SYNTENY BROWSER

SYNTENY BROWSER ABOUT DOCS

JAX Synteny Browser Use Cases

http://syntenybrowser.jax.org/

Last revised: November 2019

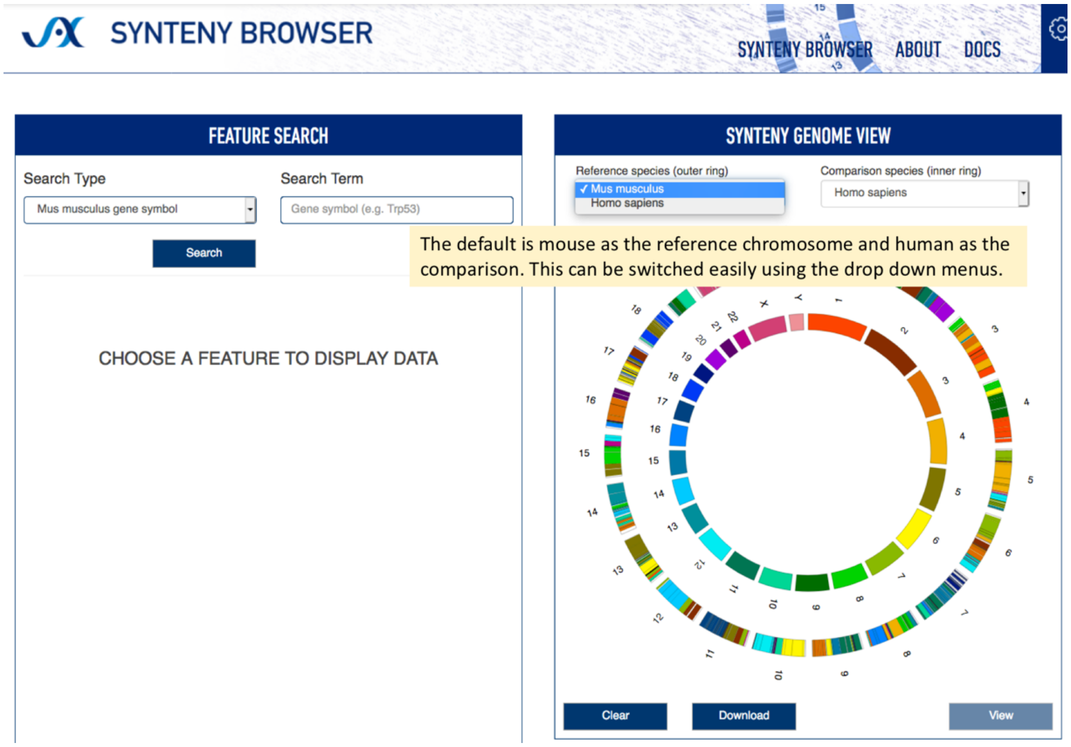
The basic workflow for using the JAX Synteny Browser involves four steps:
(1) selecting the Reference genome,
(2) specifying a region of interest on the Reference,
(3) visualizing the region of interest and its corresponding conserved syntenic block(s) in the Comparison genome, and
(4) selectively highlighting genes in the Reference and Comparison genomes based on their biological attributes.

Two use cases described below serve to demonstrate this workflow. As the user interfaces for the JAX Synteny Browser evolve with software updates, this document illustrating different use cases will be updated. The most recent version will be available here: http://syntenybrowser.jax.org/docs.html

Use Case #1: Identify candidate genes in a mapped interval for human lung cancer susceptibility

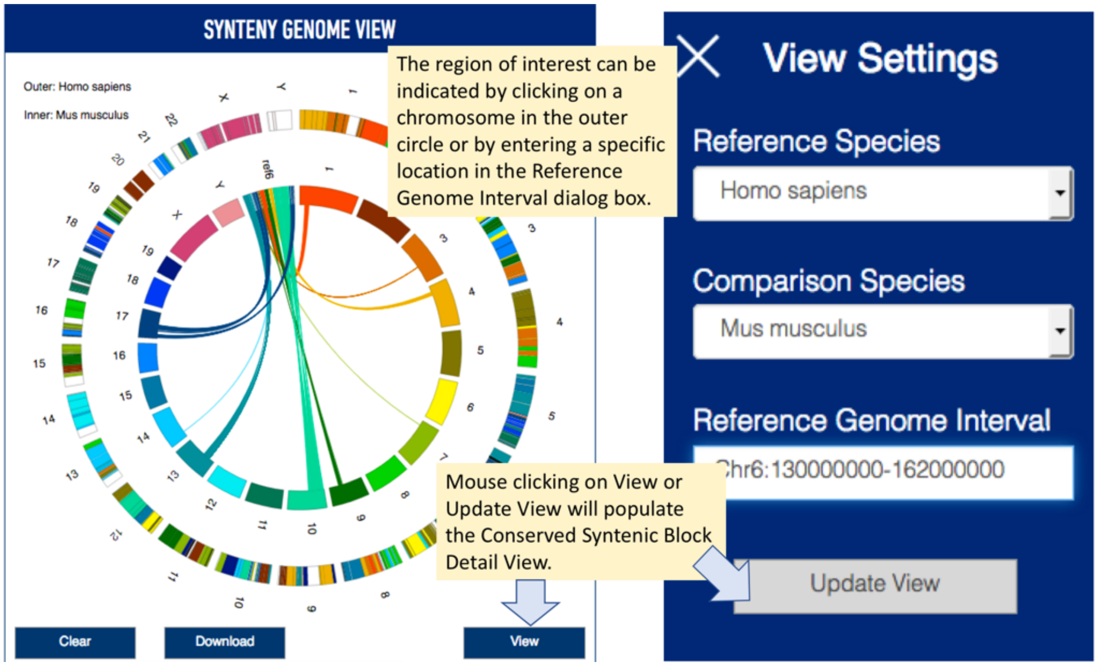
A region of human chromosome 6 (6q23–25; GRCm38 chr6: 130300000-161000000 bp) was identified previously as a linkage interval associated with human lung cancer susceptibility (Bailey-Wilson, et al., 2004). Because this linkage interval also overlaps regions of allelic loss observed in several cancers, the authors hypothesized that genes involved in regulating apoptosis would be good candidates for the susceptibility phenotype.

The first step in using the JAX Synteny Browser to find potential candidate genes for the lung cancer susceptibility locus is to select human as the Reference genome.



The default is mouse as the reference chromosome and human as the comparison. This can be switched easily using the drop down menus.

Next, the user navigates to the region of interest on chromosome 6 using one of two options. For the first option, human chromosome 6 is selected in the **Synteny Genome View** graphic. Clicking on the View button in this panel results in the entire chromosome being displayed in the **Syntenic Block Detail** window. The display interval can then be refined interactively using the slider on the chromosome overview graphic. Alternatively, the coordinates of a genomic interval for the Reference genome can be entered in the appropriate dialog box within the **Settings** menu. When the "Update View" button is selected, the user-specified genomic region is then displayed in the **Syntenic Block Detail** panel.



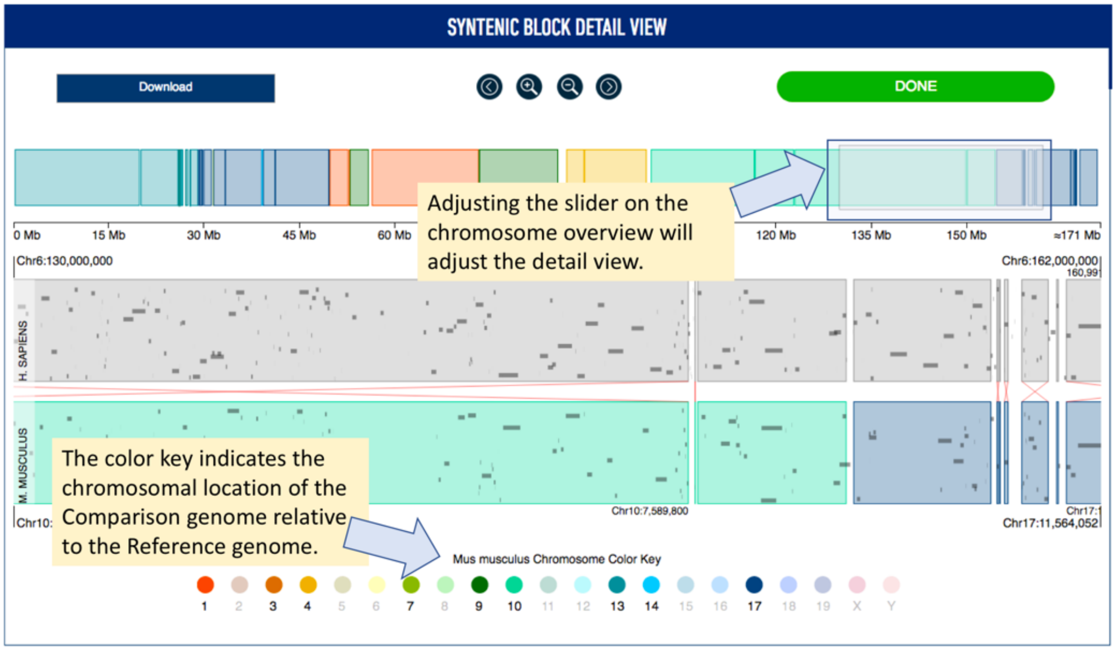
The region of interest can be indicated by clicking on a chromosome in the outer circle or by entering a specific location in the Reference Genome Interval dialog box.

Reference Species: Homo sapiens

Comparison Species: Mus musculus

Reference Genome Interval: Chr6:130000000-162000000

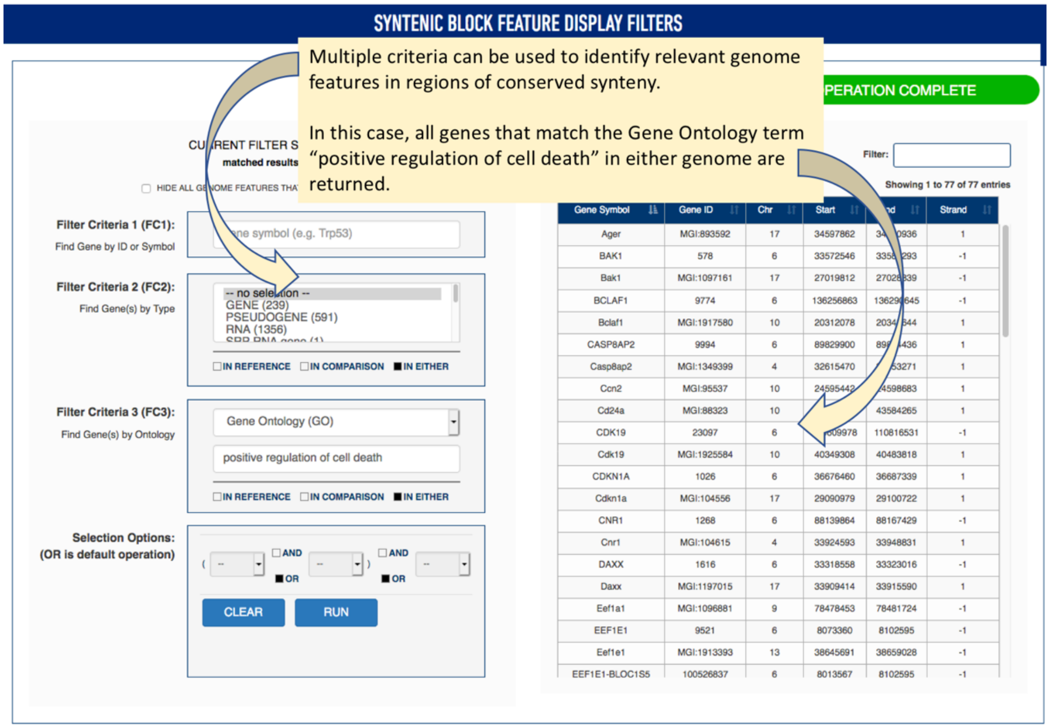
Mouse clicking on View or Update View will populate the Conserved Syntenic Block Detail View.



Adjusting the slider on the chromosome overview will adjust the detail view.

The color key indicates the chromosomal location of the Comparison genome relative to the Reference genome.

Once the **Syntenic Block Detail View** display is finalized, searches for genome features according to their biological and functional annotations can be performed using the **Syntenic Block Features Display Filters** function. For the lung cancer susceptibility interval, a search for genome features that are annotated to the GO function term of “positive regulation of cell death” in **either** genome results in eight genes (*CCN2, MAP3K5, BCLAF1, IL20RA, LATS1, FNDC1, IGR2R, and PRKN*) being highlighted in the Syntenic Block Detail View. Four of these genes (*IGR2R, PRKN, CCN2, and IL20RA*) were identified by the authors of the mapping paper as likely candidate genes. Clicking on a genome feature opens a dialog box with links to external resources with detailed annotations about the feature (MGI for mouse genes; NCBI for human genes).



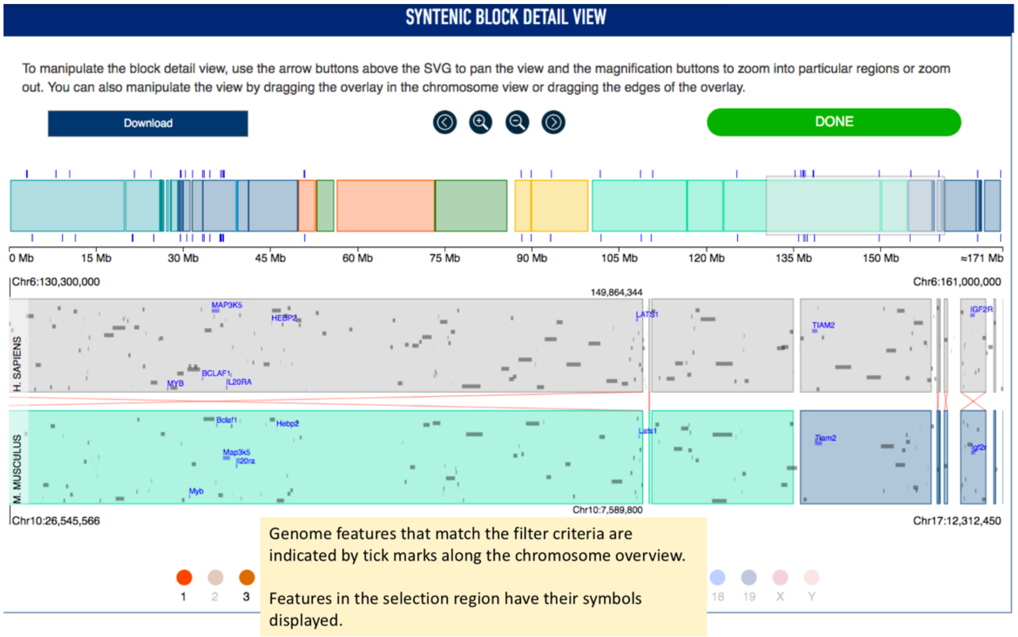
Multiple criteria can be used to identify relevant genome features in regions of conserved synteny.

In this case, all genes that match the Gene Ontology term “positive regulation of cell death” in either genome are returned.

Gene Ontology (GO)

positive regulation of cell death

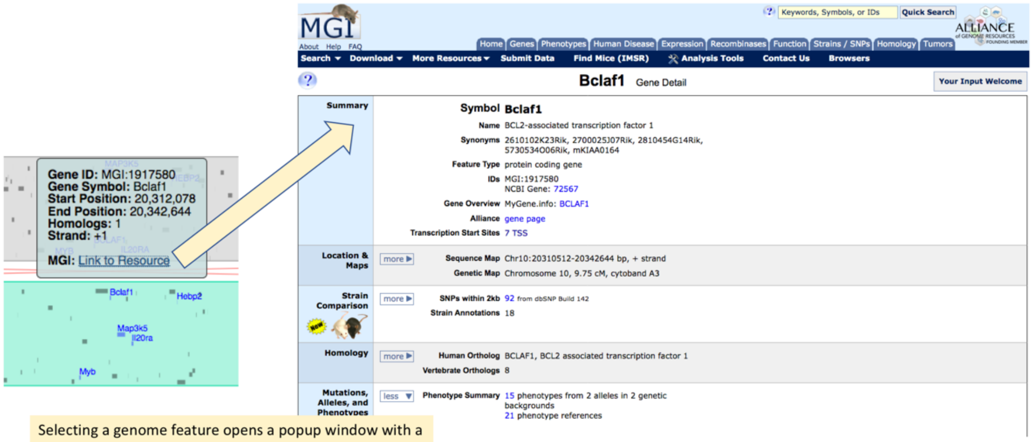
Gene Symbol	Gene ID	Chr	Start	nd	Strand
Ager	MGI:893592	17	34597862	34[illegible]0936	1
BAK1	578	6	33572546	3358[illegible]293	-1
Bak1	MGI:1097161	17	27019812	2702[illegible]39	-1
BCLAF1	9774	6	136256863	13629[illegible]645	-1
Bclaf1	MGI:1917580	10	20312078	2034[illegible]44	1
CASP8AP2	9994	6	89829900	89[illegible]436	1
Casp8ap2	MGI:1349399	4	32615470	[illegible]53271	1
Ccn2	MGI:95537	10	24595442	[illegible]4598683	1
Cd24a	MGI:88323	10	[illegible]	43584265	1
CDK19	23097	6	[illegible]609978	110816531	-1
Cdk19	MGI:1925584	10	40349308	40483818	1
CDKN1A	1026	6	36676460	36687339	1
Cdkn1a	MGI:104556	17	29090979	29100722	1
CNR1	1268	6	88139864	88167429	-1
Cnr1	MGI:104615	4	33924593	33948831	1
DAXX	1616	6	33318558	33323016	-1
Daxx	MGI:1197015	17	33909414	33915590	1
Eef1a1	MGI:1096881	9	78478453	78481724	-1
EEF1E1	9521	6	8073360	8102595	-1
Eef1e1	MGI:1913393	13	38645691	38659028	-1
EEF1E1-BLOC1S5	100526837	6	8013567	8102595	-1



To manipulate the block detail view, use the arrow buttons above the SVG to pan the view and the magnification buttons to zoom into particular regions or zoom out. You can also manipulate the view by dragging the overlay in the chromosome view or dragging the edges of the overlay.

Genome features that match the filter criteria are indicated by tick marks along the chromosome overview.

Features in the selection region have their symbols displayed.



Gene ID: MGI:1917580
Gene Symbol: Bclaf1
Start Position: 20,312,078
End Position: 20,342,644
Homologs: 1
Strand: +1

MGI: Link to Resource

Bclaf1 Gene Detail

Summary

Symbol	**Bclaf1**
Name	BCL2-associated transcription factor 1
Synonyms	2610102K23Rik, 2700025J07Rik, 2810454G14Rik, 5730534O06Rik, mKIAA0164
Feature Type	protein coding gene
IDs	MGI:1917580 NCBI Gene: 72567
Gene Overview	MyGene.info: BCLAF1
Alliance	gene page
Transcription Start Sites	7 TSS

Location & Maps

Sequence Map	Chr10:20310512-20342644 bp, + strand
Genetic Map	Chromosome 10, 9.75 cM, cytoband A3

Strain Comparison

SNPs within 2kb	92 from dbSNP Build 142
Strain Annotations	18

Homology

Human Ortholog	BCLAF1, BCL2 associated transcription factor 1
Vertebrate Orthologs	8

Mutations, Alleles, and Phenotypes

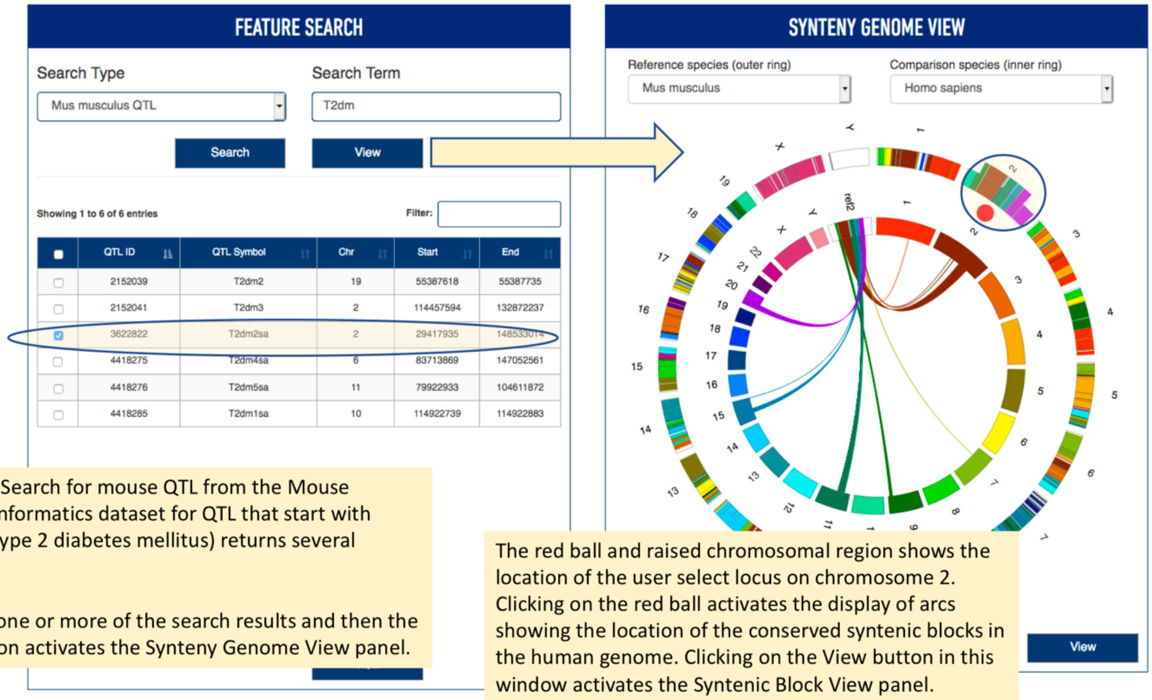
Phenotype Summary	15 phenotypes from 2 alleles in 2 genetic backgrounds 21 phenotype references

Selecting a genome feature opens a popup window with a link to more details about the feature (MGI for mouse genes; NCBI for human genes).

Use Case #2: Identifying candidate genes for Type 2 diabetes

The Quantitative Trait Locus (QTL) *T2dm2sa* (type 2 diabetes mellitus 2 in SMXA RI mice) was identified as a region of mouse chromosome 2 associated with impaired glucose tolerance, hyperinsulinemia, and high body mass index (BMI) (Kobayashi et al. 2006). To identify possible candidate genes in the QTL interval using prior biological knowledge about the genome features in this chromosomal region, a user would first use the **Feature Search** option to search for the *T2dm2sa* QTL (GRCm28; Chr2:29417935-148533014) from the Mouse Genome Informatics (MGI) database.

Selecting *T2dm2sa* from the **Feature Search** results table and then clicking on the View button activates the display of the locus on mouse chromosome 2 in the **Synteny Genome View** panel. Clicking on chromosome 2 (or the red ball) shows the location of the conserved syntenic blocks in the comparison genome. Clicking on the View button from this window activates the **Syntenic Block Detail** panel.



Search Type: Mus musculus QTL
Search Term: T2dm

Showing 1 to 6 of 6 entries

Filter:

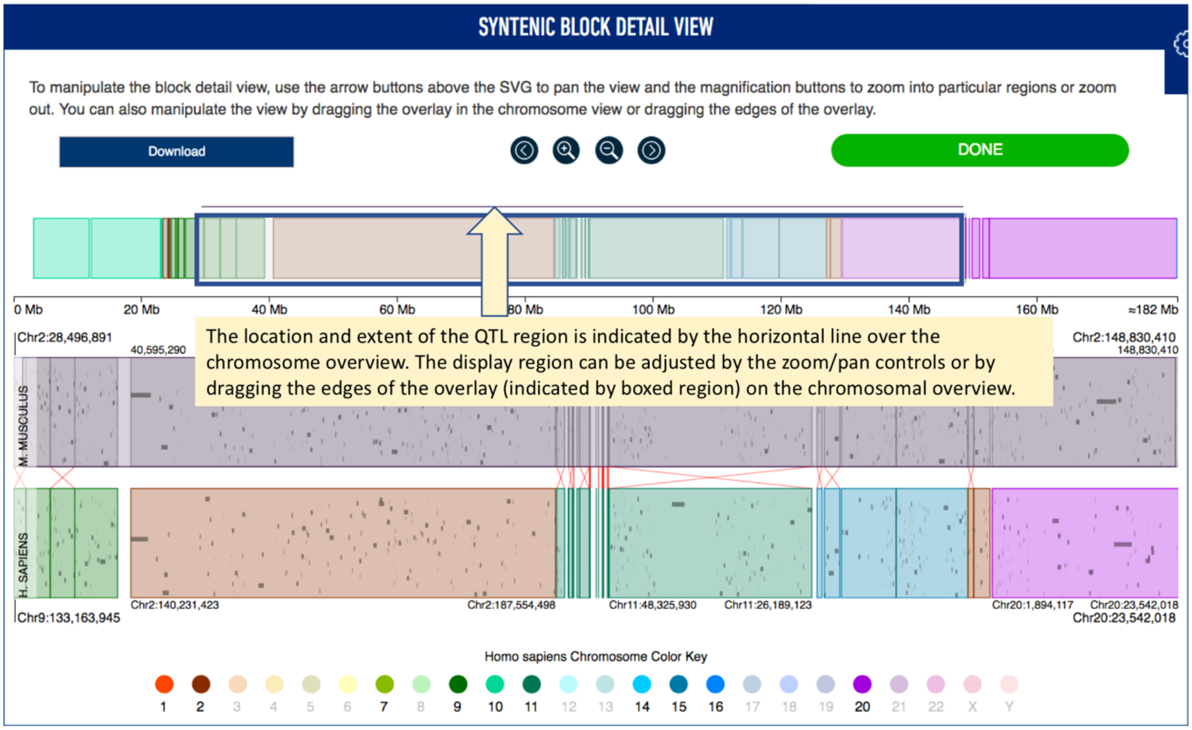
☐	QTL ID	QTL Symbol	Chr	Start	End
☐	2152039	T2dm2	19	55387618	55387735
☐	2152041	T2dm3	2	114457594	132872237
☑	3622822	T2dm2sa	2	29417935	148533014
☐	4418275	T2dm4sa	6	83713869	147052561
☐	4418276	T2dm5sa	11	79922933	104611872
☐	4418285	T2dm1sa	10	114922739	114922883

Reference species (outer ring): Mus musculus
Comparison species (inner ring): Homo sapiens

A Feature Search for mouse QTL from the Mouse Genome Informatics dataset for QTL that start with "T2dm" (type 2 diabetes mellitus) returns several results.

Selecting one or more of the search results and then the View button activates the Synteny Genome View panel.

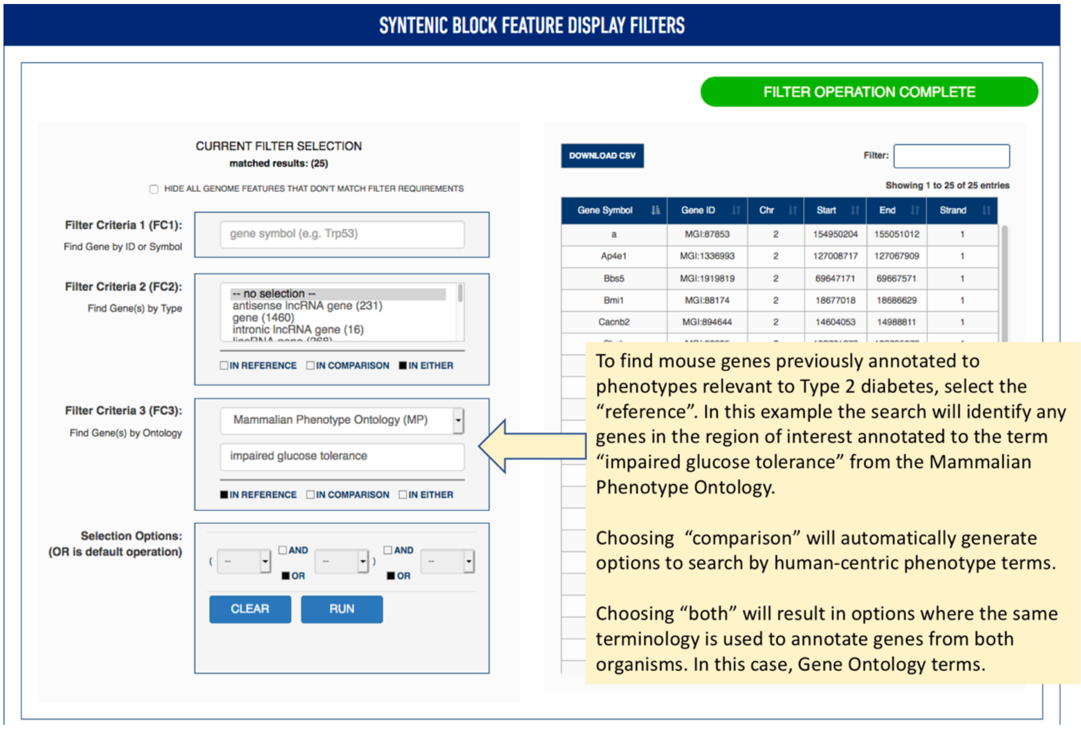
The red ball and raised chromosomal region shows the location of the user select locus on chromosome 2. Clicking on the red ball activates the display of arcs showing the location of the conserved syntenic blocks in the human genome. Clicking on the View button in this window activates the Syntenic Block View panel.


SYNTENIC BLOCK DETAIL VIEW

To manipulate the block detail view, use the arrow buttons above the SVG to pan the view and the magnification buttons to zoom into particular regions or zoom out. You can also manipulate the view by dragging the overlay in the chromosome view or dragging the edges of the overlay.

The location and extent of the QTL region is indicated by the horizontal line over the chromosome overview. The display region can be adjusted by the zoom/pan controls or by dragging the edges of the overlay (indicated by boxed region) on the chromosomal overview.

To explore annotated functions and phenotype associations of mouse genes within and around the QTL region the researcher could limit the annotation searches to the mouse (Reference) genome and then use the **Syntenic Block Features Display Filters** tool to find genes annotated to relevant phenotype terms from the Mammalian Phenotype (MP) ontology (Smith and Eppig 2012). A search for the MP term, impaired glucose tolerance, identifies thirteen genes that fall within the boundaries of the *T2dm2sa* QTL interval: *Pkn3, Lcn2, Dpm2, Zbtb43, Bbs5, Commd9, Hipk3, Pax6, Hdc, Ap4e1,Chgb, and Pcsk2*. Search results are automatically displayed in the **Syntenic Block Detail View** panel.


SYNTENIC BLOCK FEATURE DISPLAY FILTERS

FILTER OPERATION COMPLETE

CURRENT FILTER SELECTION
matched results: (25)

☐ HIDE ALL GENOME FEATURES THAT DON'T MATCH FILTER REQUIREMENTS

Filter Criteria 1 (FC1): Find Gene by ID or Symbol
gene symbol (e.g. Trp53)

Filter Criteria 2 (FC2): Find Gene(s) by Type
-- no selection --
antisense lncRNA gene (231)
gene (1460)
intronic lncRNA gene (16)
☐ IN REFERENCE ☐ IN COMPARISON ■ IN EITHER

Filter Criteria 3 (FC3): Find Gene(s) by Ontology
Mammalian Phenotype Ontology (MP)
impaired glucose tolerance
■ IN REFERENCE ☐ IN COMPARISON ☐ IN EITHER

Selection Options:
(OR is default operation)
(-- ☐ AND ■ OR --) ☐ AND ■ OR --

Filter:

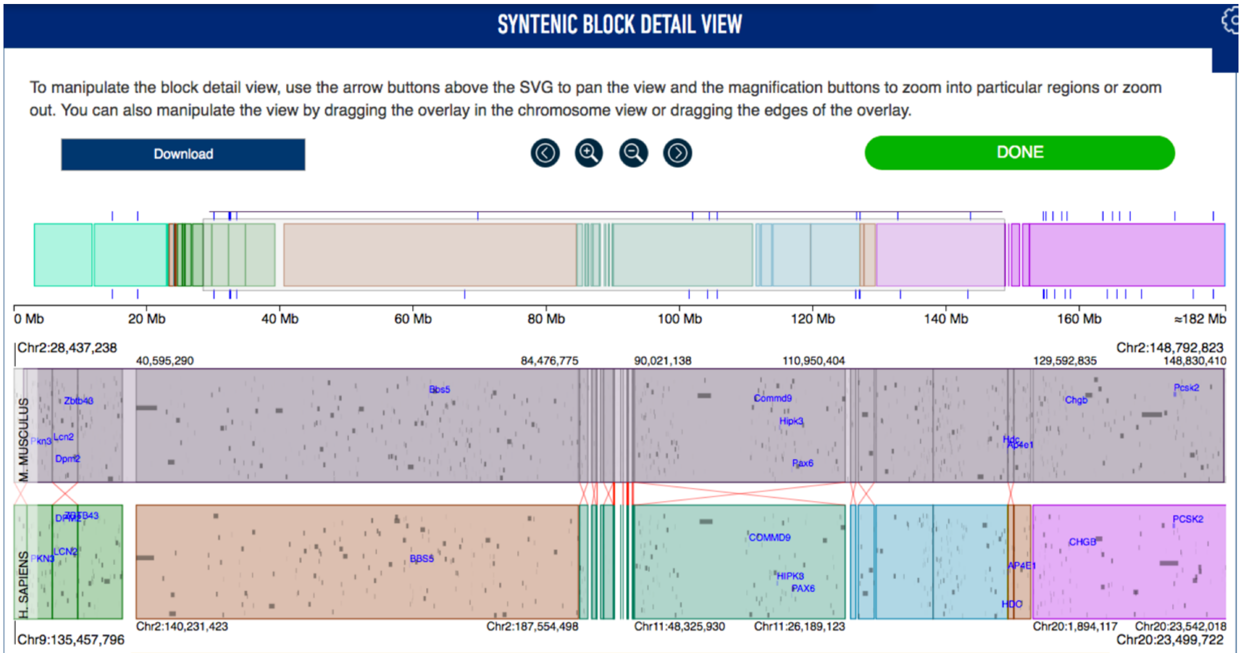
Showing 1 to 25 of 25 entries

Gene Symbol	Gene ID	Chr	Start	End	Strand
a	MGI:87853	2	154950204	155051012	1
Ap4e1	MGI:1336993	2	127008717	127067909	1
Bbs5	MGI:1919819	2	69647171	69667571	1
Bmi1	MGI:88174	2	18677018	18686629	1
Cacnb2	MGI:894644	2	14604053	14988811	1

To find mouse genes previously annotated to phenotypes relevant to Type 2 diabetes, select the "reference". In this example the search will identify any genes in the region of interest annotated to the term "impaired glucose tolerance" from the Mammalian Phenotype Ontology.

Choosing "comparison" will automatically generate options to search by human-centric phenotype terms.

Choosing "both" will result in options where the same terminology is used to annotate genes from both organisms. In this case, Gene Ontology terms.



SYNTENIC BLOCK DETAIL VIEW

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Results of the display filter search output is automatically displayed in the Syntenic Block Detail View. Hash marks along the chromosome overview show the location of the matching genome features. The orthologs in the other genome are also displayed.