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The Rat Genome Database: Genetic, Genomic, and Phenotypic Data Across Multiple Species

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Abstract

The laboratory rat, *Rattus norvegicus*, is an important model of human health and disease, and experimental findings in the rat have relevance to human physiology and disease. The Rat Genome Database (RGD, <https://rgd.mcw.edu>) is a model organism database that provides access to a wide variety of curated rat data including disease associations, phenotypes, pathways, molecular functions, biological processes, cellular components, and chemical interactions for genes, quantitative trait loci, and strains. We present an overview of the database followed by specific examples that can be used to gain experience in employing RGD to explore the wealth of functional data available for the rat and other species.

Keywords

rat; database; quantitative trait locus; ontology; gene

INTRODUCTION

The Rat Genome Database (RGD) provides the scientific community with a public source for a variety of information related to the laboratory rat (<https://rgd.mcw.edu>; (Smith, et

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CONFLICT OF INTEREST STATEMENT:

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Internet Resources

<https://rgd.mcw.edu>

The Rat Genome Database home page.

<https://download.rgd.mcw.edu/>

Site to download flat files of RGD data including genes, QTLs, microsatellites (SSLPs), maps (genetic, radiation hybrid), strains, genome annotations, and sequence files.

<http://mailman.mcw.edu/mailman/listinfo/rat-forum>

Rat Community Forum, online bulletin board for rat-related questions.

<https://www.facebook.com/RatGenomeDatabase/>

RGD on Facebook: updates on rats, rat research, and new features at the Rat Genome Database.

<https://twitter.com/ratgenome>

RGD on Twitter: updates on rats, rat research, and new features at the Rat Genome Database

<https://www.linkedin.com/company/rat-genome-database>

RGD on LinkedIn: updates on rats, rat research, new features, and general information about the Rat Genome Database.

al. 2020). RGD incorporates manually curated data and information through electronic resources into a comprehensive and dynamic database containing information on genes, strains, quantitative trait loci (QTLs), simple sequence length polymorphisms (SSLPs), sequences, maps, and orthologs, all with supporting references. RGD also provides a collection of visualization and analysis applications to assist researchers in effectively utilizing the information available in the database. This integration of manually curated data with electronically imported information obtained from major public data repositories (e.g., NCBI, UniProt), combined with diverse analysis tools, makes RGD a uniquely valuable resource to the scientific community.

This unit focuses on using RGD to access the phenotypic, functional, and genomic annotations that are available in the database. Basic Protocol 1 provides an overview of the RGD home page and illustrates the various features and entry points into the RGD Web site. The subsequent protocols explain the various routes to information in the database, how to use the more advanced querying tools, and how to interpret the individual data reports (Basic Protocols 2 and 3). The other protocols describe how to use RGD data analysis tools and how to navigate the RGD data portals.

BASIC PROTOCOL 1

NAVIGATING THE RGD HOME PAGE

The RGD Home Page provides entry points into the many features of the RGD Web site. It has several distinct sections that group together related content, and these are discussed in more detail below.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with *step annotations*

1. Locate the RGD home page at <https://rgd.mcw.edu>.
2. Examine the basic resource categories in RGD (Fig. 1).

Resource categories are arranged on tabs at the top of the page and are divided into the six major areas of the RGD Web site: Data, Analysis & Visualization, Diseases, Phenotypes & Models, Pathways, and Community (Fig. 1A). Each tab provides quick access to the corresponding section of the RGD Web site. Expanded data and tool links are also available in the center of the home page (Fig. 1C).

3. Note the location of the Keyword Search (Fig. 1B).

The Keyword search text box located in the top center of most RGD pages functions as a quick method to locate an item or items of interest (Fig. 1B).

4. Explore the remainder of the home page.

Right of center is a section containing tweets/links to RGD tweets of recent updates or rat research-related news items (Fig. 1D). Below the tweets are a list of video tutorials (Fig. 1E), which provide general introductions to various sections and topics of the RGD Web site. The bottom left portion of the home page has a list of RGD news items/links to announcements of updates, interesting journal articles, and others RGD-related information (Fig. 1F). Below the news is a list of upcoming conferences that may be of interest to RGD users (Fig. 1G). Each line in the list is a link to the home page of that conference.

BASIC PROTOCOL 2

USING THE RGD SEARCH FUNCTIONS

The RGD Web site has several ways to search for data, depending on the scope of the specific information desired. The keyword search text box, available at the top center of most RGD Web pages (Fig. 1B), provides a fast way to get at specific data, such as gene or QTL information, when a name, keyword, or accession number is known. It searches across most object types (genes, QTLs, strains, homologs, SSLPs, ESTs, and references) and many data types. It also searches the many controlled vocabularies used at RGD, including gene ontology (biological process, molecular function, and cellular component), mammalian phenotype ontology, pathway ontology, and disease vocabulary. Also, one can search specific object types and ontologies directly through the Data choice in the menu bar or through the “Search” bar near the top of the RGD homepage.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with step annotations

1. Go to the RGD Web site as described in Basic Protocol 1. Enter a key word or phrase in the keyword search box in the upper center of any RGD web page (Fig. 1B). For example, enter “protease”, then click the search icon or press the Enter key.

Any text can be entered, and the search looks for an exact or partial match of whatever word or phrase is entered. Wildcards can be used at either end of a word, and punctuation is ignored. Certain short, common words, such as “a” or “the,” cannot be searched. See Figure 2 for results of the “protease” search. An intermediate results page is shown that groups result by category. In this instance data objects, ontology terms, and references represent the result categories.

2. Click “GO: Molecular Function” on the results page (Fig. 2A) to display a list of result terms from that ontology (Fig 3a) as well as the list of the other ontologies

from the original results list (Fig 3b). Open the ontology browser by clicking on the branch icon next to “protease binding” (Fig. 4A). Click the “A” icon next to “protease binding” (Fig. 4B) to open the corresponding ontology report annotation page (Fig. 4C) with rat as the default species selected.

The ontology report page lists all annotations to “protease binding” and its children terms by gene and species. A view of chromosomal location of the annotated genes is shown in an ideogram above the gene list.

3. Hover over the “Data” dropdown to the right of the RGD logo of any RGD Web page (seen with white font on a black background in Fig. 1A).

The Data dropdown menu has a list of all available data categories.

4. Select a data type by clicking the data name. For example, click “Genes”. A new page is returned for gene-specific searches. Enter the gene symbol “lepr” in the Keyword search box on the left side of the page (Fig. 5A-a).
5. In the optional “Limit Results” section under the keyword text box, leave the default Rat for choice of species (Fig. 5A-b), and click either of the “Search Genes” buttons.

By selecting Rat species for the search, the results page returns with the rat tab selected, where 19 genes/gene variants are listed (Fig. 5B-b).

6. If it is desirable to view gene lists in other species, click another species from the dropdown list (Fig. 5A-b).
7. The dropdown list gives a selection option of RGD’s 9 non-rat species.
8. The results can be sorted alphabetically or by relevance (Fig 5B-a).
9. To send any of the results to an RGD analysis tool or to an Excel file, click one or more selection boxes to the left of any line in the results (Fig. 5B-b) and then click one of the icons on the right of the results list (Fig. 5B-c).
10. To display a certain gene report page, click anywhere on the result line (Fig. 5B-d).
11. Return to the “Data” dropdown to the right of the RGD logo of any RGD Web page as described in step 3.
12. Click on the Ontologies link in the data dropdown list from the menu bar. Then, click on the ontology dropdown menu (Fig. 6A-a) and select GO: Molecular Function”. Enter the word “peptidase” in the textbox adjacent to the dropdown and click the Search button to the right of the textbox (Fig. 6A-b).

This will lead to a results page showing Ontology Terms by ontology with a count of terms which match the query term directly, via definition, or via synonym (Fig. 6B-a) and a list of molecular function terms which at least partially match the query term (Fig. 6B-b). A term marked with an “A” in a red square means that data objects in RGD have been annotated for that term. Additional columns in the table

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include a count of annotations, to the term and its children, accession ID number of the ontology term, and links to a summary of the matches for the result.

12. Click on “peptidase activator activity” in the molecular function term list (Fig. 6B–c).

An ontology report page (Fig. 7) is returned with a definition of the term, synonyms, and a list of genes annotated to that term and its children. Above the list of genes is the GViewer (Fig. 7A), which illustrates the genomic location of each gene with an idiogram. The species tabs underneath the GViewer allow a separate view of annotated genes from rat, mouse, human, or the seven other species in RGD (Fig. 7B). Above the species tabs is a check box to display genes annotated to the ontology term or both the term and its child terms (default). There are also two drop-down menus for sorting the annotation gene list by any of its columns (Fig. 7c). The Symbols, Evidence, Source, Reference IDs, and JBrowse links in the gene list are all hyperlinked to relevant information at RGD and at external databases (Fig. 7D).

13. Scroll down to the bottom of the page to see text (Fig. 8A) and graph representations (Fig. 8B) of the branch of the ontology where the term “peptidase activator activity” resides. Click on the branch icon (Fig. 8C) next to the annotation count for “peptidase activator activity” to access the main RGD ontology term browser (Fig. 9).

The term “peptidase activator activity” is highlighted in yellow in the center column, listed with its siblings, while its child terms are in a column to the right and its parent terms are in a column to the left.

14. Click on “peptidase activator activity involved in apoptotic process” (Fig. 9A–a).

When any term is clicked, it gets highlighted and shown in the center column with its sibling terms, and the other columns refresh to show parent terms in the left column and children terms in the right column. This allows horizontal navigation of the ontology in both directions, with three levels of terms always visible. An “A” icon to the right of a term signifies that annotations for that term exist in RGD.

15. Click on the red square “A” icon adjacent to “peptidase activator activity involved in apoptotic process” (Fig. 9B–a), now in the “Term With Siblings” (center) column.

The returned page is the ontology report page for “peptidase activator activity involved in apoptotic process”, which has annotations that represent a subset of those on the page for the parent term “peptidase activator activity” (step 13) (Fig. 7).

Visualizing search results using GViewer: The GViewer tool provides a graphic representation of the genomic locations of all genes, QTLs, and congenic strains that are

annotated to an ontology term or terms. The GViewer tool is visible on all the ontology report pages (see Fig. 7A).

16. On either the ontology report page (Fig. 7, upper left) or the ontology browser homepage (Fig. 6A–a), enter “hypertension” in the ontology text search box. Click the magnifying glass icon to the right of the search box or press Enter on your keyboard. This will return an ontology results list on which you should click “RDO: RGD Disease Ontology,” and then click “hypertension” in the returned term results list.

The GViewer image shows all the chromosomes that have a gene (brown), QTL (blue), or congenic strain (green) annotated to the term hypertension and its children terms (Fig. 10A).

17. Click on the center of chromosome 11 to view a more detailed image in a zoom pane (Fig. 10B). Scroll the zoom pane by dragging the highlighted (gray) slider on the chromosome or by using the zoom pane’s horizontal scroll bar to see all the targeted genes and QTLs on chromosome 11 in more detail. Click the chromosome a second time to lock the slider (now red). Click “send to JBrowse” (Fig. 10B–a) to see a JBrowse model of the genes from the zoom pane (Fig. 10C) (see Basic Protocol 4).

The zoom pane shows all objects by symbol (on the left end of QTL and strain bars) and color code (brown—gene, blue—QTL, and green—strain). For further analysis, the mapped data can be downloaded into a spreadsheet by clicking the “CVS export” link at the bottom of the GViewer image (Fig. 10B–b)

18. Click on the gene symbol “Drd3” in the zoom pane (Fig. 10B–c) to go to the gene report, which opens in a new window (Fig. 11).

BASIC PROTOCOL 3

SEARCHING FOR QUANTITATIVE TRAIT LOCI

As mentioned earlier, RGD contains data related to various types of biological “objects” such as genes, strains, and Quantitative Trait Loci (QTLs). The complete list of data objects is accessible via the Data dropdown list on the menu bar at the top of most pages on the RGD Web site. Basic Protocol 2 describes how to search the database for any object using keywords and ontology terms. RGD also provides object-specific queries focused on a particular type of data (e.g., QTLs). As an example of these types of object-specific queries, this protocol illustrates how to search for QTLs related to blood pressure phenotypes.

While a QTL query or report page differs in some respects, such as search options or data available, from the corresponding pages for other types of data, there are substantial similarities. RGD report pages contain many of the same elements regardless of the data type. These include official nomenclature for the object, annotations in the form of both ontology terms and free-text notes, and links to related information in other databases. In addition, reports for genomic and genetic data types include information on mapping and

a link to various genome browsers to permit viewing of the object in its genomic context. Many of these elements are reciprocally linked to information of other data types. A link on a QTL report page, for instance, will lead to a gene report page which will, in turn, link back to the QTL. Each of these characteristics is reviewed in this protocol.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with *step annotations*

1. From the RGD home page (<https://rgd.mcw.edu>), or any internal page, scroll over “Data” in the top menu bar to get to a listing of the various types of biological data stored in RGD. Click “QTLs” to open the QTL query page.

Using the RGD Specific Query pages allows the user to enter query criteria specific for a particular data object. These other query pages can be reached by selecting the appropriate data object from the menu bar.

2. In the Keyword search box in the left center of the page, type “blood pressure” (Fig. 12A-a). Change the chromosome selection from “All” to “8” in the Chr (chromosome) dropdown menu (Fig. 12A-b). Click on the Search QTLs button to run the search.

When using the Start and Stop parameters for chromosomal position, the positions given must be positions from the reference genome assembly for the selected species (rat, mouse, or human). In the case of rat, the current reference assembly is mRatBN7.2. The addition of new data often shifts the absolute base-pair positions of genes and markers slightly from one assembly to the next, which is why it is important that the positions match the underlying assembly if they are to be accurate.

3. Examine the QTL results page (Fig. 12B).

The QTL search results page contains a list of all the rat QTLs in RGD that match the search criteria (in this case, 18 hits). Mouse and human QTLs for the same search may be found by selecting the appropriate species on the Species dropdown on the QTL search page (Fig. 12A). For each QTL, the list gives the official symbol and name, chromosome, the start and stop base-pair positions, number of ontology annotations associated with the QTL, strains crossed, and RGD ID (Fig. 12B).

4. Click on the symbol for Bp263, at the top of the results list, to go to the RGD report page for that QTL (Fig. 13).

RGD report pages are divided into sections depending on the type of data being displayed. The QTL report page has sections for general information, annotations, references, genomic region, and additional information (Fig. 13-a), all linked from the navigation list on the left

side of the page. Note, however, that not all QTL report pages will have all the possible subsections in each section.

5. The names of the strains used in the linkage analysis (“Strains Crossed” in the summary/general section at the top of the page) provide links to the strain report pages. Click on HTG (Fig. 13-b) to access the report page for that rat strain.

The strain pages contain extensive information on characteristics such as derivation and disease associations, as well as links to related strains and associated ontology terms to aid in data mining.
6. Return to the QTL report page. Click the term “hypertension” (Fig. 14A-a) in the RGD Manual Disease Annotations subsection to go to the details page for that annotation (Fig. 14B).

Each annotation report page provides information on evidence code, a link to the reference from which the annotation was made, the number of RGD objects annotated to the ontology term, a link to the ontology term report page (Fig. 14B-a), and the number of references in RGD curated for the object of that annotation.
7. Return to the QTL report page. In the “Region” section/”Genes in Region” subsection click on the link “Tgfbr2” under “Symbol” (Fig. 15-a) to access the gene report page for Tgfbr2.

The Genes in Region table can be downloaded as a CSV (comma-separated values) or TAB (tab separated) file, sent to a printer, or loaded into various RGD analysis tools (Basic Protocol 6).
8. Click on the subsection navigation link for/or scroll to “Position Markers” (Fig. 16). Adjacent to “Flank 1” (Fig. 16-a), click on “(D8Rat19)” to go to the SSLP report for that marker.
9. Return to the QTL report page and scroll down to the “References-curated” subsection of the Annotations section or click on “References” in the left side navigation column to view the reference for the paper with information about Bp263 (Fig. 17A). Click on the “Reference Citation” link on the right side of the page to read the abstract on the reference report page and see what other objects and what other annotations are associated with the same reference.
10. Return to the QTL report page. The “RGD Curation Notes” subsection of the “Additional Information” section (Fig. 17B) contains free-text notes giving additional details about the QTL that are not included elsewhere in the report. Click the link “1303386” in the Reference column (Fig. 17B-a) to view the abstract of the paper detailing the sexual dimorphism and drug dependence linked to this blood pressure QTL. The reference page includes a link to the abstract at PubMed, which in turn often links to a copy of the full text of the article.

BASIC PROTOCOL 4

USING THE RGD GENOME BROWSER (JBrowse) TO FIND PHENOTYPIC ANNOTATIONS

The JBrowse genome browser (Buels, et al. 2016) from the Generic Model Organism Database project (<http://www.gmod.org>) is an interactive tool that allows researchers to visualize a variety of genetic and phenotypic data types in their genomic context. Virtually all the data within the Rat Genome Database have been associated with the genome sequence in one way or another. As fundamental datasets such as genes, quantitative trait loci, microsatellite and SNP markers, and sequence resources such as ESTs are aligned with the genome sequence, they bring with them phenotypic and other information. This information includes methylation data, associations with disease, human synteny, and many types of variant/mutation data. Any or all of these can be accessed via the JBrowse genome browser and their relationship to the genomic sequence explored.

This protocol details the use of the JBrowse tool to look at a genomic region associated with hypertension.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with step annotations

1. From the RGD home page (<https://rgd.mcw.edu>, Fig. 1), click on the box labelled JBrowse Genome Browser on the left side of the page to access RGD's rat genome browser.

From RGD pages other than the home page, scroll over “Analysis & Visualization” on the menu bar at the top of the page. Click on “JBrowse (genome browser)” from the list that appears.

The RGD JBrowse home page has a list of species and genome assemblies from which to choose.

2. At the top of the genome assemblies list click “RGD mRatBN7.2” (Fig. 18A). At the top center of the right frame, choose chromosome 1 from the drop-down menu (Fig. 18B-a). In the left-side frame under “Available Tracks”, click “Disease Related Tracks”, then “Disease and Phenotype”, “Cardiovascular Diseases”, and finally “Cardiovascular Diseases Related Genes” (Fig. 18B-b). Cardiovascular disease-related genes will immediately load as a track in the right frame of the viewer (Fig. 18B-c).

Zoom out using the “-“ buttons next to the chromosome dropdown menu if no genes are visible. Full view of the track can be seen by scrolling left and right along the chromosome. Relevant genes on other chromosomes can be seen by choosing another chromosome from the dropdown at the top of the frame (Fig. 18B-a).

3. Click any red bar/gene symbol in the cardiovascular disease-related genes track (Fig. 18B–b, in this example Kcnj11 or Abcc8). A pop-up window appears (Fig. 18C) with specific gene information, including Disease Ontology annotations.

The listed annotations all have links, via the term ID, to specific ontology report pages (as in Fig. 10).
4. To see cardiovascular-related QTLs and strains click the check boxes adjacent to “Cardiovascular Diseases Related QTLs” and “Cardiovascular Diseases Related Strains” directly below “Cardiovascular Diseases Related Genes” (Fig. 18B–b).

The QTL cardiovascular disease track (blue bars) and the strain cardiovascular disease track (green bars) are added to the current view in the JBrowse display frame (Fig. 19). Clicking on any QTL bar or strain bar reveals a pop-up window with data like the gene pop-up window (Fig. 18C).

BASIC PROTOCOL 5

USING ONTOMATE TO FIND GENE-DISEASE DATA

The OntoMate tool is a biomedical literature search engine with data tagging and filtering. OntoMate provides an ontology-driven, concept-based literature search as a substitute for the PubMed search (<http://www.ncbi.nlm.nih.gov/pubmed>). OntoMate tags abstracts with gene names, gene mutations, organism name and most of the 19 ontologies/vocabularies used at RGD. Any of the ontologies can be used as the focus of an OntoMate search. All terms/entities tagged to an abstract are listed with the abstract in the search results.

This protocol will show how users can customize their queries by selecting from multiple categories: genes, disease, and multiple subsets thereof.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with step annotations

1. From the RGD home page (<https://rgd.mcw.edu/>, Fig. 1), scroll over “Analysis & Visualization” on the menu bar at the top of the page and click on “OntoMate (Literature Search)” (Fig. 20A–a).

Alternatively, OntoMate can be accessed by clicking “Ontomate (Literature)” in the light blue banner in the “Search” section (Fig. 20A–b) on the homepage, clicking the “OntoMate” box in the lower center of the hompage (Fig. 20A–c, or using the menu bar dropdown from most RGD web pages.
2. Click on the arrowhead in the drop-down selection box on the left side of the OntoMate homepage (Fig. 20B–a) and choose “Disease Ontology (RDO)”

(Fig. 20C-a). Type “hypertension” in the textbox (Fig. 21A) to the right of the ontology selection box.

The textbox has an autocomplete/suggest function, so any term that comes up in the list may be selected as an option.

3. To combine a gene with “hypertension” for a gene-disease search, click “Add term condition” under the term textbox (Fig. 21A-a). Click on the arrowhead in the drop-down selection box that appears in the center of the page (Fig. 21B-a) and select “gene” (Fig. 21B-b). Type “Abcc8” in the textbox adjacent to the ontology selection box (Fig. 21B-c).

The selection of multiple terms/genes is possible by repeating step 3.

Note that “AND”, “OR”, and “NOT” are available with each choice to perform a Boolean search.

4. Submit the query by clicking the “Search OntoMate” button beneath the ontology and term selection boxes (Fig. 21B-d).

The query result is a list of abstracts tagged with both “Abcc8” and “hypertension”. The number of abstracts and the number of result pages are given above the first abstract (Fig. 22A-a). On the left side of the page there is a tally of abstracts by publication date (Fig. 22A-b), by organism, gene, mutation, and disease.

5. Scroll down the list of abstracts to #5. Hover over the “D” in the upper right corner of the abstract box to reveal a pop-up window (Fig. 22B-a) showing RGD disease annotations to the rat, mouse, and human orthologs of gene “Abcc8”.

The abstract box contains numerous things in addition to the citation including a link to the PubMed record of that abstract, a link to full text of that abstract, and a link to the RGD reference record for that abstract (Fig. 22B-b). Also included is a toggle (“show”) (Fig. 22B-c) to show the text of the abstract in the same window. Below the abstract is a listing (Fig. 22B-d) of all genes and ontology terms tagged in the abstract. The ontology terms are links to the respective ontology term report pages in RGD.

BASIC PROTOCOL 6

USING MOET TO FIND GENE-ONTOLOGY ENRICHMENT

The purpose of the MOET or the Multi-Ontology Enrichment Tool (Vedi, et al. 2022) (<https://rgd.mcw.edu/rgdweb/enrichment/start.html>), is to leverage curated data at RGD for analysis of gene or protein lists. Given a gene or protein list, MOET analysis identifies significantly overrepresented ontology terms using a hypergeometric test.

The data available in MOET comes from manual RGD literature curation, as well as imported data from external databases including the National Center for Biotechnology

Information (NCBI), Mouse Genome Informatics (MGI), The Kyoto Encyclopedia of Genes and Genomes (KEGG), The Gene Ontology Consortium, UniProt-GOA, and others.

This protocol will show how users can find patterns of association among genes through ontology annotations.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with step annotations

1. From the RGD home page (<https://rgd.mcw.edu/>, Fig. 1), scroll over “Analysis & Visualization” on the menu bar at the top of the page and click on “Multi-Ontology Enrichment (MOET)”.

Alternatively, MOET can be accessed by clicking the box labelled MOET on the left side of the homepage or from the menu bar dropdown on most RGD web pages.

2. In the large text box on the right side of the page (Fig. 23A–a), enter the following list of gene symbols:

Abat Abca3 Abcc1 Abcc8 Abcc9 Abi2 Abo Acadl Ace Ace2
Acsm3 Acta2 Actc1 Acvrl1 Ada Adad2 Adam23 Adamts10 Adamts13
Adamts16 Adamts16em1Bj Adamts17 Adcy5 Add1 Add2 Add3

3. Click on the “Continue” button on the lower left side of the page (Fig. 23B–a) to run the analysis.

In lieu of entering a list of gene or protein names/symbols/IDs, a specific region of the genome can be entered with chromosome, start and stop coordinates, and genome assembly at the bottom of the page (Fig. 23B–b).

On the results page (the default is “rat” and “Disease Ontology) the gene symbols entered are listed above the enrichment results (Fig. 24A–a). The results are presented as a table (Fig. 24A–b) with the most highly used terms listed at the top, together with the number of annotated genes from the entered list, p value, Bonferroni Correction, and other parameters. The same data is shown in graph form (Fig. 24B) to the right of the table.

4. More analysis can be done on the same list of genes by clicking a different species (Fig. 24A–c) and/or selecting a different ontology (Fig. 24A–d) for the term enrichment.

BASIC PROTOCOL 7

USING OLGA TO GENERATE GENE LISTS FOR ANALYSIS

The OLGA (object list generator) tool (Laulederkind, et al. 2018); <https://rgd.mcw.edu/rgdweb/generator/list.html>), at RGD allows the building of object lists for analysis of genes, QTLs, or rat strains. OLGA can find objects in RGD using any of RGD's functional annotations or genomic positions.

The data available in OLGA comes from manual RGD literature curation, as well as imported data from external databases including the National Center for Biotechnology Information (NCBI), Mouse Genome Informatics (MGI), The Kyoto Encyclopedia of Genes and Genomes (KEGG), The Gene Ontology Consortium, UniProt-GOA, and others.

This protocol will show how users can generate a list of genes and analyze it.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with step annotations

1. From the RGD homepage (<https://rgd.mcw.edu/>, Fig. 1), scroll over “Analysis & Visualization” on the menu bar at the top of the page and click on “OLGA (Gene List Generator)”.

Alternatively, OLGA can be accessed by clicking the box labelled OLGA on the left side of the homepage or from the menu bar dropdown on most RGD web pages.

2. Select “Ontology Annotation” at the top left of the OLGA homepage (Fig. 25A-a), followed by selecting “Disease Ontology” (Fig. 25B-a). Type “hypertension” in the autocomplete textbox that appears for Disease Ontology (Fig. 25C-a). Select “hypertension” and click the “continue” button (Fig. 25C-b) under the textbox to generate the gene list (Fig. 25D).

The gene list returned is, by default, rat genes from rat genome assembly v7.2 (mRatBN7.2). Other results can be explored by changing the options in the drop-down menus at the top of the OLGA homepage. Other options are QTL or strain and genome assemblies of human, mouse, and other RGD species.

3. Click “Add Another Gene List” (Fig. 25D-a) and proceed with “squamous cell carcinoma” as done with “hypertension”. On the results page select “intersection” (Fig. 26A-a). The consequent “Result Set” (Fig. 26B-a) is a list of genes found in both the “hypertension” list and the “squamous cell carcinoma” list.

The option of “Union” or “Subtract” can be made before (Fig. 26A) or after (drop down menu between the two lists in Fig. 26B) the selection of “intersection”.

4. After intersecting the lists click “Analyze Result Set” (Fig. 25B–b). A pop-up window (Fig. 26C) appears with links to further analysis tools at RGD.

Clicking any of the tool icons will transfer the “Result Set” genes to that tool for further evaluation.

BASIC PROTOCOL 8

USING THE GA TOOL TO ANALYZE ONTOLOGY ANNOTATIONS FOR GENES

The purpose of the Gene Annotator (GA tool) (Laulederkind, et al. 2019); <https://rgd.mcw.edu/rgdweb/generator/list.html>, is to take a list of identifiers or a chromosomal region and retrieve gene annotation data stored at RGD. The tool retrieves annotations for rat genes and their orthologs, as well as additional information.

The analysis function of the tool allows an enrichment type view of the data and a cross-ontology comparison of annotations for the list of genes.

This protocol will show how users can analyze genes via the annotations made to those genes.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with step annotations

1. From the RGD homepage (<https://rgd.mcw.edu/>, Fig. 1), hover over “Analysis & Visualization” on the menu bar at the top of the page and click on “Gene Annotator”.

Alternatively, the Gene Annotator can be accessed by clicking the box labelled “GA Tool” on the lower center of the homepage or from the menu bar dropdown on most RGD Web pages.

2. In the large text box in the center side of the page (Fig. 27A), enter the following list of gene symbols:

Abat Abca3 Abcc1 Abcc8 Abcc9 Abi2 Abo Acadl Ace Ace2
Acsm3 Acta2 Actc1 Acvrl1 Ada Adad2 Adam23 Adamts10 Adamts13
Adamts16 Adamts16em1Bj Adamts17 Adcy5 Add1 Add2 Add3

3. Click on the “Continue” button in the lower left corner of the page (Fig. 27A-a) to run the annotation search.

In lieu of entering a list of gene or protein names/symbols/IDs, a specific region of the genome can be entered with chromosome, start and stop coordinates, and genome assembly at the bottom of the page (Fig. 27A–b).

4. The first GA page after a search is a selection page where the user chooses amongst species, annotations, and external links. The tool retrieves annotations across many ontologies for genes and their orthologs, as well as links to other information.

Deselect all the ontology annotation categories except “disease” (Fig. 27B–a). Deselect all the “External Links” by clicking “(toggle)” (Fig. 27B–b). Deselect all species under “Select Orthologs” except Human and Mouse (Fig. 27B–c).

5. Click the “submit” button (Fig. 27B–d) to return a page with all annotations for the first listed gene (default) and select orthologs in the submitted list. The page has links to RGD gene pages, ontology term pages (Accession column), and annotation pages (Reference/Evidence column).

A different gene and ortholog set can be selected from the horizontal list (submitted list) at the top of the page (Fig. 27C–a).

6. From the list of links at the top of the page, select “Annotation Distribution” (Fig. 27C–b) for an enrichment analysis-type of view (Fig. 28A) of the whole list of genes submitted.

The “Annotation Distribution” lists all ontology terms assigned to genes in the list and reports what percentage of the genes in the list are annotated to that term.

7. Click the “+” beside any term to toggle a list of the genes annotated with that term and/or its children term(s) (Fig. 28B–a).

The gene symbols in the toggled list link to the “Annotations” page of the GA tool for that gene and its orthologs. The “Explore this Gene Set” link at the top right of the toggled list refreshes the whole page with just the subset of genes from the toggled list.

8. Select “Comparison Heat Map” (Fig. 28B–b) to see a cross-ontology analysis of the gene list. The map shows by number/color density how many genes are annotated with two terms from two ontologies (horizontal and vertical axis) (Fig. 29).

The default heat map view compares disease terms versus pathway terms associated with all genes in the submitted list. Any other ontology comparisons can be made by using the drop-down menus to the upper left of the heat map (Fig. 29-a). Clicking on any of the terms labeling the rows or columns of the heat map will display a subset that only shows child terms of the selected term. By clicking any numbered square in the heat map, a list of all genes annotated to both intersecting terms will be displayed.

9. Select “All Analysis Tools” (Fig. 29-b) to see a pop-up window (Fig. 27C) with options to send the gene list from the GA tool to another analysis tool at RGD.

The option of sending data object lists to other tools via the “All Analysis Tools” choice is on many of the RGD pages that feature individual analysis tools.

BASIC PROTOCOL 9

USING THE RGD INTERVIEWER TOOL TO FIND PROTEIN INTERACTION DATA

InterViewer, RGD’s Cytoscape-based (<https://www.cytoscape.org/>) (Shannon, et al. 2003) protein–protein interaction visualization software, takes gene or protein symbols and/or IDs for rat, mouse, human, and/or dog and creates an interactive display of pairwise protein interactions for them. Information about the interactions, links to the associated genes in RGD, and links to the originating interaction records at IMEX (Orchard, et al. 2012) (Orchard, et al. 2014) are provided.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with *step annotations*

1. On the RGD homepage (<https://rgd.mcw.edu/>, Fig. 1), hover over “Analysis & Visualization” on the menu bar at the top of the page and click on “Interviewer (Protein-Protein Interactions)”.

This action leads to the Interviewer homepage (Fig. 30). The Interviewer can also be accessed by clicking on the box labelled “Interviewer Protein-Protein Interactions” in the lower left-center of the RGD homepage.

2. In the large text box on the left-center of the page (Fig. 30-a), enter the gene “Acadl”.

More than one gene name/protein name/identifier may be entered at the same time.

3. Click the “Submit” button on the lower left side of the page to see the protein-protein interaction results for the gene (Fig. 31A).

The results page features an interactive graphic display (linked to an interactive thumbnail display in lower right) (Fig. 31A–a), a list of interactions (Fig. 31A–b), detail/control options, and a legend for the graphic display (Fig. 31A–c).

4. Click on the red circle in the center of the largest interaction graphic (Fig. 31B). This action highlights all the nodes in the interaction group and enlarges the labels. Also, this action generates a detail box in the details/control frame (Fig.

31B-a), which gives information about the protein and provides a link to the UniProt page for that protein.

Clicking on any circle in the display generates a detail box in the details/control frame, which gives information about the protein and provides a link to the UniProt page for that protein. The interaction edges between circles can also be clicked. Again, a detail box appears with information about the specific interaction. A link to the PubMed source(s) of information is included.

5. On the upper right-hand side of the page, click “Report” to see an option to print the graphic display with the data table or “Graph PNG” to see an option to print the graphic display alone (Fig. 31B-b). A download link for the interactions list is available at the upper right side of the table (Fig. 31B-c).

BASIC PROTOCOL 10

USING THE RGD VARIANT VISUALIZER TOOL TO FIND GENETIC VARIANT DATA

Variant Visualizer is a viewing and analysis software tool for rat strain-specific sequence variants and human ClinVar variants. Rat strains or a variety of human assemblies may be selected, defined by genomic regions and, if desired, parameters may be set for the type(s) of desired variants. The tool will display all the single nucleotide variants (SNVs) matching the input criteria, with information on read depth, zygosity, conservation score and more.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with step annotations

1. On the RGD homepage (<https://rgd.mcw.edu/>, Fig. 1), hover over “Analysis & Visualization” on the menu bar at the top of the page and click on “Variant Visualizer”.

The Variant Visualizer can also be accessed by clicking on the box labelled “Variant Visualizer” in the center of the RGD homepage. Either action leads to the Variant Visualizer homepage (Fig. 32A).

2. Click on the “Select Strains” button in the middle left of the Variant Visualizer homepage (Fig. 32A-a) to return a page (Fig. 32B) listing all available rat strains with mRatBN7.2 assembly sequence.

The default is the rat 7.2 assembly (Fig. 32A-b), but the dropdown menu gives the options of rat assembly 3.4, 5.0, 6.0, human assembly 37 or 38, and dog assembly 3.1.

3. Under “Select Samples” choose BN/NHsdMcwi (2020), LEW/Crl (2019), and MWF/Hsd (2019) by clicking the toggle boxes to the left of each strain name

(Fig. 32B–a), followed by clicking “Continue” on the right side of the page (Fig. 32B–b).

Clicking “Continue” takes you to another selection page (Fig. 32C) to limit the variant search by genomic position, function, or gene.

4. Click the “Enter a Gene List” button on the right side of the page. In the large text box that appears on the subsequent page (Fig. 32D), enter this list of genes:

Abat Abca3 Abcc1 Abcc8 Abcc9 Abi2 Abo Acadl Ace Ace2
Acsm3 Acta2 Actc1 Acvrl1 Ada Adad2 Adam23 Adamts10 Adamts13
Adamts16 Adamts16em1Bj Adamts17 Adcy5 Add1 Add2 Add3

These are the top 26 genes listed for “hypertension” in the OLGA tool (Fig. 25D). Click “Continue” to see a page (Fig. 32E) with optional choices for filtering on variant type, variant location, variant at protein level, and call statistics for variants.

5. Click the “Find Variants” button on the top right side of the page to see the variant distribution across the chosen rat strains and genes as shown via heat map of variant numbers (Fig. 33A). Click on the square at the intersection of MWF/Hsd and Acvrl1 (Fig. 33A–a) to see the 29 variants of the MWF/Hsd strain and the 11 variants of the LEW/Crl strain within the sequence of the Acvrl1 gene (Fig. 33B).

The results feature a horizontal view of DNA sequence of strain/assembly compared to reference sequence (Fig. 33B). Variants are labeled with chromosome coordinates and base designations. The graphic display makes it easy to compare many rat strains simultaneously because the variants are shown vertically aligned based on chromosome coordinate in a scrollable display frame.

6. For details of any variant, click on the base to (Fig. 32B–a) open a popup window with details (Fig. 33C).

From the sequence display page optional views and a link to additional analysis options in the upper right corner of the display page (Fig. 33B–b) are available. The options include an overview plot of the data, a distribution graph of the data, help documentation, a download link for the data, and a link to the GA tool (Gene Annotator—see Basic Protocol 8) for functional analysis of the selected region.

BASIC PROTOCOL 11

USING THE RGD DISEASE PORTALS TO FIND DISEASE, PHENOTYPE, AND OTHER INFORMATION

There are some types of data at RGD that are presented in their own sections of the web site called “portals.” Disease information is currently divided into 15 different “portals,” separated by disease category. Phenotype data is accessible through the “Phenotypes & Models” portal, which includes quantitative PhenoMiner data, strain medical records, and

more. Finally, the pathway portal contains both molecular pathway and physiological pathway diagrams. Whereas the physiological pathways are limited to a few interactive diagrams, the pathway portal currently has 200 interactive molecular pathway diagrams across five nodes (classic metabolic pathway, signaling pathway, regulatory pathway, disease pathway, and drug pathway) of the Pathway Ontology. Related pathway diagrams are organized in “suites” and “suite networks.”

The RGD Disease Portals home page (Fig. 34A) has icons that link to the individual disease portals. RGD maintains a growing list of disease portals, each designed to be an entry point for researchers to access consolidated data and tools related to a particular category of disease.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with *step annotations*

1. From the RGD homepage (<https://rgd.mcw.edu/>, Fig. 1), click “Diseases” on the menu bar at the top of the page to display the Disease Portals homepage. Alternately, click the “Disease Portals” box on the lower left middle of the RGD homepage to access the Disease Portals homepage.

The disease portals homepage has fifteen different disease logos/names/links displayed. Any of the portals can also be accessed by hovering the computer cursor over “Disease” in the menu bar and clicking on the portal of choice.

2. Click on “Cardiovascular Disease” (Fig. 34A-a) to access the Cardiovascular Disease Portal (Fig. 34B)

The default selected species is rat with the other nine RGD species pictured to the right and below “Rat”. To change the data shown on the lower half of the page, click on any of the species’ icons.

3. To find genes, QTLs, and strains annotated to “hypertension”, click “vascular disease” in the embedded term browser (Fig. 35A-a), followed by “artery disease” (Fig. 35B-a), and finally “hypertension” (Fig. 35C-a).
4. Genes, QTLs, and strains annotated to “hypertension” are listed in separate columns (Fig. 36A) below the term browser and shown visually in the GViewer-style ideogram (Fig. 36B) (genes-brown bars, QTLs – blue bars, strains – green bars) under “Genome View”. Click on any of the choices under “Gene Enrichment Set” (Fig. 36B-a) to see an analysis as in Fig. 24. Enrichment analysis can be done with disease (DO), pathway (PW), phenotype (MP/HP), Gene Ontology (BP, CC, or MF), or chemical (ChEBI) annotations.

BASIC PROTOCOL 12

USING THE RGD PHENOTYPE & MODELS PORTAL TO FIND QUALITATIVE AND QUANTITATIVE PHENOTYPE DATA AND OTHER RAT STRAIN-RELATED INFORMATION

The Phenotypes & Models Portal contains data related to rat strains, phenotypes, identifying disease models, community forums for gathering feedback from the scientific community and essential information for conducting physiological research. Icons on the portal home page link to the respective data or tools, which include the “PhenoMiner” quantitative phenotype tool, phenotype analysis in “Expected Ranges” and “PhenoMiner Term Comparisons”, extensive aid in finding appropriate animal models, commercial rat strain availability, animal husbandry, and links to outside sources of rat strain information.

This protocol will show how users can customize their queries in PhenoMiner by selecting from four categories: rat strains, experimental conditions, clinical measurements, and measurement methods. The queries are built step by step and a tally of results obtained at each step of the query building process is provided.

The data currently in PhenoMiner is comprised of results from the rat physiological literature, two large-scale phenotyping projects (the PhysGen Program for Genomic Applications at the Medical College of Wisconsin (Malek, et al. 2006) and the National BioResource Project in Japan (Serikawa, et al. 2009), and data submitted directly from laboratories engaged in the study of rat physiology.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with step annotations

1. From the RGD homepage (<https://rgd.mcw.edu/>, Fig. 1), click “Phenotypes & Models” on the menu bar at the top of the page to display the Phenotypes and Models Portal homepage (Fig. 36). *The Phenotypes and Models portal homepage can also be accessed by clicking on the box labelled ‘Phenotypes and Models’ in the lower middle of the RGD homepage.*

To access PhenoMiner (the RGD quantitative phenotype database) click on the “Phenominer” box on the left side of the Phenotypes and Models Portal homepage (Fig. 37a) or hover over “Phenotypes & Models” on the menu bar at the top of the page and select “PhenoMiner (Quantitative Phenotypes)”.

The PhenoMiner homepage has selection data input options of Rat Strains, Clinical Measurements, Measurement Methods, and Experimental Conditions. Rat Strains is the default start point in the selection area at the bottom of the page, but the term selection may begin in any of the four options.

2. Click on the “Clinical Measurements” tab on the lower right side of the page (38A-a), followed by typing “systolic blood pressure” in the text box (38A-b)

under “Clinical Measurement Selection” in the lower left side of the page. Then click “select” adjacent to “systolic blood pressure” (38A-c) under the text box.

The selections made in the lower part of the page are tracked in the boxes in the top half of the page.

3. Click on the “strains” tab on the lower right side of the page (38B-a), followed by typing “SR” in the text box on the lower left side of the page (38B-b), and finally click “select” next to “SR” under the text box (38B-c).

The boxes in the top half of the page now contain “SR (6)” and “systolic blood pressure (6)” with the numbers in parentheses meaning there are six records in Phenominer that have both “SR” and “systolic blood pressure” as annotated terms.

4. Repeat step 3 with the strain “SS”. Repeat step 3 again with “Experimental Conditions” (38C-a) and “controlled sodium content diet” (Fig. 38C-b).
5. To see systolic blood pressure data from SS and SR strains on controlled sodium content diets click “Generate Report” (Fig. 38C-c).

“Generate Report” may be selected at any time during the term selection process. “Generate Report” returns a graph that compiles all records that meet the combined criteria of the term selection process (Fig. 39). The final data selected for the graph can be filtered by selecting boxes adjacent to terms listed in the left frame of the results page (Fig. 39A-a). The data from the graph is also available in the table beneath the graph (Fig. 39A-b).

6. Hover over the first column on the left side of the graph (Fig. 40-a) to see all the details of the experiment record associated with that column.

This view gives finer detail than the mean values shown in the graph and is the same data shown in the table below the graph. The data seen in the experiment-specific pop-up can be changed by hovering over any of the columns in the graph.

BASIC PROTOCOL 13

USING THE RGD PATHWAY PORTAL TO FIND DISEASE AND PHENOTYPE DATA VIA MOLECULAR PATHWAYS

The RGD Pathway Portal is a way to access the list of molecular pathway diagrams via the Pathway Portal homepage. The molecular pathway diagrams were designed at RGD using Elsevier’s Pathway Studio software (<http://support.pathwaystudio.com/>). The diagrams feature hyperlinks from most of the objects in the diagram to RGD pages representing the respective term, gene, chemical, or associated secondary pathway. Additional relevant data can be found beneath the diagrams on the molecular pathway pages in several lists: pathway genes/associated disease annotations, pathway genes/all associated pathway annotations, and pathway genes/associated phenotype annotations.

This protocol shows how users can access RGD pathway diagrams and related data.

Necessary Resources

Hardware: Computer with functioning Internet connection

Software: Web browser (Microsoft Edge, Mozilla Firefox, Google Chrome, or Apple Safari)

Protocol steps with step annotations

1. To access pathway diagrams from the Pathway Portal homepage, click the “Pathway Explorer” box on the lower left side of the RGD homepage (Fig. 1) or click “Pathways” on the menu bar at the top of the page. On the Pathway Portal homepage click the “Individual Diagram Pages” icon on the top left side of the page (Fig. 41A–a) or the “Molecular Pathway Suites and Suite Networks” on the top right side of the page (Fig. 41A–b).

Both icons link to a page (“Molecular Pathways”) (Fig. 41B) with lists of pathway diagrams available at RGD.

Click on “de novo pyrimidine biosynthetic pathway” in the “classic metabolic pathway” list (Fig. 41B–a). This link accesses the de novo *Below the diagrams on the pages of molecular pathways there are several lists: 1. “Genes in Pathway”: A list of genes showing annotations to the title term of the diagram and to children terms of the title term from the Pathway Ontology* (Petri, et al. 2014) (Fig. 43A). 2. *“Additional Elements in Pathway”: A list found on a subset of pathway diagram pages. This list may include small molecules, gene groups, other pathways, etc.* (Fig. 43B). 3. *“Pathway Gene Annotations”: A list of disease terms annotated to the genes involved in the pathway. This list can be toggled between disease term to genes and gene to disease terms* (Fig. 43C). 4. *A list of additional pathways in which the genes in the diagram are involved. This list can be toggled between pathway term to genes and gene to pathway terms* (Fig. 43D). 5. *A subset of diagram pages have a list of phenotype terms annotated to the genes involved in the pathway. This list can be toggled between phenotype term to genes and gene to phenotype terms* (Fig. 43E).

Background Information: The Rat Genome Database was established in 1999 as a resource to support the already growing set of genomic reagents for the rat. This role has continued to expand with continuing work on the rat reference genome sequence (Aitman, et al. 2008) (Howe, et al. 2021), strain-specific DNA sequencing (Kalbfleisch, et al. 2023), expanded SNP discovery, and large-scale phenotyping projects such as the PhysGen project (Kunert, et al. 2008) and NBRP (Serikawa, et al. 2009) (<http://www.anim.med.kyoto-u.ac.jp/nbr/>). All of the indicated sequence and phenotypic data has been integrated with existing and newly published research data. As the amount of data has grown, so has the need to add more types of data and more ways to present that data. Much effort has gone into the development and incorporation of biomedical ontologies such as the Gene Ontology (Ashburner, et al. 2000), the Mammalian Phenotype Ontology (Smith, et al. 2005), the Pathway Ontology (Petri, et al. 2011), and others (Laulederkind, et al. 2012) (Laulederkind and Peoples 2022; Shimoyama, et al. 2012). These are incorporated into the search and analysis tools, greatly facilitating the discovery of information and interpretation of its meaning.

As this unit has demonstrated, interaction with a database is primarily through a web browser and other software developed on top of the database. A concerted effort has gone into developing tools that provide access to the underlying data in a manner that is aligned with a researcher's overall goal. GViewer presents data in the context of the entire genome; JBrowse shows genes, QTLs, markers, and phenotypic annotations also from a genome-based perspective; and PhenoMiner presents quantitative phenotype data in an easy modular format. With the fundamental data curation processes in place to acquire and integrate data, the tools constructed to visualize and analyze this data are important to provide access to the data for researchers.

Many researchers using the rat as a model system are ultimately studying a specific phenotype or disease with the goal of applying this knowledge to humans. To meet this need, RGD has developed “disease portals” that present RGD data and tools from the perspective of a particular disease. The disease portals allow researchers to visit a single page that is focused on a single disease area like cardiovascular, neurological, or respiratory disease (<https://rgd.mcw.edu/rgdweb/portal/index.jsp>). These disease categories have been targeted by specific curation projects to create portals which cover most of the breadth of human pathology. The rest of RGD is accessible via these portals, but researchers can find the items of greatest relevance to their disease interest first, reducing the challenge of finding the data and interpreting its meaning.

Utilizing RGD beyond the Web site: RGD has a staff of experienced curators and bioinformaticians that have a great deal of experience dealing with rat data specifically and genomic data in general. The authors of this unit welcome the opportunity to discuss data from impending publications to work with researchers to establish correct nomenclature for rat strains, genes, QTLs, and markers. Nomenclature guidelines are available online (<https://rgd.mcw.edu/nomen/nomen.shtml>). Authors can also make direct submissions of published data so that they can be more rapidly integrated into RGD and other online resources (<https://rgd.mcw.edu/registration-entry.shtml>). If users have questions about tools or data or would like advice on methods of online data mining of RGD resources and integration of this data with the experimental work of an individual laboratory, they should contact the RGD team via the Contact page (<https://rgd.mcw.edu/contact/>), and each request will be answered to the best of the staff's ability.

Suggestions for Further Analysis

Other databases relevant to the rat: RGD maintains a resources page that contains links to other online resources for rat research (<https://rgd.mcw.edu/wg/resource-links>). The sequence and genomic databases are well known, but for the animals themselves, some very useful rat strain resources exist, including the Rat Resource and Research Center (<http://www.rrrc.us/>) at the University of Missouri and The National Bio Resource for the Rat in Japan (<http://www.anim.med.kyoto-u.ac.jp/nbr/>) at Kyoto University.

Downloading bulk data: The RGD download site maintains regularly updated files of all RGD data that can be downloaded and used in subsequent studies. These include the curated gene, QTL, strain and marker datasets, mapping information, genome annotation (in GFF format), and sequence files for RGD data. The download site can be reached by clicking the

“Download” link found in the menu bar on the top of most RGD web pages (Fig. 1). This link will lead to the download page (<https://download.rgd.mcw.edu/>) where one can browse the files available for download.

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DATA AVAILABILITY STATEMENT:

The data referenced in this report are available in the Rat Genome Database at <https://rgd.mcw.edu/>. These data were derived from the following resources available in the public domain: PubMed (<https://pubmed.ncbi.nlm.nih.gov/>), Gene Ontology Consortium (<http://geneontology.org/>), Mouse Genome Informatics (<https://www.informatics.jax.org/>), HGNC (<https://www.genenames.org/>), UniProt (<https://www.uniprot.org/>), Ensembl (<http://useast.ensembl.org/index.html>), and NCBI (<https://www.ncbi.nlm.nih.gov/>).

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B Enter Search Term... Advanced Search (OLGA) f t in

RGD virtual office hours are now by appointment.
When: At your convenience! Contact us to schedule a time.
Who: Anyone is welcome!

Search Other Species Portals Genes Strains Ontology & Annotation Ontomate (Literature) QTL Orthologs Genomic Region All...

C Analysis and Visualization

- JBrowse Genome Browser
- Variant Visualizer
- Genome Information
- OLGA Gene List Generator
- Disease Portals
- Phenotypes and Models
- MOET Multi-Ontology Enrichment
- OntoMate Advanced Literature Search
- GA Tool Gene Annotator
- Pathway Explorer Interactive Diagrams
- Interviewer Protein-Protein Interactions
- Ratmine

D Tweets from @ratgenome

- Rat Genome ... @ratgenome · 8h
- Fee free to stop by our booth at the CTC & the Rat Genomics Meeting #CTC_RG. Topics include: Completion of genomic rat variant analysis of the Hybrid Rat Diversity Panel & Phenominer: RGD's quantitative phenotype data repository.
- Rat Genome ... @ratgenome · Sep 28
- @ratgenome Jennifer Smith is presenting RGD resources for de novo rat strain assemblies on Sept 29 at the Complex Trait Community (CTC) and the Rat Genomics Meeting (RGM). Community Meeting #CTC_RG. Registration is free for virtual attendees: tinyurl.com/y24468&#atgenomics
- ucdenver.zo... Welcome! You are invited to...

E RGD Video Tutorials

- Introduction to RGD Disease Portals
- JBrowse Genome Browser
- Introduction to Biomedical Ontologies
- Introduction to Biomedical Nomenclature
- Gene Report Pages
- Variant Visualizer
- OLGA (Gene list builder and analyzer)
- GA Tool (Gene Annotator)
- Molecular Pathways

F RGD News

- 09/22/2022 - RGD announces the release of an updated Phenominer tool
- 08/31/2022 - GENETICOSIS Call for Papers: Genetic Models of Rare Disease
- 08/31/2022 - New Video Tutorial added to RGD YouTube channel
- 07/26/2022 - Submissions are open for RGD's 2022 Rat Calendar
- 07/15/2022 - RGD announces a updated Cancer & Neurologic Disease Portal
- 06/24/2022 - New paper alert Published in Frontiers in Genetics
- 04/06/2022 - GENETICOSIS special issue featuring Model Organism Database updates
- 03/16/2022 - Mammalian Genome Special Issue: Mammalian Genetic Resources
- 02/11/2022 - RGD announces office hours now by appointment only
- 02/08/2022 - Recent RGD papers discuss new data and tools
- 01/28/2022 - Additional older News notices can be found on the News page in the upper menu, or click HERE

G Conference Watch

- 09/25/2022 - ICBO 2022 International Conference on Biomedical Ontology (Hybrid), University of Michigan, Ann Arbor, MI, USA - September 25-28, 2022 Abstract deadline: June 17, 2022
- 09/29/2022 - 19th Annual Meeting of the Complex Trait Community/Rat Genomics, University of Colorado Anschutz Medical Campus (hybrid), Denver, CO, USA - September 29-30, 2022 Abstract deadline: September 1, 2022
- 10/04/2022 - 19th Annual Bioconductor Conference (Virtual), Session 3, October 4, 2022
- 10/11/2022 - 20th Fall Gene Ontology Consortium Meeting (Virtual), California Institute of Technology, Pasadena, CA, USA - October 11-13, 2022
- 10/16/2022 - Cardiovascular Disease Model Satellite 2022, 20th International SHR Symposium & 8th Japanese SHR Meeting, Shirinkankan Kyoto, Kyoto, Japan - October 16-17, 2022 Abstract deadline: July 29, 2022
- 10/25/2022 - Metabolome (Hybrid), Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, USA - October 25-29, 2022 Abstract deadline: August 5, 2022
- 10/25/2022 - American Society of Human Genetics Annual Meeting, Los Angeles Convention Center, Los Angeles, CA, USA - October 25-29, 2022 Abstract deadline: June 9, 2022
- 10/28/2022 - 8th American Physiological Society Intersections Meeting in Comparative Physiology: From Organisms to Omics in an Uncertain World, San Diego, CA, USA - October 28-31, 2022
- 11/05/2022 - AMIA 2022 Annual Symposium, Washington DC, USA - November 5-9, 2022 Submission deadline: March 9, 2022
- 11/05/2022 - Biological Data Science (Hybrid), Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, USA - November 9-10, 2022 Abstract deadline: March 10, 2022
- 02/12/2023 - Gordon Research Conference - Quantitative Genetics and Genomics, Four Points Sheraton/Holiday Inn Express, Ventura, CA, USA - February 13-15, 2023 Abstract deadline: January 13, 2023
- 03/08/2023 - Probabilistic Modeling in Genomics (Hybrid), Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, USA - March 8-11, 2023 Abstract deadline: January 13, 2023
- 03/12/2023 - Gordon Research Conference - Glycobiology - Biological Roles of Glycans as Major Building Blocks of Life, Four Points Sheraton/Holiday Inn Express, Ventura, CA, USA - March 12-17, 2023 Abstract deadline: February 12, 2023
- 03/25/2023 - Discover BMB 2023 - American Society for Biochemistry and Molecular Biology, Seattle Convention Center, Seattle, WA, USA - March 25-28, 2023 Abstract deadline: November 30, 2022

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Figure 1.

The RGD home page. Tabs and links to all the data and analysis tools at RGD are found here: Menu bar (A), General text search box (B), Links to data visualization and analysis software tools (C), and RGD messages made on Twitter (D). The bottom half of the page covers RGD tutorial videos (E), RGD news (F), and a conference list for users (G).

RGD Search Results..

5148 results found for "protease".

	Rat	Mouse	Human	Chinchilla	Bonobo	Dog	Squirrel	Pig	Green Monkey	Naked Mole-rat	All
Gene	413	448	512	171	202	204	174	179	198	197	2698
Strain	-	-	-	-	-	-	-	-	-	-	-
QTL	-	-	-	-	-	-	-	-	-	-	-
SSLP	-	-	-	-	-	-	-	-	-	-	-
Variant	-	-	-	103	-	-	-	-	-	-	103
Promoter	-	-	-	-	-	-	-	-	-	-	-
Cell line	-	-	-	68	-	-	-	-	-	-	68

Results Matrix

A

- [CL: Cell Ontology](#) 3
- [CMO: Clinical Measurement](#) 18
- [ChEBI: ChEBI Ontology](#) 24
- [GO: Biological Process](#) 27
- [GO: Cellular Component](#) 26
- [GO: Molecular Function](#) 27
- [HP: Human Phenotype](#) 8
- [MI: Molecular Interactions](#) 11
- [MP: Mammalian Phenotype](#) 22
- [PW: Pathway Ontology](#) 13
- [RDO: RGD Disease Ontology](#) 4
- [SO: Sequence Ontology](#) 4
- [VT: Vertebrate Trait Ontology](#) 6
- [XCO: Experimental Condition](#) 2

Ontology Terms (265)

[Reference](#) 2014

[References](#)

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RGD is funded by grant HL64541 from the National Heart, Lung, and Blood Institute on behalf of the NIH.

Figure 2.

Intermediate search results page. This page shows results grouped by category (ontology category example: A. Gene Ontology) with links to the specific groups of data.

The screenshot shows the RGD Search Results page with a search term "protease" entered in the search bar. The results are categorized under "Ontology Terms: (266)". A red box labeled "b" highlights the filter section, and another red box labeled "a" highlights the main results table.

Filters

- View All Results
- Other Categories:
 - Ontology Terms: (266)
 - CL: Cell Ontology (3)
 - CMO: Clinical Measurement (18)
 - ChEBI: ChEBI Ontology (84)
 - GO: Biological Process (37)
 - GO: Cellular Component (26)
 - GO: Molecular Function (27)
 - HP: Human Phenotype (9)
 - MI: Molecular Interactions (11)
 - MP: Mammalian Phenotype (22)
 - PW: Pathway Ontology (13)
 - RDO: RGD Disease Ontology (4)
 - SO: Sequence Ontology (4)
 - VT: Vertebrate Trait Ontology (6)
 - XCO: Experimental Condition (2)

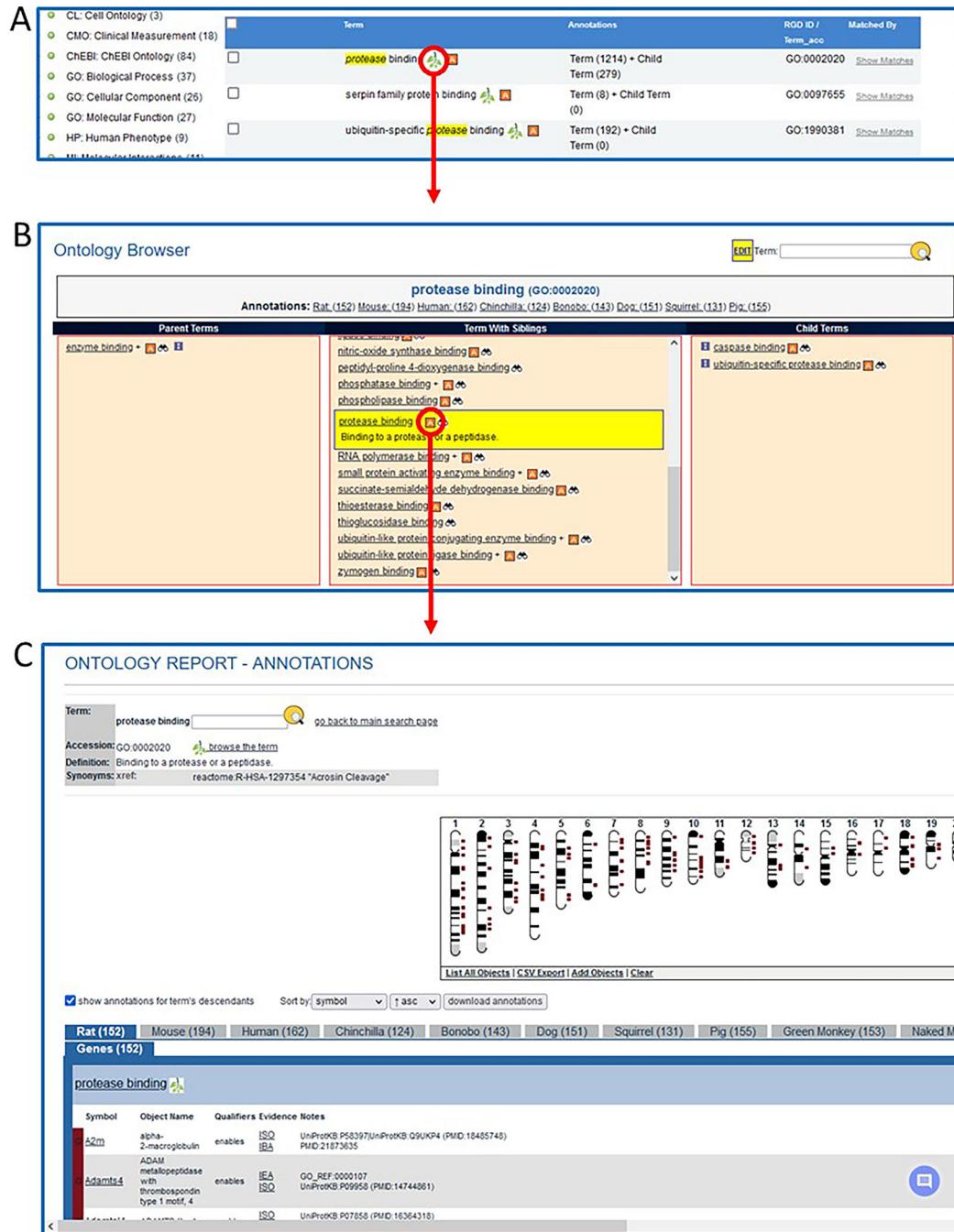
27 GO: Molecular Function records found for "protease"

Showing results 1 - 27 of 27 results

Term	Annotations	RGD ID / Matched By
protease binding	Term (1214) + Child Term (279)	GO:0002020 Show Matches
serpin family protein binding	Term (8) + Child Term (0)	GO:0097655 Show Matches
ubiquitin-specific protease binding	Term (192) + Child Term (0)	GO:1990381 Show Matches
proteinase-activated receptor activity	Term (20) + Child Term (19)	GO:0001648 Show Matches
peptidase inhibitor activity	Term (536) + Child Term (1093)	GO:0030414 Show Matches
peptidase activator activity	Term (134) + Child Term (281)	GO:0016504 Show Matches
serine-type peptidase activity	Term (1122) + Child Term (555)	GO:0008236 Show Matches
cysteine-type endopeptidase inhibitor activity	Term (296) + Child Term (212)	GO:0004869 Show Matches
Alg3-specific peptidase activity	Term (37) + Child Term (0)	GO:0019786 Show Matches
threonine-type endopeptidase activity	Term (96) + Child Term (0)	GO:0004298 Show Matches
acrosin binding	Term (44) + Child	GO:0032190 Show Matches

Figure 3.

Intermediate search results page. This page provides the ontology results of a general search for "protease".

**Figure 4.**

Search results for the Gene Ontology term “protease binding”. This figure tracks the search of “protease binding” through the general search and the RGD term browser to the ontology report page.

A Gene Search

Gene reports include a comprehensive description of function and biological process as well as disease, expression, regulation and phenotype information.
Example searches: [Δ2m_2004 serine threonine kinase](#), [NM_0124880](#), [Adora2a](#)

Keyword **lepr** **Search Genes** **a**

Limit Results (optional)
Chr: All Start (bp) Stop (bp)
Species: Rat **b** **Search Genes**

B RGD Search Results..
19 results found for term "lepr" in category "Gene"
Filters: Rat (19), Gene (19), allele (9), protein-coding (8), splice (2), Other Categories: **b**
Assembly: mRatBN7.2 **a**
Sort By: Relevance **c** Go To Page: View Results Page 1 of 1 Got 50

Symbol	Name	Chr	Start	Stop	Annotations	RGO ID / Term_id
Lepr	leptin receptor	5	116294409	116477904	586	3001
Lepr ^{1R1}	leptin receptor, mutant 1, Rudolph L. Leibel			0		9835400
Lepr ^{4Liz}	leptin receptor, CRISPR/Cas9 induced mutant 4, Lizh			17		21079476
Lepr_v1	leptin receptor, variant 1			7		728330
Lepr ^{m2}	leptin receptor, TALEN induced mutant 2			1		12910518
Lepr_v2	leptin receptor, variant 2			10		728313
Lepr ^{cp}	leptin receptor, corpulent			2		11570565
Lepr ^{m1}	leptin receptor, TALEN induced mutant 1			0		12910515
Lepr ^{fα}	leptin receptor, fa mutant			33		13432153
Lepr ^{m3}	leptin receptor, TALEN induced mutant 3			7		12910546
Lepr ^{m2MowI}	leptin receptor, zinc finger nuclease induced mutant 2, Medical College of Wisconsin			22		6484701
Leprot1	leptin receptor overlapping transcript-like 1	16	58040934	58053600	58	1307168
Leprot	leptin receptor overlapping transcript	5	116289843	116301951	66	621034

C RGD Tools
Analyze selected Genes with RGD Tools
Annotation
Distribution
Functional Annotation
OLGA
Annotation Comparison
Excel Download
InterViewer
Genome Viewer
MOET
Damaging Variants
Variant Visualizer **d**

Figure 5.

A. Gene Search page. This page provides a gene-specific version of the RGD data search.
 B. Genes results page. This page displays gene search data for rat with multiple options for viewing and analyzing the results.

A

RGD uses ontologies: hierarchical, controlled vocabularies to annotate genes, QTLs, strains and homologs: Gene Ontology; Mammalian Phenotype Ontology; Disease Ontology; Pathway Ontology and others.

The Ontology Browser allows you to retrieve all genes, QTLs, strains and homologs annotated to a particular term.

Search Ontology

Examples: ave, SS, BN, Most, Kinase, pathway

GO: Molecular Function **b** Search

Any Ontology

- CHEBI: ChEBI Ontology
- CL: Cell Ontology
- CMO: Clinical Measurement
- GO: Biological Process
- GO: Cellular Component
- GO: Molecular Function**
- HP: Human Phenotype
- MA: Mouse Anatomy
- Mi: Molecular Interactions
- MMO: Measurement Methods
- MP: Mammalian Phenotype
- NBO: Neuro Behavioral Ontology
- PW: Pathway Ontology
- RDO: RGD Disease Ontology
- RS: Rat Strains
- SO: Sequence Ontology
- UBERON: Cross-Species Anatomy
- VT: Vertebrate Trait Ontology
- XCO: Experimental Condition

ed weekly from the GO Consortium website (<http://geneontology.org/docs/download-ontology>). For more information, please see The Gene Ontology Consortium. Gene ontology: tool for the 2000;25(1):25-9.

ogy and Mammalian Phenotype Ontology are downloaded weekly from the Mouse Genome Informatics databases at Jackson Laboratories (<http://www.informatics.jax.org/home/other/publications.shtml>), see the MGI Publications Page at <http://www.informatics.jax.org/pub/reports/index.html>.

(DO, <https://disease-ontology.org/>) for disease curation across species. RGD automatically downloads each new release of the ontology on a monthly basis. Some additional terms which

ses but are not currently covered in the official version of DO have been added. As corresponding terms are added to DO, these custom terms are retired and the DO terms substituted in

y used for curation.

(CMO), Measurement Methods Ontology (MMO), and Experimental Condition Ontology (XCO) are currently being developed at the Rat Genome Database. For more information about these

et al. Three ontologies to define phenotype measurement data. Front Genet. 2012;3:87. Epub 2012 May 28 or contact us (<http://rgd.mcw.edu/contact/index.shtml>).

ntly being developed at the Rat Genome Database. For more information about this vocabulary, please see Peter et al. The rat genome database pathway portal. Database (Oxford). 2011 Apr

us (<http://rgd.mcw.edu/contact/index.shtml>).

ntly being developed at the Rat Genome Database. For more information about this vocabulary or to request additions or changes, please contact us (<http://rgd.mcw.edu/contact/index.shtml>).

B

Submit Data | Help | Video Tutorials | News | Publications | Download | REST API | Citing RGD | Contact | Sign In

peptidase **a** Advanced Search (OLGA) **b** **c**

27 results found for term "peptidase" in category "Ontology"

Ontology Search: peptidase

Filters View All Results **a**

Annotations Go To Page: View Results Page 1 of 1
1 Go! 50 < >

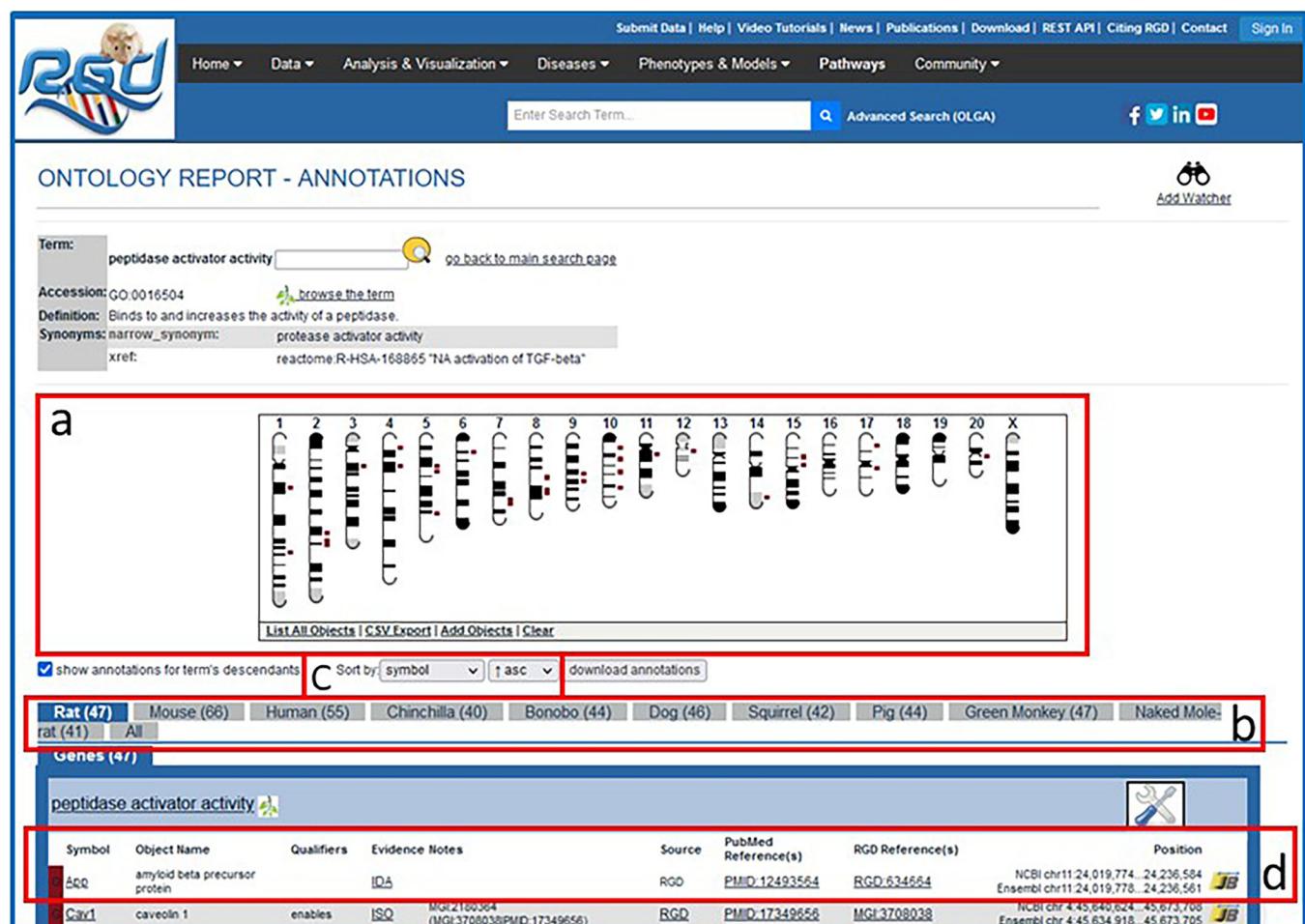
27 GO: Molecular Function records found for "peptidase"
Showing results 1 - 27 of 27 results

Term	Annotations	ROD ID / Term_acc	Matched By
peptidase regulator activity	Term (0) + Child Term (2150)	GO.0061134	Show Matches
peptidase activator activity involved in apoptotic process	Term (24) + Child Term (147)	GO.0016504	Show Matches
C peptidase activator activity	Term (136) + Child Term (367)	GO.0016504	Show Matches
peptidase activity	Term (3532) + Child Term (2227)	GO.00008233	Show Matches
peptidase inhibitor activity	Term (552) + Child Term (444)	GO.0030414	Show Matches

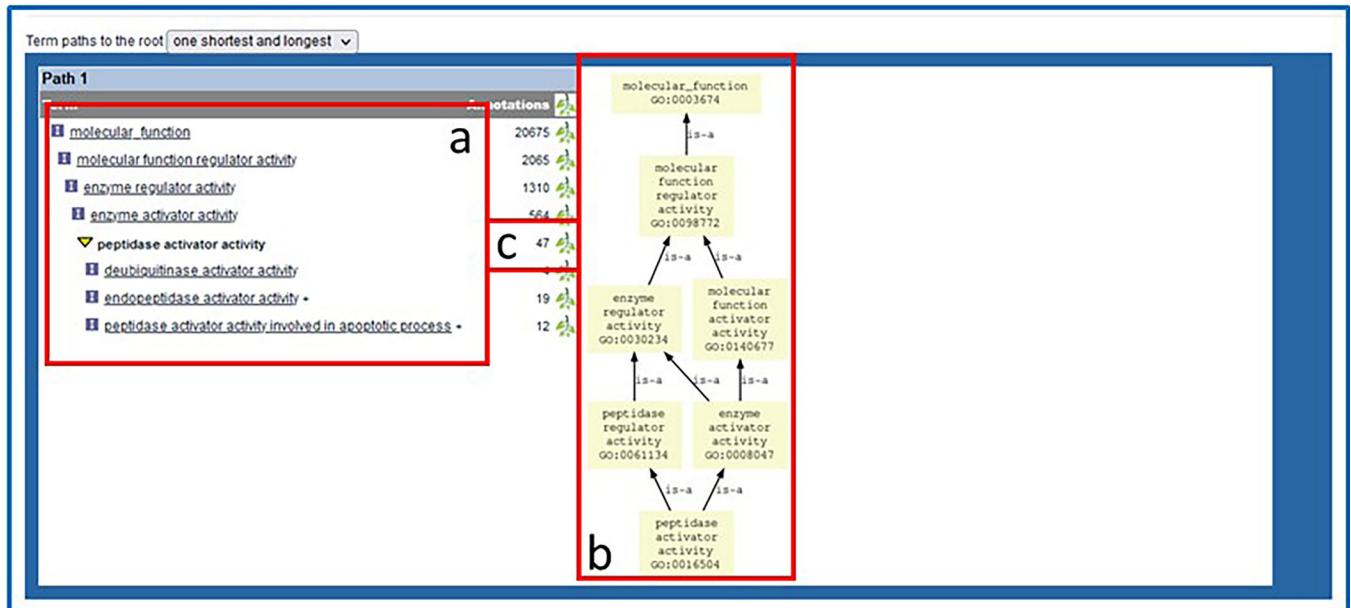
b

Figure 6.

Ontology general search results for the word “protease”. These pages highlight the narrowing of the search results down to a single Gene Ontology-Molecular Function term.

**Figure 7.**

Ontology report page. This page defines the selected ontology term, lists all RGD objects annotated with that term and its children, and displays the genomic location of annotated genes, QTLs, and congenic strains.

**Figure 8.**

Bottom of ontology report page. Underneath the annotated object list are text and graph representations of the ontology branch(es) containing the selected term.

A

Ontology Browser

Term:

peptidase activator activity (GO:0016504)

Annotations: Rat_(47) Mouse_(66) Human_(55) Chinchilla_(40) Bonobo_(44) Dog_(48) Squirrel_(42) Pig_(44)

Parent Terms	Term With Siblings	Child Terms
enzyme activator activity +	lipase activator activity + m7G(5')pppN diphosphatase activator activity ornithine decarboxylase activator activity peptidase activator activity + Binds to and increases the activity of a peptidase. peptidase inhibitor activity + phosphatase activator activity + phosphatidylcholine-sterol O-acetyltransferase activator activity polynucleotide adenylyltransferase activator activity recombinase activator activity ribulose-1,5-bisphosphate carboxylase/oxygenase activator activity RNA lariat debranching enzyme activator activity single-stranded DNA endodeoxyribonuclease activator activity sphingolipid activator protein activity	deubiquitinase activator activity endopeptidase activator activity + peptidase activator activity involved in apoptotic process + a

Commonly used browser icons:
 Term Relationships: Navigation:

Synonyms

Narrow Synonyms: protease activator activity
Xrefs: reactome:R-HSA-168865 "NA activation of TGF-beta"
Definition Sources: GOC:all

B

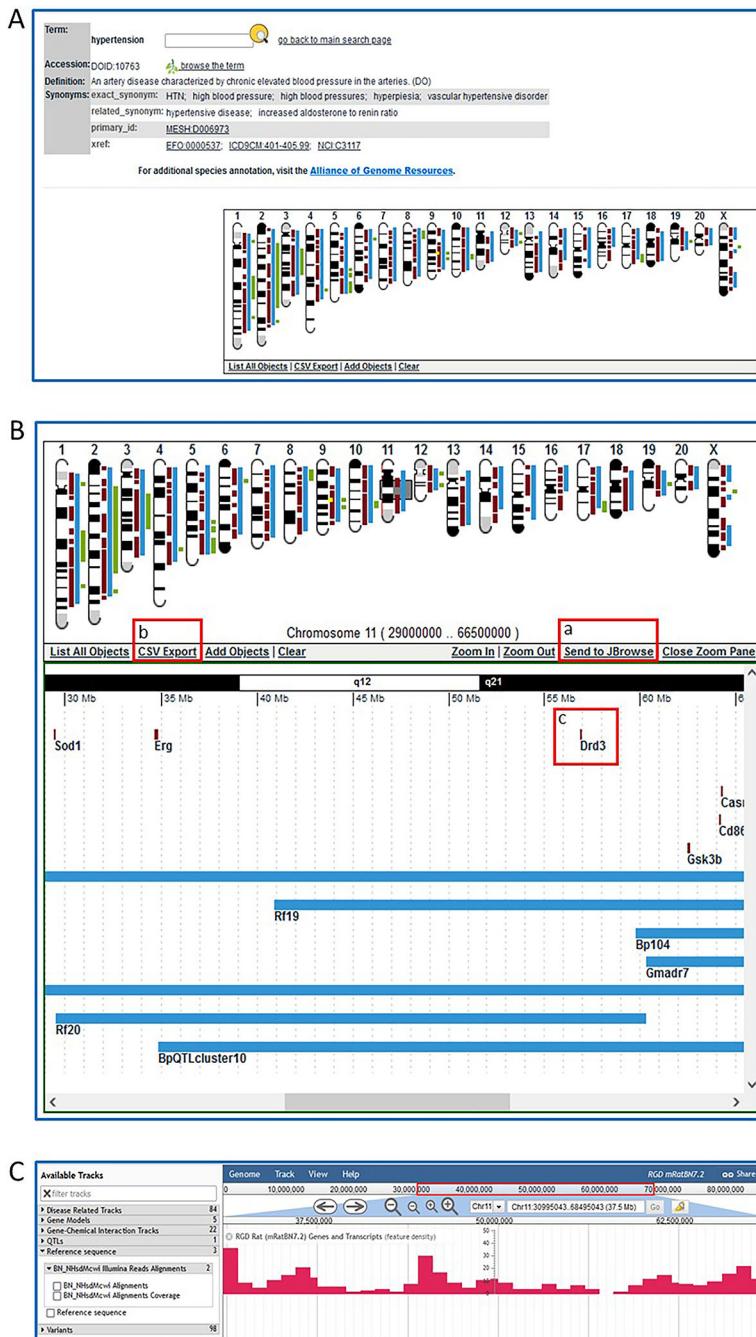
peptidase activator activity involved in apoptotic process (GO:0016505)

Annotations: Rat_(12) Mouse_(28) Human_(22) Chinchilla_(11) Bonobo_(12) Dog_(14) Squirrel_(11) Pig_(11)

Parent Terms	Term With Siblings	Child Terms
peptidase activator activity +	deubiquitinase activator activity endopeptidase activator activity + peptidase activator activity involved in apoptotic process + Binds to and increases the activity of a peptidase that is involved in the apoptotic process. a	cysteine-type endopeptidase activator activity involved in apoptotic process

Figure 9.

The RGD ontology browser. Any of the ontologies/vocabularies used at RGD can be displayed in this horizontally oriented term browser.

**Figure 10.**

The GViewer. All genes, QTLs, and congenic strains annotated to the selected term and its descendants are shown at the appropriate chromosomal location.

RGD

Home ▾ Data ▾ Analysis & Visualization ▾ Diseases ▾ Phenotypes & Models ▾ Pathways ▾ Community ▾

Enter Search Term... Advanced Search (OLGA) [f](#) [t](#) [in](#) [y](#)

Gene: Drd3 (dopamine receptor D3) Rattus norvegicus

[Add Watcher](#) [Analyze](#) [Play the RGD Video Tutorial](#)

General Array IDs

Symbol: Drd3
Name: dopamine receptor D3
RGD ID: 2521
Description: Involved in several processes, including adenylate cyclase-inhibiting dopamine receptor signaling pathway; regulation of secretion; and regulation of transcription by RNA polymerase II. Located in several cellular components, including apical part of cell; endocytic vesicle; and plasma membrane. Is act GABA-ergic synapse; glutamatergic synapse; and postsynaptic density membrane. Used to study Parkinsonism; amnesia disorder; essential tremor; ar hypertension. Biomarker of heroin dependence and visual epilepsy. Human ortholog(s) of this gene implicated in Parkinson's disease; essential tremor; ar hypertension. Orthologous to human DRD3 (dopamine receptor D3); PARTICIPATES IN dopamine signaling pathway; dopamine signaling pathway via D2 family of receptors; G protein mediated signaling pathway via Galphai family; INTERACTS WITH (R,R)-tramadol; (S)-colchicine; 17beta-estradiol.
Type: protein-coding
RefSeq Status: VALIDATED
Previously known as: D(3) dopamine receptor; D3 receptor; dopamine D3 receptor; dopamine D3 receptor isoform; dopaminergic receptor D3

RGD Orthologs:

Alliance Genes:

More Info: [more info...](#)

Latest Assembly: mRatBN7.2 - mRatBN7.2 Assembly

Position:

Rat Assembly	Chr	Position (strand)	Source	Genome Browsers			
				JBrowse	NCBI	UCSC	Ensembl
mRatBN7.2	11	56,879,689 - 56,931,901 (-)	NCBI	mRatBN7.2	mRatBN7.2		
mRatBN7.2 Ensembl	11	56,879,689 - 56,940,596 (-)	Ensembl		mRatBN7.2 Ensembl		
UTH_Rnor_SHR_Utx	11	65,692,856 - 65,745,058 (-)	NCBI	Rnor_SHR			
UTH_Rnor_SHRSP_BbbUtx_1.0	11	58,355,098 - 58,407,302 (-)	NCBI	Rnor_SHRSP			
UTH_Rnor_WKY_Bbb_1.0	11	57,403,823 - 57,463,424 (-)	NCBI	Rnor_WKY			
Rnor_6.0	11	61,819,102 - 61,883,223 (-)	NCBI	Rnor_6.0	Rnor_6.0	rn6	Rnor6.0
Rnor_6.0 Ensembl	11	61,822,077 - 61,874,327 (-)	Ensembl	Rnor_6.0		rn6	Rnor6.0
Rnor_5.0	11	60,955,136 - 61,016,058 (-)	NCBI	Rnor_5.0	Rnor_5.0	rn5	Rnor5.0
RGSC_v3.4	11	58,446,901 - 58,520,589 (-)	NCBI	RGSC3.4	RGSC_v3.4	rn4	RGSC3.4

Figure 11.

The RGD gene report page for Drd3. The summary/general section has a textual description of the gene, shows orthologs, has links to Alliance of Genome Resources gene pages, and genomic position information. Links on the left side lead to the Annotation, References, Genomics, and other sections of the page.

A

Submit Data | Help | Video Tutorials | News | Pathway

Home ▾ Data ▾ Analysis & Visualization ▾ Diseases ▾ Phenotypes & Models ▾ Pathway:

Enter Search Term... Advanced

QTL Search

QTL reports provide phenotype and disease descriptions, mapping, and strain information as well as links to markers and candidate genes.

Example searches: [Mcs_61387](#), [renal function](#), [bo1](#).

Select at least one field

a Keyword

b Chr Start (bp) Stop (bp)

Species: Rat

B

RGD Search Results..

18 results found for term "blood pressure" in category "QTL"

QTL Search: blood pressure

Assembly: mRatBN7.2 Sort By: Relevance Go To Page: 1 View Results Page 1 of 1

Filters: Rat (18), QTL (18), arterial blood pressure trait (VT:2000000) (18), Other Categories:

18 QTL records found for "blood pressure" of species Rat on chromosome 8

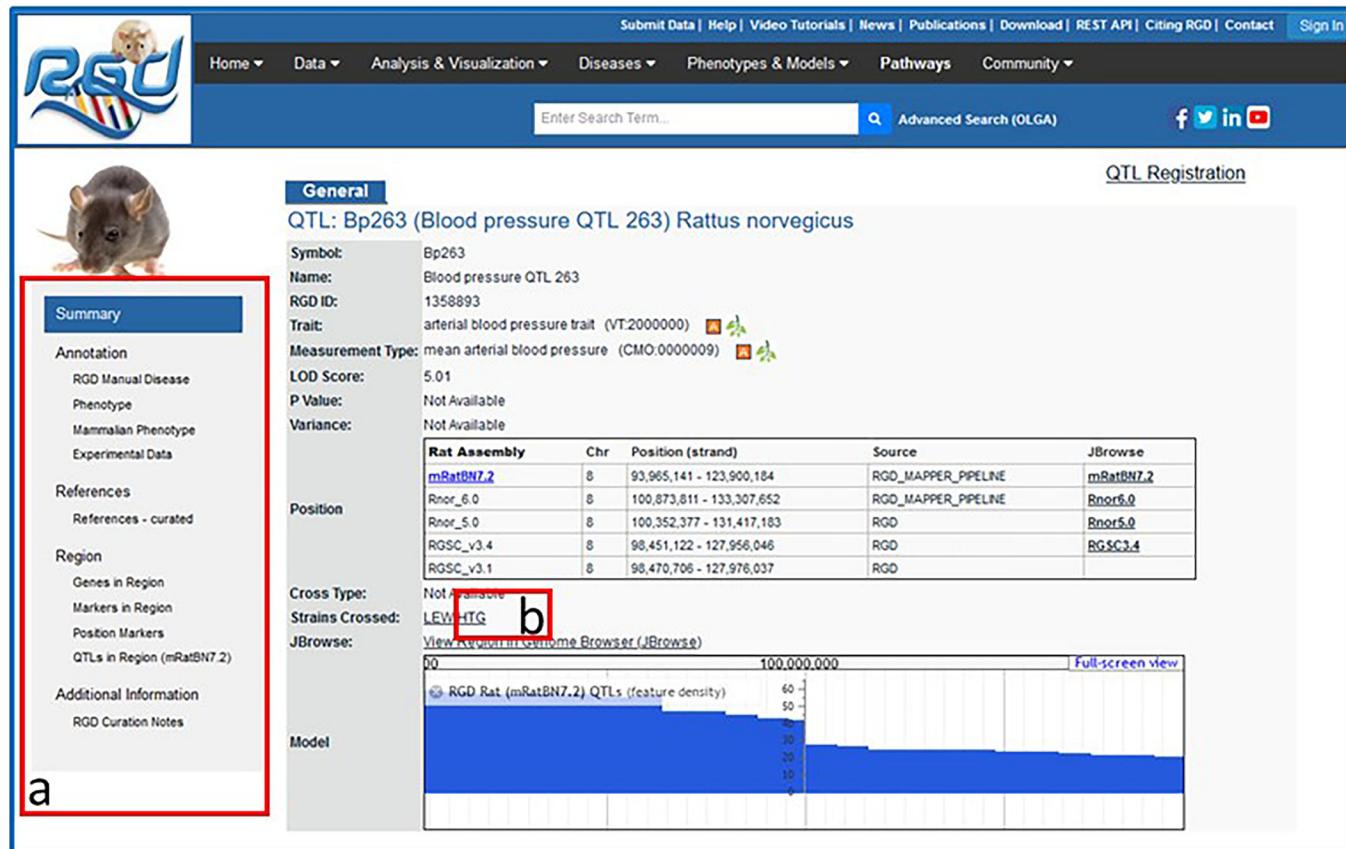
Showing results 1 - 18 of 18 results

<input type="checkbox"/>	Symbol	Name	Chr	Start	Stop	Annotations	Strains Crossed	ROD ID / Term_acc
<input type="checkbox"/>	Bp263	Blood pressure QTL 263	8	93965141	123900184	10	LEW, HTG	1358893
<input type="checkbox"/>	Bp253	Blood pressure QTL 253	8	40713066	93965294	8	LEW, HTG	1358906
<input type="checkbox"/>	Bp62	Blood pressure QTL 62	8	42692684	90165460	8	SS/Jr, SHR/NHsd	70161
<input type="checkbox"/>	Bp252	Blood pressure QTL 252	8	93965141	123900184	8	LEW, HTG	1358903
<input type="checkbox"/>	Bp331	Blood pressure QTL 331	8	61290298	119084929	8	WKY/NCrCrlj, SHR/Kyo	2303171
<input type="checkbox"/>	Bp315	Blood pressure QTL 315	8	7670578	52670578	7	SS, LEW-(D8Rat56-D8Rat51)/Ayd	2301416
<input type="checkbox"/>	Bp380	Blood pressure QTL 380	8	53968765	98968765	7	LEW, SS-(D8Chm12-	10402857

RGD Tools: Analyze selected QTLs with RGD Tools. [Genome Viewer](#) [Excel Download](#)

Figure 12.

A. The QTL-specific search. This page uses a keyword search with optional restrictions to narrow the search. B. QTL search results for “blood pressure” on rat chromosome 8.

**Figure 13.**

QTL report page including general information section, Annotation section, and others.

A

The screenshot shows the RGD QTL report page. On the left, a sidebar lists categories like Summary, Annotation, References, Region, and Additional Information. The main content area includes a table of QTL positions, a genome browser plot for RGD Rat (mRatBN7.2) QTLs, and an annotation table. A red box highlights the term "hypertension" in the annotation table.

Position	Rnor_6.0	8	100,873,611 - 133,307,652	RGD_MAPPER_PIPELINE	Rnor6.0
Cross Type:	Rnor_5.0	8	100,352,377 - 131,417,183	RGD	Rnor5.0
Strains Crossed:	RGSC_v3.4	8	98,451,122 - 127,956,046	RGD	RGSC3.4
JBrowse:	RGSC_v3.1	8	98,470,706 - 127,976,037	RGD	

Annotation [Click to see Annotation Summary View](#)

RGD Manual Disease Annotations [Click to see Annotation Summary View](#)

Only show annotations with direct experimental evidence (0 objects hidden)

Term	Qualifier	Evidence	With	Reference	Notes	Source	Original Reference(s)
a hypertension	IAGP			1303386		RGD	

B

The screenshot shows the RGD QTL-term report page for hypertension. It features a navigation bar with links like Home, Data, Analysis & Visualization, Diseases, Phenotypes & Models, Pathways, and Communications. Below the navigation is a search bar. The main content displays a list of annotations found, with a summary statement: "An association has been curated linking Bp263 and hypertension in Rattus norvegicus." A red box highlights the term "hypertension".

View As List [View As Table](#)

QTL - TERM ANNOTATION REPORT

1 Annotations Found.

An association has been curated linking Bp263 and hypertension in Rattus norvegicus.

- The association was inferred by association of genotype and phenotype (IAGP)
- The annotation was made from Ueno T. et al., Physiol Res 2003;52(6):689-700.
- 259 additional annotations were made from Ueno T. et al., Physiol Res 2003;52(6):689-700.
- 1618 RGD objects have been annotated to **hypertension** (DOID:10763)
- 1 papers in RGD have been used to annotate **Bp263**

[Go Back to source page](#) [Continue to Ontology report](#)

Figure 14.

QTL report page (A) and QTL-term report page (B). The QTL-term report page gives annotation information such as type of evidence, data source, number of annotations from that data source, and number of references associated with the QTL.

Region

Genes in Region

The following Genes overlap with this region. [Full Report](#) [CSV](#) [TAB](#) [Printer](#) [Analysis Tools](#)

RGD ID	Symbol	Name	Chr	Start	Stop	Species
69651	Igfb2	a transforming growth factor, beta receptor 2	8	115794537	115883615	Rat
69653	Snrk	SNF related kinase	8	121779704	121833949	Rat
3630	Scn11a	sodium voltage-gated channel alpha subunit 11	8	119495550	119587044	Rat
3544	Rbp2	retinol binding protein 2	8	99079293	99104489	Rat
3629	Scn10a	sodium voltage-gated channel alpha subunit 10	8	119350723	119462882	Rat
3637	Scn5a	sodium voltage-gated channel alpha subunit 5	8	119220905	119318816	Rat
2223	Bsn	bassoon (presynaptic cytomatrix protein)	8	108784849	108875819	Rat
3961	Vipr1	vasoactive intestinal peptide receptor 1	8	121303739	121339587	Rat
2729	Gpx1	glutathione peroxidase 1	8	109026905	109028031	Rat
3265	Pccb	propionyl-CoA carboxylase subunit beta	8	101591218	101641213	Rat
2743	Grm2	glutamate metabotropic receptor 2	8	107280099	107293159	Rat
2556	Ephb1	Eph receptor B1	8	102507549	102944839	Rat
3310	Prmf4	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4	8	109643558	109687006	Rat
2288	Cck	cholecystokinin	8	121153499	121160194	Rat
3111	Mras	muscle RAS oncogene homolog	8	99944036	100006771	Rat
61896	Nme6	NME/NM23 nucleoside diphosphate kinase 6	8	109832085	109839301	Rat
619892	Pten23	protein tyrosine phosphatase, non-receptor type 23	8	110360804	110383271	Rat
69261	Cish	cytokine inducible SH2-containing protein	8	107972306	107977254	Rat
3538	Rasa2	RAS p21 protein activator 2	8	97119983	97236687	Rat
619783	Troc1	transient receptor potential cation channel, subfamily C, member 1	8	96263322	96314197	Rat

Figure 15.
Genes in Region subsection of the QTL report page.

Position Markers					
Summary	a Flank 1: (D8Rat119)	Rat Assembly	Chr	Position (strand)	Source
Annotation	mRatBN7.2		8	93,965,141 - 93,965,294 (+)	MAPPER
RGD Manual Disease	Rnor_6.0		8	100,873,811 - 100,873,963	NCBI
Phenotype	Rnor_5.0		8	100,352,377 - 100,352,529	UnSTS
Mammalian Phenotype	RGSC_v3.4		8	98,451,122 - 98,451,660	RGD
Experimental Data	RGSC_v3.4		8	98,451,251 - 98,451,403	UnSTS
References	RGSC_v3.1		8	98,470,706 - 98,470,858	RGD
References - curated	Celera		8	93,462,642 - 93,462,800	UnSTS
Region	RH 3.4 Map		8	1043.1	UnSTS
Genes in Region	RH 3.4 Map		8	1043.1	RGD
Markers in Region	RH 2.0 Map		8	807.3	RGD
Position Markers	SHRSP x BN Map		8	56.1699	RGD
QTLs in Region (mRatBN7.2)	FHH x ACIMap		8	63.6299	RGD
Additional Information	Peak: (D8Rat59)	Rat Assembly	Chr	Position (strand)	Source
RGD Curation Notes	Rnor_5.0		8	115,112,735 - 115,113,003	NCBI
	RGSC_v3.4		8	112,242,639 - 112,242,906	RGD
	RGSC_v3.1		8	112,262,094 - 112,262,361	RGD
	RH 3.4 Map		8	1127.5	UnSTS
	RH 3.4 Map		8	1127.5	RGD
	RH 2.0 Map		8	872.8	RGD
	SHRSP x BN Map		8	71.0	RGD
	FHH x ACIMap		8	79.01	RGD
	Flank 2: (D8Rat171)	Rat Assembly	Chr	Position (strand)	Source
	Rnor_5.0		8	131,416,934 - 131,417,183	NCBI
	RGSC_v3.4		8	127,955,798 - 127,956,046	RGD
	RGSC_v3.1		8	127,975,484 - 127,976,037	RGD
	SHRSP x BN Map		8	84.2299	RGD
	SHRSP x BN Map		8	84.2299	UnSTS

Figure 16.

Position Markers subsection of the QTL report page.

A

References

References - curated

RGD Manual Disease
Phenotype
Mammalian Phenotype
Experimental Data

References

References - curated

B

Additional Information

RGD Curation Notes

Additional Information

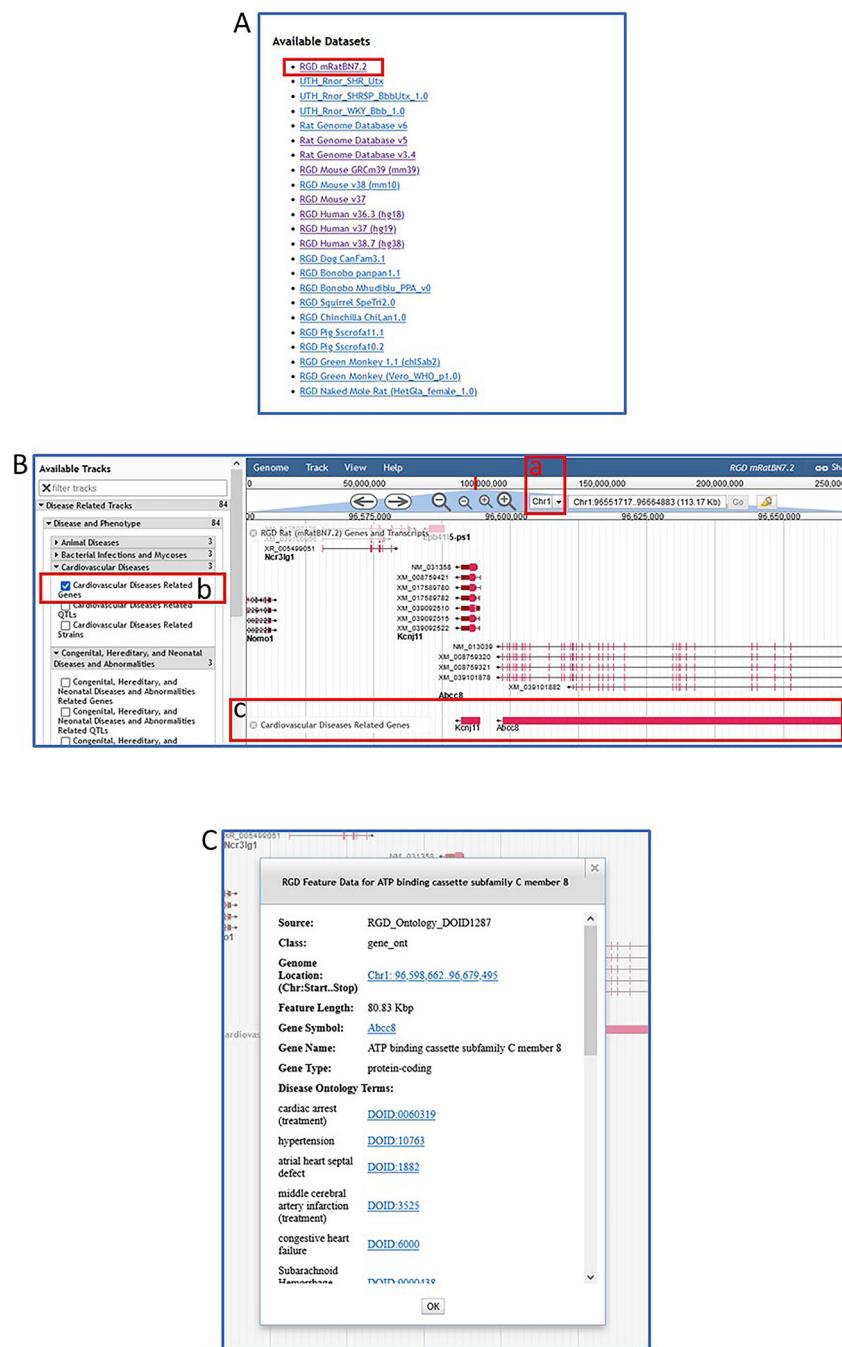
RGD Curation Notes

Note Type	Note	Reference
qtl_general	QTL detected in F2 males	1303386
qtl_statistics_details	QTL linkage is not observed in baseline MAP and is only detected after pharmacological inhibition of NO synthase	1303386
qtl_statistics_details	QTL mapping was carried out with the Map Manager QT program and is consistent with results obtained through one way analysis of variance (ANOVA) testing	1303386

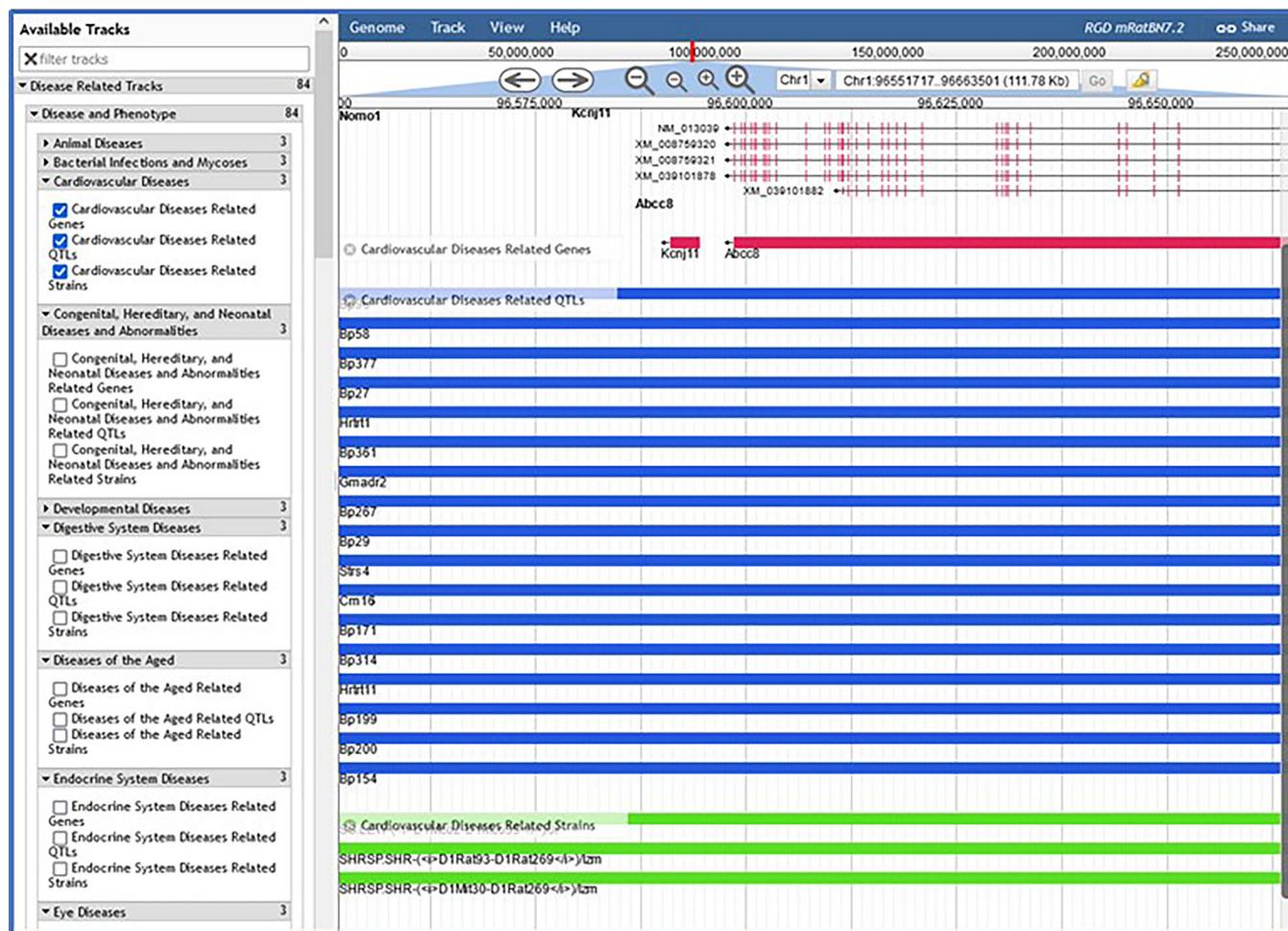
a

Figure 17.

The References (A) and Additional Information (B) sections of the QTL report page.

**Figure 18.**

A default view of rat JBrowse with an RGD genes track selected.

**Figure 19.**

JBrowse page with “Cardiovascular Diseases” selected, showing rat genes, rat QTLs, and rat strains.

A

RGD virtual office hours are available by appointment. Contact us to schedule a time.

Other Species Portals: Other Species Portals

Search: Genes, Strains, Ontology & Annotation, OntoMate (Literature), QTL, Orthologs, Genomic Region, All...

Analysis and Visualization:

- JBrowse Genome Browser
- Variant Visualizer
- VCMap Synteny Browser (beta)
- OLGA Gene List Generator
- Disease Portals
- Phenotypes and Models
- MOET Multi-Ontology Enrichment
- OntoMate Advanced Literature Search
- GA Tool Gene Annotator

Tweets from @ratgenome

Rat Genome ... @ratge... - Feb 4
Replying to @ratgenome
Use our help pages: rgd.mcw.edu/wg/help3/ or Video Tutorials page for more information: rgd.mcw.edu /wg/home/rgd_r...
Alternatively, RGD offers virtual office hours available by appointment.

Send us a Message

Rat Genome ... @ratge... - Feb 4
Replying to @ratgenome
Find rat strains specific to cancer using: rgd.mcw.edu

B

An ontology-driven, concept-based literature search engine developed at RGD.

Pubmed COVID-19 Preprint

Any ontology/Gene

Enter Search Term Examples: Hypertension, Cancer, A2m

Add term condition More Search Options Clear Form Search OntoMate

C

Help | Video Tutorials | News | Publications | Download | REST API | Citing RGD | Contact

Diseases | Phenotypes & Models | Pathways | Community

Enter Search Term... Search RGD Advanced Search (OLGA) f in

OntoMate

An ontology-driven, concept-based literature search engine developed at RGD.

Pubmed COVID-19 Preprint

Any ontology/Gene

Disease Ontology (RODO)

Drug and Chemical, Experimental Condition, Gene, Mammalian Phenotype, Measurement Methods, Molecular Function, Mouse Anatomy, Mutation, Neuro Behavioral, Organism Taxonomy

Any ontology/Gene

Figure 20.

Navigating to OntoMate, the ontology-driven, literature search tool at RGD.

A

An ontology-driven, concept-based literature search engine developed at RGD.

Pubmed COVID-19 Preprint

Disease Ontology (RDO) hypertension Examples: Hypertension, Cancer, A2m

Add term condition More Search Options Clear Form Search OntoMate

B

Home Data Analysis & Vi

Pathways Community

Advanced Search (OLGA)

Disease Ontology (RDO)

Any ontology

Biological Process

Cell Ontology

Cellular Component

CheBI Ontology

Clinical Measurement

Disease Ontology (RDO)

Drug and Chemical

Experimental Condition

Gene

Mammalian Phenotype

Measurement Methods

Molecular Function

Mouse Anatomy

Mutation

Neuro Behavioral

Organism Scientific Name

Pathway Ontology

Rat Strain Ontology

AND OR Not

Abcc8

Search OntoMate

Figure 21.
OntoMate homepage with search choices of the disease term “hypertension” and the gene “Abcc8”.

A

OntoMate Query Result

Query condition: Disease(hypertension) AND (gene(abcc8)^10 OR text(abcc8))

Year
After 2010 (22)
2000 ~ 2009 (3)
1990 ~ 1999 (2)
Before 1960 (0)

Organisms
Genes
Mutations
Diseases
All
Homo sapiens (22)
Rattus sp. (3)
Rattus norvegicus (2)
Mus musculus (1)
Salvia miltiorrhiza (1)
Sesamum indicum (1)

b

Start Record: 1 Go to Sort by: next
27 results found in 1811 ms
Page 1 of 2

1. PMID: 30484364 Journal Article Research Support, N.I.H., Extramural Research Support, Non-U.S. Govt NCBI page Free PMC Article
Journal of neurotrauma, 2018;11;29, 36(11): 1804-1817
Downstream TRPM4 Polymorphisms Are Associated with Intracranial Hypertension and Statistically Interact with ABCC8 Polymorphisms in a Prospective Cohort of Severe Traumatic Brain Injury.
Jha, Ruchira M; Desai, Shashvat M; Zusman, Benjamin E; Koleck, Theresa A; Puccio, Ava M; Okonkwo, David O; Park, Seo-Young; Shutter, Lori A; Kochanek, Patrick M; Conley, Yvette P;

ABSTRACT show

Disease terms: Intraparenchymal Hypertension Hypertension cerebral edema traumatic brain injury
Genes: > TRPM4 TRPM4 rs8104571 SUR1 > ABCC8 ABCC8/SUR1 > ABCC8 SNPs Human-Core-Exome v1.0 rs150391806 (exon-24 ABCC8 protein ???=?70.0015) ICPs TRPM4 protein rs150391806 SUR1-TRPM4 rs2283261 rs8104571 (intron-20) rs11024286
Mutations: rs8104571 rs150391806 rs2237982 rs2283261 rs11024286
Biological Process Terms: segment
Zebrafish Anatomy Terms: pore Scale
CHEBI Terms: cluster Sulfonylurea Calton Sulfonylurea cohort protein DNA Male
Cellular Component Terms: pore Core
Organism: Homo sapiens
Measurement Method Terms: Scale
Experimental Condition Terms: glyburid
Sequence Ontology Terms: predict downstream region Genotype Single exon intron valid score intron
Mammalian Phenotype Terms: Hypertension cerebral edema
Neuro Behavioral Terms: model

2. PMID: 34309670 Journal Article Research Support, N.I.H., Extramural Research Support, Non-U.S. Govt NCBI page Free PMC Article

a

B

Mouse Anatomy Terms: arteri
Mammalian Phenotype Terms: hypertens inflamm hypoxia
5. PMID: 11030411 Journal Article Research Support, Non-U.S. Govt NCBI page Full Text Article via DOI
Human genetics, 2000;10;13, 107(2): 138-44
Association of a variant in exon 31 of the sulfonylurea receptor 1 (SUR1) gene with type 2 diabetes mellitus in French Canadians
Reis, A.F.; Ye, W.Z.; Dubois-Laforgue, D.; Bellannet, C.; Timsit, J.; Velho, G;

ABSTRACT show
b

Disease terms: type 2 diabetes mellitus pancreat obes hyperinsulinemia hypertens
Genes: SUR1 gene SUR1 insulin ABCC8 protein sulfonylurea receptor 1 G allele T2DM
Biological Process Terms: ago insulin secret sensit
Zebrafish Anatomy Terms: cell
CHEBI Terms: Potassium Sulfonylurea Sulfonylurea ATP ATP Arg protein Male
Molecular Function Terms: Bind
Organism: Homo sapiens
Rat strains: AGA
Experimental Condition Terms: glucos
Sequence Ontology Terms: allel genotyp Exon Bind GeneticMarker variant single nucleotide polymorph
Mouse Anatomy Terms: arteri
Cell Ontology Terms: cell
Mammalian Phenotype Terms: obes pancreat hypertens hyperinsulinemia
Neuro Behavioral Terms: obes sensit

a

ABCC8--hypertension:
Human (IAGP), Rat (ISO), Mouse (ISO)
ABCC8--type 2 diabetes mellitus:
Human (IAGP), Rat (ISO), Mouse (ISO)

d

6. PMID: 10625598 Journal Article Research Support, Non-U.S. Govt Research Support, U.S. Govt, P.H.S. NCBI page Full Text Article via DOI

c

Figure 22.

OntoMate results page for a search of “hypertension” and “Abcc8”. Various features are pointed out (A-a & b, B-a through B-d).

A

MOET - Multi Ontology Enrichment Tool

The New MOET Algorithm (v.2 released in May 2021)*

Select a Species to view enrichment for all RGD ontologies

Rat

Select an Ontology to view enrichment in all RGD species

Disease

Enter Symbols
Please select an identifier type

Affymetrix Array ID GenBank Nucleotide GO Term ID
 Ensembl Gene GenBank Protein Gene RGD ID
 Ensembl Protein Gene Symbol EntrezGene ID

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

(Or)

Enter a Genomic Region

Chr: 1 Start: Stop: Assembly: mRatBN7.2

XP_038959247 Highlight All Match Case Match Diacritics Whole Words Phrase not found

B

Select a Species to view enrichment for all RGD ontologies

Rat

Select an Ontology to view enrichment in all RGD species

Disease

Enter Symbols
Please select an identifier type

Affymetrix Array ID GenBank Nucleotide GO Term ID
 Ensembl Gene GenBank Protein Gene RGD ID
 Ensembl Protein Gene Symbol EntrezGene ID

Abat Abca3 Abcc1 Abcc8 Abc9 Abi2 Abo Acadl Ace
 Ace2 Acsm3 Acta2 Actc1 Acvr11 Ada Adad2 Adam23
 Adamts10 Adamts13 Adamts16 Adamts16em1B
 Adamts17 Adcy5 Add1
 Add2 Add3

(Or)

Enter a Genomic Region

Chr: 1 Start: Stop: Assembly: mRatBN7.2

a

b

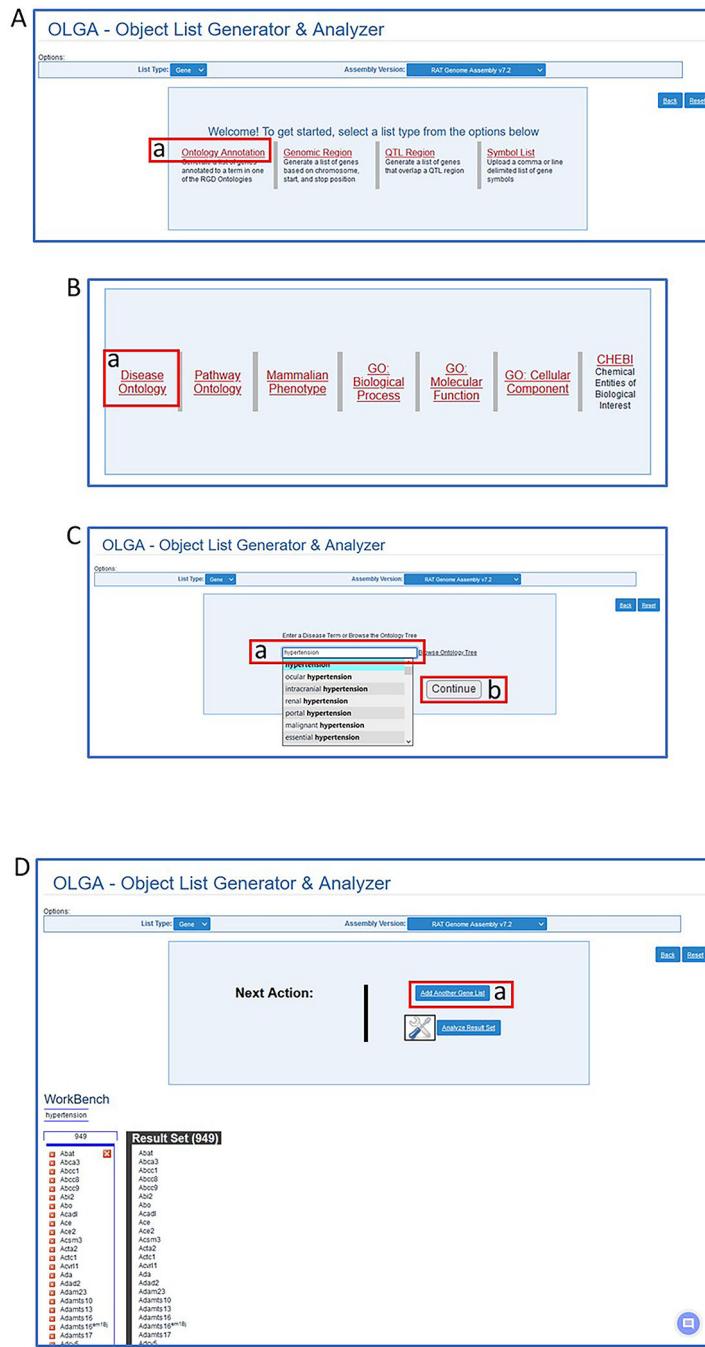
Figure 23.

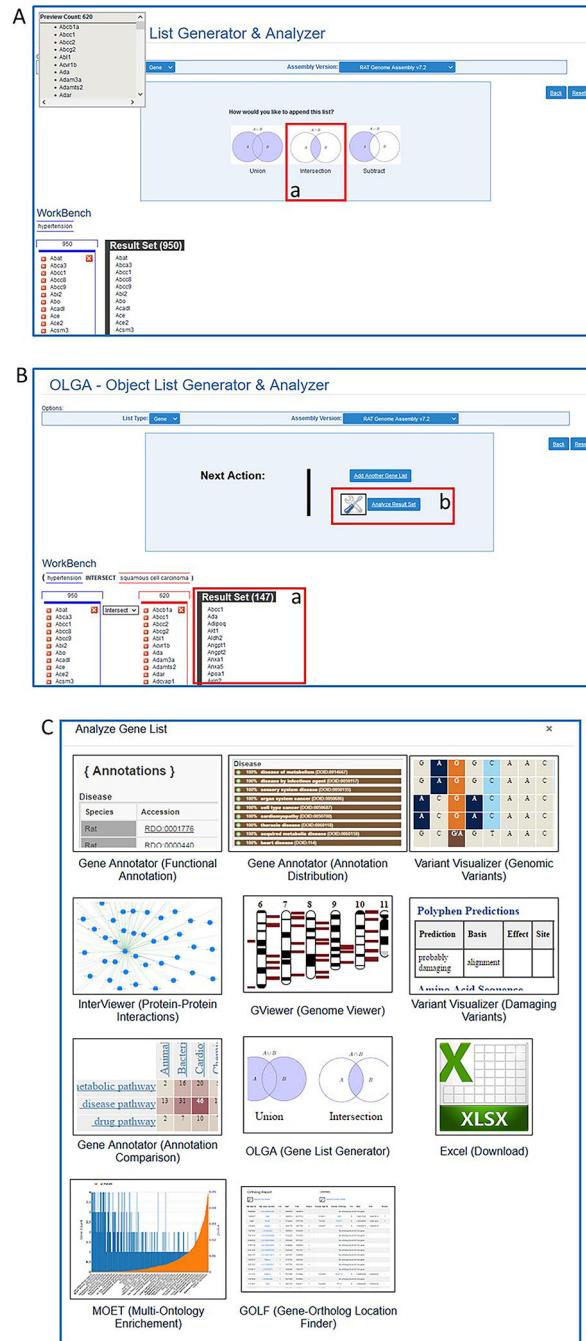
A. MOET tool homepage B. MOET homepage with gene list entered in textbox.



Figure 24.

A. MOET results page with enrichment results for the entered rat gene list and Disease Ontology (default ontology view, table A-b). Data for orthologs in other species are accessed by the tabs shown in A-c. Data for the same genes in other ontologies are accessed by the tabs in A-d. B. Graph of results shown in table (A-b).



**Figure 26.**

A. Further steps in OLGA tool for analysis of two gene lists. B. Final result of overlapping gene sets (B-a) and link to more analysis options (B-b). C. Page of links to other RGD tools for further analysis of final gene result list.

Figure 27.
A. GA tool homepage with sample gene list entered in textbox and option of entering genomic region (A-b). B. Selection page for annotation ontologies, external links, and orthologs desired in search result. C. Result page with annotations for entered gene list (C-a) and further options for results display (C-b).

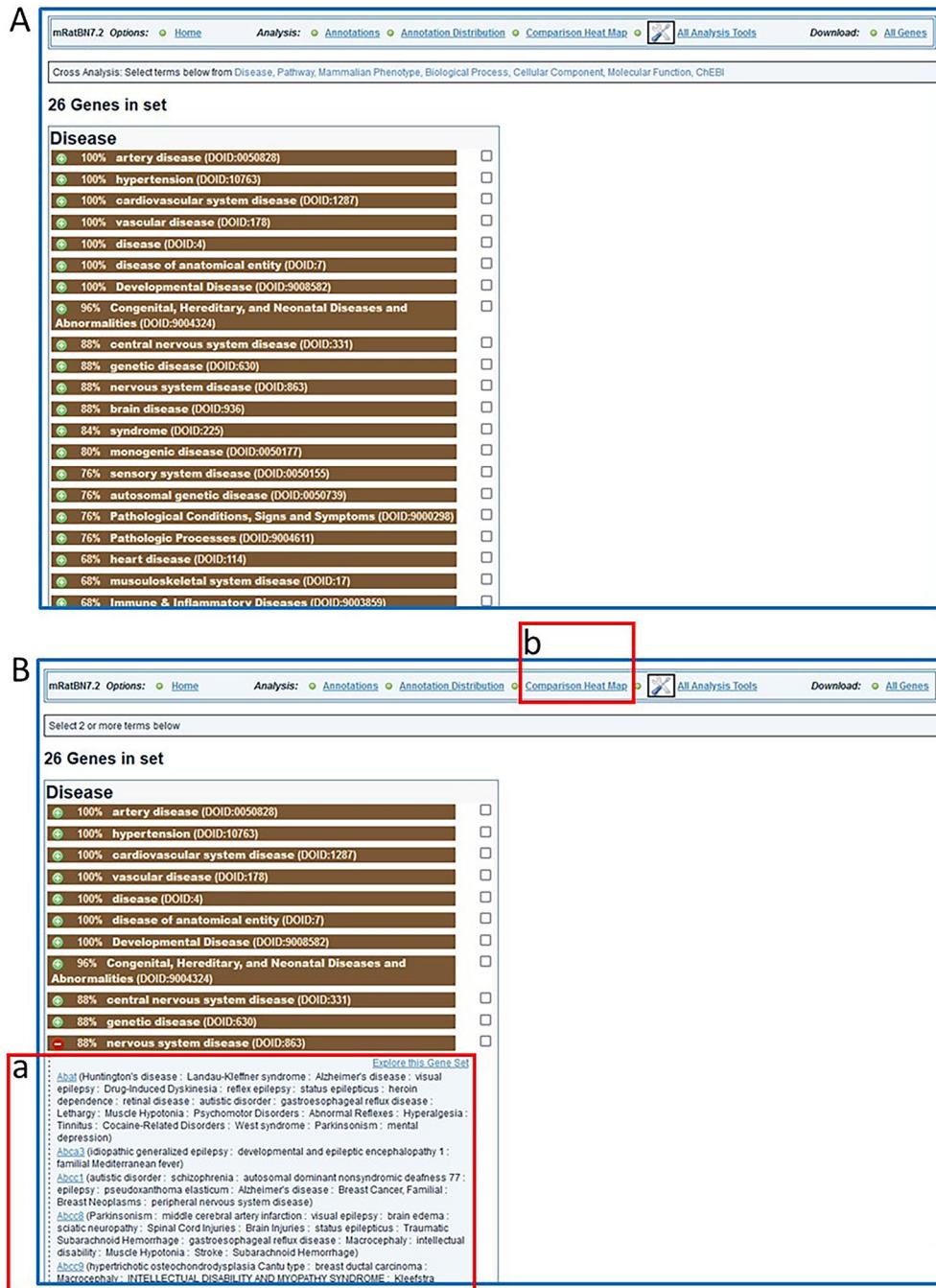


Figure 28.
A. Display of “Annotation Distribution” (enrichment-type analysis). **B.** Details for genes associated with one of the disease terms (nervous system disease, B-a) in the list and link (B-b) to “Comparison Heat Map” analysis.

**Figure 29.**

Display of “Comparison Heat Map” results from data entered in Figure 27 with viewing options (29-a) and a link (29-b) to additional analysis tools.

The screenshot shows the RGD InterViewer homepage. At the top, there is a navigation bar with links for Home, Data, Analysis & Visualization, Diseases, Phenotypes & Models, Pathways, and Community. There is also a sign-in link. Below the navigation bar is a search bar with the placeholder "Enter Search Term..." and a "Advanced Search (OLGA)" button. To the right of the search bar are social media icons for Facebook, Twitter, LinkedIn, and YouTube. The main title "InterViewer - Protein Interactions" is displayed in blue. Below the title is a text input field with the placeholder "Enter a protein or list of proteins to analyse." To the left of this field is a dropdown menu labeled "Select a Species" with "All" selected. Below the species selection is a section for "Enter Protein Identifiers" with instructions: "When entering multiple identifiers your list can be separated by commas, spaces, tabs, or line feeds". A red box labeled "a" highlights the text input field for entering identifiers. To the left of the input field is a list of "Valid identifier types": UniProtKB, Gene RGD ID, and Gene Symbol. At the bottom of the page are links for "Download All Interactions By Species" and "Browse all Rat interactions".

Figure 30.

The Interviewer homepage with textbox (30-a) for entering protein/gene identifiers.

**Figure 31.**

A. The Interviewer results page for rat protein ACADL with graphic display (A-a), data table (A-b), and tool controls (A-c). B. Highlighted gene in graphic with details pane (B-b & B-c) and download options (B-b & B-c).

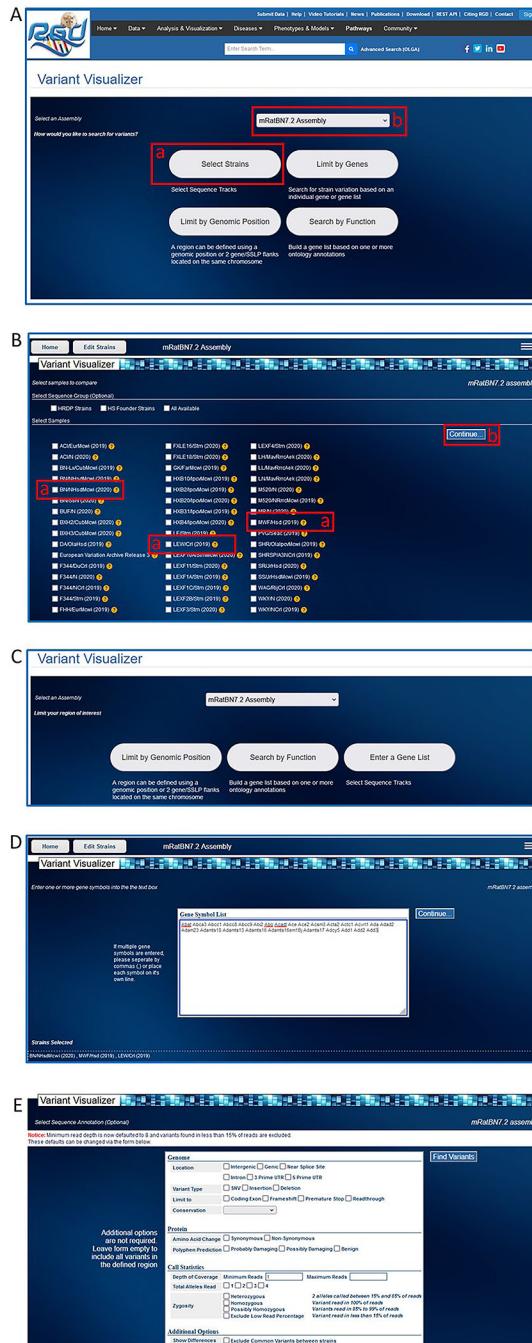
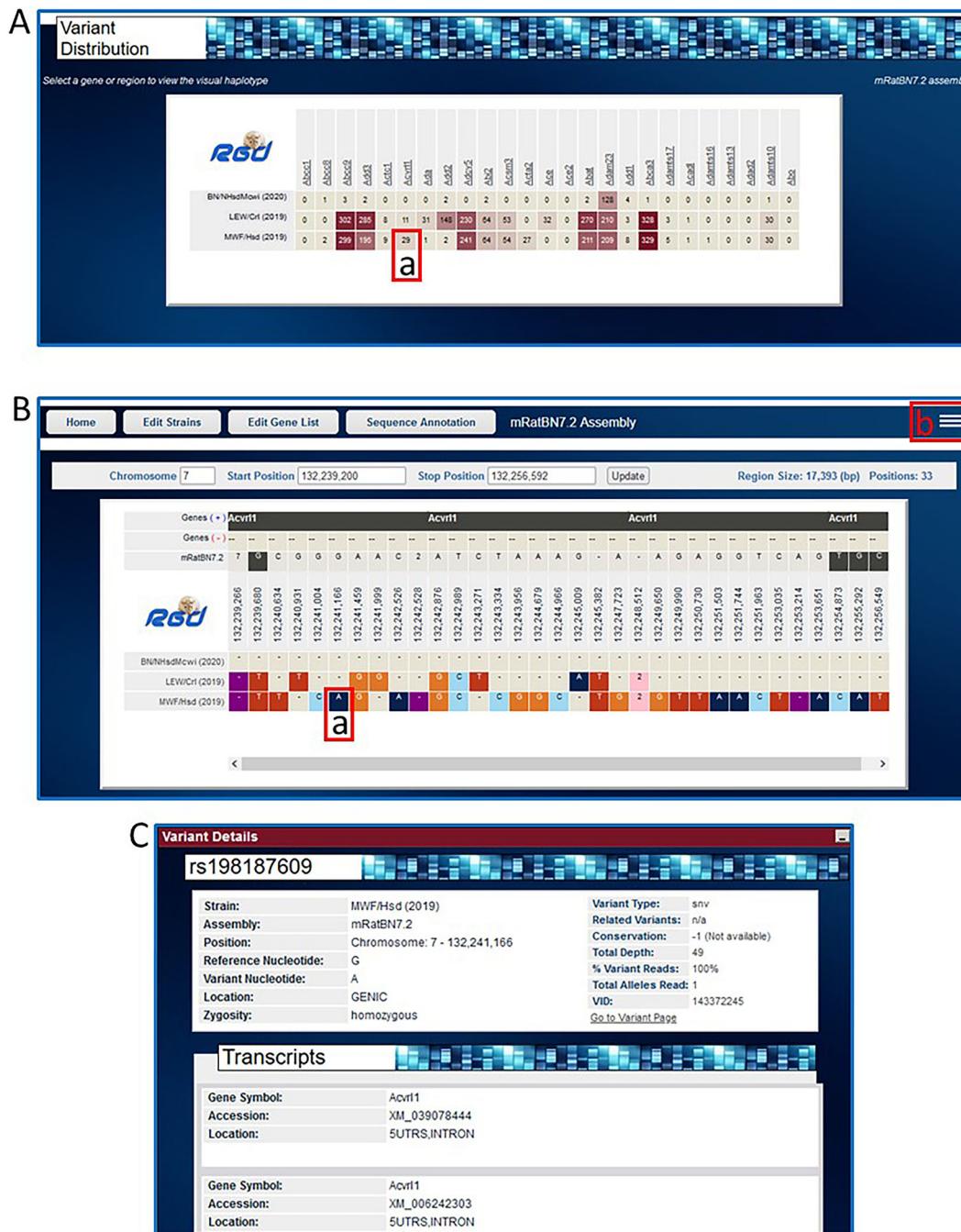


Figure 32.

Steps in use of the Variant Visualizer tool. A. Variant Visualizer homepage showing rat strain selection button (A-a) and default assembly (A-b) ready for analysis. B. Rat strain selection page. C. Options for limiting analysis based on assembly, genomic position, function, and gene(s). D. Entry page for a selected gene list. E. Option page for limiting the analysis.

**Figure 33.**

A. Variant Visualizer results page for the entered genes showing variant distribution across the three selected strains (A-a, Acvr1l in MWF/Hsd). B. Results page showing nucleotide variants for Acvr1l across the three strains compared to the reference assembly mRatBN7.2. Individual color-coded variants (B-a) are linked to detailed pop-up pages (C). Optional views and links to further analysis are available from a pop-up selection box accessed by a link in the upper right corner of the display (B-b).

A

Disease Portals

Welcome to the RGD Disease Portals. These portals are designed to be entry points for disease researchers to access data and tools related to their area of interest. [Click Here](#) for help with the RGD Disease Portals.

About the RGD Disease Portals

RGD has numerous Disease Portals, where relationships between diseases and genes, QTLs and strains can be explored in human, rat, mouse and in the other five species at RGD. The portals contain data sections for eight other ontologies related to the portal disease category, as well as links to visualization / analysis tools and additional information.

Download Data

Disease Ontology (RDO) Annotations - RDO - Gene (8 Species), QTL (Rat & Human) and Rat Strain

- [Ontology Term IDs Only](#)
- [Ontology Term IDs and Text](#)

Aging & Age Related Disease	Cancer & Neoplastic Disease
Cardiovascular Disease a	COVID-19
Developmental Disease	Diabetes
Hematologic Disease	Immune & Inflammatory Disease
Infectious Disease <small>(NEW)</small>	Liver Disease
Neurological Disease	Obesity & Metabolic Syndrome
Renal Disease	Respiratory Disease
Sensory Organ Disease	

B

Cardiovascular Disease Portal

Rattus norvegicus (Rat)

Select a category

Diseases Cardiovascular Disease	Mammalian Phenotype Cardiovascular Disease	Human Phenotype Cardiovascular Disease
Biological Processes Cardiovascular Disease	Pathways Cardiovascular Disease	Chemicals and Drugs Cardiovascular Disease
Vertebrate Traits Cardiovascular Disease	Clinical Measurements Cardiovascular Disease	Experimental Conditions Cardiovascular Disease

Select a species

Rat Genes: 4036 QTL: 704 Strains: 174	Mouse Genes: 4077 QTL: 0	Human Genes: 4511 QTL: 113	Chinchilla Genes: 3649 QTL: 0	Bonobo Genes: 3835 QTL: 0
--	--------------------------------	----------------------------------	-------------------------------------	---------------------------------

Figure 34.

A. RGD Disease Portals homepage with link (A-a) to Cardiovascular Disease Portal. B. Cardiovascular Disease Portal homepage with default selection of “*Rattus norvegicus* (rat)”.

A

Select a term

cardiovascular system disease (DOID:1287)

<< Back

Parent Terms	Term With Siblings	Child Terms
	cardiovascular system disease A disease of anatomical entity which occurs in the blood, heart, blood vessels, lymphatic system, that carries nutrients (such as amino acids and electrolytes), gases, hormones, blood cells or lymph to and from cells in the body to help fight diseases and help stabilize body temperature and pH to maintain homeostasis. (DO)	autoimmune disease of cardiovascular system cardiovascular Abnormalities cardiovascular cancer cardiovascular organ benign neoplasm Cardiovascular Pregnancy Complications Diastolic Dysfunction heart disease vascular disease a

B

Select a term

vascular disease (DOID:178)

<< Back

Parent Terms	Term With Siblings	Child Terms
cardiovascular system disease	autoimmune disease of cardiovascular system Cardiovascular Abnormalities cardiovascular cancer cardiovascular organ benign neoplasm Cardiovascular Pregnancy Complications Diastolic Dysfunction heart disease vascular disease A cardiovascular system disease that primarily affects the blood vessels which includes the arteries, veins and capillaries that carry blood to and from the heart. (DO)	Aneurysm angiodyplasia Angiomatosis anterior ischemic optic neuropathy Arterial Injury Arterial Occlusive Diseases artery disease a capillary disease cerebrovascular disease cholesterol embolism compartment syndrome Embolism and Thrombosis hepatic vascular disease hereditary arterial and articular multiple calcification syndrome

C

Select a term

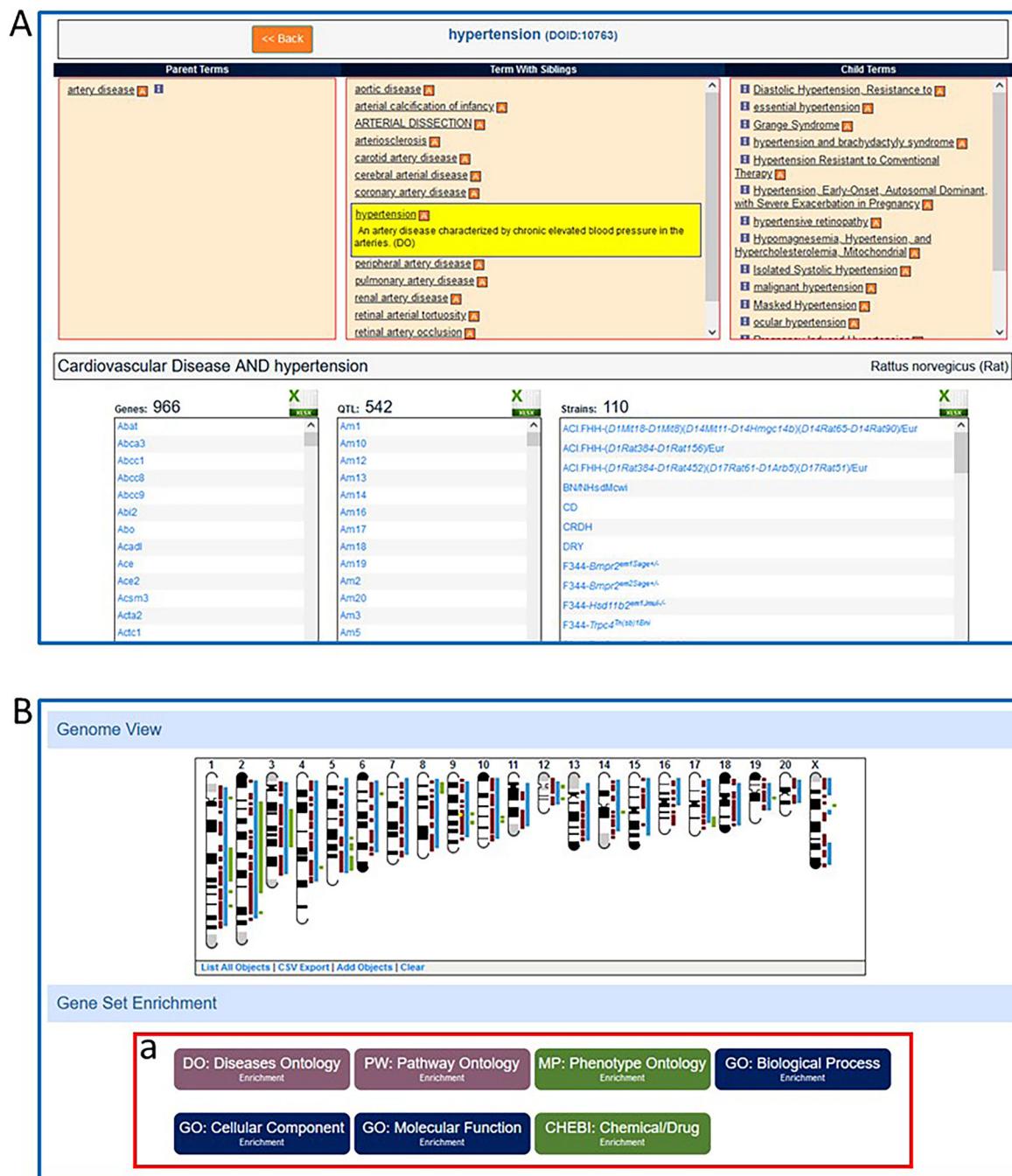
artery disease (DOID:0050828)

<< Back

Parent Terms	Term With Siblings	Child Terms
vascular disease	Aneurysm angiodyplasia Angiomatosis anterior ischemic optic neuropathy Arterial Injury Arterial Occlusive Diseases artery disease A vascular disease that is located in an artery. (DO) capillary disease cerebrovascular disease cholesterol embolism compartment syndrome Embolism and Thrombosis hepatic vascular disease hereditary arterial and articular multiple calcification syndrome	aortic disease arterial calcification of infancy ARTERIAL DISSECTION arteriosclerosis carotid artery disease cerebral arterial disease coronary artery disease hypertension a hypertension pulmonary artery disease renal artery disease retinal arterial tortuosity retinal artery occlusion Sneddon syndrome

Figure 35.

The embedded ontology term browser in the Cardiovascular Disease Portal showing a sequence of selections: A-a. vascular disease B-a. artery disease C-a. hypertension.

**Figure 36.**

A. The embedded ontology term browser in the Cardiovascular Disease Portal showing the selection of “hypertension” and the lists of genes, QTLs, and strains annotated with the term “hypertension”. B. The Cardiovascular Disease Portal page for “hypertension” with an ideogram showing the genomic locations of genes, QTLs, and regions responsible for strains annotated to “hypertension”. B-a. Gene Set Enrichment section of the Cardiovascular Disease Portal page for “hypertension” which shows the option of MOET enrichment analysis of genes in the “hypertension” annotation set.

Phenotypes and Models

Welcome to the Phenotypes & Models Portal within RGD. This portal contains data related to rat strains and phenotypes, as well as essential information for conducting physiological research, identifying disease models, and community forums for gathering feedback from the scientific community. Please feel free to contact us with suggestions for additional data or tools that would help advance your research.

a

PhenoMiner

Rat Strains
Experimental Conditions
Phenotypes
Measurement Methods

Find Models by Disease or Phenotype

Expected Ranges

PhenoMiner Term Comparisons

Phenotypes in other animal models

Strain Availability

Phenotypes

All Rat Genetic Models

Autism Rat Model Resource

Calender

Submit Data

Hybrid Rat Diversity Panel Portal

Phylogenetics

Strain Development

Animal Husbandry

Links and Resources

- Strain Nomenclature
- Strain Submission/Registration

Related Sites

- RGD Disease Portals
- American Physiological Society
- Physiology Online
- National Bio Resource Project
- NHLBI
- American Heart Association
- American Lung Association
- MGD Mouse Strains
- ILAR Lab Codes
- ILAR Resources
- RRRC: Rat Resource and Research Center
- USNW Rat Developmental Stages
- PolyGene Transgenics

Publications

- The Year of the Rat: The Rat Genome Database at 20: a multi-species knowledgebase and analysis platform.
- The Rat Genome Database (RGD) facilitates genomic and phenotypic data integration across multiple species for biomedical research
- Ontology searching and browsing at the Rat Genome Database.
- MOET: a web-based gene set enrichment tool at the Rat Genome Database for multontology and multispecies analyses
- The Rat Genome Database (RGD) facilitates genomic and phenotypic data integration across multiple species for biomedical research.
- PhenoMiner: quantitative phenotype curation at the rat genome database.
- Ontology searching and browsing at the Rat Genome Database.

Selected Reviews

- Rat models of human diseases and related phenotypes: a systematic inventory of the causative genes
- Learning-based animal models: task-specific focal
- Pathophysiological tissue changes associated
- Uric acid: bystander or culprit in hypertension

Figure 37.

The Phenotypes and Models homepage showing the various options of data and tools available, including the PhenoMiner tool (37-a).

A **PhenoMiner Database**
 Select a Category Tab in the lower right panel, then select values from categories of interest and select "Generate Report" to build report

Rat Strains Search for data related to one or more rat strains.	Clinical Measurements Query by clinical measurement.	Measurement Methods Filter results by Measurement method.	Experimental Conditions Filter based condition.
--	---	--	--

Generate Report

Clinical Measurement Selection

b systolic blood pressure
c **systolic blood pressure(1419)**

a **Strains** **Clinical Measurements** **Measurement Methods** **Experimental Conditions**

a **systolic blood pressure**
 alimentary/gastrointestinal measurement(35)
 blood measurement(34530)
 body morphological measurement(12873)
 body movement/balance measurement(347)
 body temperature(1258)
 cardiovascular measurement(21503)
 blood pressure measurement(7215)
 calculated blood pressure(4324)
 central venous pressure(2)
 diastolic blood pressure(909)
 pulse pressure(42)
 maximum rate of positive change in left ventricular systolic blood pressure(46)
 left ventricle end-systolic wall stress(12)

B **Rat Strains**
 Search for data related to one or more rat strains.

<input checked="" type="checkbox"/> SR(6)	Clinical Measurements Query by clinical measurement.	Measurement Methods Filter results by Measurement method.	Experimental Conditions Filter based condition.
--	---	--	--

Generate Report

Rat Strain Selection

b SR
c **select SR(6)**

a **Strains** **Clinical Measurements** **Measurement Methods** **Experimental Conditions**

a **SR(6)**

C **Rat Strains**
 Search for data related to one or more rat strains.

<input checked="" type="checkbox"/> SR(6) <input checked="" type="checkbox"/> SS(6)	Clinical Measurements Query by clinical measurement.	Measurement Methods Filter results by Measurement method.	Experimental Conditions Filter based condition.
--	---	--	--

Generate Report

Experimental Condition Selection

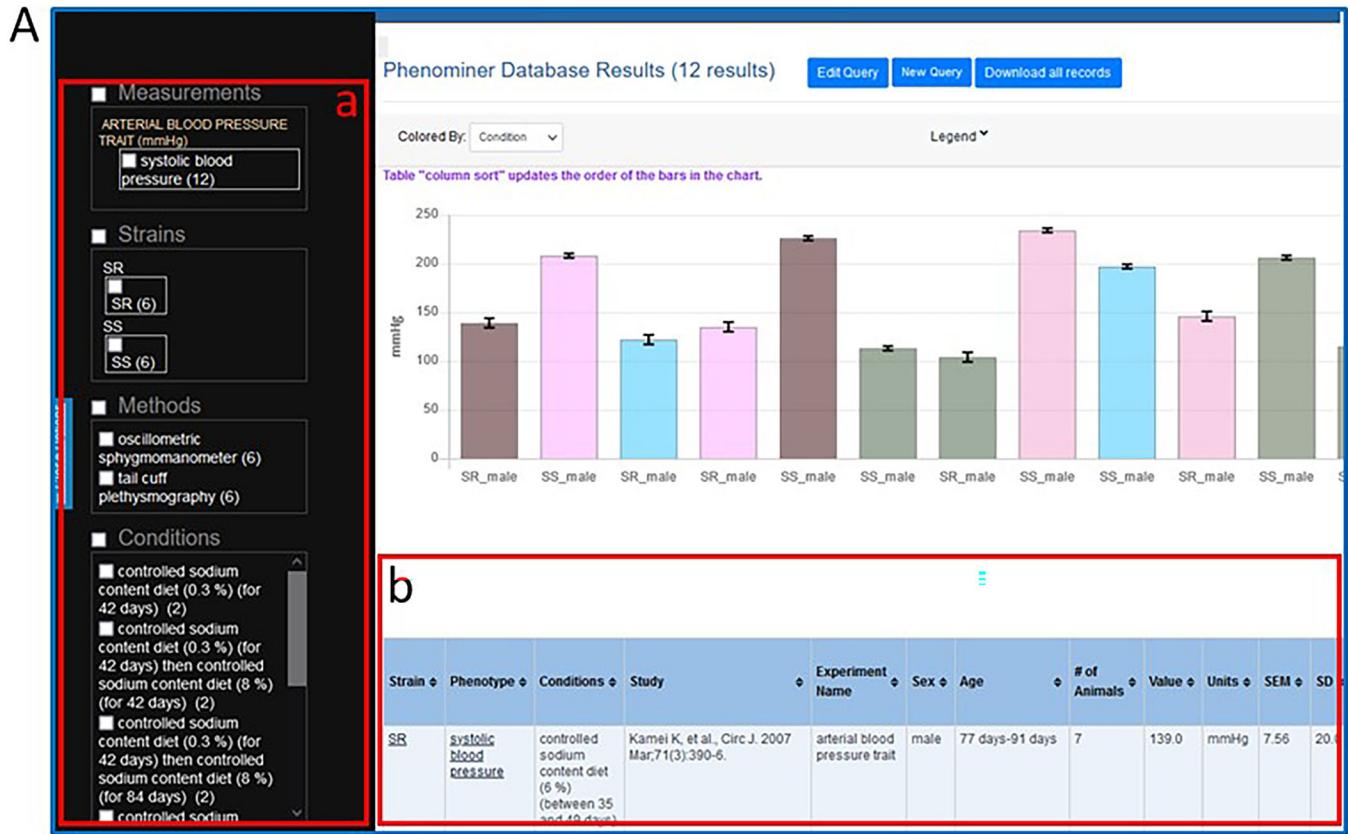
b controlled sodium content diet
c **select controlled sodium content diet(12)**

a **Strains** **Clinical Measurements** **Measurement Methods** **Experimental Conditions**

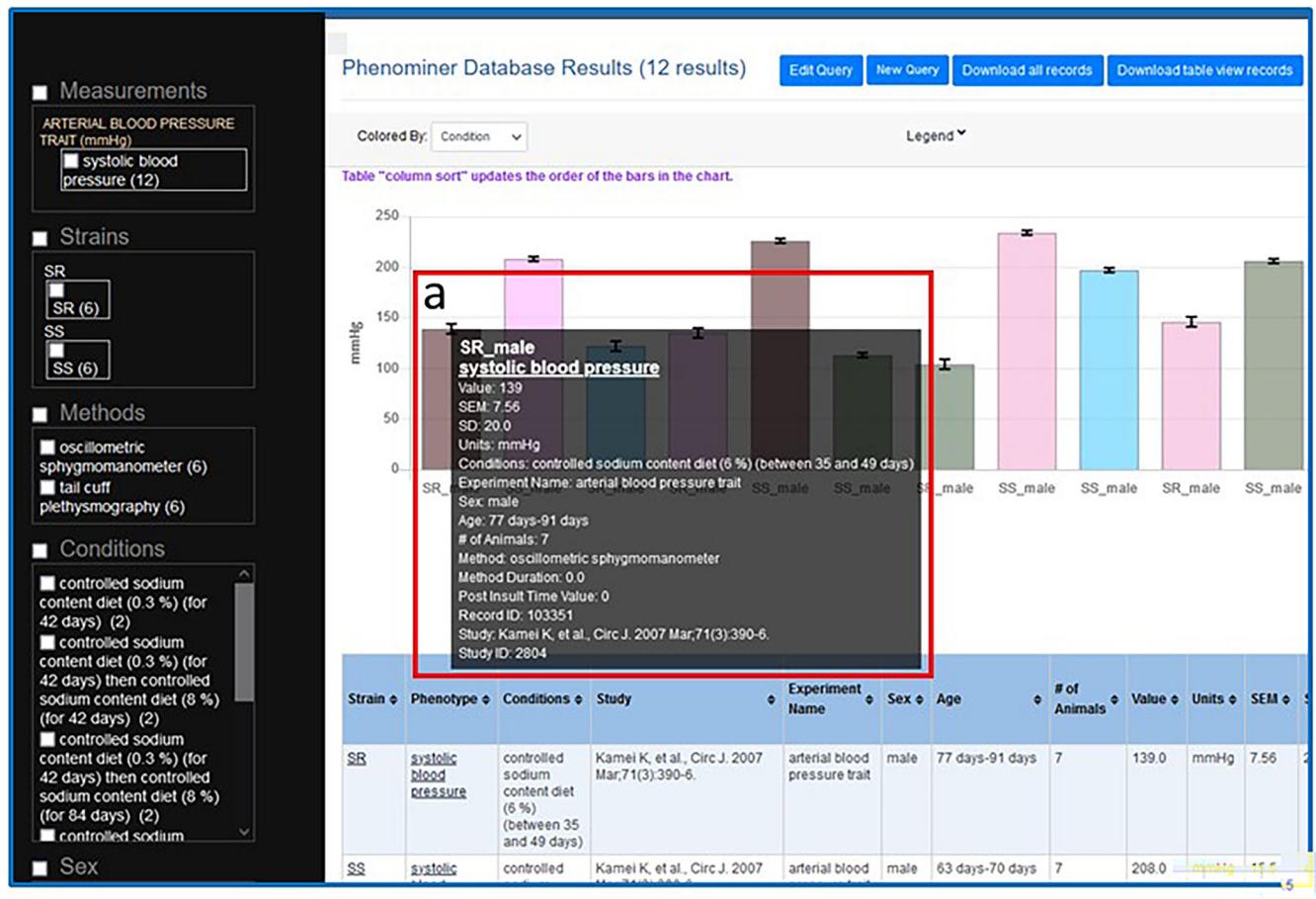
a **diet(12)**
 solid diet(12)
 controlled content diet(12)
 controlled sodium content diet(12)

Figure 38.

Steps in querying the PhenoMiner database. A. After a selection of “Clinical Measurements” (A-a), “systolic blood pressure” is entered in a textbox (A-b) and selected (A-c). B. After a selection of “Strains” (B-a), “SR” is entered in a textbox (B-b) and selected (B-c). C. After repeating B-a, -b, -c for “SS”, “Experimental Conditions” (C-a) is selected, “controlled sodium content diet” is entered in a textbox and selected (C-b), and “Generate Report” is selected to activate the query.

**Figure 39.**

A. The PhenoMiner results page showing the graphed results of the SR/SS/systolic blood pressure/controlled sodium content diet query, the data filtering options (A-a), and the query results in table form (A-b).

**Figure 40.**

The PhenoMiner results page showing the graphed results of the SR/SS/systolic blood pressure/controlled sodium content diet query with details of the first column (a) being shown in a pop-up window when the mouse cursor hovers over the column.

A

The screenshot shows the RGD Pathway Portal homepage. At the top, there is a navigation bar with links to "Submit Data", "Help", "Video Tutorials", "News", "Publications", "Download", "REST API", "Citing RGD", "Contact", and "Sign In". Below the navigation bar is a search bar with the placeholder "Enter Search Term..." and a "Search RGD" button. To the right of the search bar are links for "Advanced Search (OLGA)" and social media icons for Facebook, Twitter, LinkedIn, and YouTube.

The main content area is titled "Molecular Pathway Diagrams". It features two sections: "Individual Diagram Pages" (labeled "a") and "Molecular Pathway Suites and Suite Networks" (labeled "b"). Both sections are highlighted with red boxes. Below each section is a brief description and a link to more information.

Individual Diagram Pages:
These can be accessed directly from the list that catalogs them alphabetically based on the major nodes of the pathway ontology. Alternatively, one can search the pathway ontology for terms of interest; the ontology report page provides an icon with a link to the diagram page if one exists for that term. [Click here](#) to view choices of molecular pathways.

Molecular Pathway Suites and Suite Networks:
The suites and suite networks offer an instant snapshot of pathways that are suites inter-related within a higher order network. The alphabetically listed suites are accessible [here](#).

Pathway-related Publications by RGD Members

Disease models, variants and altered pathways – journeying RGD through the magnifying glass.
Petri V, Hayman GT, Tutaj M, Smith JR, Laulederkind SJ, Wang SJ, Nigam R, De Pons J, Shimoyama M, Dwinell MR. Comput Struct Biotechnol J. 2015 Nov; 14:35-48. PMID: 27602200

Disease pathways at the Rat Genome Database Pathway Portal: genes in context – a network approach to understanding the molecular mechanisms of disease.
Petri V, Hayman GT, Tutaj M, Smith JR, Laulederkind SJF, Wang S-J, Nigam R, De Pons J, Shimoyama M, Dwinell MR, Worthey EA, Jacob HJ. Hum Genomics. 2014 Sep; 8(1):17. PMID: 2526595

The pathway ontology – updates and applications.
Petri V, Jayaraman P, Petri V, Tutaj M, Liu W, De Pons J, Laulederkind SJ, Lowry TF, Nigam R, Wang SJ, Shimoyama M, Dwinell MR, Munzenmaier DH, Worthey EA, Jacob HJ. J Biomed Semantics. 2014 Feb; 5:1. PMID: 24499703

The updated RGD Pathway Portal utilizes increased curation efficiency and provides expanded pathway information.
Hayman GT, Jayaraman P, Petri V, Tutaj M, Liu W, De Pons J, Dwinell MR, Shimoyama M, Worthey EA, Munzenmaier DH, Jacob HJ. Hum Genomics. 2013 Feb; 7(1):4. PMID: 23379628

Pathway Resources at the Rat Genome Database: A Dynamic Platform for Integrating Gene, Pathway and Disease Information.
Petri V, Oshiro K, Hayman GT, Dwinell MR, Jacob HJ. *J Clin Pathol*. 2014; 67(10):733-738. doi: 10.1136/jcp.2014.133304

B

The screenshot shows the RGD Pathway Portal homepage. At the top right is a "Play the RGD Video Tutorial" button. The main content area is titled "Molecular Pathways".

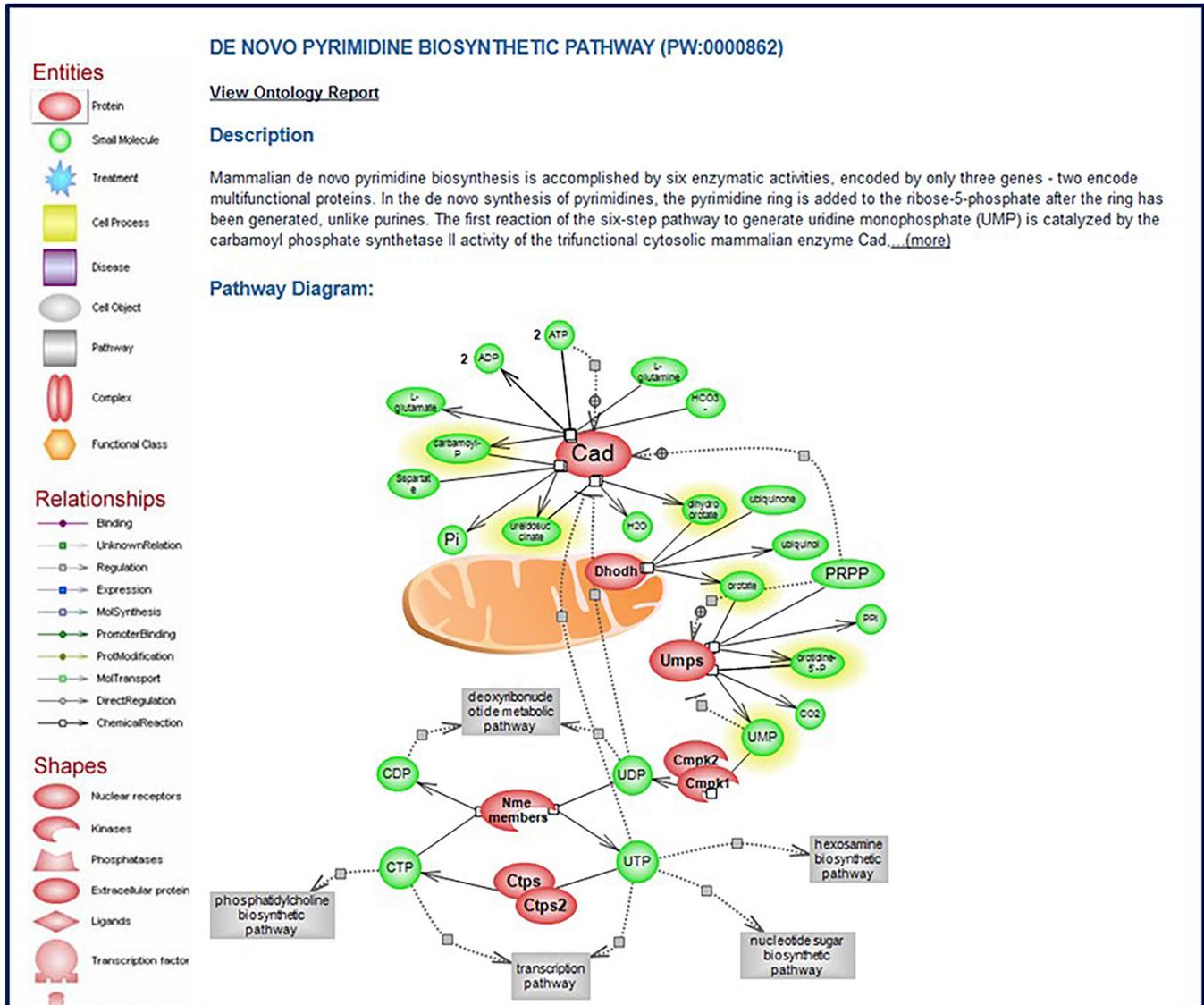
Interactive Pathway Diagrams:
Each pathway diagram contains links to genes and related pathways. Additional diagrams will be added on a regular basis, so check back often.

RGD Pathway Suites and Suite Networks:
Pathways that revolve around a concept and are globally related are brought together within a pathway suite. When two or more suites are needed to capture distinct aspects of that concept, they are brought together within a pathway suite network. Pathway suites and suite networks offer an instant snapshot of these broader, system-level views of connected molecular pathways. To explore such suites of related pathways and suite networks of related suites, click any of the links below.

- Balancing Blood Pressure Regulatory Mechanisms Pathway Suite Network
 - Mechanisms Mediating and Pertinent to Increased Blood Pressure Pathway Suite
 - Mechanisms Mediating and Pertinent to Decreased Blood Pressure Pathway Suite
 - Mechanisms Mediating and Pertinent to Both Increased and Decreased Blood Pressure Pathway Suite
- Balancing Inflammatory Responses Pathway Suite Network
 - Anti-inflammatory HPA Axis, Interleukin-10 and Related Pathways Suite
 - Pro-inflammatory Nuclear Factor kappa B, Toll-like Receptor, Interleukins and Related Signaling Pathways Suite
- Beta Adrenergic Receptor Pathway Suite
- Calcium Homeostasis Pathway Suite
- Developmental Pathway Suite
- DNA Damage Response Pathway Suite
- Doxorubicin Pathway Suite
- Energy Homeostasis Pathway Suite
- Estrogen Pathway Suite
- Gene Expression and Regulation Pathway Suite Network
 - Epigenetic Regulation/Control – Chromatin Modification/Remodeling Pathway Suite
 - Transcription and Transcription-Coupled Events Pathway Suite
 - RNA maturation, Transport and Surveillance (QC) and Protein Translation Pathway Suite
- Glucose Homeostasis Pathway Suite Network
 - Pathway Suite for the Glucose Homeostasis-related Regulatory and Signaling Pathways
 - Pathway Suite for the Metabolism of Glucose and Related Molecules Pathways

Figure 41.

A. Homepage of the RGD Pathway Portal showing the options of “Molecular Pathway Diagrams” (41-a) and “Molecular Pathway Suites and Suite Networks” (41-b), links that lead to the pathway diagrams homepage (41B). B. Pathway diagram homepage with links to all pathway diagrams in RGD, including “de novo pyrimidine biosynthetic pathway” (B-a).

**Figure 42.**

The pathway diagram page for “de novo pyrimidine biosynthetic pathway” (PW:0000862).

A Genes in Pathway:

Rat Mouse Human All show annotations for term's descendants Sort by symbol ↑ asc

[download](#) view all columns

de novo pyrimidine biosynthetic pathway

Symbol	Object Name	JBrowse	Chr	Start	Stop	Reference
G Cad	carbamoyl-phosphate synthetase 2, aspartate transcarbamylase, and dihydroorotate	JBrowse	6	26,657,507	26,680,459	RGD:5133412
G Cmpk1	cytidine/uridine monophosphate kinase 1	JBrowse	5	133,759,722	133,786,452	RGD:5133414
G Cmpk2	cytidine/uridine monophosphate kinase 2	JBrowse	6	45,683,242	45,694,824	RGD:5133256
G Clps1	CTP synthase 1	JBrowse	5	139,475,934	139,505,065	RGD:5133414
G Clps2	CTP synthase 2	JBrowse	X	33,383,087	33,522,852	RGD:5133410

B Additional Elements in Pathway:

(includes Gene Groups, Small Molecules, Other Pathways..etc.)

Object Type	Pathway Object	Pathway Object Description
Small Molecule	ADP	adenosine diphosphate
Small Molecule	ATP	adenosine triphosphate
Small Molecule	CDP	cytidine diphosphate
Small Molecule	CTP	cytidine triphosphate
Functional Class	Nme members	members of the nucleoside diphosphate kinase family

C Pathway Gene Annotations

Disease Annotations Associated with Genes in the de novo pyrimidine biosynthetic pathway

Diseases/Genes	Genes/Diseases
alkaptonuria	Umps
arteriosclerosis	Nme2
autistic disorder	Cts2
autosomal dominant dyskeratosis congenita	Dhodh

D Pathway Annotations Associated with Genes in the de novo pyrimidine biosynthetic pathway

Pathways/Genes	Genes/Pathways
2-hydroxyglutaric aciduria pathway	Cad
adefovir pharmacokinetics pathway	Nme1 , Nme2
adenine phosphoribosyltransferase deficiency pathway	Nme6
adenosine monophosphate deaminase deficiency pathway	Nme6

E Phenotype Annotations Associated with Genes in the de novo pyrimidine biosynthetic pathway

Phenotype/Gene	Gene/Phenotype
decreased metastatic potential	Nme2

Figure 43.

Additional sections of the “de novo pyrimidine biosynthetic pathway” diagram page which appear below the diagram on the webpage. A. “Genes in Pathway”: A list of genes with annotations to the title term of the diagram and to child terms of the title pathway from the Pathway Ontology. B. “Additional Elements in Pathway” is a list of small molecules and a gene group. C. “Pathway Gene Annotations” is a list of disease terms associated with the genes involved in the diagrammed pathway. This list toggles between disease term to genes and gene to disease terms. D. A list of additional pathways with which the

diagrammed pathway genes are involved. This list toggles between pathway term to genes and gene to pathway terms. E. A list of phenotype terms associated with the genes involved in the diagrammed pathway. This list toggles between phenotype term to genes and gene to phenotype terms.

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