

Finding and Using Addiction Data in RGD

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1. Keyword search

The screenshot shows the RGD homepage with several search and browse features highlighted:

- Keyw ord** search bar [1a]
- Search RGD** link [1b]
- Genes**: Map positions, functions and more.
- Strains**: Search Strains.
- QTL**: Phenotypes & Traits linked to the genome.
- Function**: Gene Ontology, Phenotype, Pathway info.
- Diseases**: Genes, QTL & Strains related to Disease.
- Phenotypes & Models**: Phenotype data, Assays, Husbandry and more.
- Rat JBrowse** and **Rat GBrowse** links [5].
- Genome Tools**: Data mining, analysis and visualization.
- Pathways**: Pathway reports and diagrams.

The keyword search appears at the top of most RGD pages [1a]. It can also be accessed from the "Search RGD" link in the blue menu bar [1b]. Search RGD also contains a "search by position" option which returns a list of all genes, quantitative trait loci (QTLs) and markers which overlap the input position. The "Genes", "Strains" and "QTL" buttons on the main page access searches specific for those data types.

The keyword search is a "begins with" search by default and is case insensitive. If you enter a number it will search for that number as an RGD ID. To search for numeric external database IDs, enter a colon ":" or other text character before the number.

Enter "alcohol" into the search box or [click here](#) to view the search results for the word alcohol.

Keyword Search Results:

RGD Search Result

518 records found for search term **alcohol**

GENES
271 Found [View Genes for All Species](#) [A]

	Rat	Mouse	Human
Genes	110	82	79
QTLs	62	79	0
Strains	19	0	0
SSLPs	0	0	0
References	0	0	0
Promoters	0	0	0
Cell Lines	0	0	0
Variants	0	0	24

QTLs
141 Found [View QTLs for All Species](#)

	Rat	Mouse	Human
QTLs	62	79	0

STRAINS
19 Found
Rattus norvegicus 19 [View Rat Strains Report](#)

VARIANTS
24 Found [View Variants for All Species](#)

Ontologies [C]

Curators at RGD make annotations to genes, QTLs and strains using standardized vocabularies/ontologies. Your search returned annotations to the terms below.

CHEBI: Chebi Ontology

- (+)-artemisinic alcohol
- (+)-caryolan-1-ol
- (+)-diversonol
- (+)-dihydrocaryolan-1-ol

The RGD keyword search results show a summary of the number of each type of object that matched the search term (in this case, alcohol). The total number of records that matched is shown at the top, followed by the details of the number of matches in list format to the left and as a scoreboard to the right. View the list of all records of a given type that match your search regardless of species by clicking the "View...for All Species" link [A]. See the

list of objects of a given type (e.g. gene) and species (e.g. rat) by clicking the "View Rat Genes Report" link to the left or the number of matches in the scoreboard to the right [B].

The search also returns all of the ontology/controlled vocabulary terms that match your search term [C]. Click the "leaf" icon to the left of a term to browse the ontology, that is, to see the more general terms above and the more specific terms below your term of interest. If a term has associated annotations, it will be shown as a link. Click the term to go to the ontology report page. For a general introduction to ontologies and ontology annotations, view the "Introduction to Biomedical Ontologies" video tutorial series at <http://rgd.mcw.edu/wg/home/the-introduction-to-biomedical-ontologies-video-series>. For more about ontology searches and ontology search results, see below.

RGD ID	Symbol	Name	Description	Chr	Start	Stop	Species	Annotations	Match	Type
2012	Acadm	acyl-CoA dehydrogenase, C-4 to C-12 straight chain	ENCODES a protein that exhibits acyl-CoA dehydrogenase activity; fatty acyl-CoA binding; flavin adenine dinucleotide binding; INVOLVED IN fatty acid beta-oxidation using acyl-CoA dehydrogenase; medium-chain fatty acid catabolic process protein homotetramerization; PARTICIPATES IN fatty acid beta-de... (more)	2	278786485	278812856	Rat	283	description	gene, protein-coding, VALIDATED [RefSeq]
2014	Acadyl	acyl-CoA dehydrogenase, very long chain	ENCODES a protein that exhibits acyl-CoA dehydrogenase activity; fatty acyl-CoA binding; flavin adenine dinucleotide binding; INVOLVED IN fatty acid beta-oxidation, fatty acid beta-oxidation using acyl-CoA dehydrogenase; very long-chain fatty acid catabolic process; PARTICIPATES IN fatty acid beta d... (more)	10	56364440	56369587	Rat	142	description	gene, protein-coding, PROVISIONAL [RefSeq]
2044	Adh1	alcohol dehydrogenase 1 (class I)	ENCODES a protein that exhibits alcohol dehydrogenase (NAD) activity; drug binding; ethanol binding; INVOLVED IN acetaldehyde biosynthetic process; ethanol oxidation; organ regeneration; ASSOCIATED WITH Alcoholism (ortholog)... (more)	2	262090818	262102977	Rat	196	description, name, old_gene_name	gene, protein-coding, VALIDATED [RefSeq]
71028	Adh4	alcohol dehydrogenase 4 (class II), pi polypeptide	ENCODES a protein that exhibits alcohol dehydrogenase (NAD) activity; ethanol binding; NAD binding; INVOLVED IN aging; ethanol oxidation; oxidation cycle; PARTICIPATES IN fatty acid metabolic process. ASSOCIATED WITH Alcoholism (ortholog)... (more)	2	262237059	262254499	Rat	191	description, name, old_gene_name	gene, protein-coding, PROVISIONAL

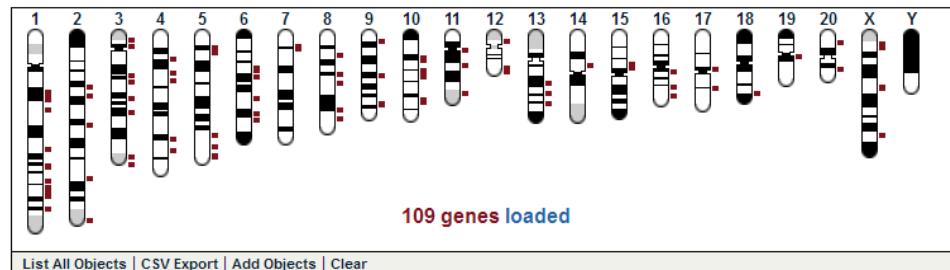
Clicking the "View Rat Genes Report" link takes you to the list of rat genes that match the search term "alcohol". The top of the report [A] gives the data type, species, a link to the previous result summary and the number of records listed (as of this writing, there are 111 rat genes that match but, since data is continuously updated, you may see a different number).

The box at the top right [B] gives you the option to refine your search or to search rat genes for another term. You can also change the genome assembly for which position data is shown and/or change the criteria by which the results are sorted. The default is to search by a relevance score. Change this to "symbol" to see the results as they are shown above.

The tabs at the top of the main results box [C] allow you to change the species from rat to mouse, human or all.

The result includes data about each gene such as the RGD ID, symbol, name, description and position. The gene symbol [D] links to the gene report page (see below for more about gene reports).

You can download the report for your records or print a copy of the results [E]. Click "Genome Viewer" (GViewer) to see the positions of the genes in your result set in relation to a karyotype of the rat chromosomes:



Note that because some genes are not mapped to the current assembly, the number of genes loaded into the GViewer may be less than the original number returned.

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2. Ontology Search

Going back to the RGD home page (e.g. by clicking the "Home" tab or the RGD logo at the top of the page), click the "Function" button ([2] in the first figure) to access the RGD ontology search/browser function.

This is the "landing" page for the ontology search and browse functions. Note that the page can also be accessed by clicking the "Data" tab at the top of the page and selecting "Ontologies" [★].

You have two options for finding an ontology term: you can search for a term by entering a keyword, or you can start at the top of the ontology, i.e. the most general concept in the vocabulary, and select more and more specific terms until you find the one you want. We will start by searching for the term "alcohol". Type this into the search box in the "Search Ontology" section and click "Search".

Ontology Search Results

Term	Accession	Annotations To	Browse
(click term name to see term annotations)		rat - this term only all - this term only all - term with children	
Alcohol Amnestic Disorder	RDO:0004589	0 0 0	0 browse tree
Alcohol fetopathy	RDO:0015850	0 0 0	0 browse tree
Alcohol induced encephalopathy	RDO:0004588	0 0 0	0 browse tree
ALCOHOL SENSITIVITY_ACUTE	RDO:0009406	2 6 6	6 browse tree
Alcohol Withdrawal Delirium	RDO:0004795	2 6 6	6 browse tree
Alcohol Withdrawal Seizures	RDO:0007384	0 0 0	0 browse tree
Alcohol-Induced Disorders	RDO:0005132	42 42 186	186 browse tree
Alcohol-Induced Disorders_Nervous System	RDO:0004793	1 3 9	9 browse tree
Alcohol-Related Disorders	RDO:0004794	0 0 371	371 browse tree
Alcoholic Intoxication	RDO:0004797	2 6 6	6 browse tree
Alcoholic Neuropathy	RDO:0007383	0 0 0	0 browse tree
Alcoholism	RDO:0004798	91 164 164	164 browse tree
Amblyopia	RDO:0004809	0 0 0	0 browse tree
Ascorbic Acid Deficiency	RDO:0004923	1 1 4	4 browse tree
Binge Drinking	RDO:0012117	2 6 6	6 browse tree
Cardiomyopathies	RDO:0000791	170 1950 7790	7790 browse tree
Cardiomyopathy_Alcoholic	RDO:0005131	5 15 15	15 browse tree

Hint: click ontology name to see terms matching your search phrase.
Hint: if a term shown has annotations, click it to see the annotations.

When you first see the ontology search results, only the search box and the result summary are displayed. The summary shows the number of matching terms in each applicable RGD ontology. Note that if an ontology does not have any matching terms it will not appear in the list. Click on "RDO: RGD Disease Ontology" to open the results for your search in the RDO. The details box on the right displays a list of the ontology terms which match your search term as part of the term, a synonym or the term definition.

Notice that terms which have annotation counts following them are shown as links, whereas terms which do not appear as links have no associated annotations (arrow). In the former case, you can click the term itself or one of the annotation count numbers to access the ontology report page for that term. For more about the ontology report, see below.

Ontology Browser

Click the leaf icon beside the term "Alcohol-Related Disorders" to access the tree at that point. You can also access the browser for an ontology from the ontology landing page by clicking on the name of the ontology.

Ontology Browser

Term:

Alcohol-Related Disorders (RDO:0004794)
371 annotations ([View Annotations](#))

Parent Terms	Term With Siblings	Child Terms
Substance-Related Disorders +	Alcohol-Related Disorders + Disorders related to or resulting from abuse or mis-use of alcohol. Amphetamine-Related Disorders Cocaine-Related Disorders Drug Overdose Inhalant Abuse Marijuana Abuse Neonatal Abstinence Syndrome Opioid-Related Disorders + Phencyclidine Abuse Psychoses, Substance-Induced + Substance Abuse, Intravenous Substance Withdrawal Syndrome + Tobacco Use Disorder +	Alcohol Amnestic Disorder + ALCOHOL SENSITIVITY ACUTE Alcohol Withdrawal Delirium Alcohol-Induced Disorders + Alcoholic Intoxication Alcoholism Binge Drinking Psychoses, Alcoholic Wermicke Encephalopathy

Parent(s)

Children

Synonyms

Exact Synonyms: Alcohol-Related Disorder
 Primary IDs: MESH:D019973
 Definition Sources: MESH:D019973

C

D

The RGD ontology browser shows three panels. The left shows the immediate parent term(s) for the highlighted term in the center panel. The center panel shows the selected term [A] and its definition highlighted in yellow, along with the list of all other children of the parent term(s) on the left (i.e. siblings of the highlighted term). The panel on the right shows all of the direct children of the highlighted term. Note that some terms have a plus (+) sign to their right. This indicates that that term has one or more child terms underneath it, so "Alcohol-Related Disorders" has children (as shown), but "Alcoholism" does not.

Above the browser the selected term [A] is listed with its RDO ID, the count of the number of annotations to that term and any of its descendent term(s), and a link to view those annotations in the ontology report. Below the browser all synonyms for the selected term are listed [B] as are external database IDs with links to those databases. Below this is a graphic of the path from the selected term back to the root of the tree [C]. Each term in the graphic of the tree links to that term in the browser, making it easy to "hop" to a higher node without traversing the tree one level at a time.

You will notice that many of the terms in the browser view have an icon beside them [D]. This indicates that there are annotations for that term and/or one or more child terms under it. Click the icon beside the term "Alcoholism" to access the ontology report page for that term.

Ontology Report Page

ONTOLOGY REPORT - ANNOTATIONS

Term: **Alcoholism** [go back to main search page](#)

Accession: RDO:0004798 [browse the term](#)

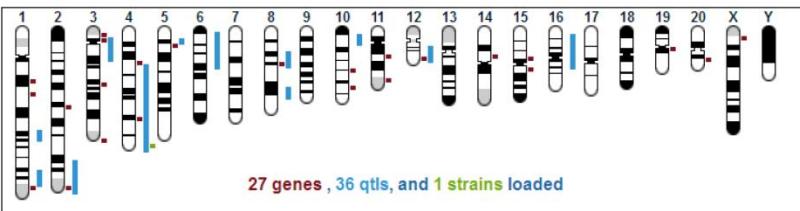
Definition: A primary, chronic disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. The disease is often progressive and fatal. It is characterized by impaired control over drinking, preoccupation with the drug alcohol, use of alcohol despite adverse consequences, and distortions in thinking, most notably denial. Each of these symptoms may be continuous or periodic. (Morse & Flavin for the Joint Commission of the National Council on Alcoholism and Drug Dependence and the American Society of Addiction Medicine to Study the Definition and Criteria for the Diagnosis of Alcoholism: in JAMA 1992;268:1012-4)

Synonyms: exact_synonym: ALCOHOL DEPENDENCE; Alcohol Abuse; Alcohol Addiction; Chronic Alcoholic Intoxication

related_synonym: Alcohol dependence, susceptibility to; Beta-glycopyranoside tasting

primary_id: MESH:D000437

alt_id: OMIM:103780



[List All Objects](#) | [CSV Export](#) | [Add Objects](#) | [Clear](#)

Rat Mouse Human All show annotations for term's descendants Sort by: symbol download view all columns

Alcoholism						
Symbol	Object Name	GBrowse	Chr	Start	Stop	Reference
Adh1	alcohol dehydrogenase 1 (class I)	GBrowse	2	262,090,818	262,102,977	RGD:7240710 RGD:8554872
Adh5	alcohol dehydrogenase 5 (class III), chi polypeptide	GBrowse	2	262,262,936	262,275,343	RGD:5129091
Aldh2	aldehyde dehydrogenase 2 family (mitochondrial)	GBrowse	12	42,334,057	42,366,049	RGD:734551 RGD:8554872
Crh	corticotropin releasing hormone	GBrowse	2	124,182,919	124,184,783	RGD:5508173
Crhr1	corticotropin releasing hormone receptor 1	GBrowse	10	91,953,470	91,995,414	RGD:734822
Dbh	dopamine beta-hydroxylase (dopamine beta-monooxygenase)	GBrowse	3	11,073,477	11,095,363	RGD:1625571 RGD:1625572

The ontology report page has four parts, of which three are shown here. The first section [A] contains the term and information about it such as the definition, synonyms and external database links. A search box and a link to the browser are provided to simplify searching for another term or refining your selection.

The second section [B] contains a GViewer image of genes, QTLs and strains annotated to the term "alcoholism". If you scroll down the page you will see that there are more strains which are annotated to this term than are listed in the GViewer. Only congenic and mutant strains have assigned genomic positions and can be displayed in the tool.

The third section [C] lists all objects annotated to the selected term and, where applicable, to its children. The term "alcoholism" does not have children. If the selected term has children with annotations, the table will show objects annotated to the selected term followed by the descendant terms and objects annotated to them. This table gives a summary of the objects, i.e. symbol, name, chromosomal position and a link to the reference(s) from which the annotations were derived. The GBrowse link takes you to the genome browser at the position of that object so you can further explore its genomic context. For full annotation details check the "view all columns" box above the table. Options above the table also allow you to change species, change the sort order or download the results. The box for "show annotations for term's descendants" is selected by default. Uncheck this box to see annotations for the selected term only.

Below the list of annotated objects there is a tree view of the path from this term to the root of the ontology, similar to the view in the ontology browser. In this case, however, the terms link to their respective ontology report pages rather than the browser.

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3. Genome Tools

OLGA: the Object List Generator & Analyzer

Going back to the RGD home page, click on the button labelled "Genome Tools" ([3] in the first figure). Select "OLGA - Object List Generator & Analyzer".

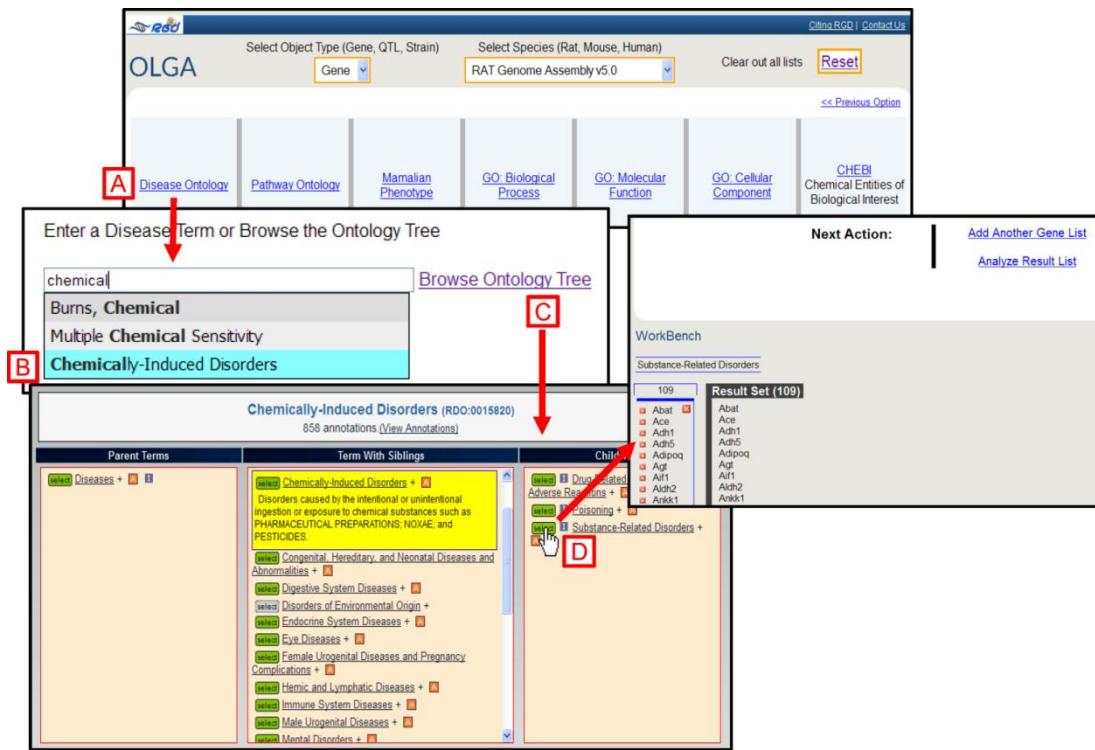
The screenshot shows the RGD home page with the "Genome Tools" section highlighted. A red arrow points from the "Genome Tools" link on the left to the "OLGA - Object List Generator & Analyzer" section on the right. The "OLGA" interface has three main sections: A dropdown menu for "Select Object Type (Gene, QTL, Strain)" with "Gene" selected, a dropdown menu for "Select Species (Rat, Mouse, Human)" with "RAT Genome Assembly v5.0" selected, and a "Reset" button. Below these are four search options: "Ontology Annotation" (selected), "Genomic Region", "QTL Region", and "Symbol List". Each option has a brief description and a "Select" button.

OLGA supports searches for genes, QTLs and strains for rat, and genes and QTLs for mouse and human [A]. The default is "Genes" and we will use that. For searching by position, select a genome assembly for the species you are interested in [B]. Selecting an assembly will not affect searches by ontology terms or searching for a list of objects, but this would be the field to change to search for mouse or human data.

Tip: At each step of the process, your options will be determined by the data type and species you are searching for. Not all options are available for all data types or all species, and in some cases there will be additional options not mentioned here.

For genes, you have four search options [C]: to search for genes annotated to an ontology term, to search by genomic position (i.e. chromosome, start and stop), to search for genes which overlap a particular QTL, or to enter your own list of gene symbols.

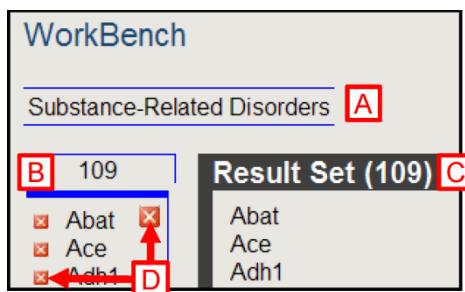
Select "Ontology Annotation".



There are 7 types of ontology annotations for rat genes: disease, pathway, phenotype, biological process, molecular function, cellular component and ChEBI (gene-chemical interactions). Select "Disease Ontology" [A].

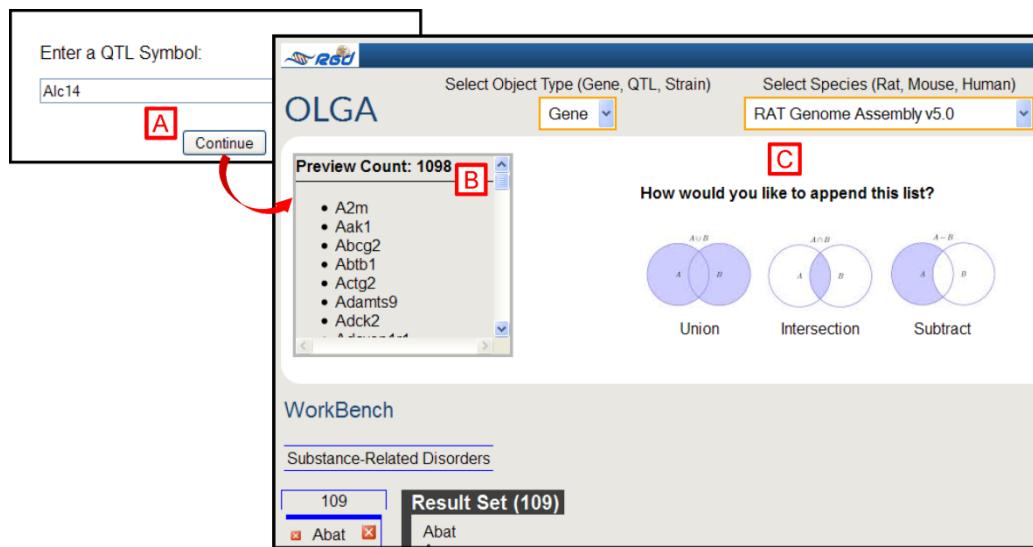
In the resulting window you can begin typing your term of interest in the search box. Notice that the tool displays term "autocomplete" options that match your input [B].

Alternatively, you can click "Browse Ontology Tree" [C]. This opens the ontology browser in a new window. The browser is the same as the one described above but with the addition of "Select" buttons. The buttons next to terms which have any gene annotations for that term and/or any of its descendants are green, but are greyed out (and inactive) for terms with no annotations. When the browser initially opens, the top term "Diseases" will be in the center panel. Click the term "Chemically-Induced Disorders" in the right panel to move that to the center, then click the "Select" button beside the term "Substance Related Disorders" in the right panel [D]. This will automatically enter that term into the search box and close the browser popup. Click "Continue" to search RGD for all rat genes annotated to "Substance Related Disorders" or any of its children.



The list of genes will appear in the "WorkBench" portion of the page. The term you searched for is shown above the list [A], as is the number of genes in the list [B]. A "Result Set" list, currently with the same number of genes in it is also shown [C]. The result set will change as we go along to reflect the search combinations we include. Note the "X" icons beside the gene symbols and at the top right side of the input list [D]. At any time you can remove individual genes by clicking the X beside them or the entire list by clicking the X at the top of the list.

At this stage, you have two options: to analyze the list as it is or to do another search and combine that list with your current "result set". We will choose the latter. Click the link that says "Add Another Gene List". This takes you back to the original four options. Select "QTL Region".



Enter the QTL symbol "Alc14" into the search box and click Continue [A].

The resulting screen gives you a preview of the genes which match the most recent search, in this case, the 1098 genes which overlap the rat Alcohol consumption QTL 14 [B]. You have three choices [C] for how you can combine this list with your list of genes annotated to "Chemically-Induced Disorders": "Union", which adds the two lists together and returns the non-redundant set of all genes from both lists; "Intersection", which gives you only the genes that appear in both lists; or "Subtract", which removes the genes which overlap between the list and returns only the non-overlapping genes from your first list. Select "Subtract".

Result Set (109)	Result Set (104) [A]
109 Abat Ace Adh1 Adh5 Adipoq Agt Aif1 Aldh2 Ankk1	1098 A2m Aak1 Abcg2 Abtb1 Actg2 Adamts9 Adck2 Adcyap1r1 Add2

The result set now has 104 genes, i.e. five genes were removed from the original list [A]. Above the lists, the new query term is shown with its combinatorial type [B]. Notice that there is a dropdown between the lists that allows you to change the combiner [C]. If you change this to "Intersect" your result set will include only the five genes that had been removed from the first gene list. If you changed this, return it to "Subtract". Note that once again the tool gives you two options for where to go next [D]. We will add one more gene list.

Choose "Add Another Gene List" and select "Ontology Annotation" again. This time, select the ChEBI ontology. Begin typing "ethanol" into the search box, click the term in the autocomplete list when it comes up and click "Continue". The search currently returns 3996 genes, although this may be slightly different for you due to ongoing curation of the data.

Tip: ChEBI annotations are imported into RGD from the Comparative Toxicogenomics Database (CTD) and constitute a relatively large dataset. The number of annotations for a ChEBI term, especially one that is higher in the ontology can be in the tens of thousands. For the sake of performance, OLGA does not allow selection of a

term with that many annotations. If there are more than 10,000 you will get an error message asking that you select a more specific term.

Select "Intersection" as the method for combining this list with your previous result set.

The screenshot shows the WorkBench interface with the following steps:

- Next Action:** Buttons for "Add Another Gene List" and "Analyze Result List".
- WorkBench:** A search bar with the query: ((Substance-Related Disorders SUBTRACT Alc14) INTERSECT ethanol).
- Gene Selection:**
 - 109 genes: Abat, Ace, Adh1, Adh5
 - 1098 genes: A2m, Aak1, Abcg2, Ahbh1
 - 3996 genes: A1bg, A2m, Aadat, Aak1
- Result Set (62):** Abat, Ace, Adh1, Adh5

Your result set should look something like this. The result set constitutes the 62 rat genes which are annotated to both "Substance-Related Disorders" and interaction with "Ethanol" and do not overlap with the rat Alc14 QTL. Note that only the input lists and the final result set are shown—at this stage you do not see the intermediary results. At this point you could add another gene list but we will analyze the list we have instead. Select "Analyze Result List".

The screenshot shows the OLGA interface with the following components:

- OLGA:** A main header with "OLGA" and various tool links: GA Tool, Variant Visualizer, Genome Viewer, and Excel (Download).
- WorkBench:** A search bar with the query: ((Substance-Related Disorders SUBTRACT Alc14) INTERSECT ethanol).
- Gene Selection:**
 - 109 genes: Abat, Ace, Adh1
 - 1098 genes: A2m, Aak1, Abcg2
 - 3996 genes: A1bg, A2m, Aadat
- Result Set (62):** Abat, Ace, Adh1
- Analysis Options:**
 - Buttons for "Gene" (selected), "Species" (RAT Genome Assembly v5.0), "Reset", and "A << Previous Option".
 - Links for "Gene Annotator" [B], "Variant Visualizer" [C], "Genome Viewer" [D], and "Excel (Download)" [E].

At this point (and actually, at any point during the process), if you decide that what you have selected is not what you want, you can click "Previous Option" [A] to go back to your last option, in this case to the selection of adding another list or analyzing the list you have, or choose "Reset" to clear all your input and start again.

OLGA gives you four options for analyzing a gene list. The Gene Annotator (GA) tool [B], the Variant Visualizer [C], the Genome Viewer [D] and an Excel Download of your list [E]. The Genome Viewer, or GViewer, is the same tool shown previously in this tutorial. The download option gives you a ".xls" file with the list of RGD IDs, symbols, genomic positions and genome assembly name for the genes in your list. Selecting the GA Tool, Variant Visualizer or GViewer opens a new window or new tab, depending on your browser settings, so that your search parameters are not lost. If you want to go back and change your queries or use a different tool for analysis, simply open the original window/tab and you are ready to go. The GA Tool and Variant Visualizer will be explained in the next sections.

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The Gene Annotator (GA) Tool

As mentioned in the previous section, the GA Tool is one of the analysis options that can be accessed from OLGA. If you enter the tool that way, the list of genes in your result set will automatically be entered and the species selected [A].

HOME DATA GENOME TOOLS DISEASES PHENOTYPES & MODELS CUSTOM RATS PATHWAYS COMMUNITY

Rat GBrowse | VCMAP | Variant Visualizer | GViewer | ACP Haplotype | Genome Scanner | Genome Conflicts | RatMine

GA Tool: Annotation Search and Export

Step One: Define a list of genes to annotate (2000 gene maximum)

Select a Species: Rat

Enter Symbols: When entering multiple identifiers, your list can be separated by commas, spaces, tabs, or line feeds.

Valid identifier types: Affymetrix, GenBank Nucleotide Ontology Term ID, Ensembl Gene, GenBank Protein, RGD ID, Ensembl Protein, Gene Symbol, dbSNP ID, EntrezGene ID, Kegg Pathway

Gene list input area [A]: Abat, Ace, Adh1, Adh5, Adipoq, Agt, Aldh2, C6, Cav1, Cd27, Cdk5, Cfh, Chrna5

Enter a genomic region (Optional): Genes in this region are appended to your gene list. Enter a Position: Chr 1 Start Stop Assembly RGSC Genome Assembly v5.0

Continue >> [D]

Play the RGD Video Tutorial [E]

The tool can also be accessed from the Genome Tools page ([3] in the first figure, or <http://rgd.mcw.edu/wg/tool-menu>). Whatever method you use to access the tool, you can change the species and enter your own list of gene identifiers (or edit the list imported from OLGA). A variety of identifier types can be used [B], and the list entered does not need to be of a single type. The tool will interpret the list based on data in RGD (i.e. it will find the rat gene with the external database ID matching the input) and convert other IDs into gene symbols for data retrieval. You may also choose a genomic region and assembly to analyze the set of genes that overlap that region [C]. If you enter both a list of genes and a genomic region the two lists will be added together and results presented for genes from both lists. Click "Continue" [D] to select the type of data you would like to retrieve. For a demonstration of the functionality of the GA Tool, RGD has produced a tutorial video about the tool. It can be accessed directly from the tool's home page [E].

Step Two: Select annotations to include in report

Ontology Annotations (toggle): Diseases, Pathway, Phenotype, GO: Biological Process, GO: Cellular Component, GO: Molecular Function, Chemical Interactions

External Links (toggle): BND, ClinVar, COSMIC, dbSNP (RS), dbSNP (SS), Ensembl Genes, Ensembl Protein, Ensembl SNP, Ensembl Transcript, Ensembl Gene, GenBank Nucleotide, GenBank Protein, Gene3D-CATH, HGNC ID, HomoloGene Group ID, HPRD ID, Human Proteome Map, InterPro, KEGG Pathway, KEGG Report, MedGen, MGC_CLONE, MGD, NCBI Nucleotide, OMM, OMM Allele, PANTHER, Pfam, PharmGKB, PhenoGen, PRSF, PRINTS, ProDom, PROSITE, PubMed, SMART, SNOMED CT, Superfamily-SCOP, TIGR, TIGRFAMs, Transposagen, UniGene, UniProt, UniSTS

Select Orthologs (toggle): Human, Mouse

Submit

Clicking "Continue" brings you to a page where you can choose which ontology annotations, external database links and orthologs you want the GA Tool to include in your result set. All options are selected by default so if you want everything, you don't need to make changes on this page. If, however, there is a type of data you do not want to include, you can uncheck any of the boxes to exclude that datatype. If you want to exclude all options of a particular type, for instance if you are not interested in seeing the external database IDs for your gene set, you can click "toggle" at the top of the appropriate box and it will uncheck all of the options in that box. Click it again to recheck all of them. Once you have selected the data you would like to get back, click "Submit", either at the bottom left of the page or on the right side under the "Select Orthologs" box.

The GA Tool Annotations View

A Options: [Home](#) Analysis: [Annotations](#) [Annotation Distribution](#) [Comparison Heat Map](#) [Genome Plot](#) **F** Download: [This Gene](#) [All Genes](#)

B Abat [\(1\)](#) Ace [\(2\)](#) Adh1 [\(3\)](#) Adh5 [\(4\)](#) Adipoq [\(5\)](#) Agt [\(6\)](#) Aldh2 [\(7\)](#) C6 [\(8\)](#) Cav1 [\(9\)](#) Cd27 [\(10\)](#) Cdk5 [\(11\)](#) Cfh [\(12\)](#) Chrna5 [\(13\)](#) Chrna7 [\(14\)](#)

C Abat : ENCODES a protein that exhibits 4-aminobutyrate transaminase activity; protein homodimerization activity (ortholog); pyridoxal phosphate binding (ortholog); INVOLVED IN aging; cerebellum development; copulation; PARTICIPATES IN alanine, aspartate and glutamate metabolic pathway; beta-alanine metabolic pathway; butanoate metabolic pathway; ASSOCIATED WITH Anorexia; Cocaine-Related Disorders; Depressive Disorder; FOUND IN mitochondrial matrix; mitochondrion; neuron projection; INTERACTS WITH 1,3-dinotrobenzene, 1-bromopropane, 2,3,7,8-tetrachlorodibenzodioxine

Gene Symbol: RGD ID: Species: Link to Gene Report	Abat 620948 Rat RGD	Human Ortholog: Ortholog RGD ID: Species: Link to Gene Page	ABAT 732065 Human RGD	Mouse Ortholog: Ortholog RGD ID: Species: Link to Gene Page	Abat 1332048 Mouse RGD
------------------------------------------------------------	----------------------------------------------	----------------------------------------------------------------------	------------------------------------------------	----------------------------------------------------------------------	-------------------------------------------------

D { Annotations }

Disease	Species	Accession	Term	Reference / Evidence
Rat	RGD:0002223		Alzheimer Disease	ISS
Rat	RGD:0001950		Anorexia	PM
Rat	RGD:0007303		Cocaine-Related Disorders	PM
Rat	RGD:0005344		Depressive Disorder	PM
Rat	RGD:0005352		Diabetes Mellitus, Experimental	ED
Rat	RGD:0005408		Dystonia, Drug-Induced	PM
Rat	RGD:0007337		Epilepsy, Reflex	ED

External Links	E	Source(s)
Ensembl Genes	ENSRNOG000000002636	Link ENTREZGENE, UniProtKB/Swiss-Prot
Ensembl Protein	ENSRNOP000000003633	Link ENTREZGENE, UniProtKB/Swiss-Prot
Ensembl Transcript	ENSRNOT000000003633	Link ENTREZGENE, UniProtKB/Swiss-Prot
Entrez Gene	81632	Link ENTREZGENE
GenBank Nucleotide	AABR07029086	Link ENTREZGENE
GenBank Nucleotide	AABR07029087	Link ENTREZGENE
GenBank Nucleotide	AABR07029088	Link ENTREZGENE
GenBank Nucleotide	AABR07029089	Link ENTREZGENE
GenBank Nucleotide	AABR07029090	Link ENTREZGENE
GenBank Nucleotide	AAHX01062595	Link ENTREZGENE

The GA Tool has four ways of viewing the data it has retrieved: Annotations, Annotation Distribution, Comparative Heat Map and Genome Plot [A]. The "Genome Plot" is the same Genome Viewer (GViewer) described before. This picture shows the "Annotations" view, the default entry point for data analysis in the GA Tool. Along the top of the page is a scrollable list of the genes that were entered [B]. Clicking on a gene symbol pulls up the data for that gene and its orthologs.

Below the gene list is the description for that gene and a table containing the Symbol, RGD ID, Species and a link to the RGD gene report for the gene and its orthologs [C]. The annotations table [D] lists all annotations for rat, mouse and human for all of the selected ontologies. The external database IDs section [E] lists the external database IDs, such as Genbank nucleotide and protein, UniProtKB IDs, etc., for the gene being displayed (not orthologs) and, for each ID, links to the record at the corresponding database.

The tool also includes options to download the data for just the gene you are viewing, or for the entire set using the links at the top of the page [F]. The result is a tab-delimited text file that can be saved to your local machine and/or opened in a spreadsheet program such as Excel.

The GA Tool Annotation Distribution View

The annotation distribution function analyzes the annotations for each ontology across the entire list of genes and displays the percentage of genes which share annotations for a given term or branch of the ontology.

Cross Term Analysis (2 terms)

11.29% of this set are annotated to [RDO:0004794 PW:0000059] [Explore this Gene Set](#)

- Ace
- Adr
- Crh
- Drd2
- Grin1
- Grin2b
- Nos1

Select 2 or more terms below

62 Genes in set

Disease

- 100% Diseases (RDO:0000001)
- 100% Mental Disorders (RDO:0004751)
- 100% Substance-Related Disorders (RDO:0005102)
- 100% Chemically-induced Disorders (RDO:0015820)
- 85.48% Pathological Conditions, Signs and Symptoms (RDO:0006304)
- 83.87% Nervous System Diseases (RDO:0001228)
- 80.65% Pathologic Processes (RDO:0004703)
- 79.03% Brain Diseases (RDO:0000283)
- 79.03% Central Nervous System Diseases (RDO:0000677)
- 79.03% Cardiovascular Diseases (RDO:0005134)
- 77.42% Vascular Diseases (RDO:0003177)
- 77.42% Alcohol-Related Disorders (RDO:0004794)
- 75.81% Signs and Symptoms (RDO:0004930)

Pathway

- 83.87% pathway (PW:0000001)
- 59.68% signaling pathway (PW:0000003)
- 51.61% regulatory pathway (PW:0000004)
- 38.71% disease pathway (PW:0000013)
- 33.87% homeostasis pathway (PW:0000035)
- 22.58% classic metabolic pathway (PW:0000002)
- 19.35% signaling pathway pertinent to the brain and nervous system (PW:0000059)
- 19.35% signaling pathway pertinent to the brain and nervous system (PW:0000059)
- Ace (kallikrein-kinin cascade pathway)
- Adr (long term potentiation)
- Cdk5 (Reelin signaling pathway)
- Chma5 (acetylcholine signaling pathway via nicotinic acetylcholine receptor)
- Chma7 (acetylcholine signaling pathway via nicotinic acetylcholine receptor)
- Ctrb (long term depression)
- Drd1 (dopamine signaling pathway - long term depression - long

Cross Analysis: Select terms below

7 Genes in set

Disease

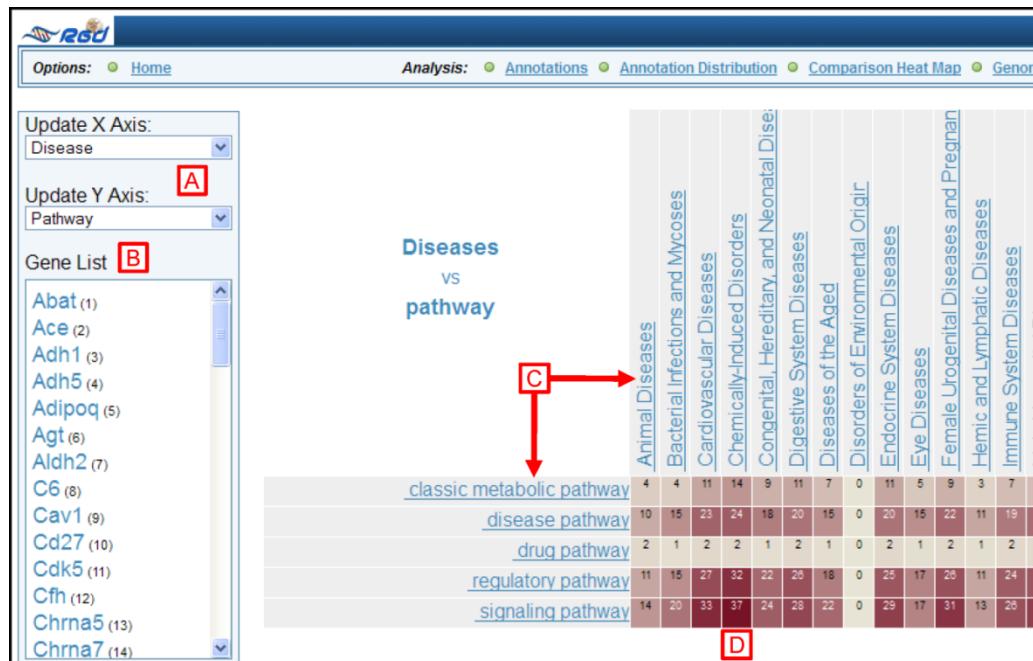
- 100% Diseases (RDO:0000001)
- 100% Brain Diseases (RDO:0000283)
- 100% Ischemia (RDO:0000285)
- 100% Central Nervous System Diseases (RDO:0000677)

The default annotation distribution view shows ontology terms and the percentage of the original list of 62 genes annotated to each, starting with the terms with the highest percentage of the gene list annotated to them and going down. Because a gene annotated to a specific disease is, by extension, annotated to the more general terms above it, and because we chose genes based on their association with a disease category, the term we selected, Substance-Related Disorders, and its parent terms all are displayed with 100% of the genes annotated to them. Click on a green circle with a plus sign to the left of a term to see the list of genes annotated to that term [A]. In this case, the list for "signaling pathway pertinent to the brain and nervous system (PW:0000059)" shows 12 genes (19.35% of the list) annotated to that term.

To view the list of genes annotated to multiple terms within or between ontologies, you can do a "Cross Term Analysis" [B]. Select your terms of interest by checking the box to the right of each term you want to include. As the red circles and check marks show, the terms "Alcohol-Related Disorders (RDO:0004794)" and "signaling pathway pertinent to the brain and nervous system (PW:0000059)" have been chosen. The cross analysis appears automatically at the top of the page as soon as at least two boxes are checked and is updated as more terms are selected. 11.29%, or 7 genes, are annotated to both the disease and pathway terms chosen. To further explore this subset of the genes, click the link in the result box for "Explore this Gene Set" [C]. This begins a new analysis using just that subset of the original list.

The GA Tool Comparison Heat Map View

The GA Tool's Comparison Heat Map gives a more global view of the annotation overlap either between ontologies or between branches of a single ontology. If you have clicked on an "Explore this Gene Set" link, use your browser's Back button to return to the analysis of the original 62 gene list. Click "Comparison Heat Map" in the menu at the top of the page.

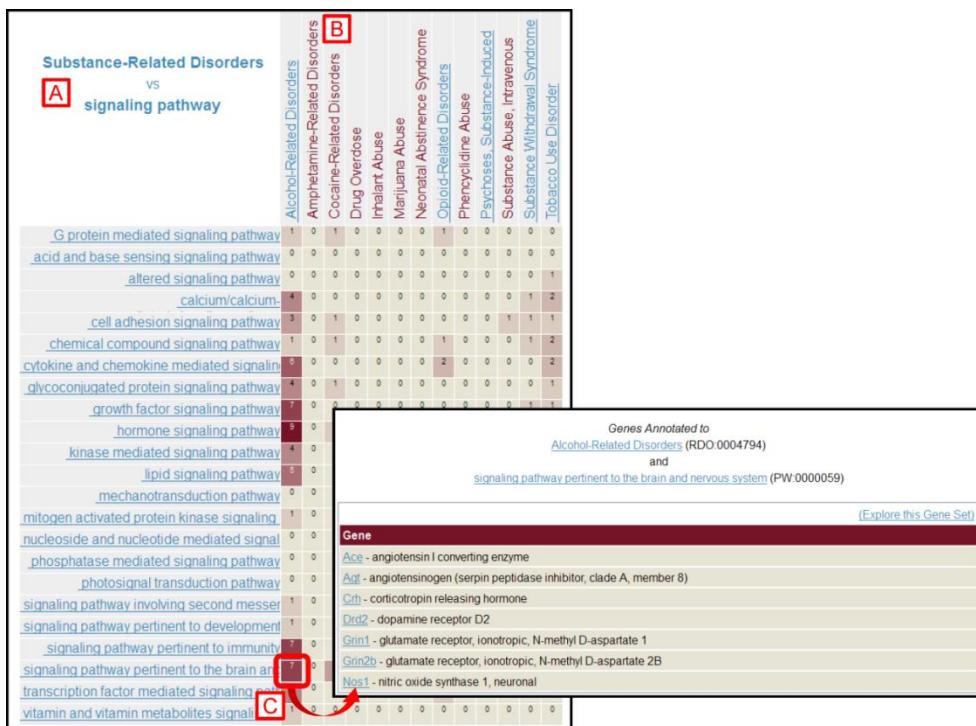


Choose the two ontologies you would like to compare using the dropdowns in the upper left corner of the page [A]. The default is to view disease along the horizontal axis and pathway along the vertical axis. You can choose any two ontologies, or select the same ontology for both to see the overlap between two branches. For instance you could find genes in your list annotated to both chemically-induced disorders and nervous system diseases, or to signaling pathways and disease pathways. We will continue with disease and pathway.

Below the dropdowns is the list of genes being used in the analysis [B].

Drill down through the ontology to the term or branch you are interested in by clicking terms on the two axes [C]. When you click a term it "anchors" the axis on that term, showing the direct children of the term you selected. The number in the box at each intersection of a row and a column is the number of genes from your list annotated to the terms that correspond to that row and column (or any of their descendants). There are 37 genes annotated both the "Chemically-Induced Disorders" branch of the disease ontology and the "signaling pathway" branch of the pathway ontology [D]. The darker the color, the higher the number of genes it represents relative to the other categories displayed.

Click the term "signaling pathway" on the vertical axis, then choose "Chemically-Induced Disorders" on the horizontal axis. In the resulting graph (Chemically-Induced Disorders vs signaling pathway), select "Substance-Related Disorders" on the horizontal axis.



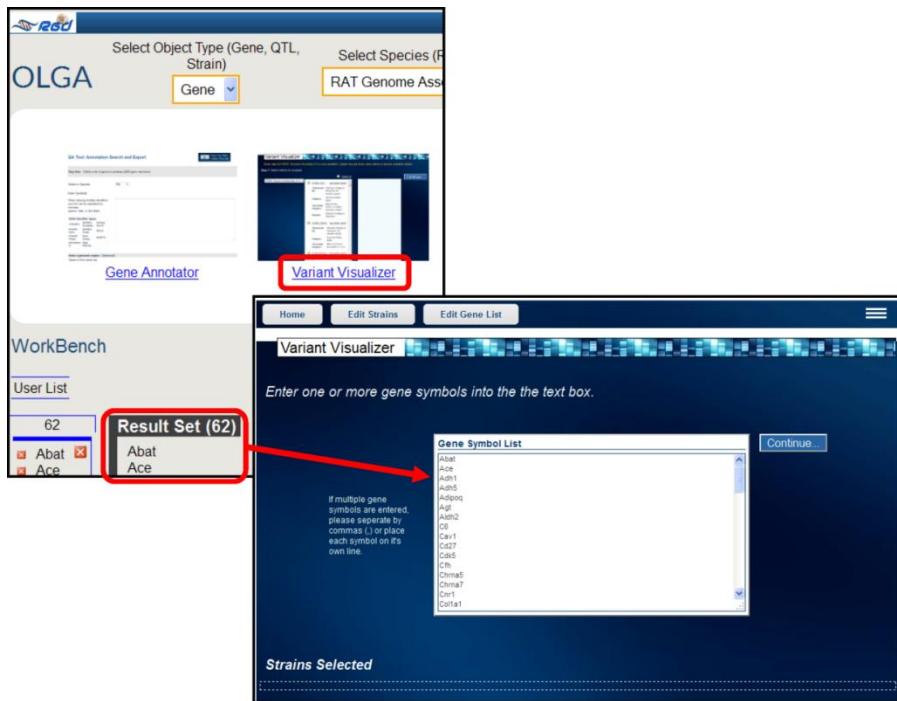
[A] shows the two anchoring terms for the current graph: Substance-Related Disorders for disease and signaling pathway for the PW ontology. Notice that some of the disease terms are no longer links [B]. These terms do not have children in the ontology. Looking at the intersection of "Alcohol-Related Disorders" and "signaling pathway pertinent to the brain and nervous system" [C], the number shown is 7. Click on that square to open the list of genes it represents and you will find the same 7 genes we saw in the cross-term comparison earlier. The advantages of the comparison heat map is the ease with which you can move up and down the trees for the ontologies to explore the different branches, and the ease with which you can look across branches at the same time.

[\[Return to top\]](#)

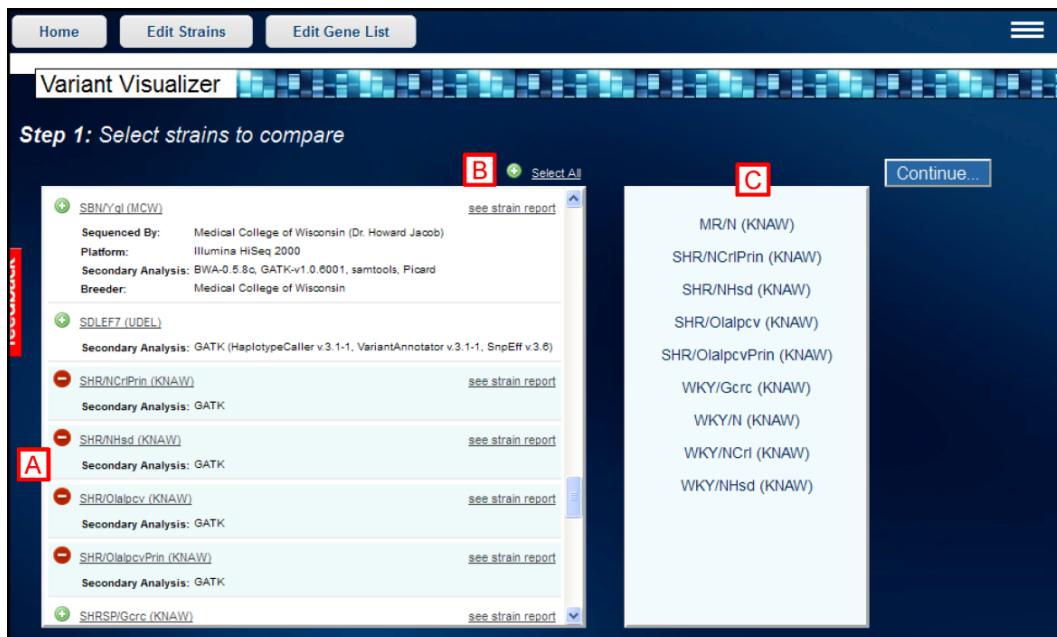
The Variant Visualizer

The Variant Visualizer is a nucleotide variant discovery and analysis tool. It can be accessed from the Genome Tools page in RGD or as part of the OLGA analysis suite.

When accessed from the Genome Tools page, you can start by selecting your strains of interest, by entering a list of genes, by entering a chromosome, start and stop position in the genome, or by searching for genes based on their ontology annotations.



When accessed from OLGA, the final list of genes is automatically entered and the assembly matched to the OLGA search parameters. In the OLGA results window, click the link for Variant Visualizer. A new window or tab will open to the gene list entry screen with the 62 genes of the OLGA result set entered. Click "Continue".



The next step is to select your strains of interest. All of the strains for which RGD currently has genomic variant data for the assembly being used are listed, along with information about the group that did the sequencing and subsequent analysis (e.g. MCW for the Medical College of Wisconsin), and in some cases information about the software program(s) used for the sequence analysis. Click the green plus circle to the left of the strain symbol to add that strain to the list to query [A]. To remove a strain from your list, click its red minus circle. To add all of the strains to the analysis, click the "Select All" link above the strain list [B]. Clicking it again will remove all the strains from the analysis. The list of strains currently included for querying is shown in the box to the right [C]. Here we've included the MR/N strain, all of the substrains of SHR and the WKY substrains. Click "Continue".

Home Edit Strains Edit Gene List

Variant Visualizer

Select Sequence Annotation (Optional)

A Genome

Location	<input type="checkbox"/> Intergenic <input type="checkbox"/> Genic <input type="checkbox"/> Near Splice Site <input type="checkbox"/> Intron <input type="checkbox"/> 3 Prime UTR <input type="checkbox"/> 5 Prime UTR
Variant Type	<input type="checkbox"/> SNV <input type="checkbox"/> Insertion <input type="checkbox"/> Deletion
Limit to	<input type="checkbox"/> Coding Exon <input type="checkbox"/> Frameshift <input type="checkbox"/> Premature Stop <input type="checkbox"/> Readthrough
Conservation	<input type="checkbox"/>
Novelty	<input type="checkbox"/> pos/change found in dbSNP 138 <input type="checkbox"/> pos/change novel to dbSNP 138

Find Variants

Additional options are not required. Leave form empty to include all variants in the defined region.

B Protein

Amino Acid Change	<input type="checkbox"/> Synonymous <input type="checkbox"/> Non-Synonymous
Polphen Prediction	<input type="checkbox"/> Probably Damaging <input type="checkbox"/> Possibly Damaging <input type="checkbox"/> Benign

C Call Statistics

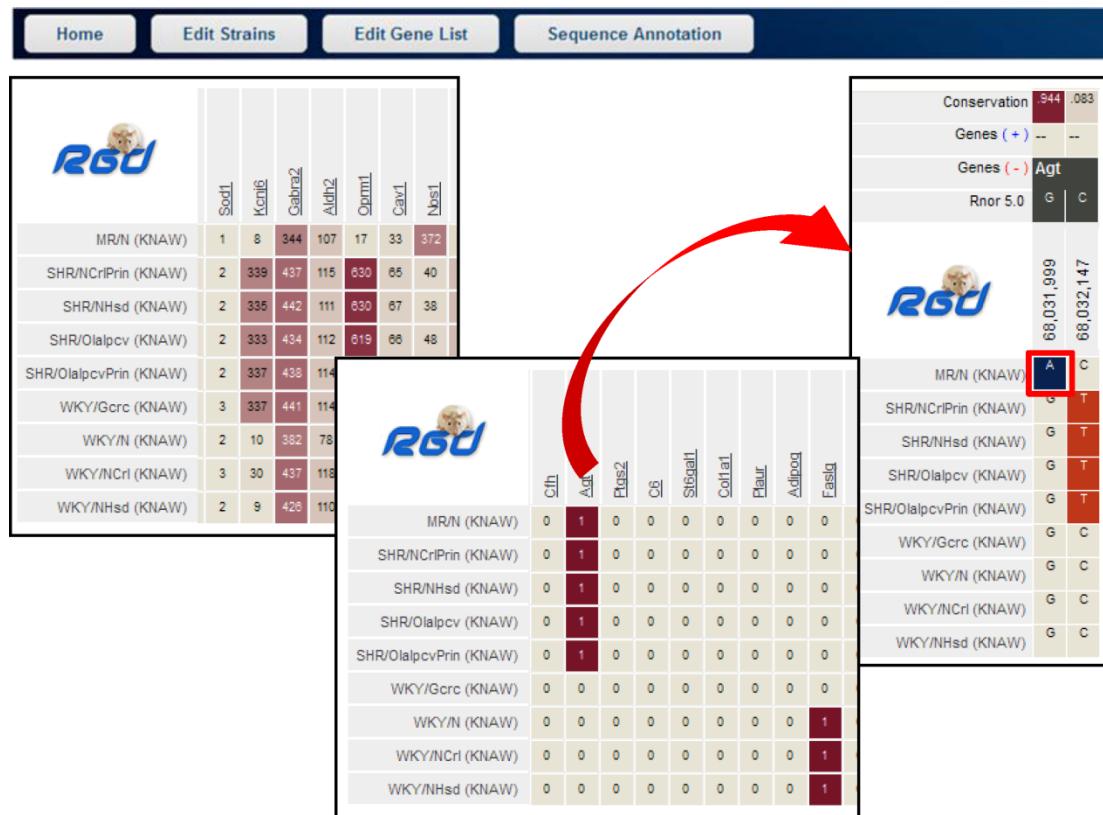
Depth of Coverage	Minimum Reads <input type="text"/> Maximum Reads <input type="text"/>
Total Alleles Read	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Zygosity	<input type="checkbox"/> Heterozygous 2 alleles called between 15% and 85% of reads <input type="checkbox"/> Homozygous Variant read in 100% of reads <input type="checkbox"/> Possibly Homozygous Variants read in 85% to 99% of reads <input type="checkbox"/> Exclude Low Read Percentage Variant read in less than 15% of reads

D Additional Options

Show Differences Exclude Common Variants between strains

MR/N (KNAW), SHR/NCrlPrin (KNAW), SHR/NHsd (KNAW), SHR/OlaLpcv (KNAW), SHR/OlaLpcvPrin (KNAW), WKY/Gcrc (KNAW), WKY/N (KNAW), WKY/NCrl (KNAW), WKY/NHsd (KNAW)

The third step is to select whether or not to limit the results of your search based on [A] the genomic properties of the variants returned such as the type or position relative to genes and exons, [B] how the variant would affect the genes' protein products such as whether it would cause a synonymous or non-synonymous change in the amino acid sequence, [C] the "call statistics" such as the number of reads or the zygosity of the variant, and/or [D] whether the variant is shared across strains. For our first query we will not select any of these filters but rather query for all available variants. Click "Find Variants".



The left panel shows some of the results for all variants for the list of 62 genes. Each gene is shown as a column in the heat map and each strain is represented by a row. The number of variants in a gene in a specific strain versus the reference sequence, in this case, Rno_5.0, is shown within the square at the intersection of the corresponding column and row. The color of the box indicates the relative number compared to all the results in

the set. As you can see, in some cases the numbers of variants are similar across all strains, while in other cases they are quite different.

To go back to the filtering options, click the button labeled "Sequence Annotation" in the bar across the top of your browser display. Click the box for "probably damaging" in the "Protein" section. This will limit your results to only variants that have Polyphen predictions that the variant will probably be damaging to the function of the protein. Click "Find Variants" again. This time, as you can see in the center panel, most of the genes do not have any variants listed in any of the strains. However, the Agt gene has damaging variants in the MR/N and SHR substrains and Faslgl has variants in three of the four WKY substrains. Click the Agt symbol to view the specific variants in that gene across the strains.

The panel on the right shows that although each affected strain has a single damaging variant in this gene, the variant for MR/N is different than the one found in the four SHR substrains. In addition to the specific variant nucleotides, this view gives additional information in the upper portion of the display. Going from the top of the display, this includes:

- The conservation score at each position (a number between a low score of 0 and a high score of 1),
- Information about whether the variant is overlapping a gene on the plus strand and/or the minus strand of the genomic sequence—in this case, Agt is on the minus strand,
- The reference nucleotide at each position. When this letter is in a box colored dark blue, it indicates that the variant is within a coding exon, and
- The genomic position of each variant.

Click the MR/N variant to see the variant details for that single nucleotide variation.

Variant Details

Strain:	MR/N (KNAW)	Variant Type:	snv
Position:	Chromosome: 19 - 68,031,999	Related Variants:	n/a
A Reference Nucleotide:	G	Conservation:	0.944 (High sequence conservation)
Variant Nucleotide:	A	Total Depth:	24
Location:	GENIC	% Variant Reads:	96%
Zygosity:	possibly homozygous	Total Alleles Read:	2
		VID:	564156358

Transcripts

Accession:	NM_134432
Location:	EXON
Amino Acid Prediction:	T to I (nonsynonymous)

PolypHEN Predictions

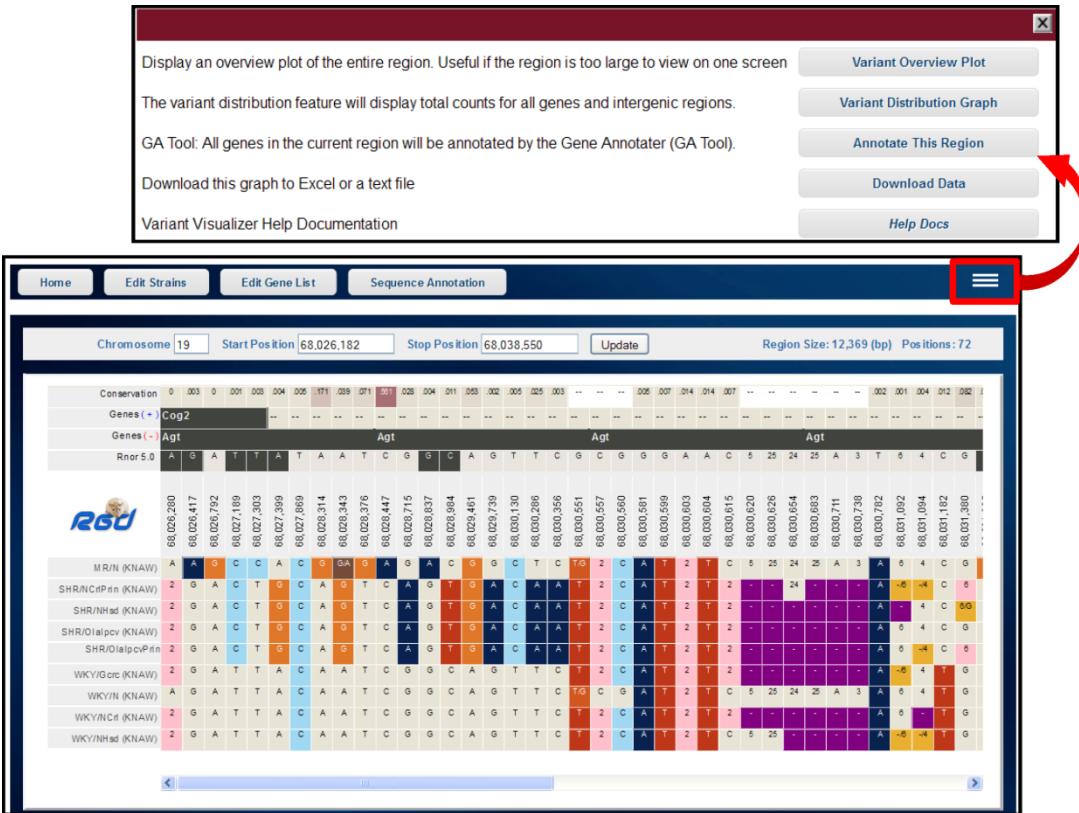
Prediction	Basis	Effect	Site	Score1	Score2	Diff	Number Observed	Structures	Protein ID	PDB ID	Inverted
probably damaging	alignment		NO	-1.244	-3.365	+2.121	107	1	NP_602308	2wxw	-

Amino Acid Sequence
(Calculated using NCBI transcript definition)

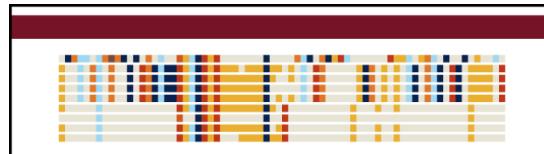
```
MPTIGAGLKAATIFCILTWVSLTAGDRVYIHFPFLLYYSKSTCAQIENPSVTELPEPTFEPVPIQAKTSPVDEKTLRDKL  
LATEKLEAEDRQRRAQVMIANFMGFRMYKMLSEARGVASGAVITPPALFGTIVSFYLGSLOPTASQLQVLLGPVKEG  
CTSLLDGHKVLTALQAVQGLLVTOGGSSSQTPLLQSTVVGLFIIAPGLRLKQPFVESLGPFPTAIFFRSLLSTDPLVLA  
KINRFVQAVITGNKMMNLPLEGVSTLFFNTYVHFQGKMRGFSQLTGHLHEFWVDNSTSVSVPMLSGTGNFQHWSDAQNN  
SVTRVPLGLGESVILLIQQCASLDRVEVLVFQHDFLTWKINPFPRAIRLTLPOLEIRGSYNLQDLLAQAKLSTLLGAE  
NLGKMGDTNPRVGEVLNSILLELQAGEEEQPTESAQQPGSPPEVLDVTLSPLLFAIYERDGSALHFLGRVDNPQNVV*
```

The top of the Variant Details pane [A] shows specific data about the variant itself and gives some of the sequencing metadata such as the read depth, the number of alleles that were read at that position (in this case 2 alleles, the variant and the reference) and the percent of reads that were called as this particular variant. In this case, 96% of the reads were called as being the variant A so the variant is considered "possibly homozygous" (for information about the percentages that are considered to be homozygous, possibly homozygous and heterozygous see the bottom of the Sequence Annotation pane).

Below the information about the variant is information about each transcript for the gene and, where applicable, the predicted consequence of the variant to the resulting protein [B]. In this case, the variant falls within a coding exon of transcript NM_134432 and causes a threonine (T) to isoleucine (I) nonsynonymous change in the protein which is predicted to be "probably damaging" to its function. Since variants are called relative to the sequence of the reference genome, the Variant Visualizer pulls the nucleotide sequence from the reference based on the start and stop of the coding region and translates it into an amino acid sequence. This sequence is shown below the Polyphen prediction data [C] with the substituted amino acid shown in red (see arrow).



In the top bar of the result panes, at the right side, there is a link to a menu of additional options for viewing, downloading and further analyzing your data. The image above shows the variants for the Agt gene without any filters (i.e. all variants for that gene). Click the menu icon to see the options. The "Variant Overview Plot" shows a display of all of the variants across your region of interest.

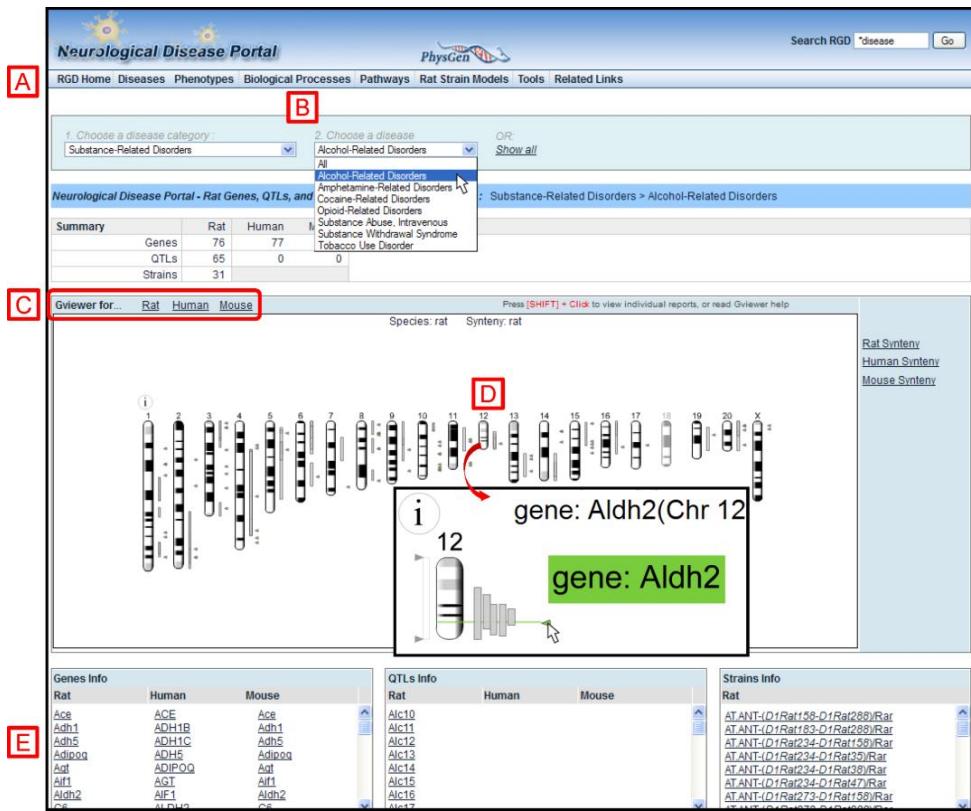


Since the variants are color coded, this can give you a region-wide view of the similarities and differences between strains even if the region has too many variants to be able to see the details all at once. The Variant distribution graph is the same type of view of the counts per gene for each strain that is displayed above (although since at this point only a single gene is selected, only a single gene will be shown in the distribution). "Annotate This Region" sends the list of genes in the region you are viewing to the Gene Annotator (GA) Tool to view and analyze the ontology annotations for those genes. In addition, there are options to Download the data to a file on your local computer to save for your records or use as input for other applications, and to view Help Documentation for more information about the Variant Visualizer tool.

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4. RGD Disease Portals

RGD Disease portals consolidate information about genes, QTLs and strains associated with a number of disease categories and make that data easy to find. To access the list of available portals, click on the "Diseases" tab or button on the RGD front page ([\[4\]](#) in the first figure). As of this writing, RGD has 9 portals: Cancer, Cardiovascular Disease, Diabetes, Immune/Inflammatory Disease, Neurological Disease, Obesity/Metabolic Syndrome, Renal Disease, Respiratory Disease, and Sensory Organ Disease. Click the button for the Neurological Disease Portal.



The disease portal opens to the disease page by default, but there are also pages for phenotypes, pathways and biological processes related to the disease category, as well as pages with information about rat models for disease in the category and with links to additional resources and tools for data analysis. These can be accessed from the menu bar at the top of the page [A].

The default view shows all of the data for all diseases in the portal, in this case, Neurological Diseases. To narrow this down, select categories using the dropdown lists at the top of the page [B]. In the first dropdown, scroll to the bottom of the list and select "Substance-Related Disorders". The options in the second dropdown will be adjusted to match the selection in the first field. Using the second dropdown, select "Alcohol-Related Disorders". As you make choices, the data being shown in the portal is updated to match your selections. Just under the selection dropdowns, a summary of the number of genes, QTLs and strains for rat, mouse and human that are annotated to any term in the selected category are shown. For rat, RGD has 76 genes, 65 QTLs and 31 strains annotated to alcohol-related disorders or any more specific child term underneath that. There are also 77 human genes and 76 mouse genes with related disease annotations.

Below this, the GViewer tool gives a genome-wide view of the corresponding genes and QTLs relative to a karyotype view of the chromosomes. The default view is rat, but there are also GViewers for mouse and human [C]. To zoom into a single chromosome, click that chromosome [D] in the display, then right click on the image and select "zoom in". Notice that although it looks in the full genome image that there is only a single QTL on chromosome 12, the zoomed-in view shows that there are actually 5 overlapping QTLs. Mouse over the gene icon to see its symbol (Aldh2) and genomic position. To the right of the karyotype view are links which change the karyotype bands on the chromosomes to colored blocks showing the corresponding syntenic region in a second species, for example you could view the human syntenic regions for the rat chromosomes.

Below the GViewer are lists of the genes, QTLs and strains with applicable disease annotations [E]. Each symbol links to the corresponding RGD report page for access to additional information about that object. At the bottom of the page are bar charts of the top 10 GO terms in each category (function, process and cellular component) found in the annotations of the included genes (not shown). Click Aldh2 in the rat gene list, or in the GViewer hold the Shift key and click the icon for the Aldh2 gene to access the rat gene report page.

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Gene Report Pages

We will take a closer look at a gene report page here. QTL and Strain report pages are structured very similarly so much of the information here will also apply to those reports. Reference reports have a similar format but a somewhat different structure—they show the citation, abstract and what data in RGD was curated from that reference.

A Gene: Aldh2 (aldehyde dehydrogenase 2 family (mitochondrial)) Rattus norvegicus Play the RGD Video Tutorial

	General	Array IDs																																			
	Symbol: Aldh2																																				
	Name: aldehyde dehydrogenase 2 family (mitochondrial)																																				
	Description: ENCODES a protein that exhibits aldehyde dehydrogenase (NAD) activity; identical protein binding; NADH binding; INVOLVED IN cellular response to fatty acid; cellular response to hormone stimulus; liver development; PARTICIPATES IN arginine and proline metabolic pathway; ascorbate and aldarate metabolic pathway; beta-alanine metabolic pathway; ASSOCIATED WITH alcohol preference; ASSOCIATED WITH Drug-Induced Liver Injury; Fatty Liver; Alcoholic Heart Diseases; FOUND IN mitochondrion; extracellular exosome (ortholog); INTERACTS WITH (S)-norlaudanosoline; 1,3-dinotrobenzene; 2,3,7,8-tetrachlorodibenzodioxine																																				
	Type: protein-coding																																				
	RefSeq Status: PROVISIONAL																																				
	Also known as: aldehyde dehydrogenase 2, aldehyde dehydrogenase 2 mitochondrial, aldehyde dehydrogenase 2, mitochondrial, aldehyde dehydrogenase, mitochondrial, ALDH class 2; ALDH-E2; ALDH1; mitochondrial aldehyde dehydrogenase																																				
	Orthologs: Homo sapiens : ALDH2 (aldehyde dehydrogenase 2 family (mitochondrial)) HGNC more info...																																				
	Mus musculus : Aldh2 (aldehyde dehydrogenase 2, mitochondrial) MGI																																				
	Allele / Splice: Aldh2m2low																																				
	Latest Assembly: RGSC Genome Assembly v5.0																																				
	NCBI Annotation Information: Annotation category suggests misassembly																																				
	Position:	<table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th>Map</th> <th>Chr</th> <th>Position</th> <th>Strand</th> <th>Source</th> </tr> </thead> <tbody> <tr> <td>RGSC Genome Assembly v6.0</td> <td>12</td> <td>40,466,425 - 40,498,813</td> <td>+</td> <td>NCBI</td> </tr> <tr> <td>Rat Cytogenetic Map</td> <td>12</td> <td>q16</td> <td></td> <td>NCBI</td> </tr> <tr> <td>RGSC Genome Assembly v5.0</td> <td>12</td> <td>42,334,057 - 42,366,049</td> <td>+</td> <td>NCBI</td> </tr> <tr> <td>RGSC Genome Assembly v3.4</td> <td>12</td> <td>36,081,778 - 36,116,445</td> <td>+</td> <td>NCBI</td> </tr> <tr> <td>Rat Celera Assembly</td> <td>12</td> <td>36,614,188 - 36,647,218</td> <td>+</td> <td>NCBI</td> </tr> <tr> <td>Genome Assembly 3.1</td> <td>12</td> <td>35,945,165 - 35,979,833</td> <td>+</td> <td>NCBI</td> </tr> </tbody> </table>	Map	Chr	Position	Strand	Source	RGSC Genome Assembly v6.0	12	40,466,425 - 40,498,813	+	NCBI	Rat Cytogenetic Map	12	q16		NCBI	RGSC Genome Assembly v5.0	12	42,334,057 - 42,366,049	+	NCBI	RGSC Genome Assembly v3.4	12	36,081,778 - 36,116,445	+	NCBI	Rat Celera Assembly	12	36,614,188 - 36,647,218	+	NCBI	Genome Assembly 3.1	12	35,945,165 - 35,979,833	+	NCBI
Map	Chr	Position	Strand	Source																																	
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		Launch Genome Browser (GBrowse) Launch JBrowse																																			

The top section of the gene report page [A] contains general information about that gene. The first item is the gene symbol and full name. In many cases these constitute the official nomenclature for the gene as assigned by RGD curators under the authority of the Rat Genome Nomenclature Committee.

The next few fields [B] include the gene description as derived from the functional annotations for the gene, the gene type, the RefSeq status of the gene at NCBI and any synonyms or aliases for the gene, including previous symbols and/or names. The orthologs for the gene are listed with links to the corresponding mouse and human gene pages in RGD. Click the "more info" button to see additional homologs for the gene if there are any. Aldh2 is a member of a gene family so there are a number of additional human homologs. RGD's ortholog and homolog assignments are either manually curated at RGD or imported from the HUGO Gene Nomenclature Committee (HGNC) Comparison of Orthology Predictions (HCOP). The source of the assignment is listed in this table.

Where they are available, mutant, transgenic and knockout alleles of a gene, whether naturally occurring or derived by genomic manipulations, are listed on the gene page under the list of orthologs.

The final part of this section of the page contains map data [C]. In addition to the genomic positions for mappable objects on the most current assembly, RGD stores legacy positions on previous genomic assemblies and genetic, radiation hybrid and cytogenetic maps. In many cases these are difficult or impossible to find elsewhere. As of this writing, RGD was using the Rno_5.0 assembly as the default, although position data for many objects in the Rno_6.0 assembly are also available. The current assembly assignment changes when most or all of RGD's mappable objects have positions on the new assembly. An image of the intron/exon structure of all available transcripts for the gene on the current assembly is displayed and links are provided to both the GBrowse and JBrowse genome browsers (see below).

The rest of the gene page is divided into sections for the various kinds of data available, specifically, Annotations, Genomics, Sequences, Strain-specific Variations and "Additional Information".

- More on Aldh2
- [Entrez Gene](#)
 - [Ensembl Gene](#)
 - [GBrowse](#)
 - [JBrowse](#)
 - [NCBI Map Viewer](#)
 - [Vista](#)
 - [Vista + UCSC](#)

RGD Object Information	
RGD ID:	69219
Created:	2001-11-13
Species:	Rattus norvegicus
Last Modified:	2015-07-28
Status:	ACTIVE

D

E

A

Annotation (Toggle Detail/Summary View)

Disease Annotations

- ALCOHOL SENSITIVITY ACUTE (ISS)
- Alcoholism (ss)
- Alzheimer Disease_ (ss)
- Asthma_ (iss)
- Brain Infarction_ (iss)
- Diabetes Mellitus_ Type 1 (iss)
- Diabetes Mellitus_ Type 2 (iss)
- Diabetic Nephropathy (ss)
- Drug-Induced Hypertension (ss)
- Fatty-Liver_ (ss)
- Heart Disease_ (ss)
- Hypertension_ (ss)
- Kidney Disease_ (ss)
- Liver Disease_ (ss)

Gene-Chemical Interaction Annotations

Gene Ontology Annotations

Molecular Pathway Annotations

Phenotype Annotations

References - curated

References - uncurated

RGD Disease Portals

RGD Manual Annotations

Term	Qualifier	Evidence	With	Reference	Notes	Source
Alcoholism		ISS	RGD 69220 734551			RGD
Alzheimer Disease	Onset	ISS	RGD 69220 1599042			RGD
Brain Infarction	Susceptibility	ISS	RGD 69220 1601161			RGD

Imported Annotations - ClinVar

Term	Qualifier	Evidence	With	Reference	Notes	Source	Original Reference(s)
ALCOHOL SENSITIVITY ACUTE		ISS	RGD 69220 8554872	match by OMIM:610251	ClinVar	PMD:10527091 more...	
Alcoholism		ISS	RGD 69220 8554872	match byterm: ALCOHOLISM	ClinVar	PMD:10527091 more...	

Imported Annotations - Genetic Association Database

Term	Qualifier	Evidence	With	Reference	Notes	Source	Original Reference(s)
Asthma		ISS	RGD 69220 1331525		GAD		

Imported Annotations - OMIM

Term	Qualifier	Evidence	With	Reference	Notes	Source	Original References
ALCOHOL SENSITIVITY ACUTE		ISS	RGD 69220 7249710		OMIM		

B

Genomics

Comparative Map Data

Position Markers

QTLs in Region (RGSC Genome Assembly v5.0)

miRNA Target Status

Predicted Targets

	Summary Value
Count of predictions	240
Count of mRNA genes	141
Interacting mature miRNAs	151
Transcripts	ENSRNTO00000001816
Prediction methods	Microra, Miranda, Rnashybrid, Targetscan
Result types	miRGate_prediction

The detailed report is available here: [Full Report](#) [CSV](#) [TAB](#) [Printer](#)

miRNA Target Status data imported from miRGate (<http://mirtarget.bioinfo.cnio.es/>)
For more information about miRGate, see [PMD:25855286](#), or access the full paper [here](#).

The Annotation section [A] contains RGD's manual and imported functional annotations for the object (i.e. in this case the rat Aldh2 gene). Click on the brown bar labelled "Disease Annotations". The default view is just the list of terms annotated to this gene with the corresponding "evidence code(s)". Click on a term to see more information, including the definition of the evidence codes as well as links to the source publication(s), other data from the same reference, other objects with the same annotation and additional references for the same object. Beside the "Annotation" header is a link labelled "(Toggle Detail/Summary View)". Click this to view more information about the individual annotations in a tabular format. Disease annotations are divided by source, with manual annotations from RGD shown first followed by imported annotations from other databases including ClinVar, Online Mendelian Inheritance in Man (OMIM) and the Genetic Association Database (GAD).

The next section covers "Genomics" [B]. The genomic positions of the mouse and human orthologs are listed under the "Comparative Map Data" heading. The positions of overlapping objects in the rat genome such as markers and QTLs are also listed as "Position Markers" and "QTLs in Region". The newest addition to this section is "miRNA Target Status". This data is imported from miRGate. Although it is not the case here, where a gene is a validated target for one or more miRNAs, the corresponding miRNAs are listed first with links to the miRNA gene records in RGD. The section also gives information about miRNAs for which the gene is predicted to be a target through computational algorithms. Aldh2 has 240 predictions for gene-miRNA interactions, but for some genes the predictions can number in the thousands. Because of the potential for the data to be large, it is not listed on the gene page. Rather, links are provided to view the full report, or to download or print the list. When looking at a gene page for an miRNA, the "miRNA Target Status" section lists that miRNA's target genes in like manner.

A

Sequence

Nucleotide Sequences

Protein Sequences

Protein RefSeqs

NP_115792 (Get FASTA)

XP_005249447 (Get FASTA)

GenBank Proteins

AAA04719 (Get FASTA)

AAA04720 (Get FASTA)

AAA04722 (Get FASTA)

AAA04723 (Get FASTA)

AAA04724 (Get FASTA)

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AAA049262 (Get FASTA)

AAA049263 (Get FASTA)

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AAA049312 (Get FASTA)

AAA049313 (Get FASTA)

AAA049314 (Get FASTA)

AAA049315 (Get FASTA)

AAA049316 (Get FASTA)

AAA04931

The Sequence section [A] gives lists of the RefSeq and Genbank nucleotide and protein identifiers associated with the gene, with links to the corresponding records at NCBI in Genbank and FASTA format. In addition, information is provided for each RefSeq sequence. Click the brown bar labelled "Protein Sequences" to see the information about the RefSeq protein sequences. Click the "show sequence" link [B] to see the FASTA protein sequence.

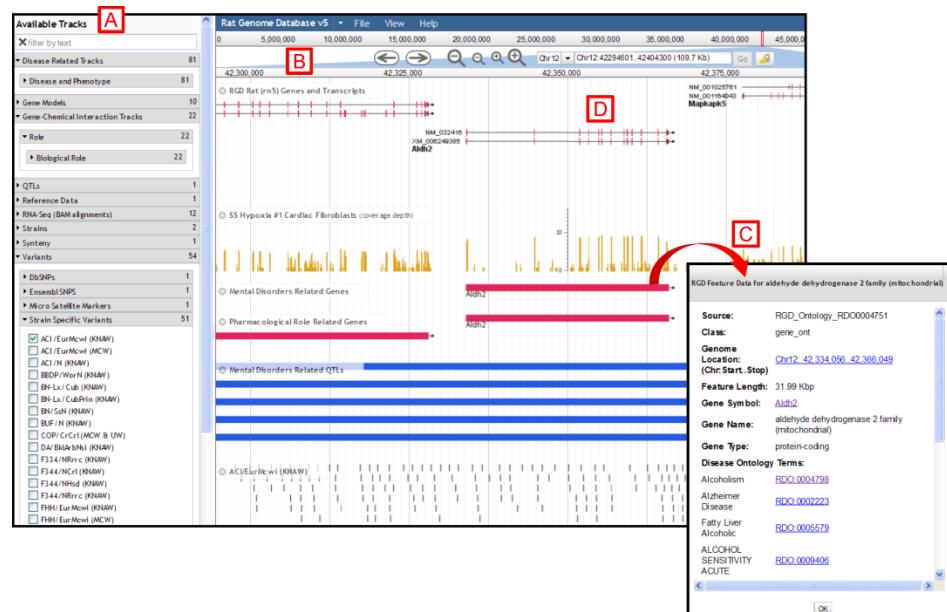
Strain Variation [C] lists the strain-specific variants that overlap this gene with links to view the data in the Variant Visualizer (see above) or to download it as a tab-delimited text file or send it to the printer.

"Additional Information" [D] includes links to information about this gene and/or its protein products in other databases. There is also a section on the "Nomenclature History" of the gene. If the gene's symbol or name has changed, or if the gene record was merged with another record, this history will be detailed here.

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5. The JBrowse Genome Browser

In the information about the Aldh2 gene's map data section, the genome browsers GBrowse and JBrowse were mentioned. RGD uses and supports both of the browsers but since the GBrowse browser is being deprecated, only JBrowse will be reviewed here. Both browsers can be accessed either from the RGD front page (see [5] in the first figure) or from RGD report pages. Either click the link from the Aldh2 gene page or access JBrowse from the RGD front page and enter "Chr12:42294601..42404300" into the search box (in the header above the D in the image below.)

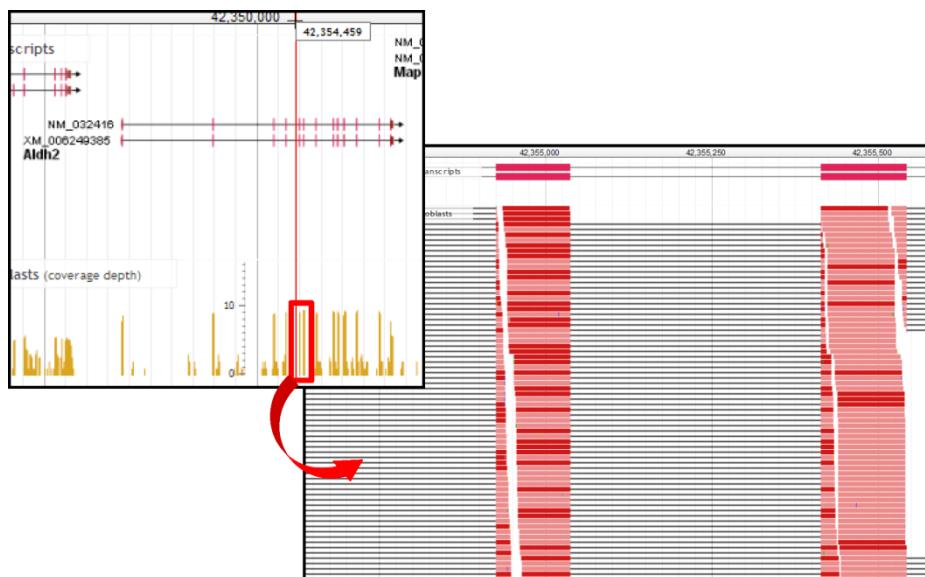


The default view will only show the "RGD Genes and Transcripts" track. You can select other tracks to view using the "Available Tracks" menu in the column on the left side of the page [A]. In the image above, the tracks showing include an RNA-Seq BAM alignment track, the "Mental Disorders Related Genes" and "Mental Disorders Related QTLs" tracks found under "Disease Related Tracks", the "Pharmacological Role Related Genes" track from the "Gene Chemical Interaction Tracks" section (click "Role", then "Biological Role" to see all of the chemical categories), and the "ACI/EurMcwi (KNAW)" variant track found under "Variants"→"Strain Specific Variants". To open a track, click the box to the left of a track name in the list of available tracks. The tracks appear in the order selected but you can "drag and drop" by clicking on the track name in the display and dragging it to the place you want it to appear.

The header section of the page [B] includes a dark blue bar showing the current species and assembly. The arrow beside that opens a dropdown with options for other genome assemblies and other species. Below that is a grey bar that represents the entire chromosome selected, in this case, rat chromosome 12, showing nucleotide positions at intervals along it. The vertical red bar on the far right delineates the region shown in the details view below. A light blue triangle extends from this bar to the start and stop of the grey position bar just above the details view. The area that contains this blue triangle also contains the navigation tools: arrows for moving up and down the chromosome, magnifying glass icons for zooming in (+) and out (-) in the details view, a dropdown for selecting a different chromosome, and the search box mentioned earlier, which also shows the genomic position currently displayed in the details view.

Click on an object in one of the tracks in the details view [C] to see a popup with information about that object. For instance, click the Aldh2 gene in the "Mental Disorders Related Genes" track to see gene-specific information, including the annotations to terms in that branch of the ontology that have been assigned to the Aldh2 gene. As you can see, "Alcoholism" is the first term listed. The ontology ID (RDO:0004798) links to the ontology report page at RGD (see above for more about ontology report pages).

The [D] in the image above is located just above two exons we want to zoom in on to see in more detail. To zoom in, click the larger of the (+) magnifying glasses, or position your mouse over the chromosome details position bar just above the D. A red line will extend down through the detail view tracks to show you the position of your "cursor". When it is just to the left of the two exons circled below click your mouse button and drag it to the right to select the smaller region in the red box.



The red box above shows the two peaks in the RNA-Seq histogram view. Tracks such as the RNA-Seq tracks, gene tracks and variant tracks are data-dense. When the data becomes too dense to easily view as individual data points, JBrowse automatically shifts to a histogram view to show the data density at each location. When you zoom in far enough, as shown here, you go back to the individual data points. Here you can see the individual BAM alignments for the RNA-Seq data.

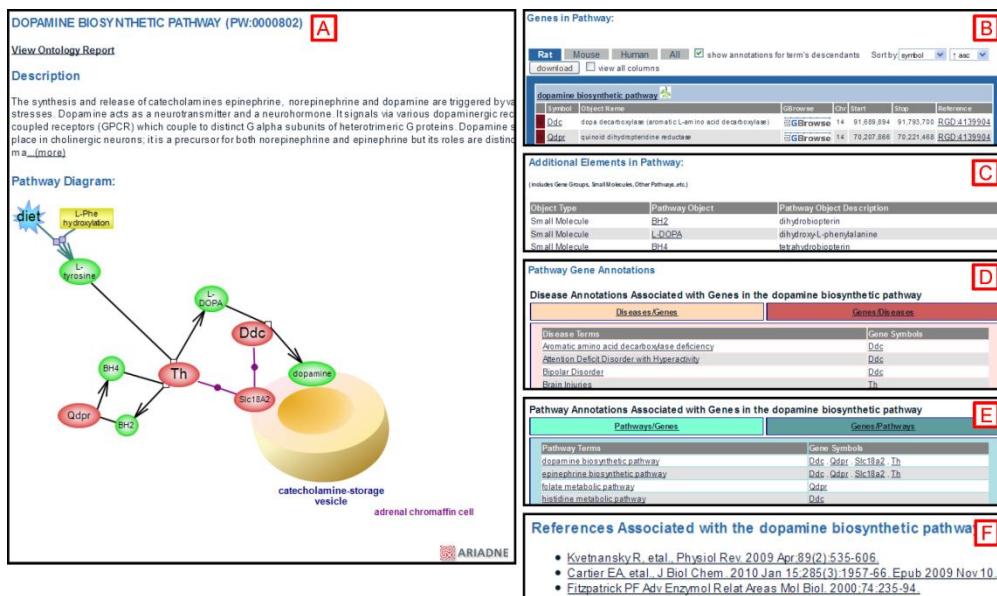
RGD has extensive help pages about our JBrowse installment. To view more information about JBrowse and how to use it, see <http://rgd.mcw.edu/wg/help3/tools/rgd-genome-browsers/the-rat-jbrowse-genome-browser>

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6. RGD Pathway Resources

RGD's Pathway resources are based on the Pathway (PW) ontology which was created and is under development at RGD. Genes with direct involvement in a particular pathway are annotated to that PW term. In addition, to aid the user in understanding how the elements of a particular pathway fit together, a series of interactive pathway diagrams are available, with more under construction. Many of these diagrams are also combined into "pathway suites" which are groups of pathways that are related by their involvement in a larger process. Some of these suites are grouped into even larger "suite networks" when related processes work together on a system level. We will concentrate on the basic pathway diagram pages.

Access the list of molecular pathways by clicking on the "Pathways" tab or button on the RGD front page (see [6] in the first figure) and click on the icon for "Individual Diagram Pages". Under "classic metabolic pathway", click the link for the "dopamine biosynthetic pathway".



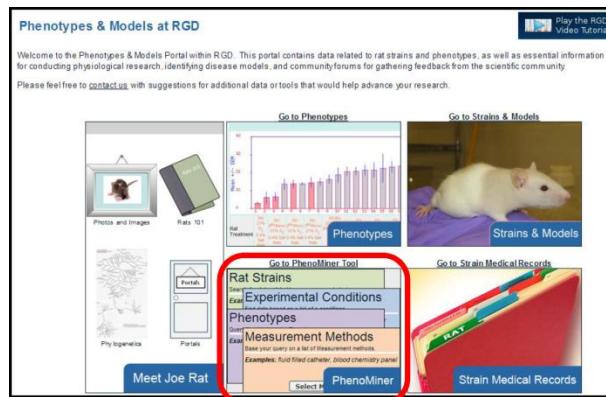
The name of the pathway and its PW ID are at the top of the page [A] with a link to the ontology report page for the term and an extensive description of the pathway and its players, often with additional information about its targets and downstream effects. The centerpiece of the pathway diagram page is the diagram itself. Each manually curated diagram is a "snapshot" of the interactions that make up the pathway. Icons denote proteins, small molecules, external influences or treatments, input and output pathways, etc. A key for the various icons is located in the left page margin (not shown). Wherever possible icons link to records for more information. For example, protein icons link to the corresponding RGD gene pages, pathway icons link to the corresponding pathway diagrams, and small molecule icons link to ChEBI.

The remaining of the sections of the diagram page give diverse information about the "players" in the pathway. These sections include the list of genes [B] and additional elements [C] in the pathway. To give a more complete picture of the genes involved in the pathway, there are lists of the disease annotations [D], phenotype annotations (not shown) and other pathway annotations [E] for the genes in the pathway. Pathway diagrams are curated from the literature and a list of references used in the curation process is included [F], as is a diagram of the location of the pathway term in the PW ontology (not shown). Each term in the ontology tree diagram links to the ontology report for that term.

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7. The PhenoMiner Tool

Up to this point, the data we have looked at has been mostly gene- or genome-related. Now let's use RGD's PhenoMiner tool to compare quantitative phenotype data across strains. The PhenoMiner database, query and analysis tool is a curated warehouse of detailed quantitative phenotype data and its associated metadata with a search engine specifically designed to mine it.



Access the tool by clicking the "Phenotypes and Models" button or tab at the top of the RGD front page ([7] in the first figure) and, on the resulting page, clicking on the "PhenoMiner" button (or the "Go to PhenoMiner Tool" link).

PhenoMiner Database

To begin, select a starting point

Rat Strains
Search for data related to one or more rat strains.
Examples: congenic strain, ACI, BN

Clinical Measurements
Query the database by clinical measurements.
Examples: heart rate, blood cell count

Experimental Conditions
Find data based on a list of conditions.
Examples: diet, atmosphere composition, activity level

Measurement Methods
Base your query on a list of measurement methods.
Examples: fluid filled catheter, blood chemistry panel

* If you would like to show your own data in PhenoMiner, please submit your data here.

Clinical Measurements Selection

Select 1 or more Clinical Measurements from the list below.
Each selection will be used to filter remaining categories.
Click the plus (+) sign to expand sub topics.
To search for a term, enter key words in the search box, e.g. ethanol

Search: ethanol

- + blood ethanol level
- + ethanol drink intake rate **B**
- + ethanol drink intake volume
- + ethanol drink intake rate
- + calculated blood ethanol level
- + blood ethanol clearance rate
- + calculated ethanol drink intake volume
- + calculated ethanol drink intake rate
- + calorie intake measurement(27)
- + drink intake measurement(119)
 - + calculated drink intake measurement(43)
 - + drink calorie intake measurement(5)
 - + drink intake rate(72)
 - + bisphenol A drink intake rate(24)
 - + calculated drink intake rate(8)
 - + drink calorie intake rate(5)
 - + ethanol drink intake rate(11) **C**
 - ethanol drink intake rate(3)
 - + calculated ethanol drink intake rate(8)
 - + fructose drink intake rate(17)

D Select Clinical Measurements Cancel

You have four choices of where to start to access PhenoMiner data. You may start by choosing rat strain(s), clinical measurement(s), experimental condition(s), or measurement method(s). For this example, click the button in the "Clinical Measurements" box [A] labeled "Select Clinical Measurement". There are two ways to find the term or terms you are interested in: search or browse the Clinical Measurement Ontology (CMO). To search, enter a term in the search box above the ontology list [B]. As you begin to type, a dropdown appears containing terms that include the text you have entered so far. Type "ethanol" into the box and select the term "ethanol drink intake rate" by clicking on the term in the dropdown. The term will be entered into the search box and the tool will automatically find that term in the ontology. The branch that the term is in is opened and term is highlighted [C]. Select that term (including all the more specific child terms beneath it) by clicking the box to the left of the term.

Alternatively, you can explore the ontology without searching by clicking on the boxes with the plus (+) signs to successively open more specific terms. When you find a term you would like to use, check the box to the left of the term. Notice that the number of annotations in the database which match your query so far are listed to the right of the term—in this case, 11 annotations.

When you have selected all of the terms you are interested in, click the "Select Clinical Measurement" button toward the bottom of the page [D]. If you were to decide this is not how you wanted to search you can click the Cancel button beside it.

PhenoMiner Database

Select values from categories of interest and select "Generate Report" to build report

Clinical Measurements
Query the database by clinical measurement.
Examples: heartrate, blood cell count

Rat Strains Selection

Select 1 or more Rat Strains from the list below.
Each selection will be used to filter remaining categories.
Click the plus (+) sign to expand sub topics.
To search for a strain, enter key words in the search box, e.g. "co"

Matching Records 11

Sex: male female both

- + inbred strain(8)
- + HAD(2) **E**
- + HEP(2)
- + LAD(2)
- + WKY(2)
- + outbred strain(3)
- + SD(3)

C Matching Records 11

D Limit By Rat Strains

E

F Generate Report

G Select Rat Strains

H Heat maps

I Additional Options...

J Limit By Experimental Conditions

K Limit By Measurement Methods

L I'm Done..

M Generate Report

N Select Rat Strains

O Heat maps

P Additional Options...

Q Limit By Experimental Conditions

R Limit By Measurement Methods

S I'm Done..

T Generate Report

U Select Rat Strains

V Heat maps

W Additional Options...

X Limit By Experimental Conditions

Y Limit By Measurement Methods

Z I'm Done..

A Generate Report

B You are limiting by Clinical Measurements (11 records)

C Matching Records 7

D Heat maps

E Additional Options...

F Limit By Experimental Conditions

G Limit By Measurement Methods

H I'm Done..

I Generate Report

J Select Rat Strains

K Heat maps

L Additional Options...

M Limit By Experimental Conditions

N Limit By Measurement Methods

O I'm Done..

P Generate Report

Q Select Rat Strains

R Heat maps

S Additional Options...

T Limit By Experimental Conditions

U Limit By Measurement Methods

V I'm Done..

W Generate Report

X Select Rat Strains

Y Heat maps

Z Additional Options...

A Limit By Experimental Conditions

B Limit By Measurement Methods

C I'm Done..

D Generate Report

E Select Rat Strains

F Heat maps

G Additional Options...

H Limit By Experimental Conditions

I Limit By Measurement Methods

J I'm Done..

K Generate Report

L Select Rat Strains

M Heat maps

N Additional Options...

O Limit By Experimental Conditions

P Limit By Measurement Methods

Q I'm Done..

R Generate Report

S Select Rat Strains

T Heat maps

U Additional Options...

V Limit By Experimental Conditions

W Limit By Measurement Methods

X I'm Done..

Y Generate Report

Z Select Rat Strains

A Heat maps

B Additional Options...

C Limit By Experimental Conditions

D Limit By Measurement Methods

E I'm Done..

F Generate Report

G Select Rat Strains

H Heat maps

I Additional Options...

J Limit By Experimental Conditions

K Limit By Measurement Methods

L I'm Done..

M Generate Report

N Select Rat Strains

O Heat maps

P Additional Options...

Q Limit By Experimental Conditions

R Limit By Measurement Methods

S I'm Done..

T Generate Report

U Select Rat Strains

V Heat maps

W Additional Options...

X Limit By Experimental Conditions

Y Limit By Measurement Methods

Z I'm Done..

A Generate Report

B Select Rat Strains

C Heat maps

D Additional Options...

E Limit By Experimental Conditions

F Limit By Measurement Methods

G I'm Done..

H Generate Report

I Select Rat Strains

J Heat maps

K Additional Options...

L Limit By Experimental Conditions

M Limit By Measurement Methods

N I'm Done..

O Generate Report

P Select Rat Strains

Q Heat maps

R Additional Options...

S Limit By Experimental Conditions

T Limit By Measurement Methods

U I'm Done..

V Generate Report

W Select Rat Strains

X Heat maps

Y Additional Options...

Z Limit By Experimental Conditions

A Limit By Measurement Methods

B I'm Done..

C Generate Report

D Select Rat Strains

E Heat maps

F Additional Options...

G Limit By Experimental Conditions

H Limit By Measurement Methods

I I'm Done..

J Generate Report

K Select Rat Strains

L Heat maps

M Additional Options...

N Limit By Experimental Conditions

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P I'm Done..

Q Generate Report

R Select Rat Strains

S Heat maps

T Additional Options...

U Limit By Experimental Conditions

V Limit By Measurement Methods

W I'm Done..

X Generate Report

Y Select Rat Strains

Z Heat maps

A Heat maps

B Additional Options...

C Limit By Experimental Conditions

D Limit By Measurement Methods

E I'm Done..

F Generate Report

G Select Rat Strains

H Heat maps

I Additional Options...

J Limit By Experimental Conditions

K Limit By Measurement Methods

L I'm Done..

M Generate Report

N Select Rat Strains

O Heat maps

P Additional Options...

Q Limit By Experimental Conditions

R Limit By Measurement Methods

S I'm Done..

T Generate Report

U Select Rat Strains

V Heat maps

W Additional Options...

X Limit By Experimental Conditions

Y Limit By Measurement Methods

Z I'm Done..

A Generate Report

B Select Rat Strains

C Heat maps

D Additional Options...

E Limit By Experimental Conditions

F Limit By Measurement Methods

G I'm Done..

H Generate Report

I Select Rat Strains

J Heat maps

K Additional Options...

L Limit By Experimental Conditions

M Limit By Measurement Methods

N I'm Done..

O Generate Report

P Select Rat Strains

Q Heat maps

R Additional Options...

S Limit By Experimental Conditions

T Limit By Measurement Methods

U I'm Done..

V Generate Report

W Select Rat Strains

X Heat maps

Y Additional Options...

Z Limit By Experimental Conditions

A Limit By Measurement Methods

B I'm Done..

C Generate Report

D Select Rat Strains

E Heat maps

F Additional Options...

G Limit By Experimental Conditions

H Limit By Measurement Methods

I I'm Done..

J Generate Report

K Select Rat Strains

L Heat maps

M Additional Options...

N Limit By Experimental Conditions

O Limit By Measurement Methods

P I'm Done..

Q Generate Report

R Select Rat Strains

S Heat maps

T Additional Options...

U Limit By Experimental Conditions

V Limit By Measurement Methods

W I'm Done..

X Generate Report

Y Select Rat Strains

Z Heat maps

A Heat maps

B Additional Options...

C Limit By Experimental Conditions

D Limit By Measurement Methods

E I'm Done..

F Generate Report

G Select Rat Strains

H Heat maps

I Additional Options...

J Limit By Experimental Conditions

K Limit By Measurement Methods

L I'm Done..

M Generate Report

N Select Rat Strains

O Heat maps

P Additional Options...

Q Limit By Experimental Conditions

R Limit By Measurement Methods

S I'm Done..

T Generate Report

U Select Rat Strains

V Heat maps

W Additional Options...

X Limit By Experimental Conditions

Y Limit By Measurement Methods

Z I'm Done..

A Generate Report

B Select Rat Strains

C Heat maps

D Additional Options...

E Limit By Experimental Conditions

F Limit By Measurement Methods

G I'm Done..

H Generate Report

I Select Rat Strains

J Heat maps

K Additional Options...

L Limit By Experimental Conditions

M Limit By Measurement Methods

N I'm Done..

O Generate Report

P Select Rat Strains

Q Heat maps

R Additional Options...

S Limit By Experimental Conditions

T Limit By Measurement Methods

U I'm Done..

V Generate Report

W Select Rat Strains

X Heat maps

Y Additional Options...

Z Limit By Experimental Conditions

A Limit By Measurement Methods

B I'm Done..

C Generate Report

D Select Rat Strains

E Heat maps

F Additional Options...

G Limit By Experimental Conditions

H Limit By Measurement Methods

I I'm Done..

J Generate Report

K Select Rat Strains

L Heat maps

M Additional Options...

N Limit By Experimental Conditions

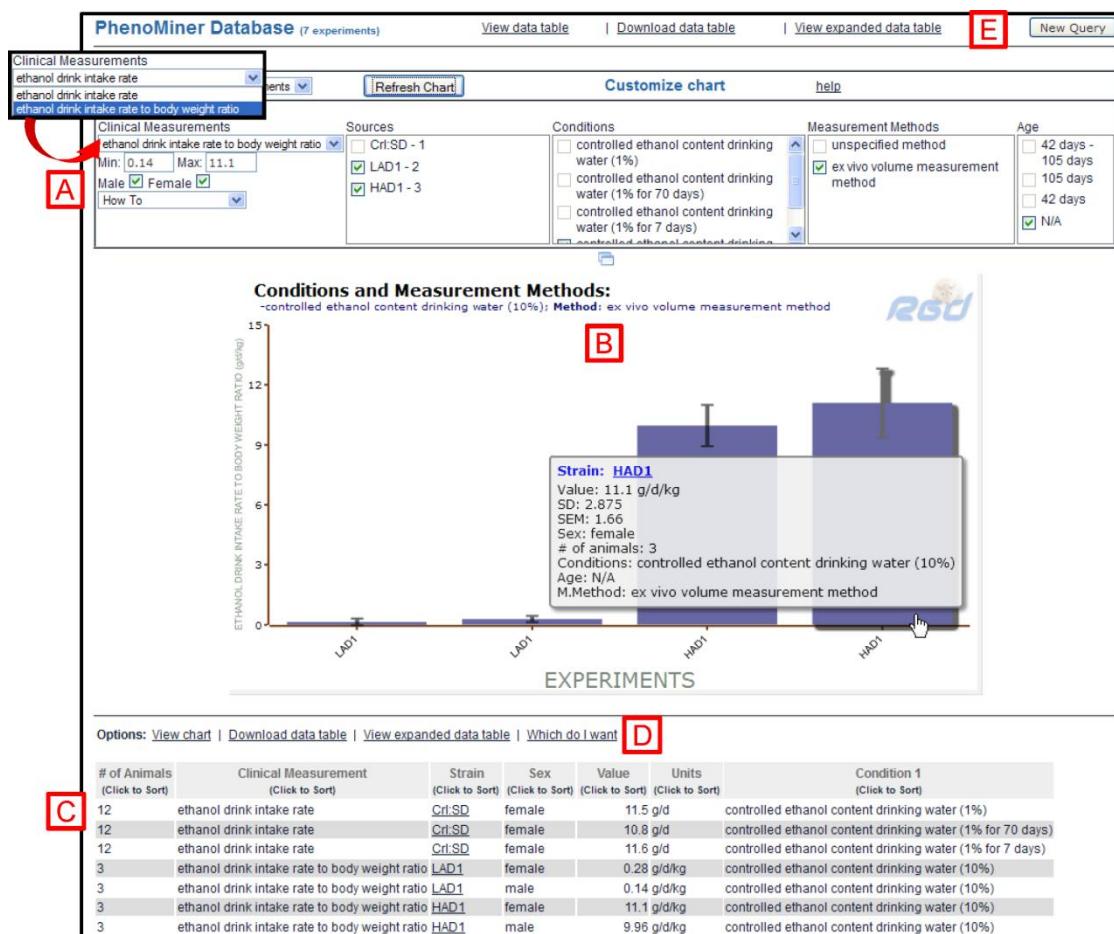
O

Selecting a CMO term takes you to an intermediate page (top left). Here the term(s) you selected are listed [A] and an "Edit Measurements" button is provided which returns you to the corresponding ontology search page, allowing you to edit your selections. A line at the bottom of the display [B] shows the vocabulary selections you have already made and the number of records that match at each step. At this point, only one vocabulary, the CMO, has been used but as you can see in the lower panel, as additional selections are made, all vocabularies selected thus far are shown in this line of text as well as in additional boxes in the display above it.

The number of records matching the current query is also shown at the top right corner of the display [C]. Here there are 11 matching records.

At this point you have the option to limit your selection further using any or all of the other three PhenoMiner ontologies [D]. Click on the button for limiting by the rat strain (RS) ontology. This takes you to a vocabulary selection page similar to the one we saw previously, except that in this case the selection pane only shows the terms for which data exists based on the selections you have already made (i.e. strains that do not have data for the CMO term we selected are not shown). This prevents you from making selections that will give no results. Click the plus signs beside the two terms "inbred strain" and "outbred strain" to view the strains selections [E]. Select the strains "HAD" and "LAD" under inbred and "SD" under outbred. Notice that the box beside outbred is now checked because you selected all the terms under that whereas the box for inbred strain is not checked but filled in with grey. This indicates that some, but not all, terms below that in the display have been selected. Click "Select Rat Strains".

As you can see, the lower panel now shows your selections for both CMO and RS ontologies. If you wanted to limit your results further, you could also limit by experimental condition and/or measurement method. Instead, we will select "Generate Report" [F].



The top of the result page [A] shows the parameters for the chart displayed below it [B], including the clinical measurement, the strains ("Sources"), the experimental conditions under which the measurements were made, the measurement method used and the age of the rats. In each case, there can be multiple options. When you open the page, the measurement listed will be "ethanol drink intake rate". Use the dropdown list at [A] to change this to "ethanol drink intake rate to body weight ratio", i.e. the ethanol intake normalized to body weight. Click "Refresh Chart" to update the chart to display results for the new term. Note that only one measurement term can be graphed at a time.

Just below the CMO term selector are options to limit the results you are viewing by the value and/or the gender of the animals. Looking across the parameters box you can see that some items are not selected. This reflects the fact that, for instance, the Crl:SD rat was not used for the measurement currently being displayed. As before, the tool prevents you from choosing options for which there are no results, so the box beside that strain symbol cannot be checked. You can, however, remove results based on the active parameters. Uncheck the box beside "LAD1" and click "Refresh Chart" to view only results for the HAD1 strain. Recheck that box and refresh the chart again to once again see all the results.

[B] shows the graph of the results for the CMO term we selected. At the top of the display the applicable experimental conditions and measurement methods are shown. In this case there is only a single one of each but in some cases there can be many. This line of text is displayed in the same color as the corresponding bars in the graph. Mouse over one of the bars in the chart to see the details for that measurement value.

Below this is a summary table of all of the measurements and their values [C]. To see the full details for all of the measurements, select "View expanded data table" [D]. This gives additional parameters as well as information about the study and a link to the reference if available. The option is given to download either the summary or the expanded data table and if you are not sure which you need, the link for "Which do I want" [D] gives information to help you decide which to choose. These options are also available at the top of the page [E]. To clear your current selections and start again, click "New Query".

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