Rat Variant Resources for Cardiovascular Disease Research

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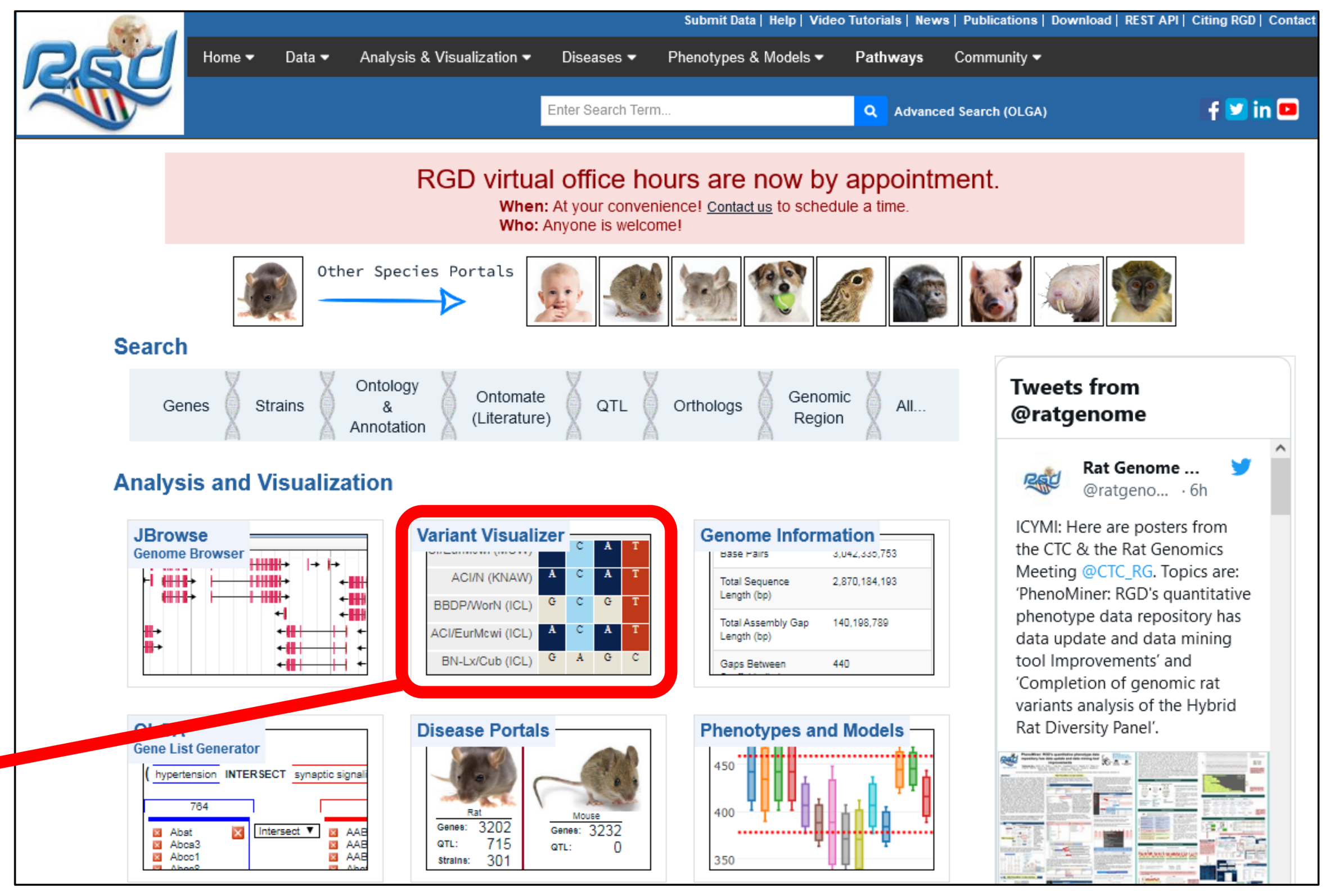
Rat Genome Database
http://rgd.mcw.edu

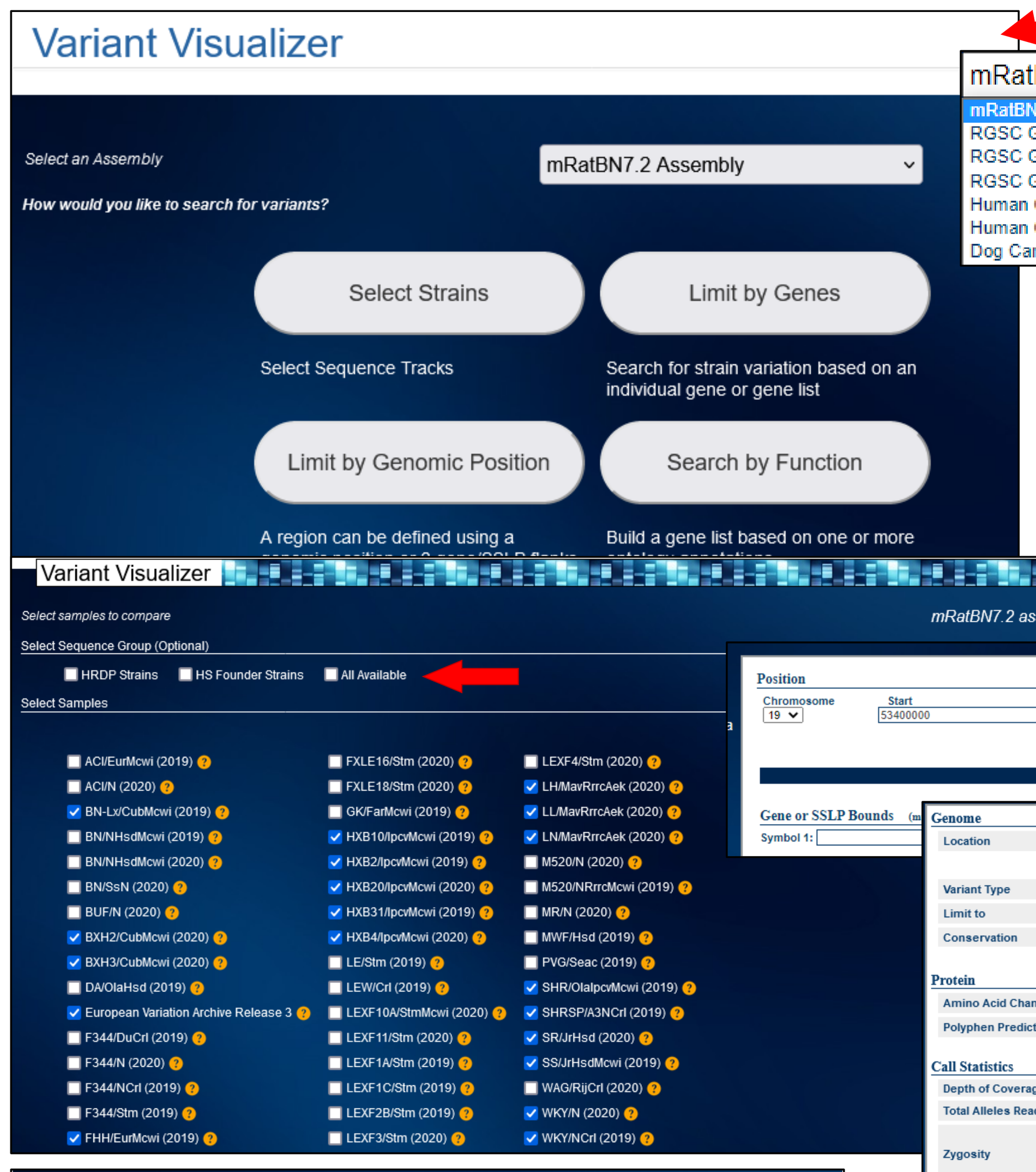
Abstract:

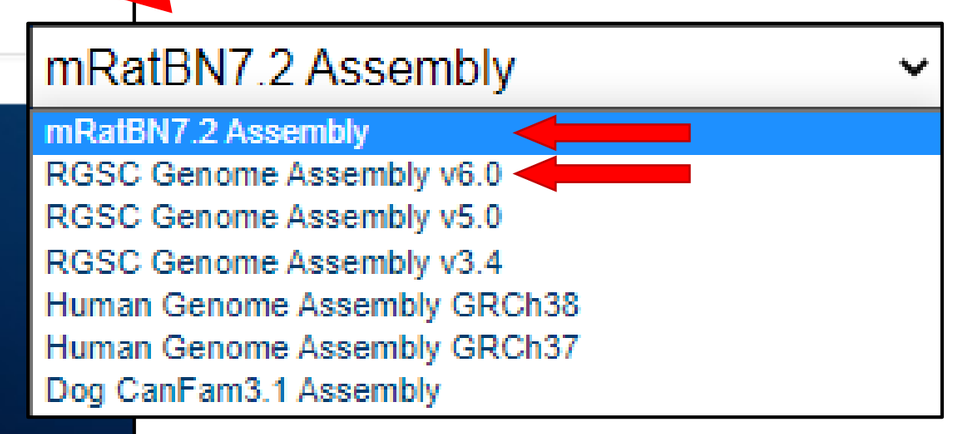
The Rat Genome Database (RGD, https://rgd.mcw.edu) is the premier online location for genomic, genetic, phenotypic and disease-related data for the laboratory rat, as well as an integrated resource for comparative data for nine other mammalian species. RGD's Variant Visualizer is a data mining and visualization tool for genomic variants from whole genome sequencing of rat strains mapped against both the Rnor6.0 and mRatBN7.2 assemblies. Most of these strains are part of the Hybrid Rat Diversity Panel (HRDP), a panel of inbred rat strains selected for their genetic diversity. For a genomic region of interest or a list of genes, researchers can compare sequence variations across cardiovascular disease and hypertension models, normotensive controls, and a number of Recombinant Inbred (RI) strains. For comparative purposes, Variant Visualizer also provides access to human clinical (ClinVar) variants and to variants for 75 dog breeds.

For an even more divergent view of sequence variations and their consequences, researchers can explore cross-species variants across six phylogenetically diverse model organisms and human at the Alliance of Genome Resources (https://www.alliancegenome.org), of which RGD is a founding member. The Alliance houses variation data from all of these organisms based on both high-throughput whole genome sequencing and manually curated phenotypic alleles. Where the data is available, the Alliance allele record links the disease and/or phenotype(s) that result from the alteration of a gene with the causative variant in that model organism. In addition, the Alliance provides disease and phenotype annotations for human genes along with a rich dataset of information.

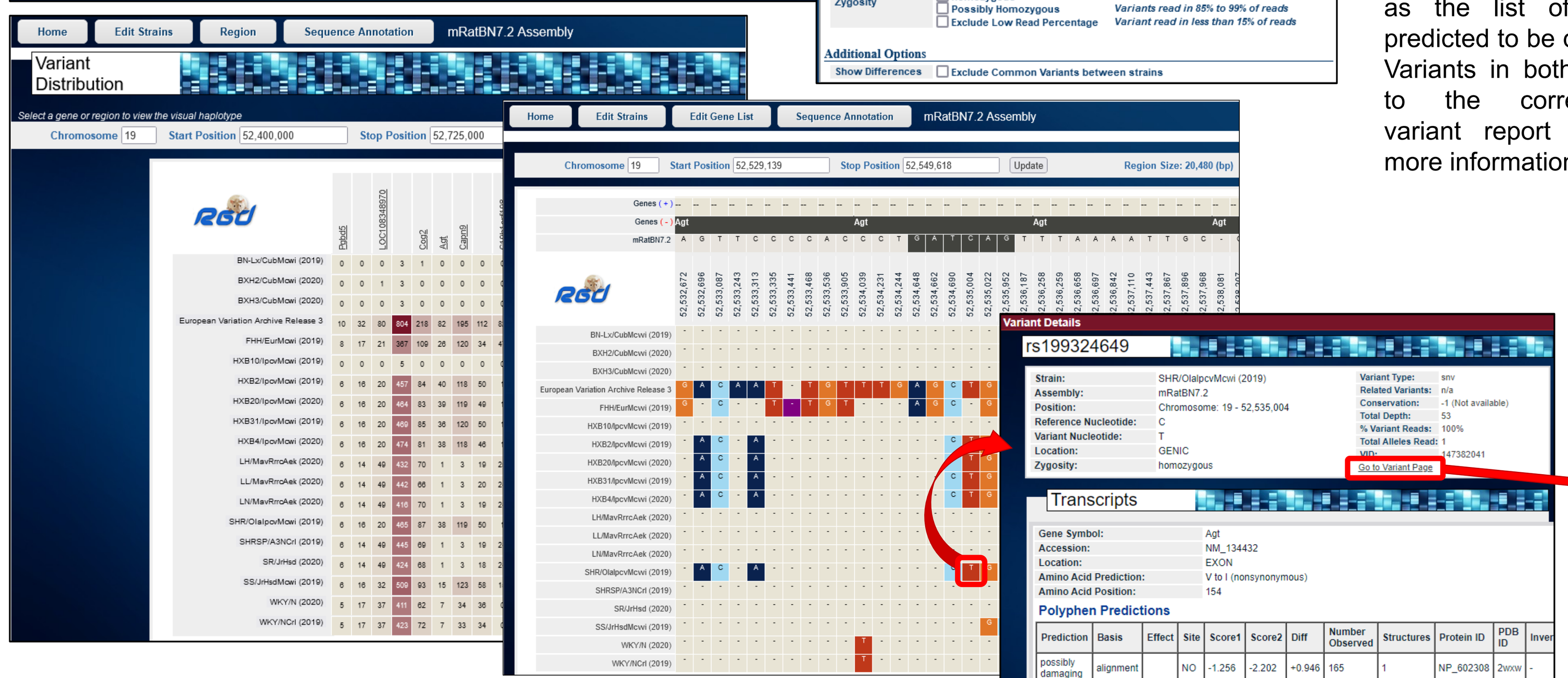


RAT VARIANT VISUALIZER





Variant Visualizer contains genomic variant data for multiple assemblies in rat, human and dog. Rat variants are derived from WGS of rat strains, e.g., from the Hybrid Rat Diversity Panel and the founder strains of the Heterogeneous Stock rats, or are imported from the EVA.

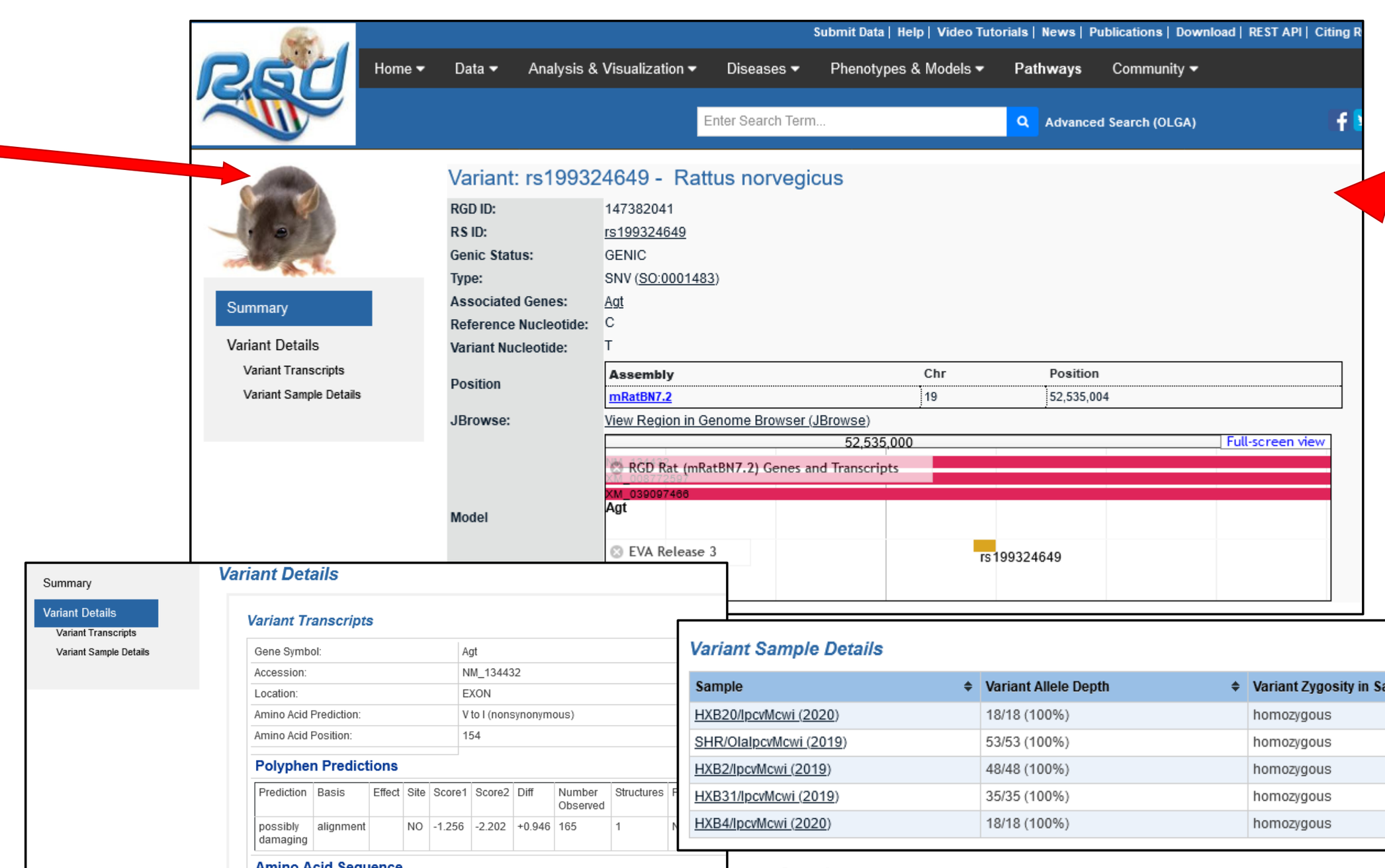


Select a group of strains such as the HRDP strains or the HS founders, and/or choose one or more individual strains. Explore variants in a region of interest or enter a list of genes to retrieve associated variants. Results can be filtered by type or location of the variants, or by Polyphen predictions of damage. For a region of interest an overview of the number of variants per gene and intergenic region is shown. Click on a gene to see all variants in the selected strains. Choose a variant to see additional details about the nucleotide and, where applicable, the amino acid change, zygosity, read depth and variant details, Polyphen predictions of damage. A link is provided to RGD's new Variant report page which provides additional information.

RGD GENE AND VARIANT PAGES

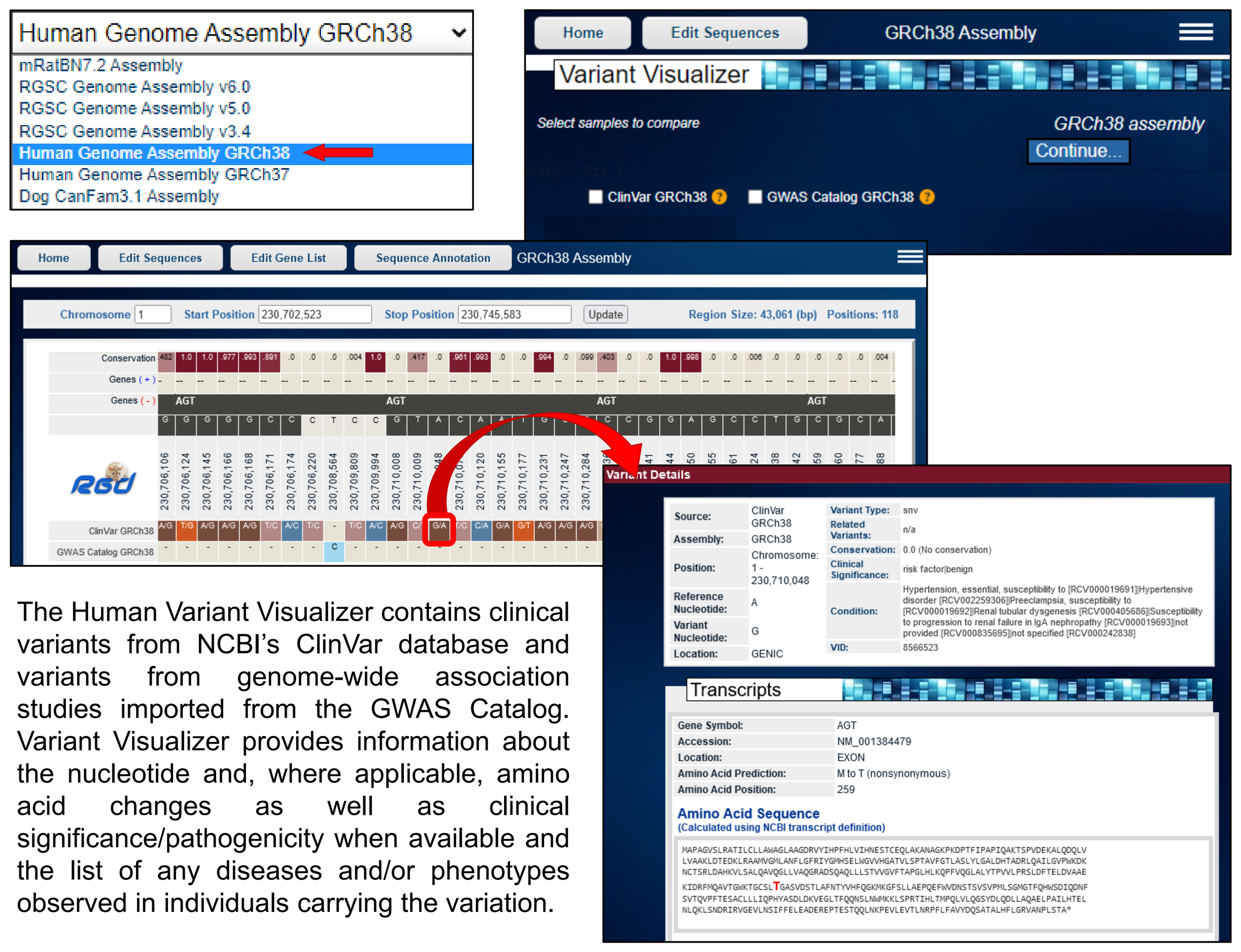
RGD's gene report page gives a link to a list of variants found in that gene as well as the list of variants predicted to be damaging. Variants in both lists link to the corresponding variant report page for more information.

RGD gene pages link to gene pages at the Alliance.



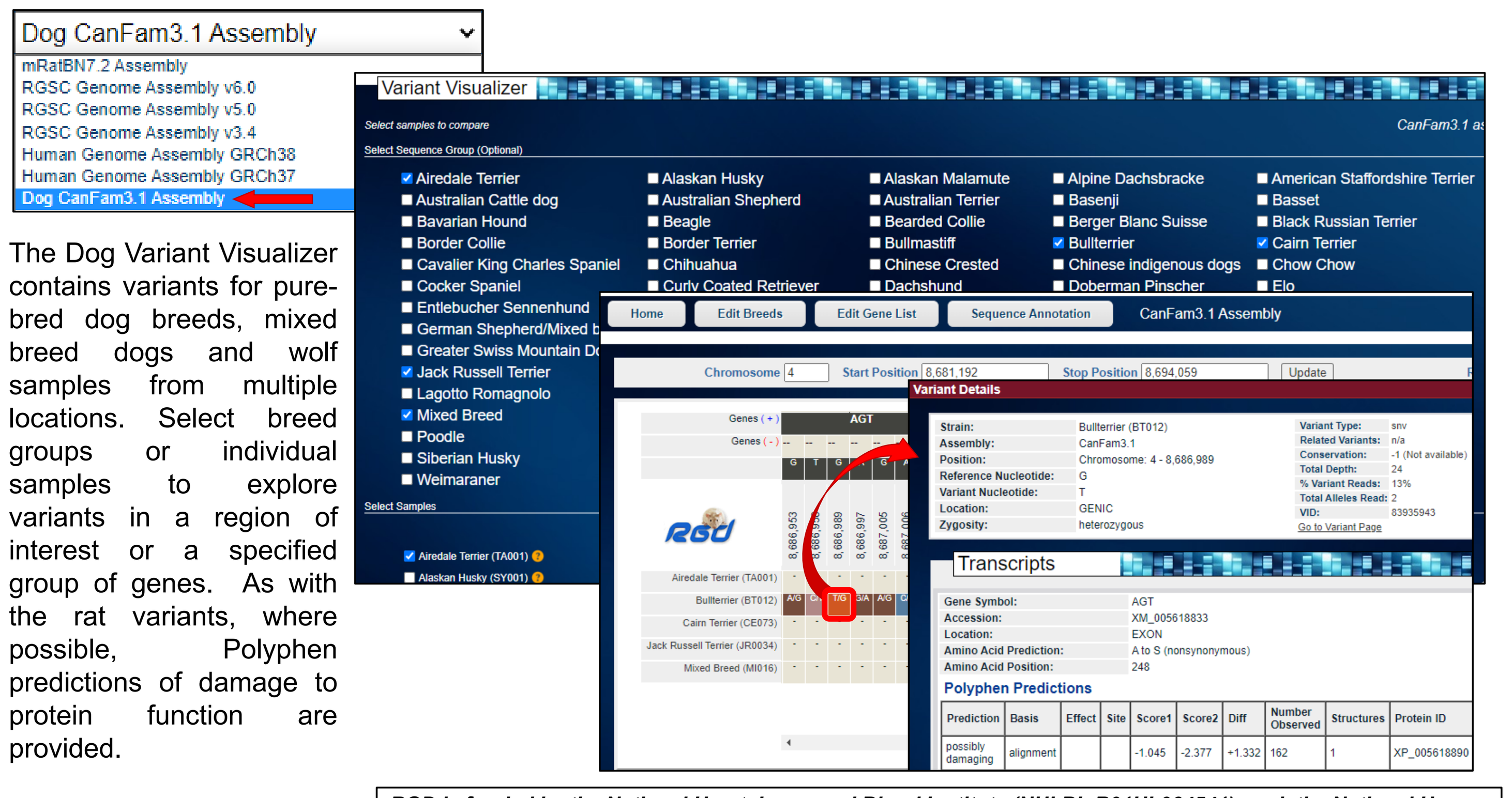
RGD's variant report page provides details about the variant location, transcript- and protein-level consequences, and the variant allele depth and zygosity for each strain sample in which the variant was seen.

HUMAN VARIANT VISUALIZER



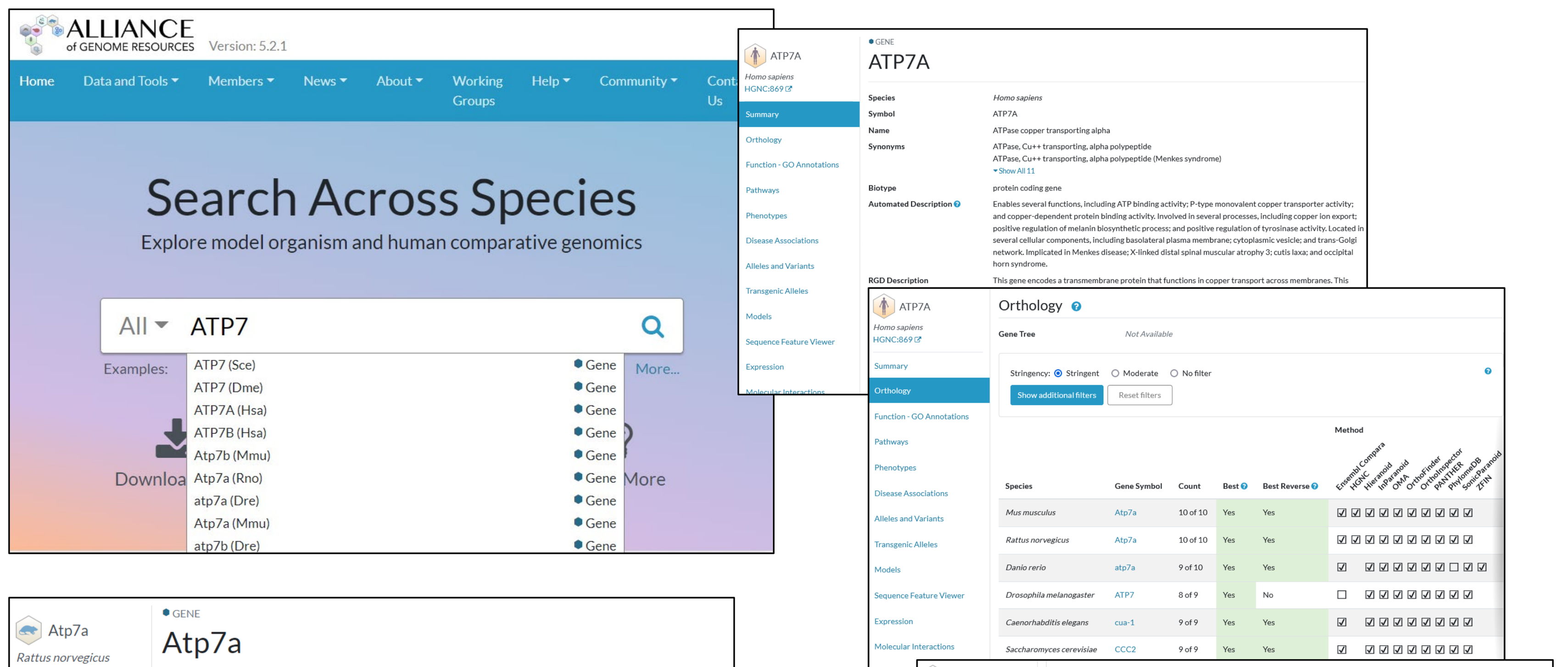
The Human Variant Visualizer contains clinical variants from NCBI's ClinVar database and variants from genome-wide association studies imported from the GWAS Catalog. Variant Visualizer provides information about the nucleotide and, where applicable, amino acid changes, as well as clinical significance/pathogenicity when available and the list of any diseases and/or phenotypes observed in individuals carrying the variation.

DOG VARIANT VISUALIZER



The Dog Variant Visualizer contains variants for pure-bred dog breeds, mixed breed dogs and wolf samples from multiple locations. Select breed groups or individual samples to explore variants in a region of interest or a specified group of genes. As with the rat variants, where possible, Polyphen predictions of damage to protein function are provided.

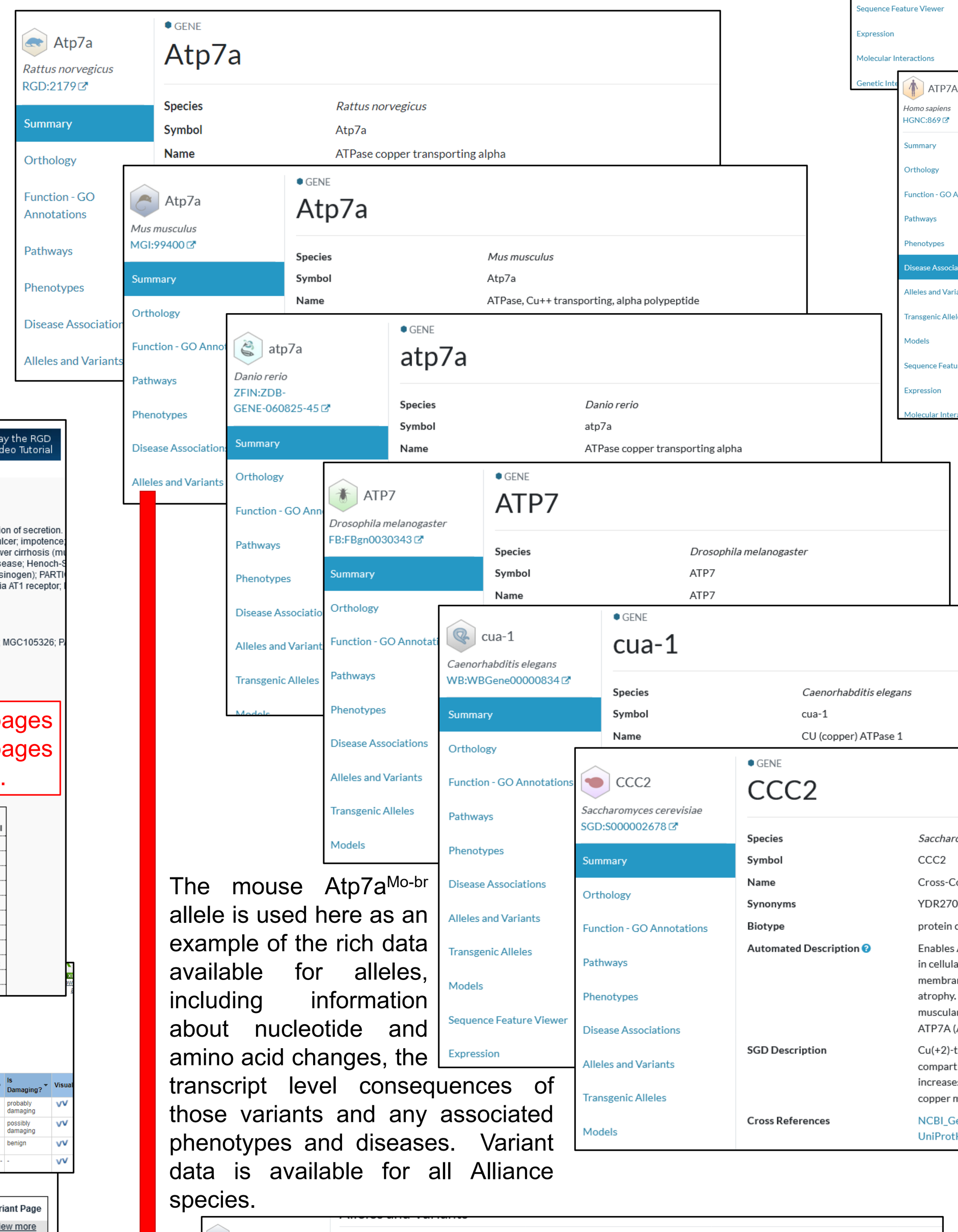
ALLIANCE OF GENOME RESOURCES GENE, ALLELE AND VARIANT PAGES



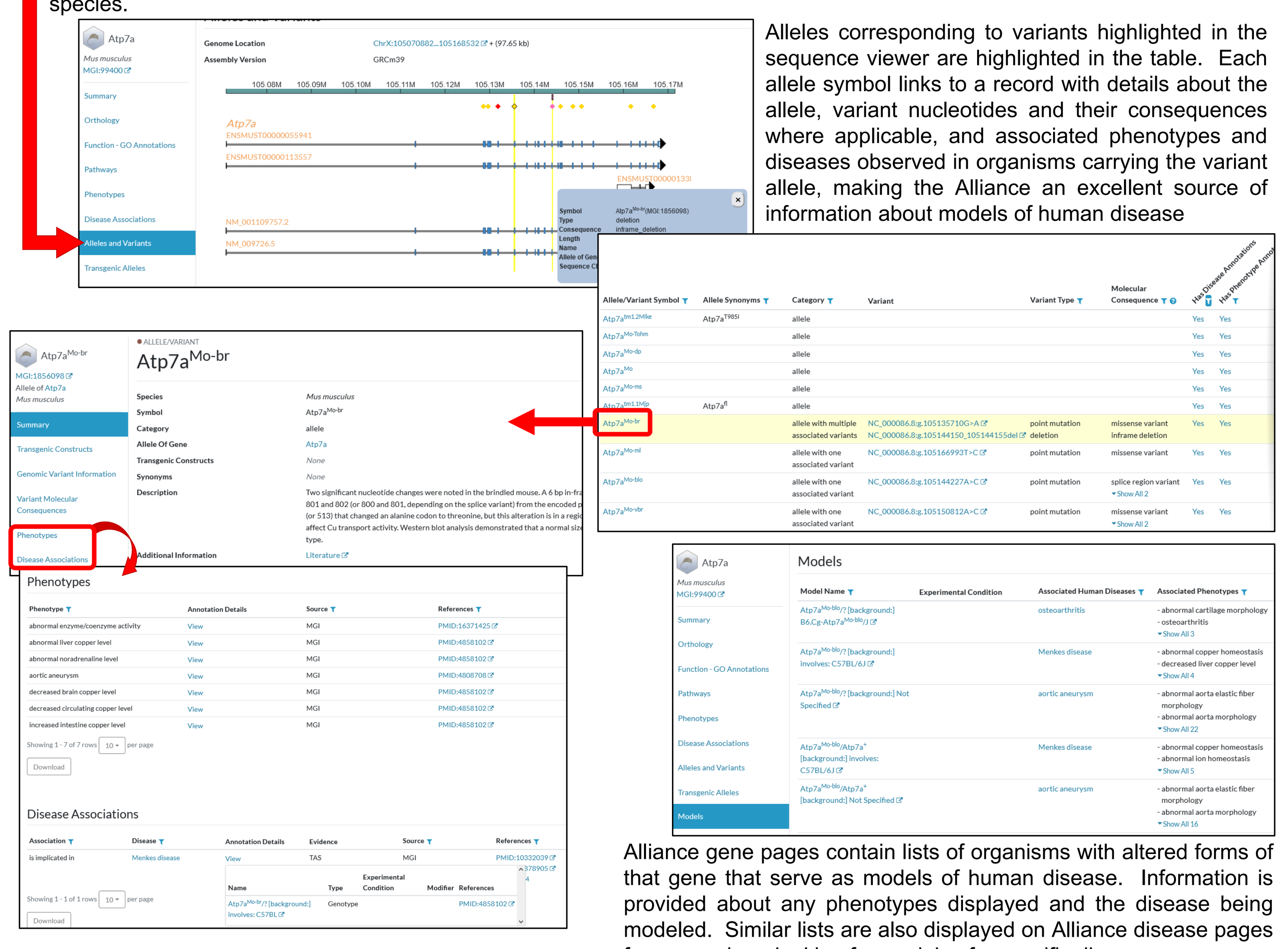
The Alliance of Genome Resources is a consolidated resource integrating data from six model organism databases and the Gene Ontology Consortium. The Alliance provides a harmonized view of data for human, rat, mouse, zebrafish, fly, worm and yeast. In addition to basic gene records, the Alliance provides a substantial body of data about models of human disease. Human gene records and disease associations are provided for comparative purposes.

The Alliance uses the DIOPT ortholog set, a robust ortholog prediction tool which leverages data from nine algorithms vetted by the Quest for Orthologs group and manual assignments from two groups. The example shown here, human ATP7A has orthologs in all six model species.

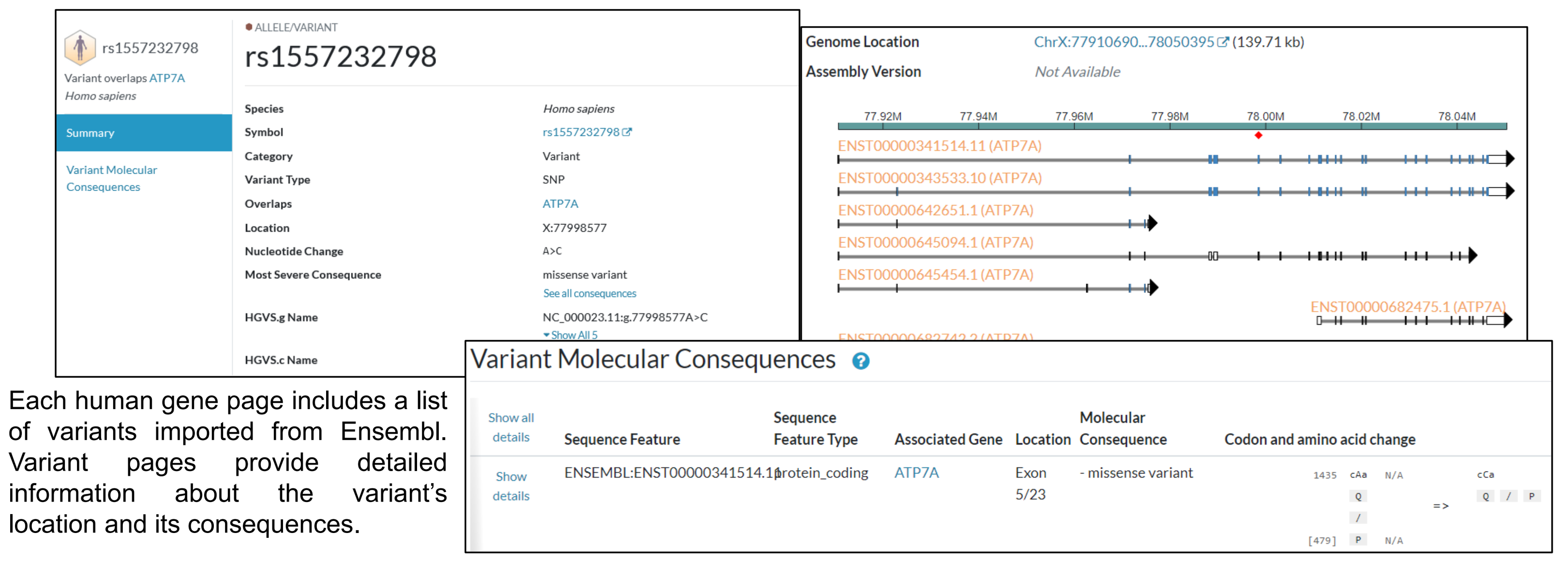
The mouse Atp7a^{Mo-br} allele is used here as an example of the rich data available for alleles, including information about nucleotide and amino acid changes, the transcript level consequences of those variants and any associated phenotypes and diseases. Variant data is available for all Alliance species.



Alleles corresponding to variants highlighted in the sequence viewer are highlighted in the table. Each allele symbol links to a record with details about the allele, variant nucleotides and their consequences where applicable, and associated phenotypes and diseases observed in organisms carrying the variant allele, making the Alliance an excellent source of information about models of human disease



Alliance gene pages contain lists of organisms with altered forms of that gene that serve as models of human disease. Information is provided about any phenotypes displayed and the disease being modeled. Similar lists are also displayed on Alliance disease pages for researchers looking for models of a specific disease.



Each human gene page includes a list of variants imported from Ensembl. Variant pages provide detailed information about the variant's location and its consequences.

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