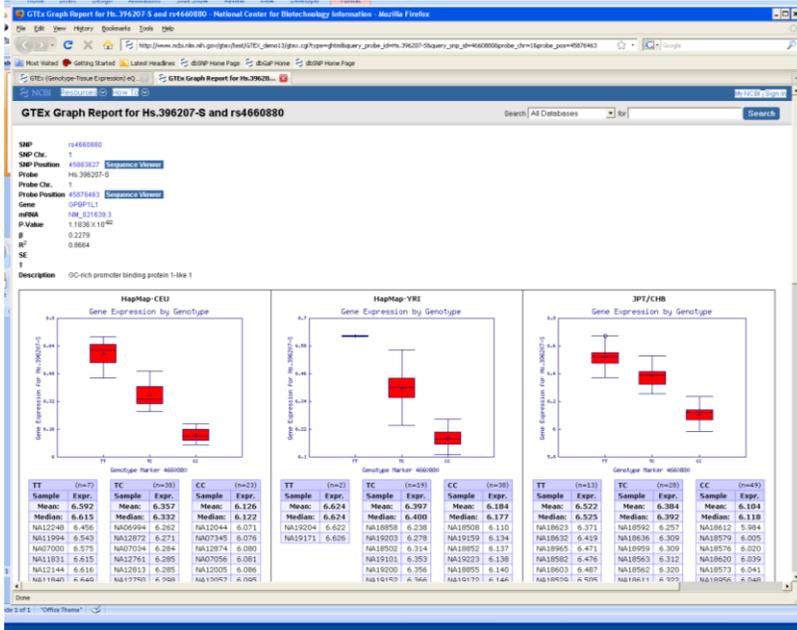
Above the Search Result table, you will see that **Current Dataset Information** and **Search Parameters** have now been collapsed. Clicking on the arrow next to each will expand it. Specifically, **Search Parameters** can be expanded to review the previous search or to enter new search parameters. Clicking **Display Results** again will refresh the search results with the new query.

Detailed Results View

A detailed “GTEx Graph report” for each row in the results table can be accessed by clicking either the box-plot icon in the second column or the P-value column.

The GTEx Graph report page contains summary information for the selected row, and a series of genotype/expression box-plots for each tested population. These box-plots contain the three genotype class categories on the horizontal axis and log normalized expression value on the vertical axis.

Below each graph the expression values for each sample is displayed in tables.



Clicking on the **Sequence Viewer** buttons by the SNP and Probe positions near the top of the page will bring the user to the NCBI sequence viewer, zoomed to that region.

Use case 2: Search by Gene(s) of interest - To display significant eQTLs for a gene(s) of interest
 On the right side of the **Search Parameters** form there is a text box labeled *Gene Symbols or ID numbers*.

A list of gene symbols or Refseq identifiers can be input, separated by spaces or on different lines, into this box in order to search for eQTL results showing association with expression of those genes. To input a text file, rather than pasting into that text box, users may click on the "Browse" button and select a file to upload. Genes can also be selected by specifying a chromosome and position range.

Comment [JPS1]: I don't know that it is necessary, but can one search on probe IDs?

Clicking **Display Results** will then search the eQTL results limited to this set of gene expression traits.

Use case 3: Search by SNPs of interest - To display significant gene expression traits associated with a SNP of interest

Similarly, the eQTL result dataset can be queried by a list of SNPs in the box, a set of SNPs uploaded in a file, or by SNPs position, under the **SNP filters** part of the Search Parameters form, on the right side.

Comment [JPS2]: At the url I can view, this box is on the left.

Use case 4: Combination search, p-value threshold, and sorting.

Both a list of SNPs and expression of a set of Genes can be queried simultaneously, combining case 2 and case 3 above. A filter on the p-value significance, beyond the default 10^{-5} level, can be applied by selecting the exponent using the drop down list on the bottom left of the Search Parameters form. Output is automatically sorted by P-value, but can be also be sorted by SNP or gene position, or names, using the controls on the bottom right.

Use case 5: Search by Phenotype

The expressed gene from the eQTL associations has been joined to the GWAS disease phenotype results from the NHGRI Genome Catalog to link eQTL results to GWAS disease results. Phenotypes can be selected from a query selection box to narrow search eQTL results to those intersecting with a specific disease (or set of diseases using the "CTRL" key).