Variation Viewer

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

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

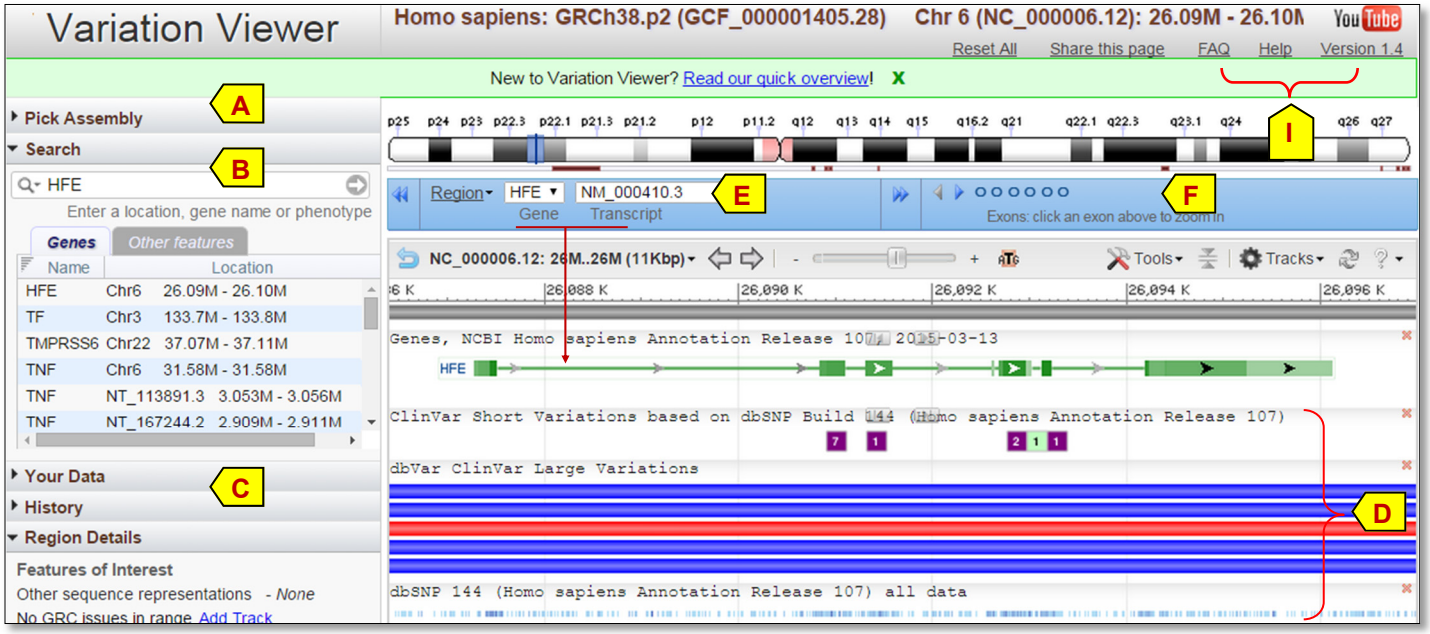
National Center for Biotechnology Information • National Library of Medicine • National Institutes of Health • Department of Health and Human Services

Overview

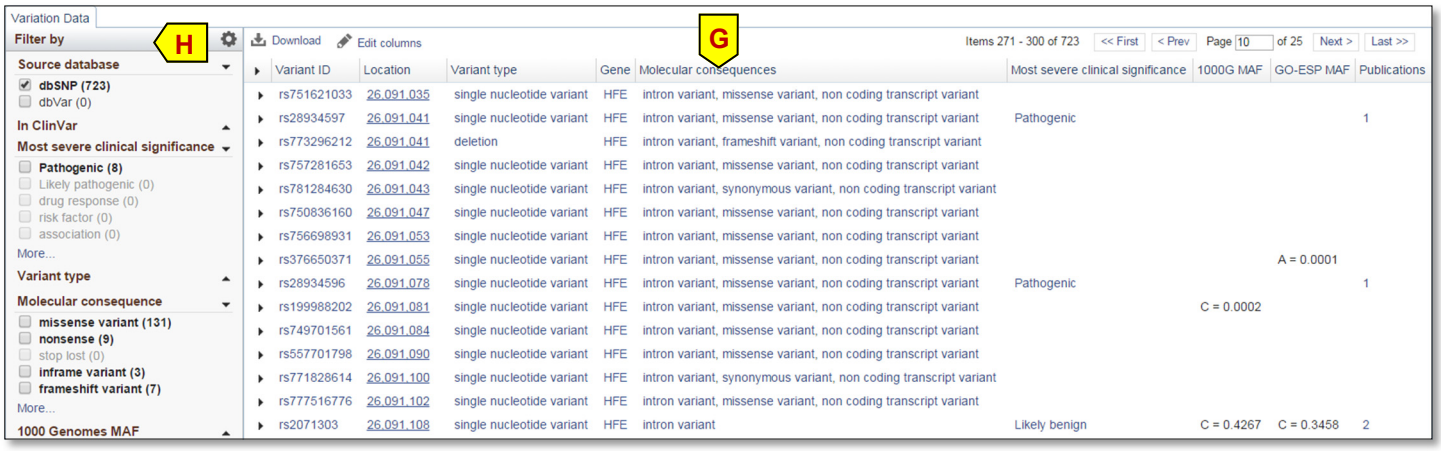
Review of nucleotide variation is important to population genetics and medical genetics alike. Several databases at NCBI (dbSNP [1], dbVar[2] and ClinVar[3]) represent these variants, their molecular consequences, and any clinical significance. The Variation Viewer tool provides an integrated way to 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.



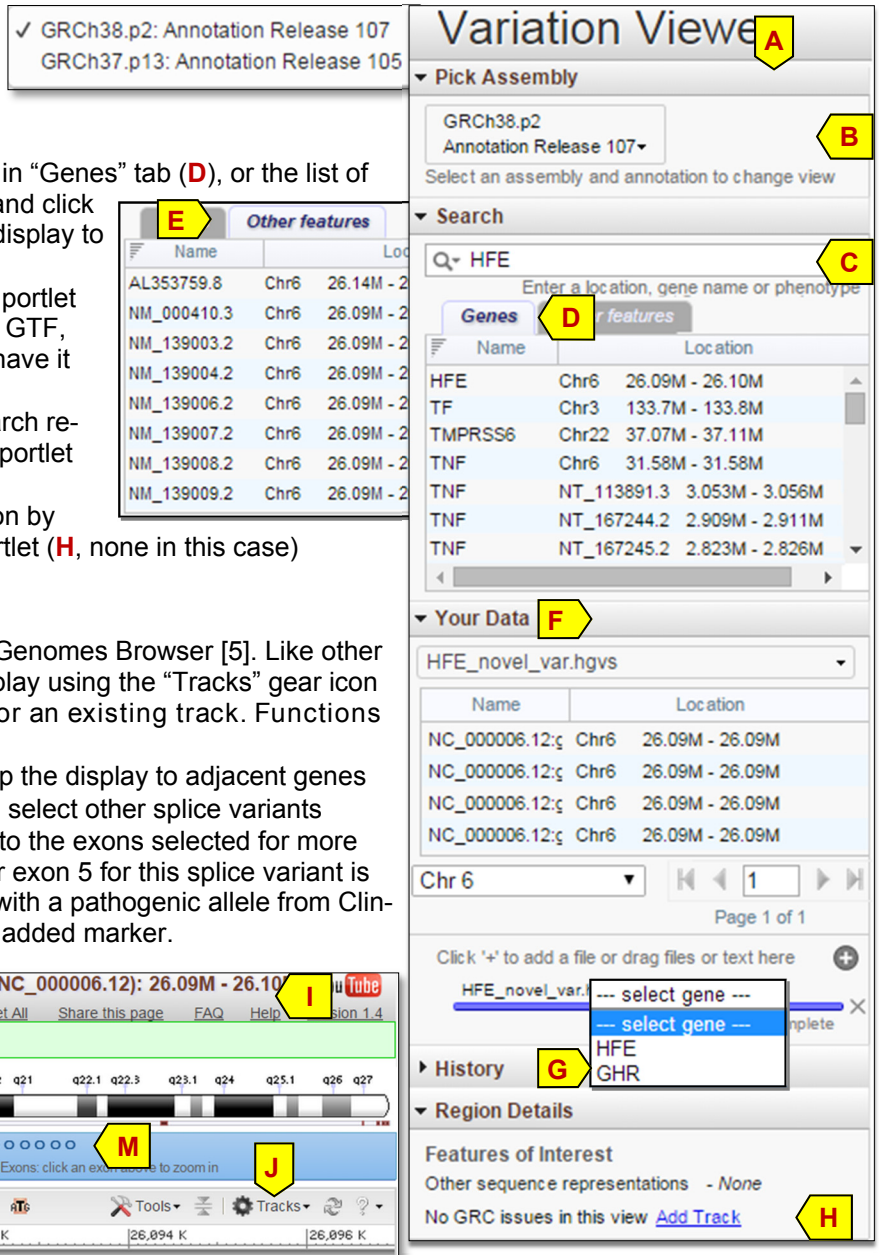
The table (**G**) below the graphical display lists variants mapped to the region and provides their ids, mapped location and gene, molecular consequence, clinical significance and minor allele frequencies, as well as number of PubMed abstracts referencing the variants. Using filter checkboxes in the 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 provides customization functions. Specifically, you can use this panel to:

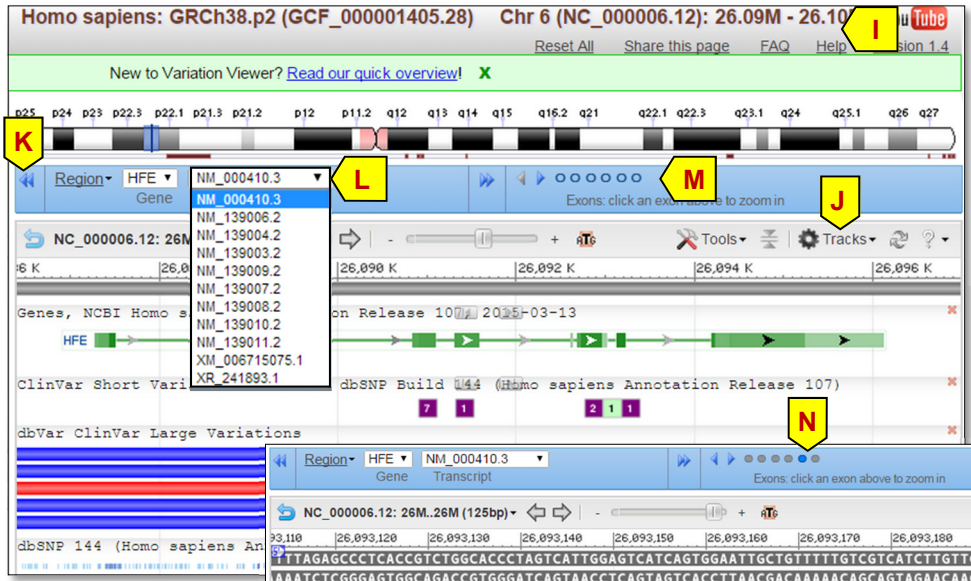
- change mapping assembly (**B**)
- Search for specific features (**C**), such as gene symbol, phenotype, chromosomal location, or rsID
- See the list of genes retrieved by a search in "Genes" tab (**D**), or the list of transcripts in the "Other features" tab (**E**), and click an entry in the list to update the graphical display to the right to show that region
- Upload custom data using the "Your Data" portlet (**F**) by clicking the "+" sign (BED, GFF3, GTF, GVF, HGVS, and VCF are accepted) and have it displayed as a separate track (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)



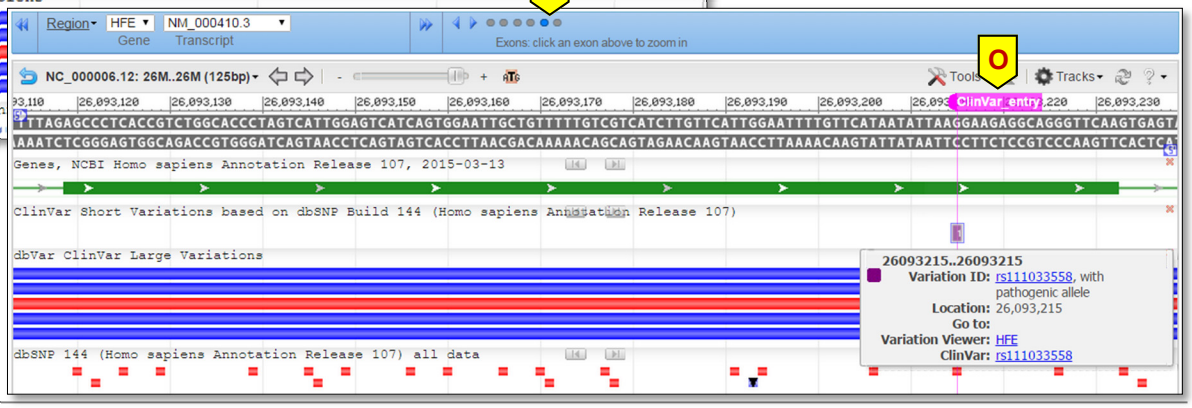
The graphical display

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

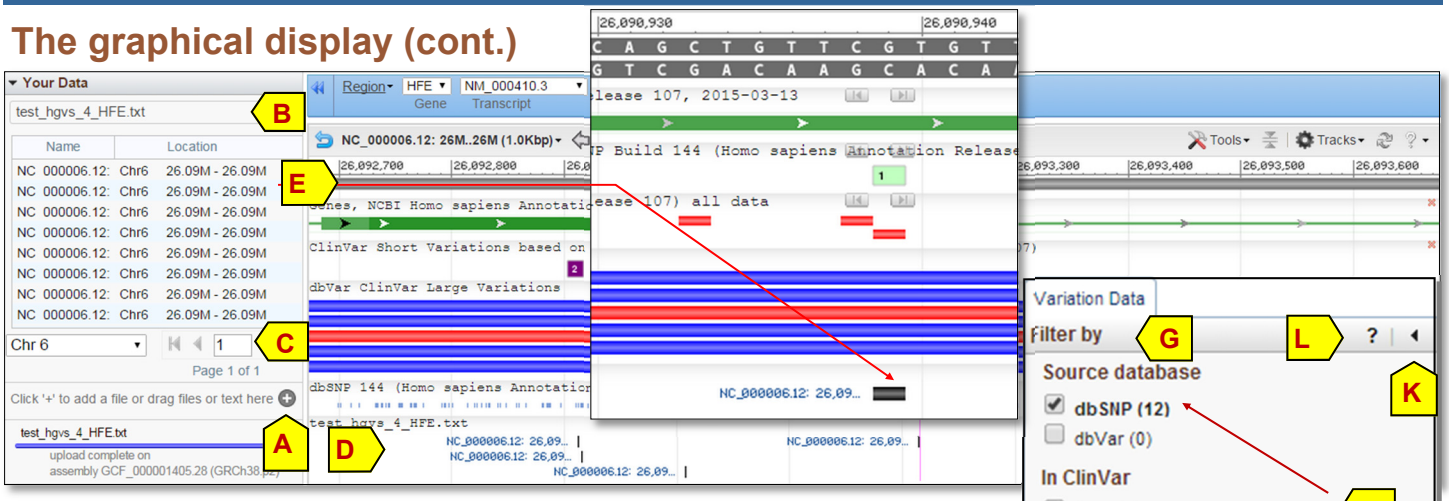
- Double-arrow icon (**K**) enables users to skip the display to adjacent genes
- Transcript pull-down list (**L**) allows users to select other splice variants
- Exon selector (**M**) enables one-click zoom to the exons selected for more detailed examination. A zoomed-in view for exon 5 for this splice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



Settings in both the control panel and graphical display affect the content displayed in the variation table.



The graphical display (cont.)



"Your data" section allows upload of a custom dataset via the "+" button (**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**).

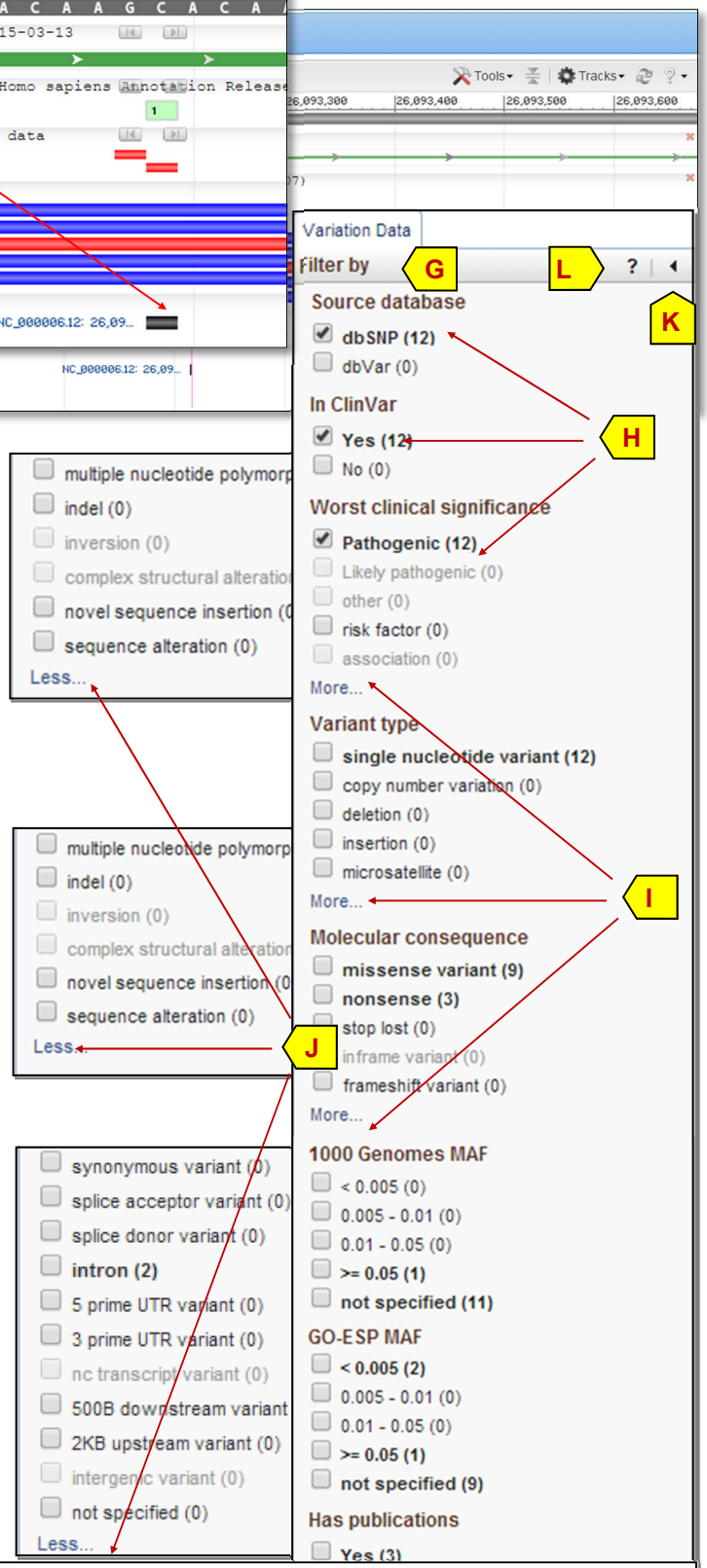
Filters for displaying selected subsets of variations

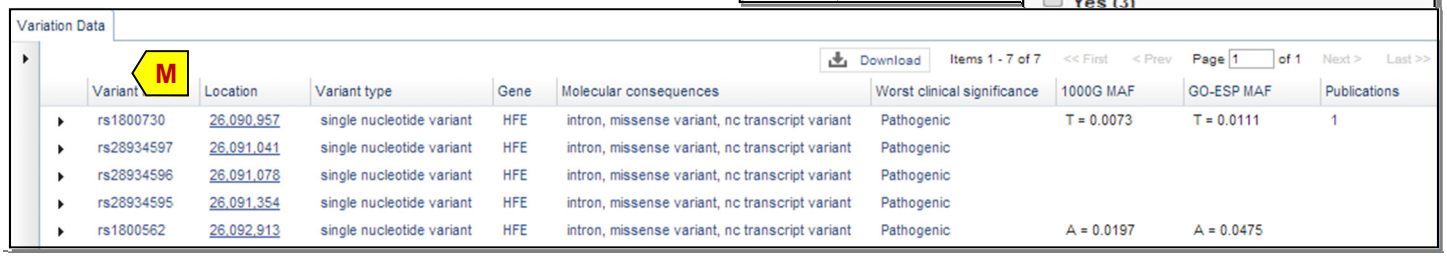
The default setting of Variation Viewer is to list all nucleotide variations available for the selected gene locus, including those large genomic variations from dbVar, short to single-nucleotide variations from dbSNP, and those with clinical significance from ClinVar. These variations are displayed in the table at the lower right of the page.

A comprehensive set of filters (**G**) to the left of the table (described in p. 1) 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 (**H**) 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 (**I**). To compress the extended list, click the "Less …" link (**J**). To maximize the column width to avoid line wrapping, the filter section can be compressed by clicking the arrow (**K**). A detailed description of the filters is available by clicking the "?" (**L**). A sample table display with filter section collapsed is shown below (**M**).

Note that filter selection only affects the variation list displayed in the table without affecting the graphical display.



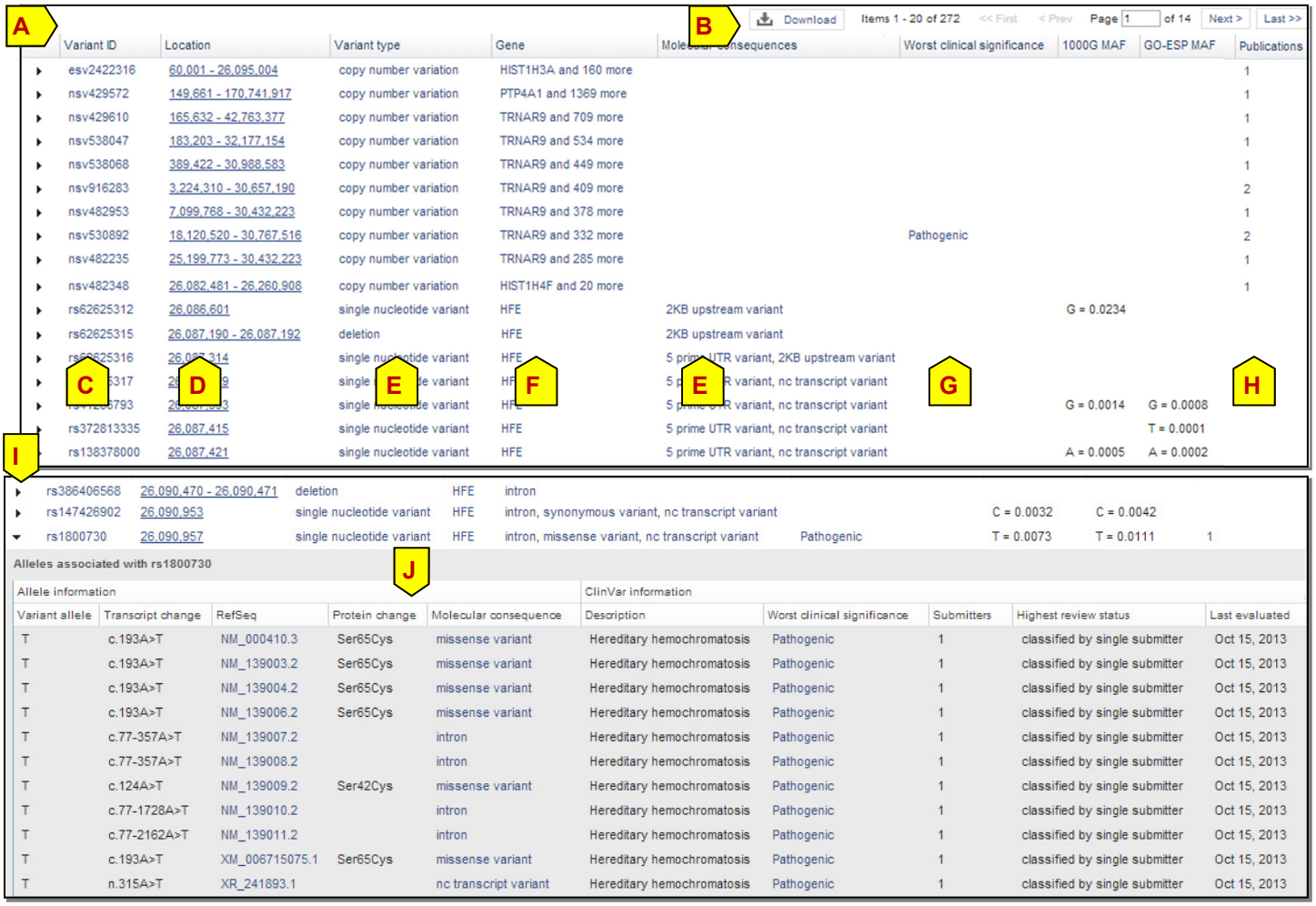


Variant	Location	Variant type	Gene	Molecular consequences	Worst clinical significance	1000G MAF	GO-ESP MAF	Publications
rs1800730	26,090,957	single nucleotide variant	HFE	intron, missense variant, nc transcript variant	Pathogenic	T = 0.0073	T = 0.0111	1
rs28934597	26,091,041	single nucleotide variant	HFE	intron, missense variant, nc transcript variant	Pathogenic			
rs28934596	26,091,078	single nucleotide variant	HFE	intron, missense variant, nc transcript variant	Pathogenic			
rs28934595	26,091,354	single nucleotide variant	HFE	intron, missense variant, nc transcript variant	Pathogenic			
rs1800562	26,092,913	single nucleotide variant	HFE	intron, missense variant, nc transcript variant	Pathogenic	A = 0.0197	A = 0.0475	

Data table

The tabular data (**A**, shown with filter panel collapsed) 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 and from GO-ESP studies, as well as the number of available publications on the variant. The complete dataset can be downloaded in XML format using the Download link (**B**). Entries in the table are hyperlinked to provide additional function as described below:

- Full report of a selected variant is available by clicking the id in the Variant ID column (**C**)
- Zoomed-in graphical presentation of a variant (in the SV display above the table) can be obtained by clicking the genomic location (**D**).
- Sequence Ontology terms [6] relevant to a given variant are linked from the Variant type and Molecular consequences columns (**E**)
- Genes to which a variant is mapped can be retrieved by clicking the link in the Gene column (**F**)
- Explanation of the clinical significance term in the Worst clinical significance column (**G**) is available from ClinVar upon click
- Relevant publications about the variants can be retrieved from PubMed using the link in the Publications column (**H**).
- Clicking the arrow (**I**) to the left of a variant provides additional details, which include the transcript and protein level mapping details for SNPs mapped onto transcribed region. An example variant with its detailed section open is shown (**J**).



Variant ID	Location	Variant type	Gene	Molecular consequences	Worst clinical significance	1000G MAF	GO-ESP MAF	Publications
esv2422316	60,001 - 26,095,004	copy number variation	HIST1H3A and 160 more					1
nsv429572	149,661 - 170,741,917	copy number variation	PTP4A1 and 1369 more					1
nsv429610	165,632 - 42,763,377	copy number variation	TRNAR9 and 709 more					1
nsv538047	183,203 - 32,177,154	copy number variation	TRNAR9 and 534 more					1
nsv538068	389,422 - 30,988,583	copy number variation	TRNAR9 and 449 more					1
nsv916283	3,224,310 - 30,657,190	copy number variation	TRNAR9 and 409 more					2
nsv482953	7,099,768 - 30,432,223	copy number variation	TRNAR9 and 378 more					1
nsv530892	18,120,520 - 30,767,516	copy number variation	TRNAR9 and 332 more		Pathogenic			2
nsv482235	25,199,773 - 30,432,223	copy number variation	TRNAR9 and 285 more					1
nsv482348	26,082,481 - 26,260,908	copy number variation	HIST1H4F and 20 more					1
rs62625312	26,086,601	single nucleotide variant	HFE	2KB upstream variant		G = 0.0234		
rs62625315	26,087,190 - 26,087,192	deletion	HFE	2KB upstream variant				
rs62625316	26,087,314	single nucleotide variant	HFE	5 prime UTR variant, 2KB upstream variant				
[illegible]	[illegible]	single [illegible] variant	HFE	5 [illegible] R variant, nc transcript variant				
[illegible]	[illegible]	single nucleotide variant	HFE	5 prime UTR variant, nc transcript variant		G = 0.0014	G = 0.0008	
rs372813335	26,087,415	single nucleotide variant	HFE	5 prime UTR variant, nc transcript variant			T = 0.0001	
rs138378000	26,087,421	single nucleotide variant	HFE	5 prime UTR variant, nc transcript variant		A = 0.0005	A = 0.0002	
rs386406568	26,090,470 - 26,090,471	deletion	HFE	intron				
rs147426902	26,090,953	single nucleotide variant	HFE	intron, synonymous variant, nc transcript variant		C = 0.0032	C = 0.0042	
rs1800730	26,090,957	single nucleotide variant	HFE	intron, missense variant, nc transcript variant	Pathogenic	T = 0.0073	T = 0.0111	1

Allele information					ClinVar information				
Variant allele	Transcript change	RefSeq	Protein change	Molecular consequence	Description	Worst clinical significance	Submitters	Highest review status	Last evaluated
T	c.193A>T	NM_000410.3	Ser65Cys	missense variant	Hereditary hemochromatosis	Pathogenic	1	classified by single submitter	Oct 15, 2013
T	c.193A>T	NM_139003.2	Ser65Cys	missense variant	Hereditary hemochromatosis	Pathogenic	1	classified by single submitter	Oct 15, 2013
T	c.193A>T	NM_139004.2	Ser65Cys	missense variant	Hereditary hemochromatosis	Pathogenic	1	classified by single submitter	Oct 15, 2013
T	c.193A>T	NM_139006.2	Ser65Cys	missense variant	Hereditary hemochromatosis	Pathogenic	1	classified by single submitter	Oct 15, 2013
T	c.77-357A>T	NM_139007.2		intron	Hereditary hemochromatosis	Pathogenic	1	classified by single submitter	Oct 15, 2013
T	c.77-357A>T	NM_139008.2		intron	Hereditary hemochromatosis	Pathogenic	1	classified by single submitter	Oct 15, 2013
T	c.124A>T	NM_139009.2	Ser42Cys	missense variant	Hereditary hemochromatosis	Pathogenic	1	classified by single submitter	Oct 15, 2013
T	c.77-1728A>T	NM_139010.2		intron	Hereditary hemochromatosis	Pathogenic	1	classified by single submitter	Oct 15, 2013
T	c.77-2162A>T	NM_139011.2		intron	Hereditary hemochromatosis	Pathogenic	1	classified by single submitter	Oct 15, 2013
T	c.193A>T	XM_006715075.1	Ser65Cys	missense variant	Hereditary hemochromatosis	Pathogenic	1	classified by single submitter	Oct 15, 2013
T	n.315A>T	XR_241893.1		nc transcript variant	Hereditary hemochromatosis	Pathogenic	1	classified by single submitter	Oct 15, 2013

References

Links to relevant documents and resources are:

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