Variation Viewer

A tool for interactive examination and download of nucleotide variants for a specific locus

https://www.ncbi.nlm.nih.gov/variation/view

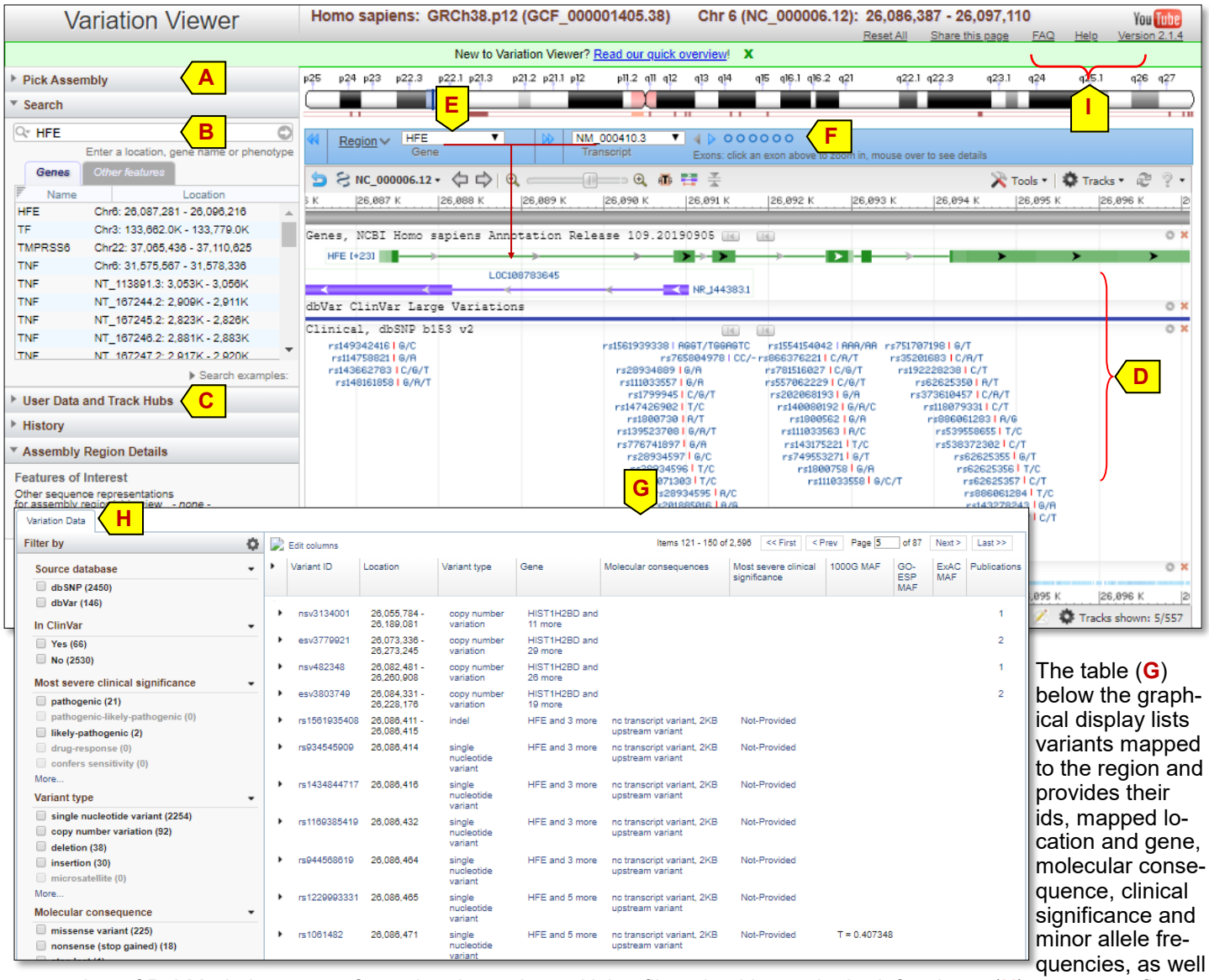
National Center for Biotechnology Information • National Library of Medicine • National Institutes of Health • Department of Health and Human Services

Overview

Review of nucleotide variation is important to population genetics and medical genetics alike. Several databases at NCBI (dbSNP [1], dbVar[2] and ClinVar[3]) represent these variants, their molecular consequences, and any clinical significance. The Variation Viewer tool provides an integrated way to present data from these sources, based on sequence location and as tabular reports. The graphical display allows navigation by exon or by neighboring gene. The tabular data table allows filtering displayed variations through a comprehensive set of options/criteria in the left-hand column, and saving of selected variants via the download link.

Access

Variation Viewer is available at www.ncbi.nlm.nih.gov/variation/view/, and via links from full reports of Gene, SNP, dbVar, and ClinVar records. The interface contains four sections, each with a specific set of functions. The top left section is the control panel, where you can select a different assembly (**A**), jump to a specific locus, region, or feature by direct querying (**B**), or import your own data (**C**). The top right section is a Sequence Viewer (SV, [4]) based graphical presentation of the genomic region selected, which puts variation-related tracks (**D**) in the context of annotated genes and transcript (**E**). Exon navigator (**F**) allows you to jump from exon to exon without scrolling through intronic regions.

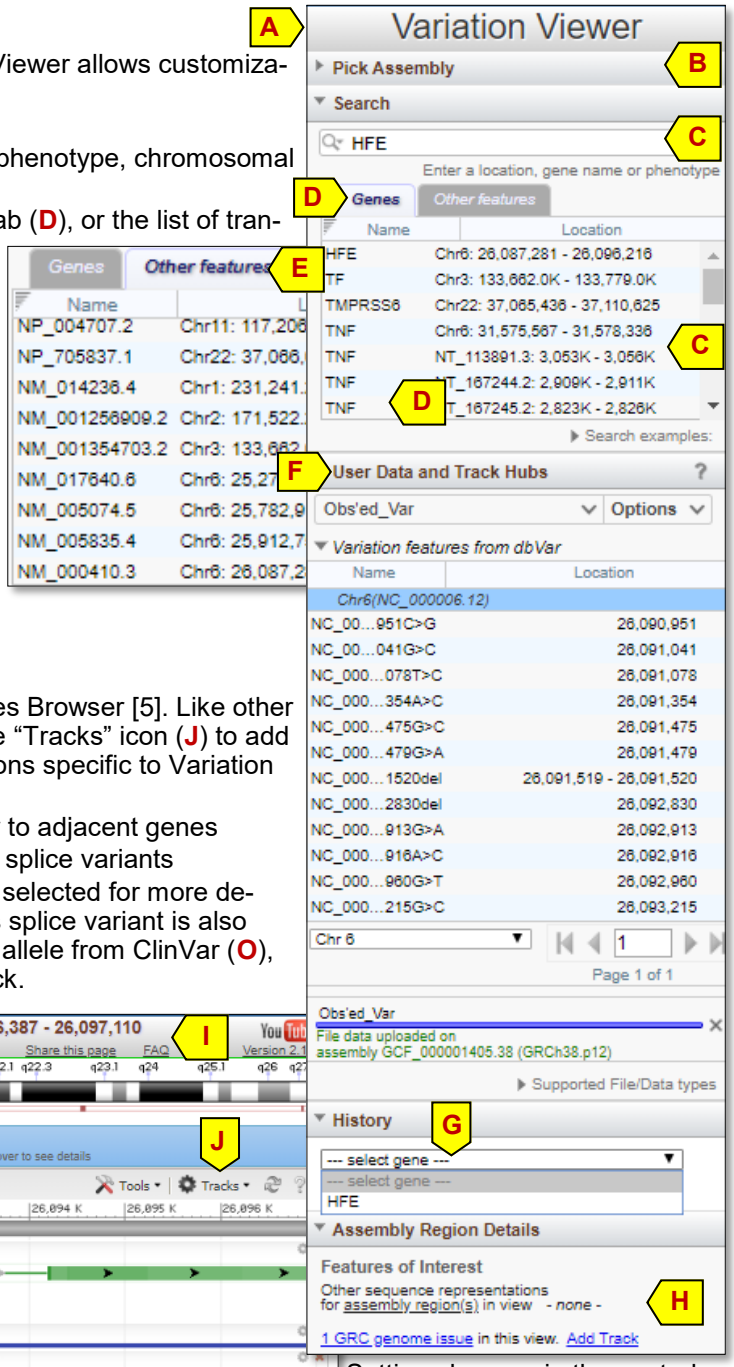


The table (**G**) below the graphical display lists variants mapped to the region and provides their ids, mapped location and gene, molecular consequence, clinical significance and minor allele frequencies, as well as number of PubMed abstracts referencing the variants. Using filter checkboxes in the left column (**H**), you can refine the list to quickly locate the variants of interest. More descriptions are in the following pages. Refer to the help document and a YouTube video introduction (**I**) at the upper right for more information on this tool.

Detailed Functions of the Control Panel

The control panel (**A**) for the graphical display of Variation Viewer allows customization of the display. Specifically, you can use this panel to:

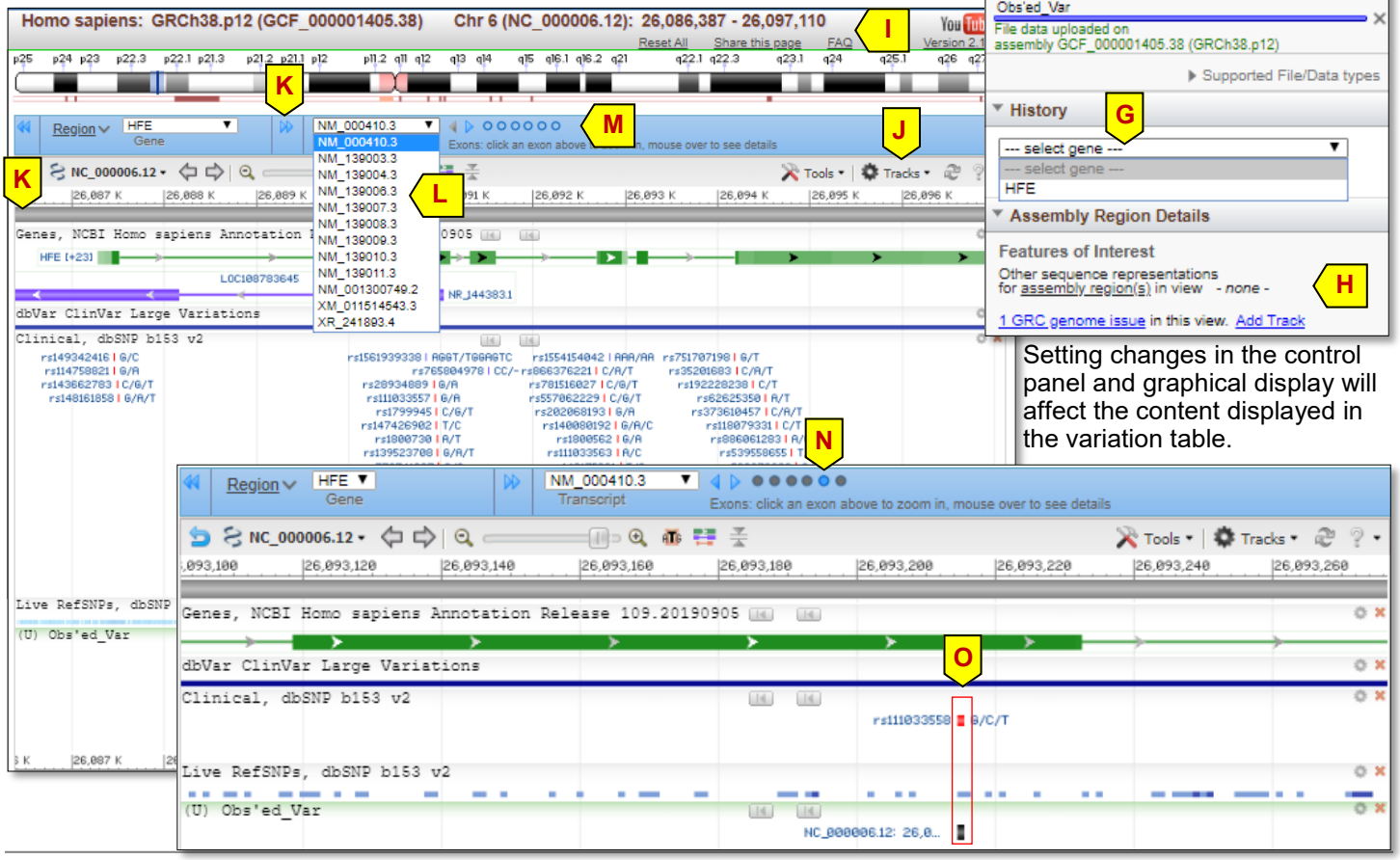
- change mapping assembly (**B**)
- Search for specific features (**C**), such as gene symbol, phenotype, chromosomal location, or rsID
- See the list of genes retrieved by a search in "Genes" tab (**D**), or the list of transcripts in the "Other features" tab (**E**), and click an entry in the list to update the graphical display to the right to show that region
- Upload custom data using the "User Data ..." portlet (**F**) to stream remote tracks, files, or direct paste in text in BED, GFF3, GTF, GVF, HGVS, or VCF format, and have them displayed as separate tracks (p. 3, **A - E**)
- Access your search history (previously search results) can be accessed using the "History" portlet via the pull-down list (**G**)
- See assembly issues for the genomic region by referring to links in the "Region Details" portlet (**H**, none in this case)



The Graphical Display

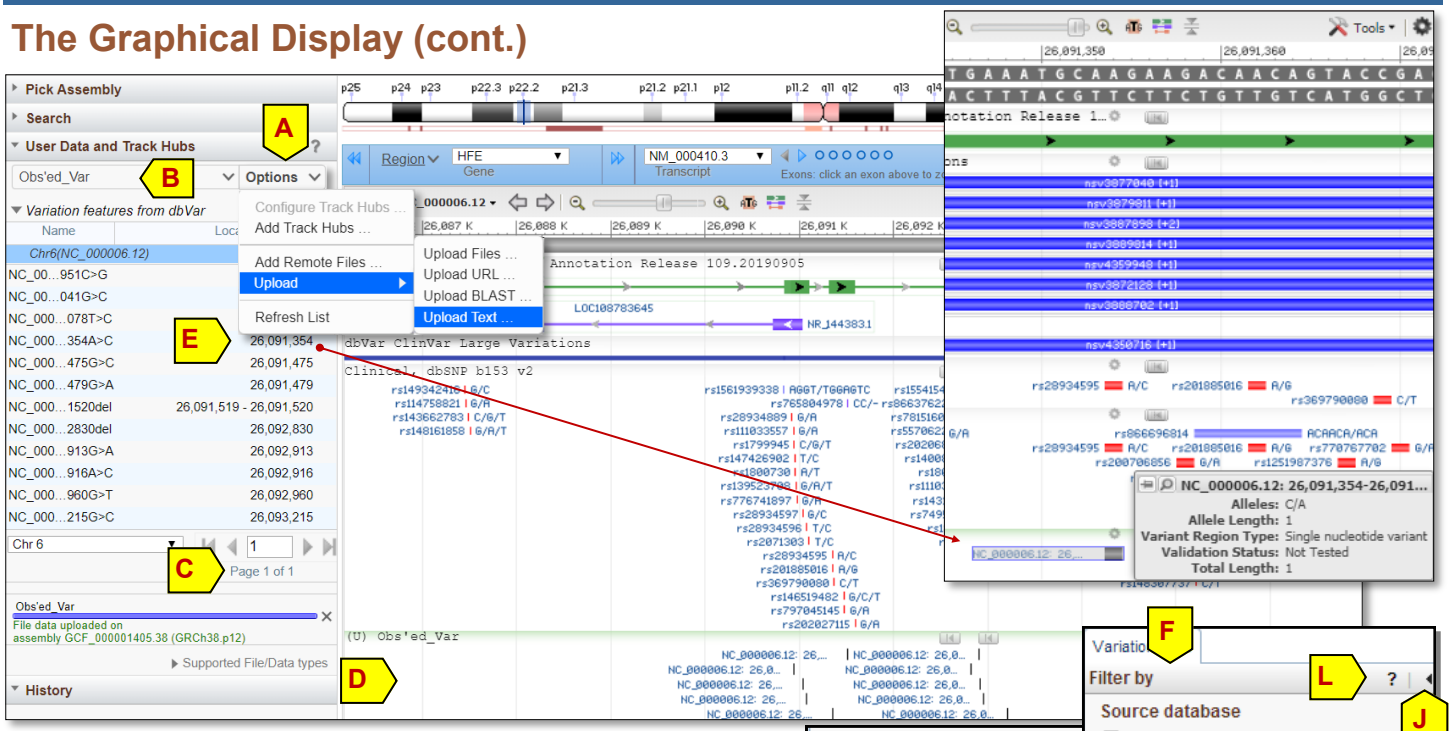
The graphical display (**I**) resembles the NCBI 1000 Genomes Browser [5]. Like other SV-based displays, you can customize the display using the "Tracks" icon (**J**) to add tracks or modify content shown for an existing track. Functions specific to Variation Viewer are also available:

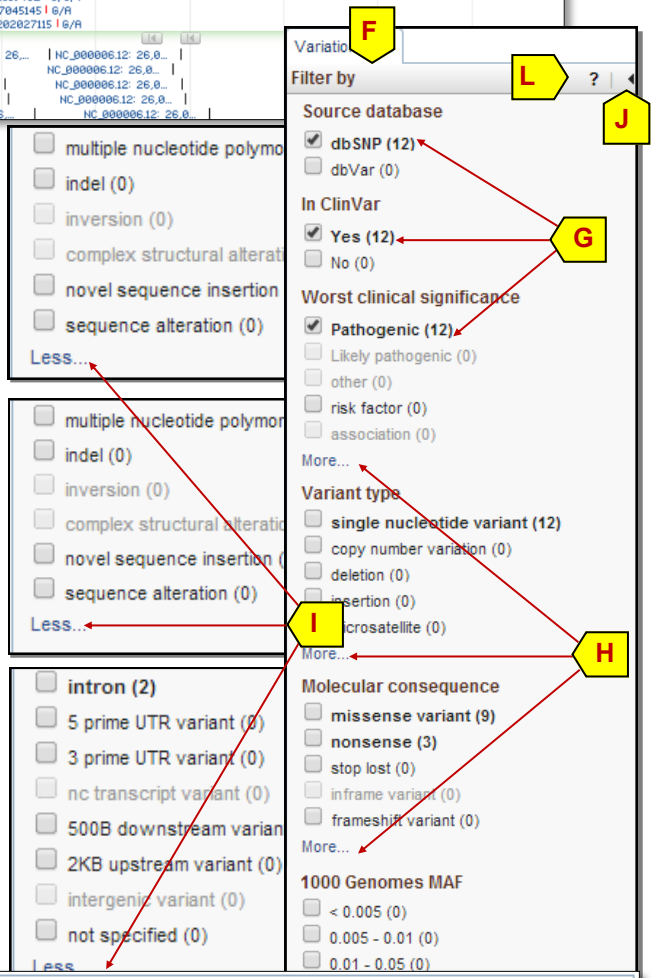
- Double-arrow icon (**K**) enables users to skip the display to adjacent genes
- Transcript pull-down list (**L**) allows users to select other splice variants
- Exon selector (**M**) enables one-click zoom to the exons selected for more detailed examination. A zoomed-in view for exon 5 for this splice variant is also shown (**N**). This exon has a variation with a pathogenic allele from ClinVar (**O**), which is also in the uploaded set in the Obs'ed_Var track.



Setting changes in the control panel and graphical display will affect the content displayed in the variation table.

The Graphical Display (cont.)





The “User data” section allows uploading of custom datasets through the “Option” cascading menu (**A**). It lists the active dataset at the top (**B**) and breaks large lists of variants/features into multiple pages (**C**). The graphical display shows the uploaded data as added tracks (**D**). Clicking a specific variant/feature zooms the display to the location of that entry (**E**).

Filtering Variations Shown in the Data Table

Variation Viewer lists all nucleotide variations available for the selected gene locus by default and presents them in the table at the bottom section of the page. A comprehensive set of filters (**F**) to the left of the table allows one-click filtering of displayed variations. Multiple filter selections can help narrow down the displayed variations to selected criteria for more focused examination. The example selection (**G**) restricts the display to show only dbSNP entries that are also in ClinVar with known pathogenic alleles. The number of variations available is given in the parentheses. For certain filter fields, additional options are available by clicking the “More …” link (**H**). To compress the extended list, click the “Less …” link (**I**). To maximize the column width to avoid line wrapping, click the arrow (**J**) to compress the filter section. For a detailed description of the filters.

A sample table display without filter section is shown below (**K**). Note that filter selection only affects the variation list displayed in the table without affecting the graphical display.

K

Edit columns

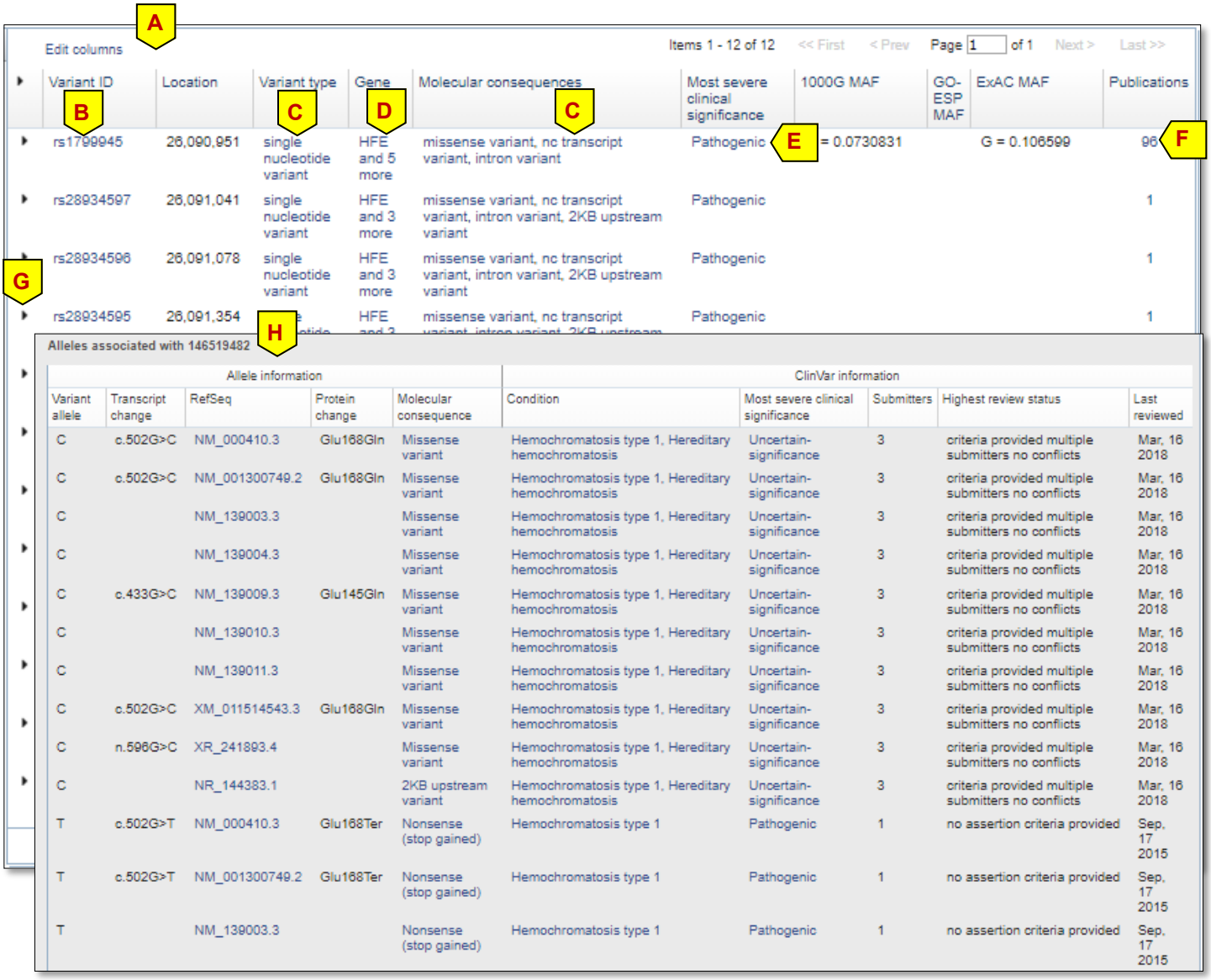
Items 1 - 12 of 12 << First < Prev Page 1 of 1 Next > Last >>

Variant ID	Location	Variant type	Gene	Molecular consequences	Most severe clinical significance	1000G MAF	GO-ESP MAF	ExAC MAF	Publications
rs1799945	26,090,951	single nucleotide variant	HFE and 5 more	missense variant, nc transcript variant, intron variant	Pathogenic	G = 0.0730831		G = 0.106599	96
rs28934597	26,091,041	single nucleotide variant	HFE and 3 more	missense variant, nc transcript variant, intron variant, 2KB upstream variant	Pathogenic				1
rs28934596	26,091,078	single nucleotide variant	HFE and 3 more	missense variant, nc transcript variant, intron variant, 2KB upstream variant	Pathogenic				1

Data Table

The tabular data (**A**, shown without the filter panel) displays the summary of nucleotide variations by providing information on the following fields: variant ID, genomic location, variant type, gene(s) the variant mapped to, the molecular consequences (only for SNPs), the most severe clinical significance, the minor allele frequency (MAF) from 1000 Genomes project, GO-ESP studies and ExAc aggregation, plus the number of available publications on the variant. Entries in the table are hyperlinked to provide additional function as described below:

- Click the id in the Variant ID column (**B**) to see the full report of a selected variant
- Follow the link in the Variant type and Molecular consequences columns (**C**) to see Sequence Ontology terms [6] relevant to a given variant
- Click the link in the Gene column (**D**) to retrieve the list of genes to which a variant is mapped
- See explanation of the term in the Most severe clinical significance column (**E**) in ClinVar by clicking on the clinical significance term
- Use the link in the Publications column (**F**) to retrieve publications about the variants from PubMed
- Click the arrow (**G**) to the left of a variant to see additional details, which include the transcript and protein level mapping details for SNPs mapped onto transcribed region in an expanded section below that variant (**H**).



References

Here are a list of links to relevant documents and resources:

1. NCBI Factsheets collection ftp://ftp.ncbi.nlm.nih.gov/pub/factsheets/README_factsheets
2. Variation Viewer Help https://www.ncbi.nlm.nih.gov/variation/view/help/
3. Sequence Ontology http://www.sequenceontology.org

Please send questions, suggestions, and bug reports on Variation Viewer to: snp-admin@ncbi.nlm.nih.gov