Read Me

varSEAK Online

Variant Table

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Contents

1 Introduction to varSEAK

varSEAK Online offers public access to the **varSEAK** database. The varSEAK database contains variants and classifications submitted by genetic experts using the **varSEAK Pilot** software. Additionally, information is provided by public databases such as ClinVar, ClinVitae, ExAC, dbSNP, 1000 Genomes Project and the prediction tools and allele frequencies of dbNSFP.

2 Searching the database

1. Search for your gene of interest and define the range up- and downstream (5.000 – 50.000 bp) of this gene as preferred.
2. The variants table is loaded. The search can be further refined within the variant table by adding one or several keywords. The whole search can be deleted by clicking the *[X]* button in the upper right corner of the gene name. Subsequently, a new gene name of interest can be entered and the range up- and downstream of this gene can be defined to start another search.

3 Content and Features in the results table

General information about the gene of interest is provided below and to the right of the search field: Below the search field there is the Gene name, Chromosome, Strand, Number of Transcripts, Aliasnames and your selection of up- and downstream ranges. On the right, you can find the Start and End Positions for hg19 and hg38, respectively, and the default transcript the location information is based on.

Only results containing entries in the column varSEAK Classification, ClinVar Classification or ClinVitae Classification will be displayed.

Overhead the results table, the amount of entries for your gene of interest is shown, together with a navigational aid.

Most of the allele frequencies and classifications of the variants from other public databases are directly linked to the respective information about the variant on the respective website. For details, see the description of the respective column.

The results table contains the following information:

Column	Description
Pos hg19 **Pos hg38** (Position)	Lists the chromosomal position of the variant for the respective reference genome.
Loc (Location)	Location of the variant. For orientation, location is calculated based on the longest transcript for the gene for all variants in the results table. The name of this default transcript is given on the right of the search field.

HGVS	Variant is reported according to HGVS with transcript number (1st line), sequence changes relative to the coding DNA reference sequence (2nd line) and protein reference sequence (3rd line). Click the field to display the complete content if it is abbreviated.
varSEAK # of Labs	Count of **varSEAK** member laboratories that detected this variant.
varSEAK Classification	Variant is classified by **varSEAK** members in five classes (ACMG-Classification, e.g. pathogenic (5.0)) (1st line) followed by a detailed explanation of the classification (2nd line), i.e.: it shows how often each classification has been chosen (e.g. 0/0/0/0/2 means that the variant has been classified as pathogenic twice).
ClinVar Classification	Clinical significance of variant (ACMG-Classification) from ClinVar. (*http://www.ncbi.nlm.nih.gov/clinvar/*, Version: 2016-11-28)
ClinVitae Classification	Clinical significance of variant (ACMG-Classification) from ClinVitae. (*http://clinvitae.invitae.com/*, Version: 2016-11-22)
gnomAD AF	Exome Dataset Allele Frequency according to the Genome Aggregation Database (gnomAD). The numbers in the columns are linked to the resepective site of the variant in the gnomAD browser. (*https://gnomad.broadinstitute.org/*, Release r.2.1.0)
ExAc AF	Exome allele frequency according to the Aggregation Consortium (ExAc). The numbers in the columns are linked to the respective site of the variants in the ExAc browser. However, in contrast to the normal AF shown in varSEAK, the ExAc browser shows the adjusted allele frequency (adjAF). (*http://exac.broadinstitute.org/*, Release r0.3.1)
dbSNP MAF	Global minor allele frequency from the Single Nucleotide Polymorphism database (dbSNP) (usually from 1000 Genomes). (*http://www.ncbi.nlm.nih.gov/SNP/*, Build 149)
1000 Genomes AF	Allele frequency of variant from 1000 Genomes using allele count (AC) and allele number (AN) values. (http://www.1000genomes.org/, link is redirected to http://grch37.ensembl.org/index.html, Version: Phase3-v5a)

dbNSFP SVM Pred.	Prediction tool to estimate the likelihood that a single-nucleotide missense variant would damage a protein's structure and function: tolerated (T) or damaging (D), calculated by the dbNSFP Support Vector Machine from several prediction tools and conservation scores. This prediction is only available for coding regions. Splice regions may have information in some individual prediction tools, but no overall prediction. The detailed prediction tool rank scores can be viewed by clicking the (i) button behind the prediction. For each tool, the prediction scores were ranked among all scores of the corresponding tool in dbNSFP. The rankscore is the ratio of the rank of a score over the total number scores of that tool in dbNSFP. If multiple scores exist, only the most damaging rankscore is presented. For some tools the scores were converted first. dbNSFP also provides Allele Counts and Allele Frequencies from several sources. These are displayed below the prediction tool rank scores (click the (i) button behind the prediction). For a detailed list of the included sources, see the dbNSFP 3.3c readme: *https://drive.google.com/file/d/0B60wROKy6OqcRkNLcG1GSG1OY3M/view* (*https://sites.google.com/site/jpopgen/dbNSFP*, Version: 3.3c)
Country	Country code of the respective initial submitter's country.
Initial Submitter	Laboratory which initially submitted the variant to **varSEAK**, described with the laboratory name (1st line), and the laboratory address (2nd line). To see the full laboratory name and address hover the cursor over this column to display a tooltip.

4 Appendix

4.1 Version History

Table 1: Version history

Version	Date *)	Author	Status **)	Changes
V02	2022-02-23	Eva Noeske	released	Corrected formatting errors
V01	2021-12-27	Eva Noeske	released	Changed format of document

*) Format: YYYY-MON-DD **) Status: Draft / released