

What is GeneTalk?

GeneTalk combines a web-based tool for filtering and analyzing human sequence variants and a professional online network for geneticists worldwide.

Clinicians and scientists looking for information about specific sequence variants can find other users with expertise for a particular variant.

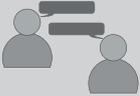
How to use Genetalk

① **Upload your sequence variants** in VCF format of single or multiple samples (*Manage Files* → *Upload VCF*). Make sure the hg19 or GRCh37 reference is used.

Uploaded files are preprocessed and listed in the file manager (*Manage Files* → *List*). Individuals in a multiple VCF file are shown after clicking the  icon. You can view the file  and share it with other users .

② **Edit the pedigree and phenotype information** of the individuals in your VCF file by clicking the  icon. Phenotypic features can be specified by terms of the *Human Phenotype Ontology* (HPO).

These information allow for powerful filtering of variants, for example,, by mode of inheritance (dominant, recessive homozygous, recessive compound heterozygous).

 Filter and prioritize sequence variants with highly effective algorithms that speed up your analysis
 Annotate sequence variants and find out what other GeneTalk users say about specific mutations
 Join the large professional online network for geneticists worldwide and discuss unclassified variants

Upload VCF File

File

Select a VCF file or a ZIP file containing one or more VCF files. The reference should be hg19 or GRCh37.

No file chosen

My VCF Files

Name	Owner	Comment	Creation date	
testABC.vcf	kamphans		November 26, 2012 23:31	   
• (1) mother 				
• (2) father 				
• (3) child 				

Edit Pedigree

Line	Individual	Father	Mother	Gender	Affection status	Origin
1	mother	<input type="text" value="0"/>	<input type="text" value="0"/>	Female	Unaffected/H	testA.vcf (12-0533)
2	father	<input type="text" value="0"/>	<input type="text" value="0"/>	Male	Unaffected/H	testB.vcf (12-0534)
3	child	<input type="text" value="2"/>	<input type="text" value="1"/>	Male	Affected/Pati	testC.vcf (11-0852b)

HPO Terms

Individual: 465

HP:0003155 (Elevated alkaline phosphatase),
HP:0001249 (Intellectual disability),
sei

Seizures (HP:0001250)
Photomyoclonic seizures (HP:0001327)

③ Filter Sequence Variants

Click on *Filter VCF* in the main menu.

The filter settings menu is organized using tabs in the top row. Choose one or more VCF files for filtering with the checkboxes in the *File* tab.

The other tabs provide several options for reducing the number of variants in your VCF file(s).

Select your filter settings and click the *Filter* button.

File							Functional	Linkage	Gene Panel	Frequency	Inheritance	Annotation
Select	Name	Owner	Comment	Upload date	Actions							
<input type="checkbox"/>	testfile1.vcf	Knaus		January 29, 2013 15:29								

Functional Filter: Reduce to variants that have an effect on the protein level.

Linkage Filter and Gene Panel Filter: Restrict the variant list to a set of genes or to a linkage interval.

Frequency Filter: Remove all variants with genotypes that occur more often in the background population than an adjustable cutoff. (Data from the 1000 genomes and 5000 exome sequencing project are used as reference.)

Inheritance Filter: Restrict analysis to genotypes that fit to a certain mode of inheritance.

Annotation Filter: Filter out variants based on ratings for medical relevance and scientific evidence.

④ View Sequence Variants

The filtered VCF file contains significantly fewer sequence variants.

Click the *Annotate* button to provide an annotation for a variant. The *More* button displays a popup with detailed variant information.

Chrom	Pos	dbSNP ID	Gene	Ref	465 (Affected)	466 (Unaffected)	467 (Unaffected)	Effect	Medical Relevance	Scientific Evidence
1	145296451	rs140256918	NBPF10	G	C/G	C/G	G/G	missense	Annotate	more
1	145368518	rs61813437	NBPF10	C	C/T	C/C	C/T	missense	Annotate	more
9	35090263	rs142164373	PIGO	G	A/G	A/G	G/G	missense	Annotate	more
9	35091529		PIGO	G	G/GG	G/G	G/GG	frameshift-insertion	Annotate	more

⑤ Find Annotations, Experts and Patients

The annotations column indicates if for the position exists at least one annotation (with the shown votings for *medical relevance* and *scientific evidence*), an expert, or another patient. Click the stars to open the list of annotations, experts, and patients.

Experts			
Expert	Gene Panel	Abstract	Level of expertise
petkraw	GPI anchor synthesis deficiency		I'm an expert for these genes

Annotations								show filter
User	Chrom	Pos	Genotype	Gene	Comment	OMIM-ID	Actions	
Alexej	9	35091529	G/GG	PIGO	HPRMS Hyperphosphatasia with mental r...		Annotate	

For position 35091529 in chromosome 9, there is an expert, *petkraw*, in GPI anchor deficiency. You can contacted this user for further discussion. Additionally, the user *Alexej* has left an annotation for this position in PIGO, rating an insertion as disease causing.

