The Virtual Comparative Map tool at the Rat Genome Database facilitates comparative and translational studies

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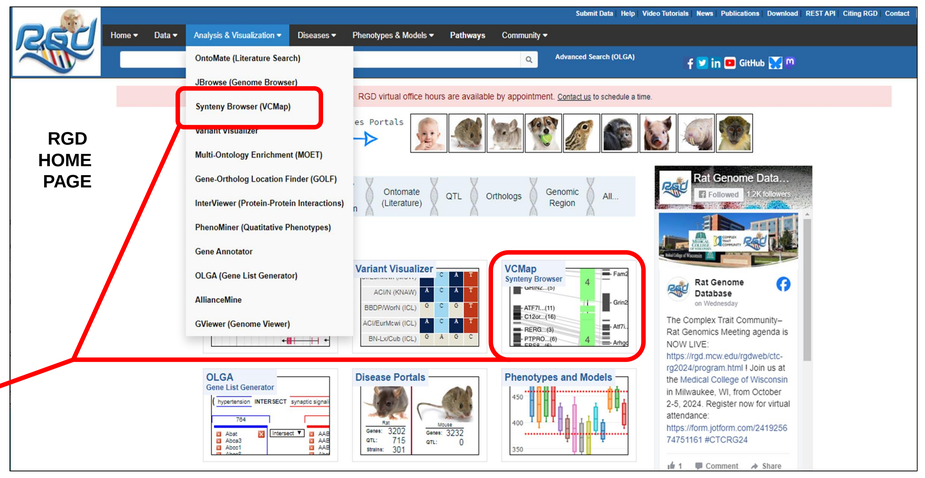
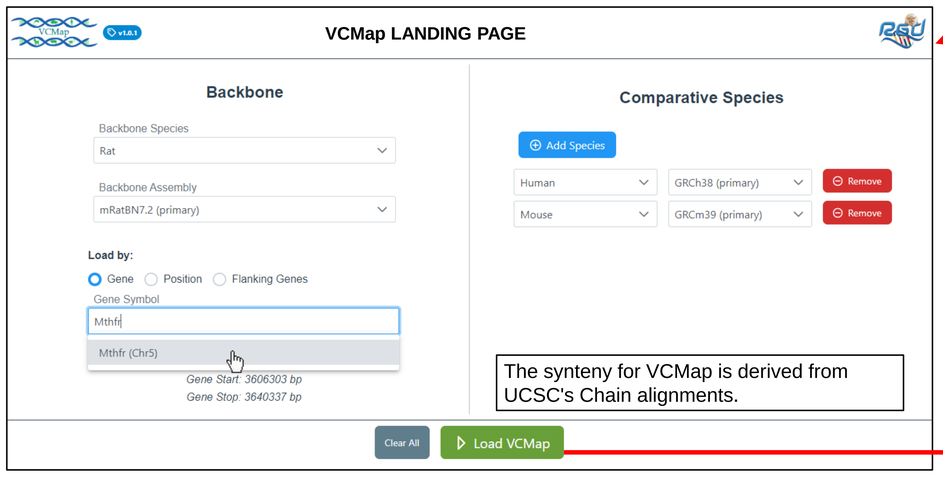
https://rgd.mcw.edu

Photography permitted

Abstract:

Rat Genome Database (RGD, https://rgd.mcw.edu), a cross-species knowledgebase and the premier online resource for rat genetic and physiologic data, has recently added an updated and expanded version of the Virtual Comparative Map tool (VCMap) to its suite of innovative analysis tools. VCMap was originally developed as a web application using rat and human radiation hybrid maps. An intermediate Java applet version included early genome assemblies of rat, mouse and human, and added agricultural species cow, pig, horse and chicken. The current version uses a synteny algorithm and multiple earlier and current genome assemblies of six species: rat, human, mouse, pig, bonobo and green monkey, with the addition of more species and genome assemblies in development. Substantial improvements have been made to performance and navigation. Examining syntenic regions across up to six species at the same time is possible, and comparing additional species, as well as comparing different assemblies of the same species will be possible in the future. A use case scenario is be presented involving interspecies gene synteny determination and analysis. In addition to genes, tracks for data such as genomic variant densities can be added to the display. The improved and expanded VCMap tool provides valuable functionality for researchers engaging in comparative genomics and translational medicine.





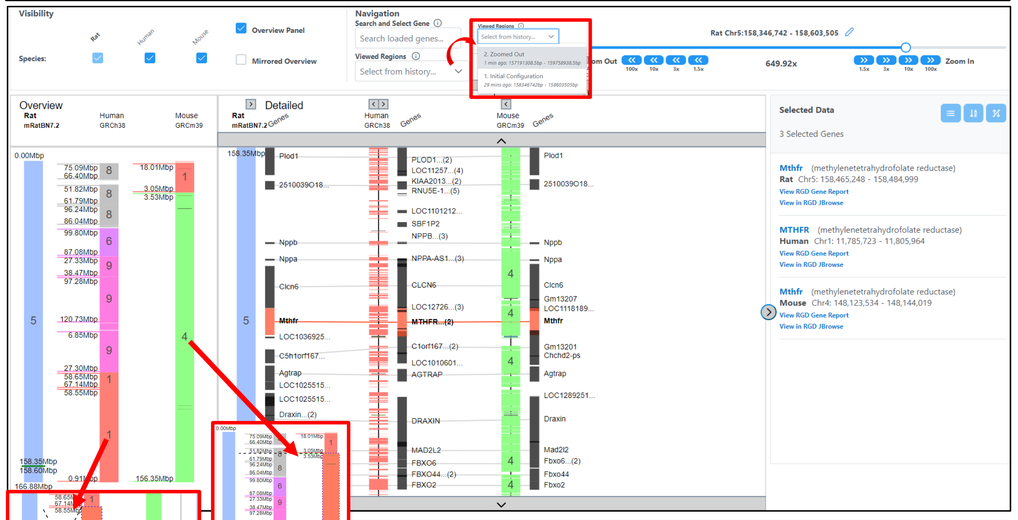
The Virtual Comparative Map (VCMap) is an innovative tool designed to allow comparisons of syntenic regions across multiple species. Currently the tool has data for rat, human, mouse, pig, bonobo and green monkey. Additional species will be added, as well as the ability to compare different genome assemblies within the same species.

Select a backbone species and a genomic region to view, then choose one or more comparator species. The region can be specified by entering a gene, a chromosomal position or two flanking genes.

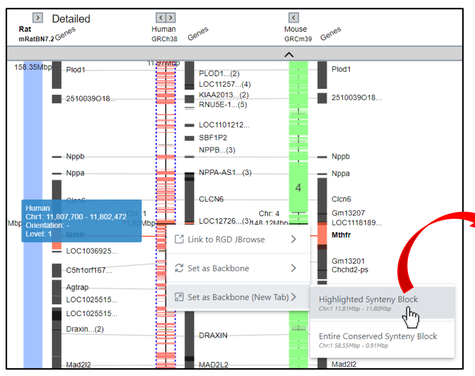
The synteny for VCMap is derived from UCSC's Chain alignments.

The browser window consists of four sections, navigation at the top, an overview panel at the left, the detail panel in the center and a sidebar on the right which shows information about selected objects such as genes or orthology groups. In the overview panel, hover over a synteny block to see information about the block, including its orientation relative to the corresponding block on the backbone.

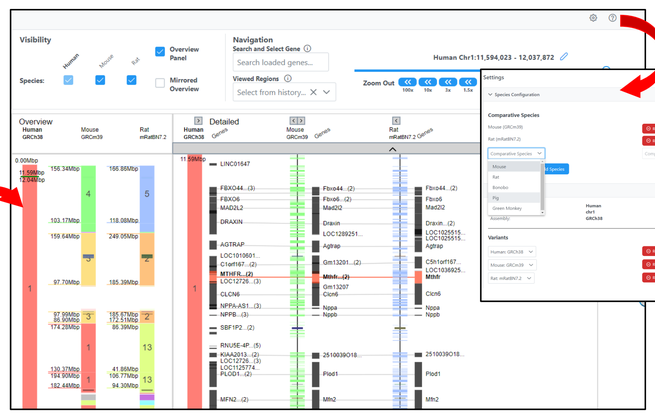
Show/hide species, change the order of the species, search for a gene within the current view, access previous views from the current session, and zoom the detail display using functions in the top section of the page.



In VCMap, syntenic blocks are aligned so that the orthologs, indicated by grey or red connecting lines, appear in the same order for the comparison species as they do for the backbone. Since the syntenic block that contains the Mthfr gene is reversed in human compared to both rat and mouse, it is shown in the opposite direction as demonstrated by the higher chromosomal position at the top of the block and the lower number at the bottom in the overview and the crossed lines between the rat and human blocks (left callout).

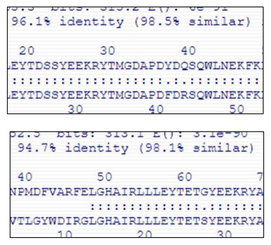


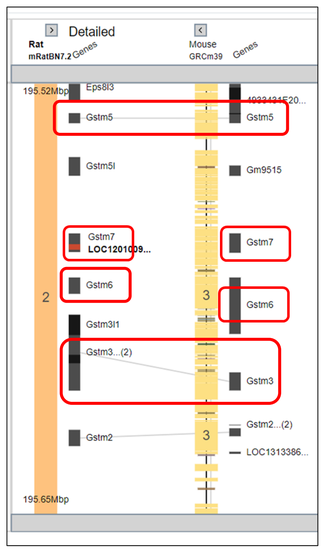
To switch which species is shown as the backbone, right click on a synteny block in the detail view.

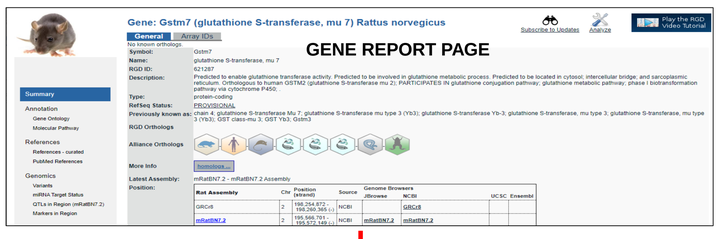


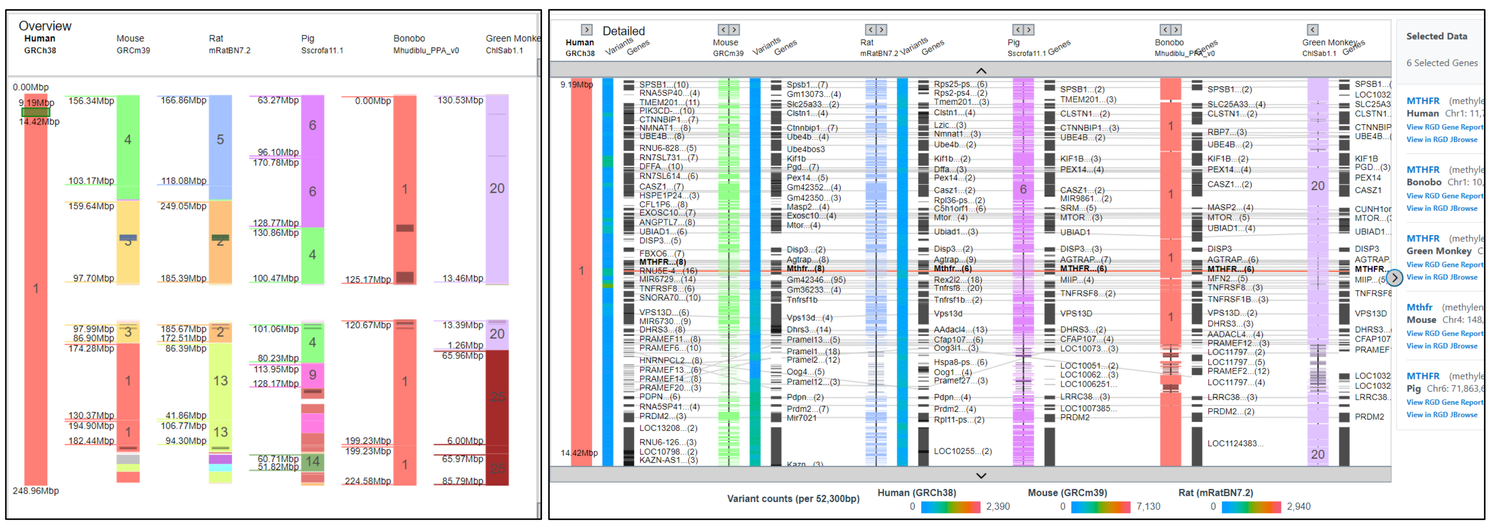
Changing the backbone species from rat to human makes it possible to add additional species to the display based on the synteny data available. As shown in the callout, the "Settings" icon provides access to a popup page where species can be added or removed and additional data tracks, currently variant density tracks, can be added to the display.

USE CASE:
Assigning rat-mouse orthologs based on synteny using VCMap and percent protein sequence identity determined by an alignment tool.









With human as the backbone, all five additional species can be compared showing MTHFR orthologs in all of the species. For human, mouse and rat, heatmaps show variant density. Human variants are imported from ClinVar and the GWAS Catalog and mouse variants are imported from the European Variant Archive. Rat variants are derived from whole genome sequencing of multiple rat strains as part of Dr. Mindy Dwinell's Hybrid Rat Diversity Project here at the Medical College of Wisconsin. Mouse over a bin to see the number of variants in that segment.

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