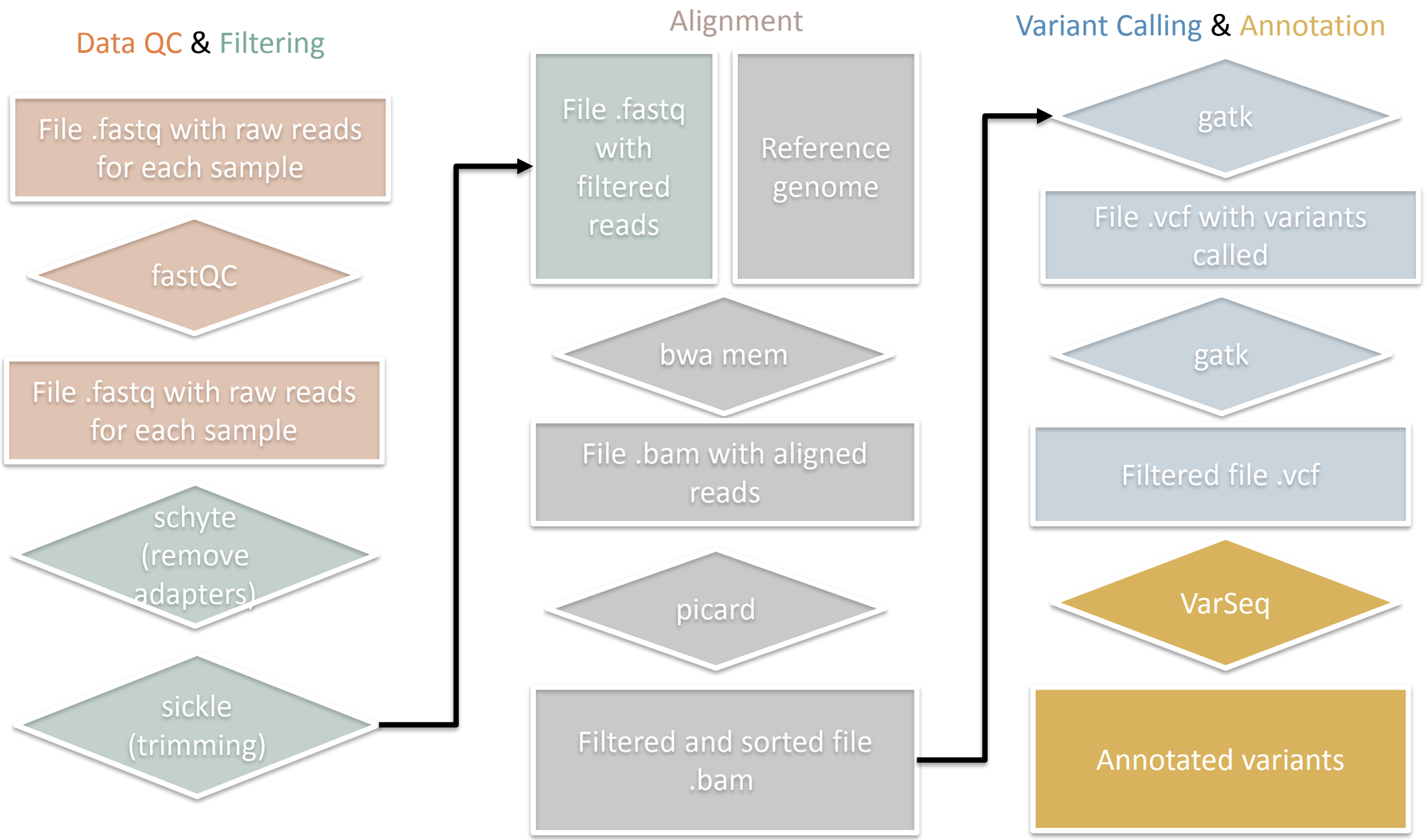
Human Genome Sequencing and Interpretation

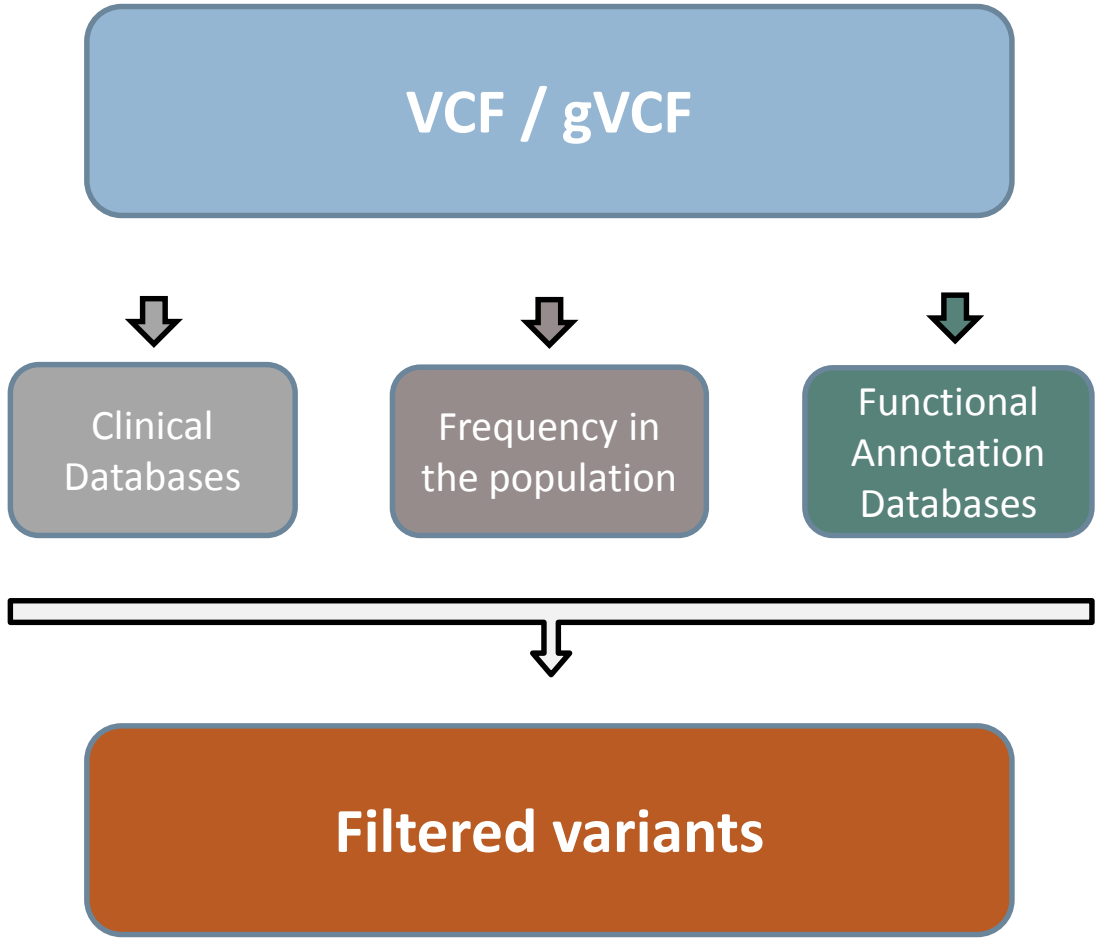
Lesson 1 - 20/01/2020
Lesson 2 - 21/01/2020
Lesson 3 - 27/01/2020
(Lesson 4 - 28/01/2020)

Prof. Massimo Delledonne
Functional Genomics lab

Pipeline


Data QC & Filtering
File .fastq with raw reads for each sample
fastQC
File .fastq with raw reads for each sample
schyte (remove adapters)
sickle (trimming)
Alignment
File .fastq with filtered reads
Reference genome
bwa mem
File .bam with aligned reads
picard
Filtered and sorted file .bam
Variant Calling & Annotation
gatk
File .vcf with variants called
gatk
Filtered file .vcf
VarSeq
Annotated variants

Variant Annotation



Others free software for the annotation

Mendel,MD

wAnnovar

Bystro

Download vcf files from server

- Single vcf files:

rsync -auv HGSI2020@157.27.26.214:/attachedvolume/HGSI2020/example/samples/135*S/ 135*S.vcf.gz

- Multiple vcf files:

rsync -auv HGSI2020@157.27.26.214:/attachedvolume/HGSI2020/example/samples/selected.variants.chr6.vcf.gz

Mendel,MD

Welcome to Mendel,MD!

This is an online tool created to help doctors and scientists to identify disease causing variants using exome/genome sequencing data from patients with mendelian disorders.

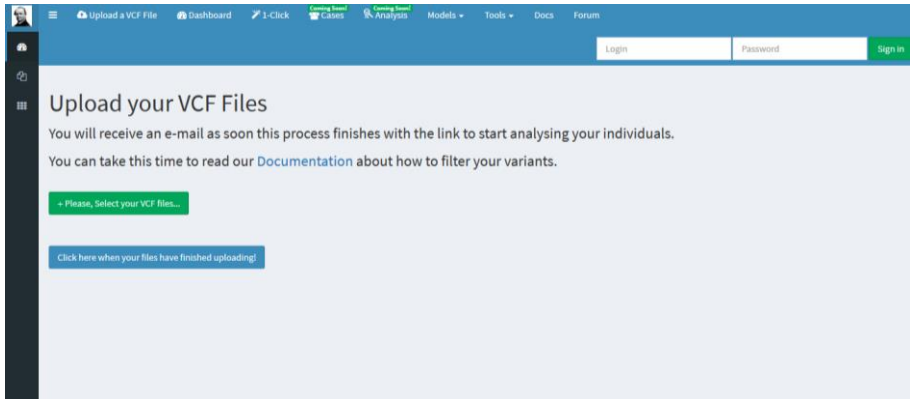
Sign Up » or Upload a VCF

LABORATÓRIO DE GENÔMICA CLÍNICA

MEDICINA UFMG

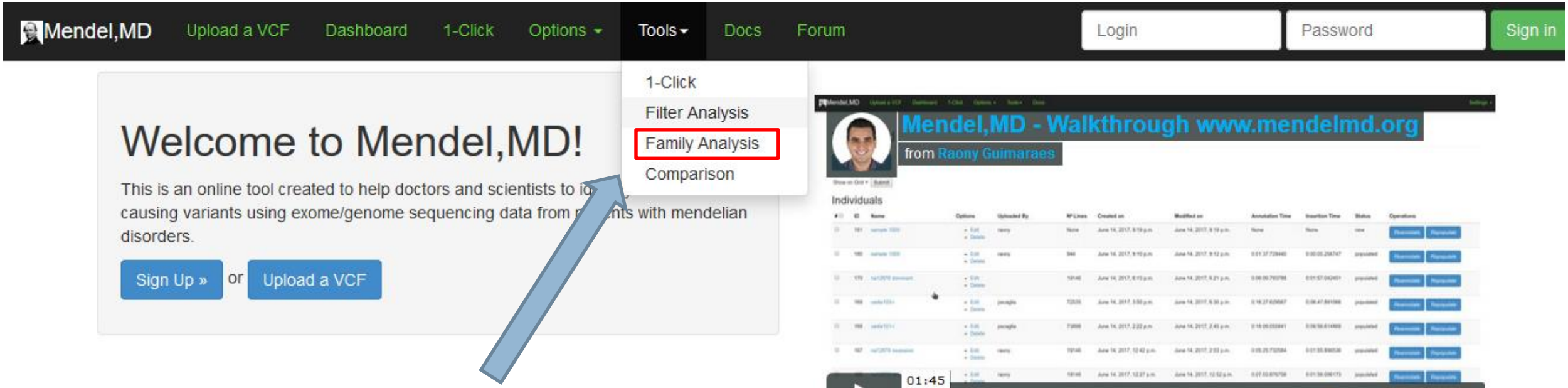
https://mendelmd.org/

Mendel,MD



https://mendelmd.org/

Mendel,MD

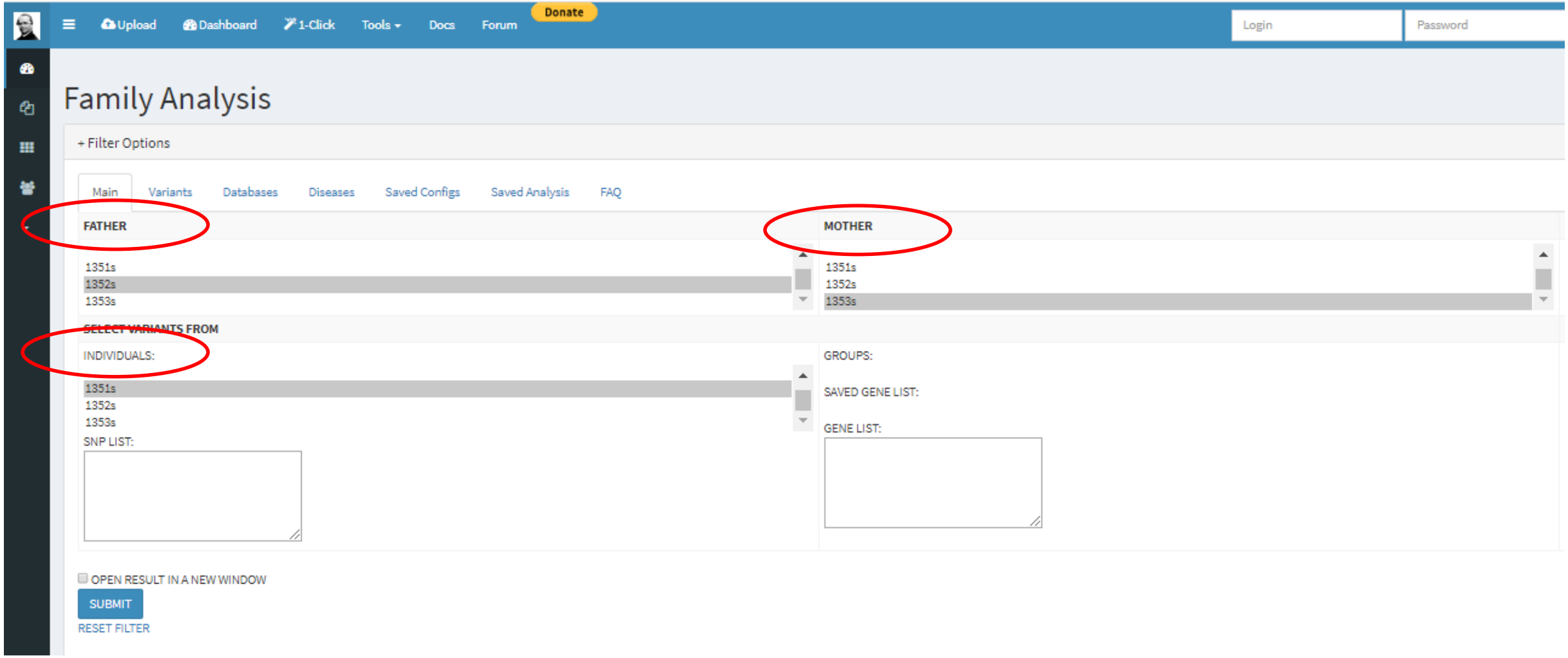


Analysis selection

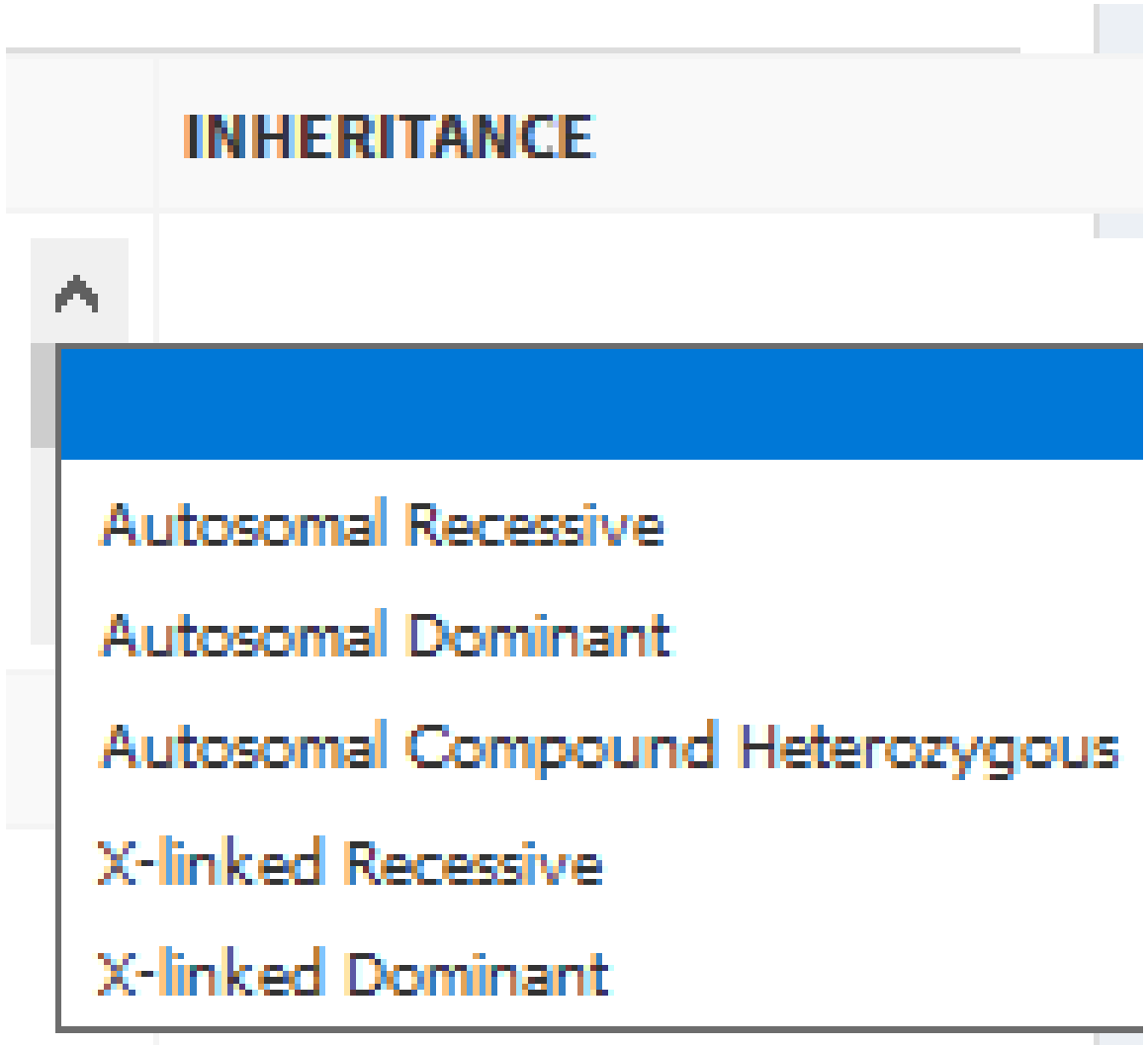
LABORATÓRIO DE GENÔMICA CLÍNICA

MEDICINA UFMG

Mendel,MD


Upload
Dashboard
1-Click
Tools
Docs
Forum
Donate
Login
Password
Family Analysis
+ Filter Options
Main
Variants
Databases
Diseases
Saved Configs
Saved Analysis
FAQ
FATHER
1351s
1352s
1353s
MOTHER
1351s
1352s
1353s
SELECT VARIANTS FROM
INDIVIDUALS:
1351s
1352s
1353s
SNP LIST:
GROUPS:
SAVED GENE LIST:
GENE LIST:
OPEN RESULT IN A NEW WINDOW
SUBMIT
RESET FILTER

Mendel,MD


INHERITANCE
Autosomal Recessive
Autosomal Dominant
Autosomal Compound Heterozygous
X-linked Recessive
X-linked Dominant

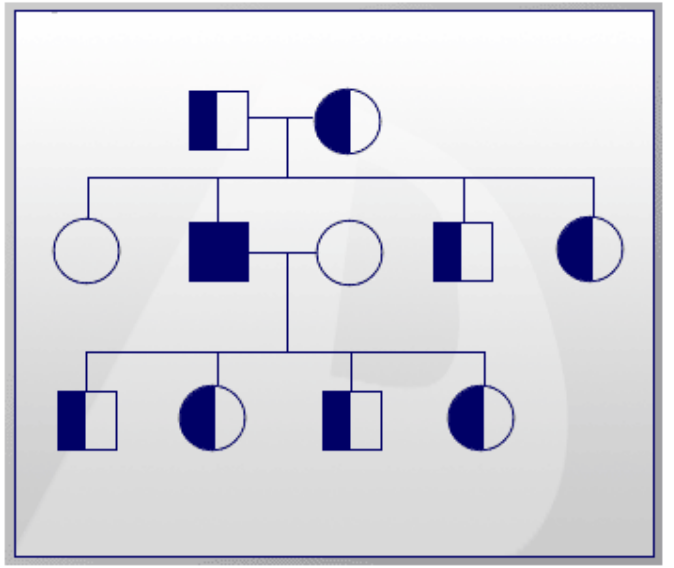
Modes of inheritance

- Inheritance patterns describe how a disease is transmitted in families.
- These patterns help to predict the recurrence risk for relatives.
- In general, inheritance patterns for single gene disorders are classified based on whether they are **autosomal** or **X-linked** and whether they have a **dominant** or **recessive** pattern of inheritance.

Example of Autosomal Recessive inheritance

→ Two copies of a disease allele are required for an individual to be susceptible to expressing the phenotype.

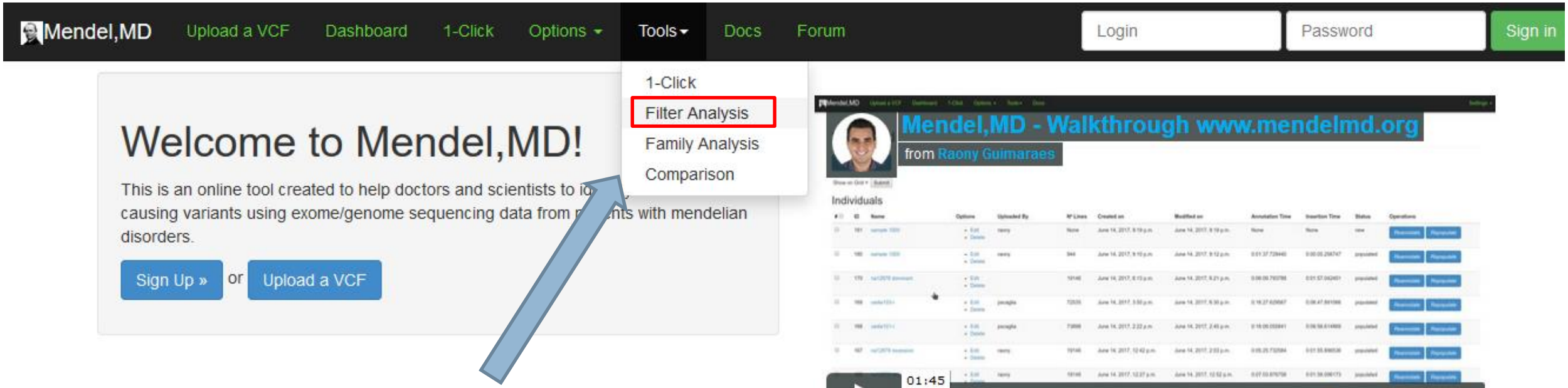
→ Typically, the parents of an affected individual are not affected but are gene carriers.



http://hihg.med.miami.edu

Mendel,MD

Options	Individual	Chr	Rsld	Pos	Qual	Ref	Alt	Filter	Gen	Father	Mother	Read Depth	Effect	Impact	Func Class	1kgenomes	dbSNP	ESP6500	Sift	PP2	DANN	CADD	OMIM	H(
CAGE1																								
Omim - GeneCards - NCBI																								
Options	Individual	Chr	Rsld	Pos	Qual	Ref	Alt	Filter	Gen	Father	Mother	Read Depth	Effect	Impact	Func Class	1kgenomes	dbSNP	ESP6500	Sift	PP2	DANN	CADD	OMIM	H(
View	1351s	6	.	7386048	532.17	A	T	PASS	1/1	HET	HET	11	NON_SYNONYMOUS_CODING	MODERATE	MISSENSE				0.06	0.13				
DEK																								
Omim - GeneCards - NCBI																								
Options	Individual	Chr	Rsld	Pos	Qual	Ref	Alt	Filter	Gen	Father	Mother	Read Depth	Effect	Impact	Func Class	1kgenomes	dbSNP	ESP6500	Sift	PP2	DANN	CADD	OMIM	H(
View	1351s	6	.	18264124	1422.16	G	A	PASS	1/1	HET	HET	27	NON_SYNONYMOUS_CODING	MODERATE	MISSENSE				0.03	0.94				
View	1351s	6	rs201160399 dbSNP	18258285	5069.16	G	A	PASS	1/1	HET	HET	77	STOP_GAINED	HIGH	NONSENSE									

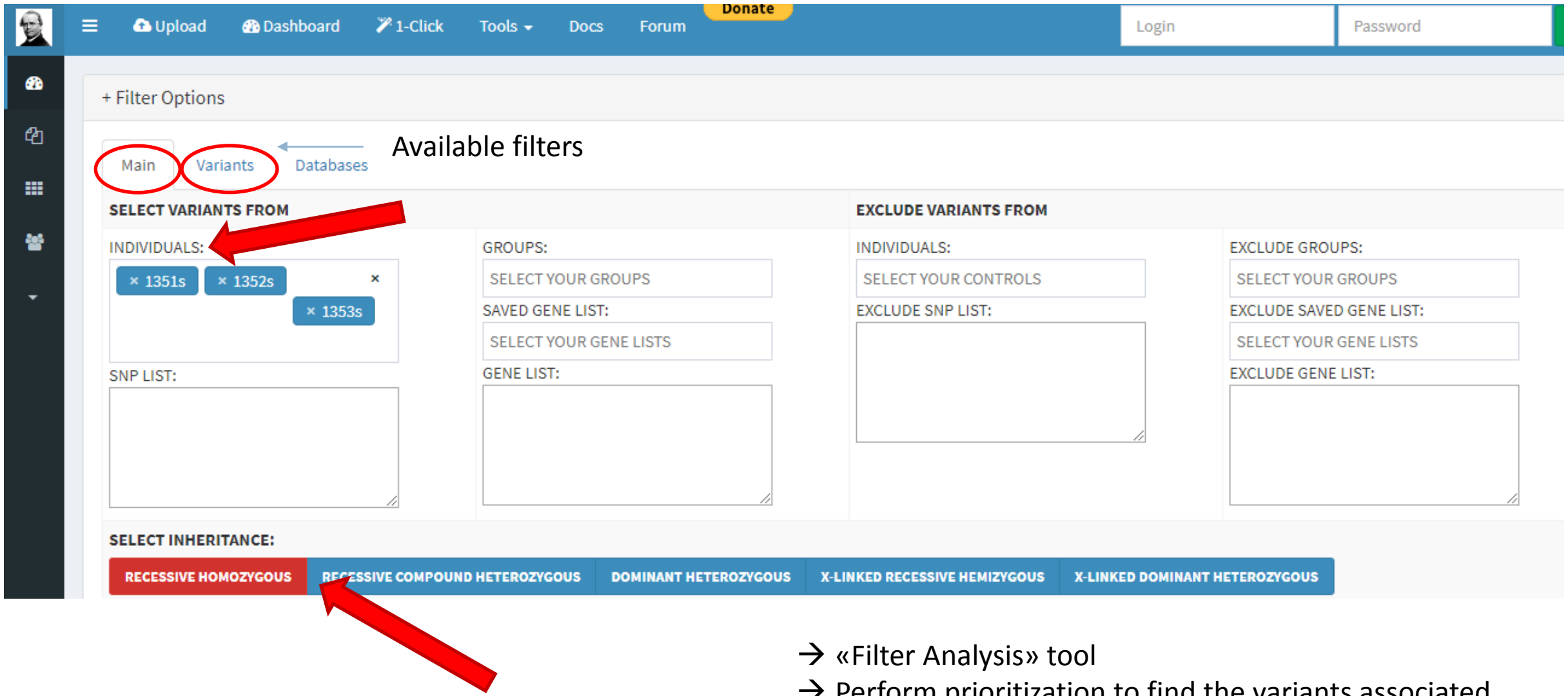


Analysis selection

LABORATÓRIO DE GENÔMICA CLÍNICA

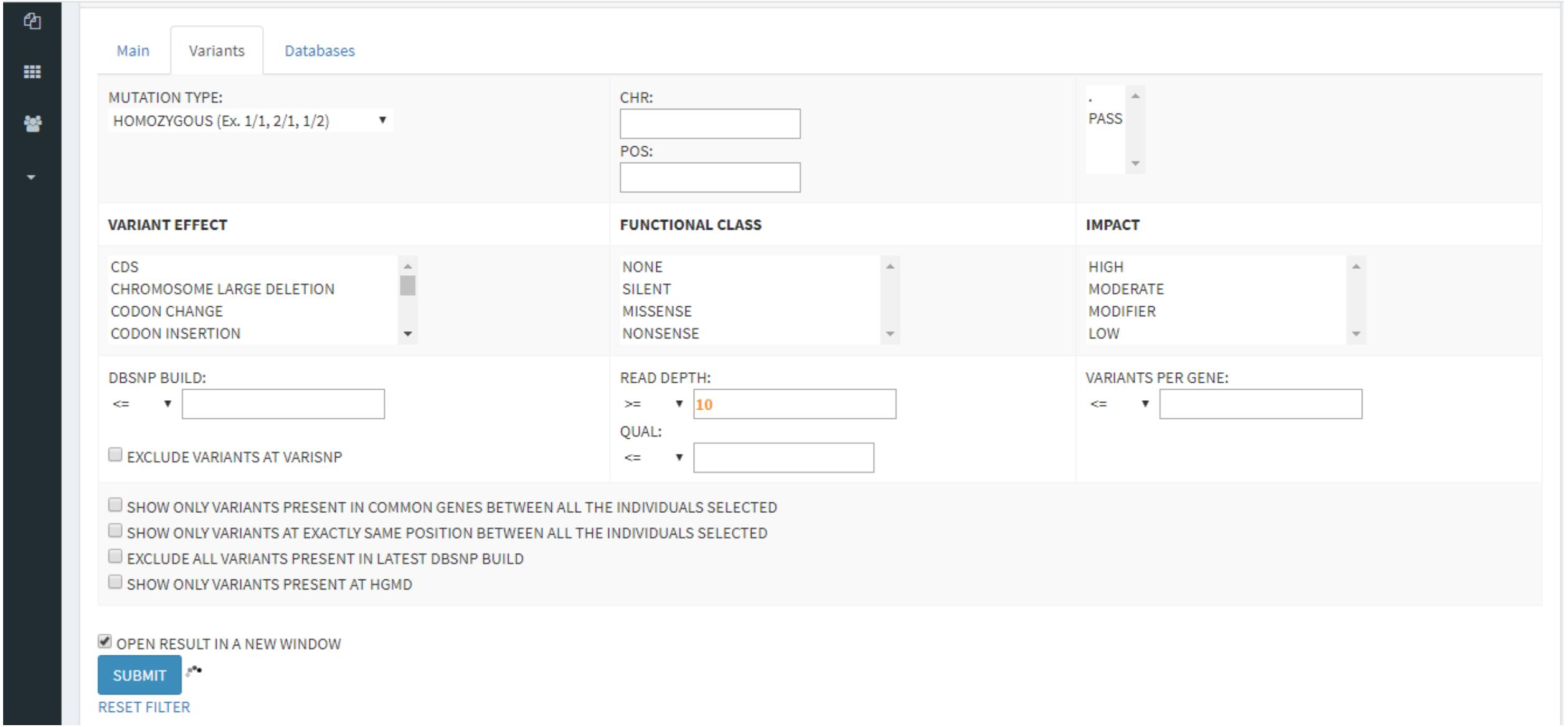
MEDICINA UFMG

Recessive Homozygous Analysis

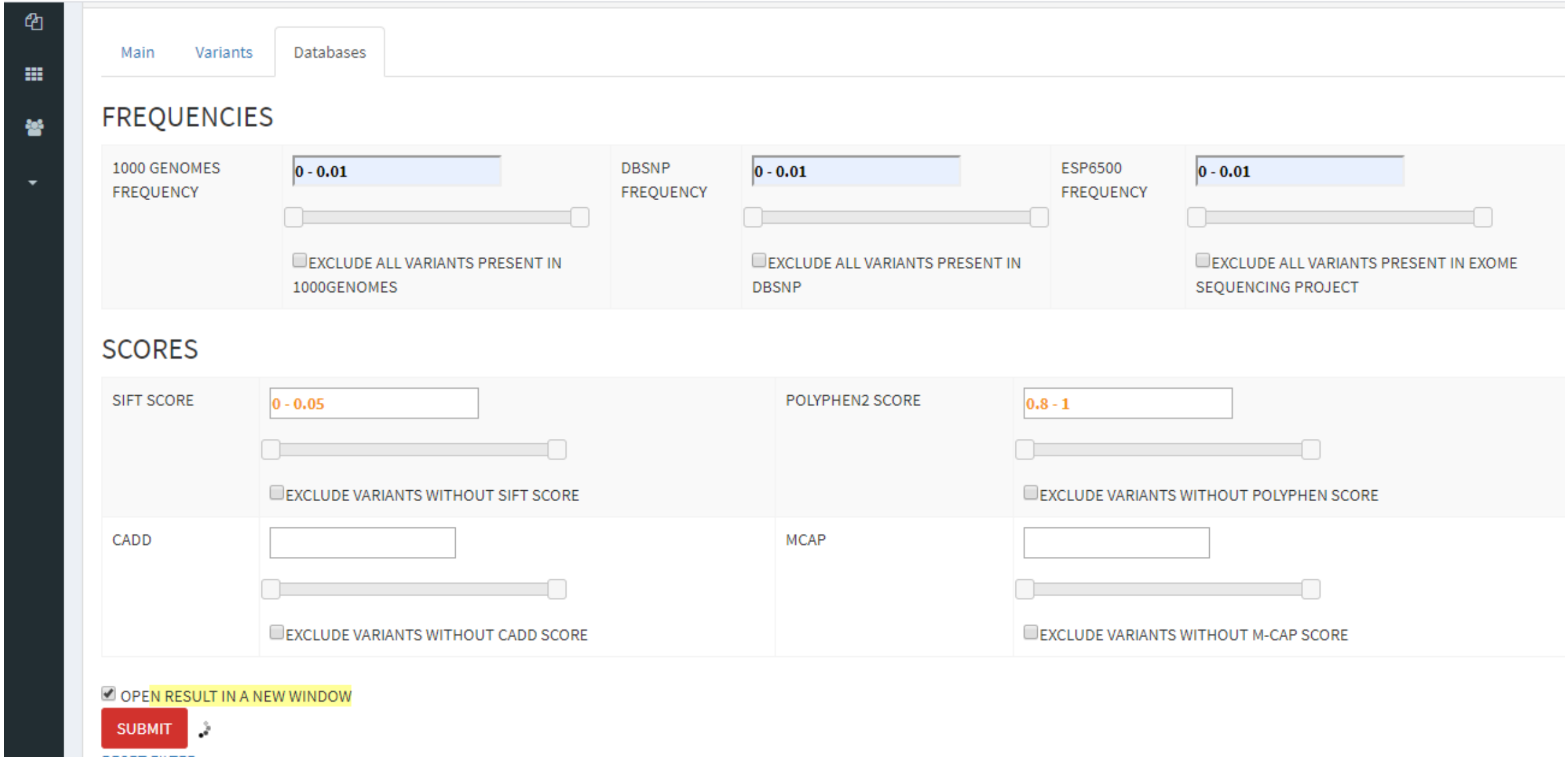


→ «Filter Analysis» tool
→ Perform prioritization to find the variants associated to Recessive Homozygous diseases

Filters (Variants)



Filters (Databases)



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+ Genes 92

+ Genes associated with diseases 21

Genes at Omim

ATXN1, C2, C4A, CD2AP, CYP21A2, DEK, DSP, ELOVL5, FANCE, FARS2, GCNT2, IGF2R, LAMA2, MAK, MOCS1, NEU1, PPP2R5D, RIMS1, SYNGAP1, TDP2, TNXB,

ATXN1	Spinocerebellar ataxia 1, 164400 (3)
C2	C2 deficiency, 217000 (3) {Macular degeneration, age-related, 14, reduced risk of}, 615489 (3)
C4A	C4a deficiency, 614380 (3) [Blood group, Rodgers], 614374 (3)

Genes at Clinical Genomics Database

ATXN1, C2, C4A, CD2AP, CYP21A2, DSP, ELOVL5, FAM65B, FANCE, FARS2, GCNT2, LAMA2, MAK, MOCS1, NEU1, PPP2R5D, RIMS1, SYNGAP1, TDP2, TNXB,

ATXN1	Spinocerebellar ataxia 1
C2	Complement component 2 deficiency
C4A	Blood group, Chido/Rodgers system
CD2AP	Focal segmental glomerulosclerosis 3
CYP21A2	Adrenal hyperplasia, congenital, due to 21-hydroxylase deficiency Hyperandrogenism, nonclassic type, due to 21-hydroxylase deficiency

Mendel,MD

Summary

Number of Variants: 7570

Number of Genes: 92

Export to: CSV

next Page 1 of 76

ABCF1

Omim - GeneCards - NCBI

	Options	Individual	Chr	Rsid	Pos	Qual	Ref	Alt	Filter	Gen	Read Depth	Effect	Impact	Func Class	1kgenomes	dbSNP	ESP6500	Sift	PP2	CADD	M-CAP	CLINVAR	HI Score
☐	View	1353s	6	.	30553360	4324.9	G	A	PASS	1/1	104	NON_SYNONYMOUS_CODING	MODERATE	MISSENSE				0.00	0.99		None None	None None None None	ABCF1|0.199313589|36.78%

ATXN1

Omim - GeneCards - NCBI

	Options	Individual	Chr	Rsid	Pos	Qual	Ref	Alt	Filter	Gen	Read Depth	Effect	Impact	Func Class	1kgenomes	dbSNP	ESP6500	Sift	PP2	CADD	M-CAP	CLINVAR	HI Score
☐	View	1351s	6	.	16327384	10929.9	A	G	PASS	1/1	101	SYNONYMOUS_CODING	LOW								None	None	ATXN1|0.832563526|5.05%

ABCF1

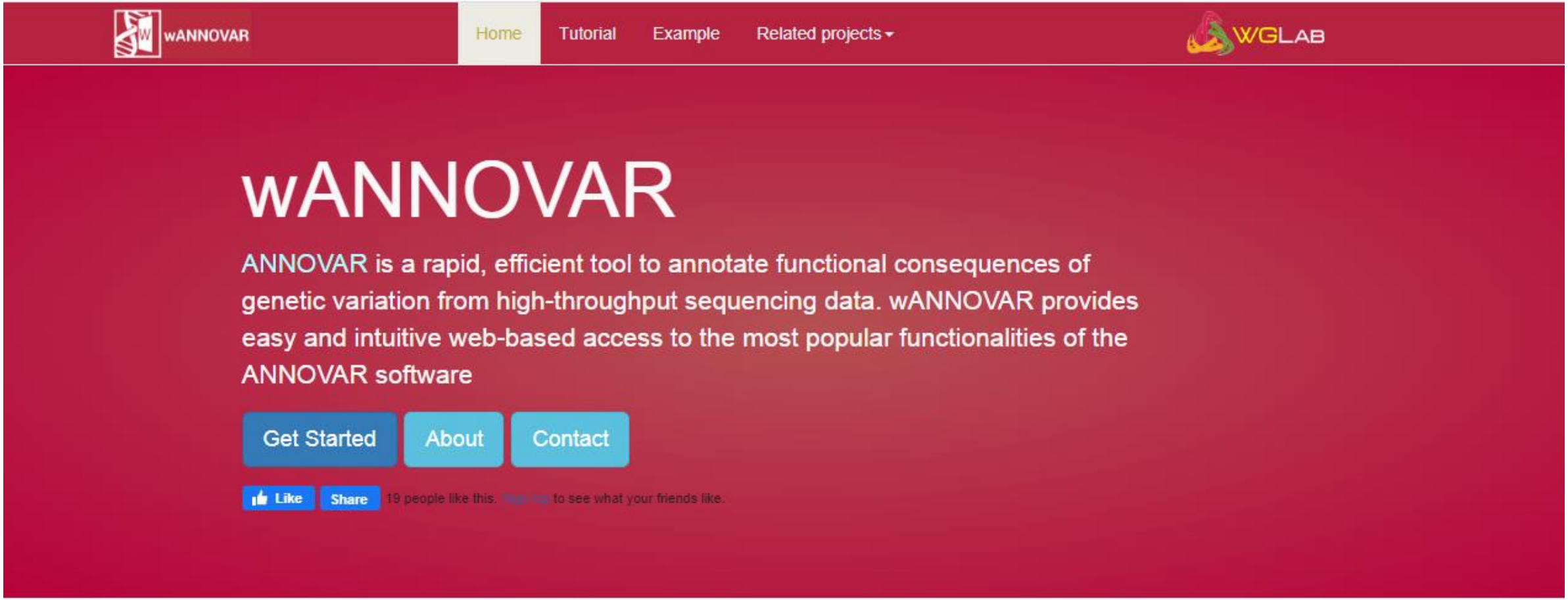
Omim - GeneCards - NCBI

	Options	Individual	Chr	Rsid	Pos	Qual	Ref	Alt	Filter	Gen	Read Depth	Effect	Impact	Func Class	1kgenomes	dbSNP	ESP6500	Sift	PP2	CADD	M-CAP	CLINVAR	HI Score
☐	View	1353s	6	.	30553360	4324.9	G	A	PASS	1/1	104	NON_SYNONYMOUS_CODING	MODERATE	MISSENSE				0.00	0.99		None None	None None None None	ABCF1|0.199313589|36.78%

→ This gene has an homozygous variant at position 6:30553360
→ NON_SYNONYMOUS_CODING effect
→ MODERATE impact
→ Sift score of 0.00
→ Polyphen2 score of 0,99

→ What if we change mode of inheritance?

wAnnovar

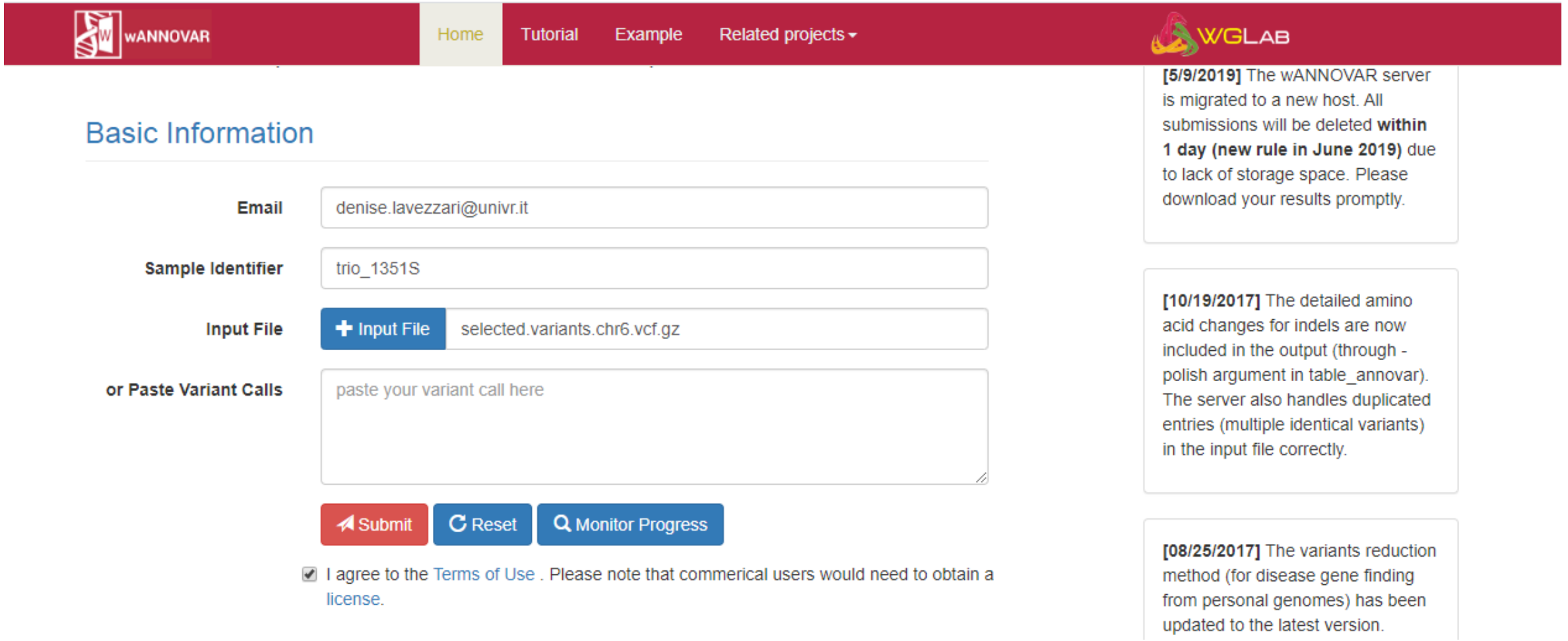


By default, wANNOVAR performs "individual analysis" on the first sample in your VCF file to help find disease genes (you may need to split your multi-sample VCF file to individual files for annotation separately to find disease genes). If you only want to annotate all variant sites in a multi-sample VCF file, select "All Annotations" option below.

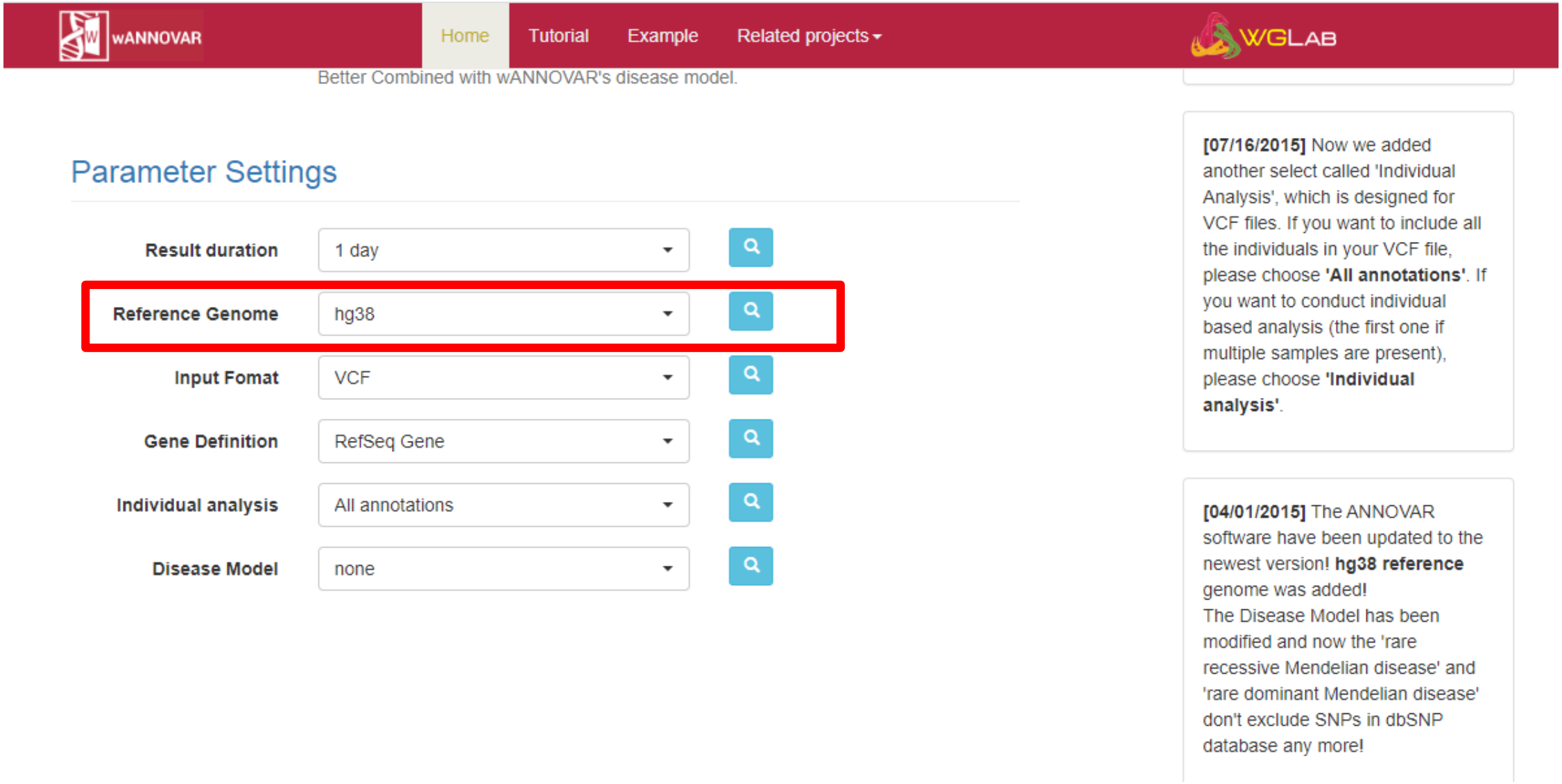
Recent Updates

http://wannovar.wglab.org/

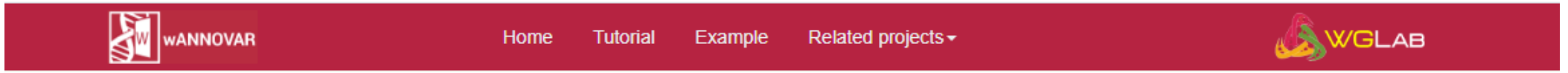
wAnnovar


wANNOVAR
Home
Tutorial
Example
Related projects
WGLAB
Basic Information
Email
denise.lavezzari@univr.it
Sample Identifier
trio_1351S
Input File
Input File
selected.variants.chr6.vcf.gz
or Paste Variant Calls
paste your variant call here
Submit
Reset
Monitor Progress
I agree to the Terms of Use . Please note that commerical users would need to obtain a license.
[5/9/2019] The wANNOVAR server is migrated to a new host. All submissions will be deleted within 1 day (new rule in June 2019) due to lack of storage space. Please download your results promptly.
[10/19/2017] The detailed amino acid changes for indels are now included in the output (through -polish argument in table_annovar). The server also handles duplicated entries (multiple identical variants) in the input file correctly.
[08/25/2017] The variants reduction method (for disease gene finding from personal genomes) has been updated to the latest version.

wAnnovar


wANNOVAR
Home
Tutorial
Example
Related projects
WGLAB
Better Combined with wANNOVAR's disease model.
Parameter Settings
Result duration
1 day
Reference Genome
hg38
Input Fomat
VCF
Gene Definition
RefSeq Gene
Individual analysis
All annotations
Disease Model
none
[07/16/2015] Now we added another select called 'Individual Analysis', which is designed for VCF files. If you want to include all the individuals in your VCF file, please choose 'All annotations'. If you want to conduct individual based analysis (the first one if multiple samples are present), please choose 'Individual analysis'.
[04/01/2015] The ANNOVAR software have been updated to the newest version! hg38 reference genome was added!
The Disease Model has been modified and now the 'rare recessive Mendelian disease' and 'rare dominant Mendelian disease' don't exclude SNPs in dbSNP database any more!

wAnnovar



Submission ID: 242620

Sample identifier = trio_1351S
File_name=selected.variants.chr6.vcf.gz
File_format=vcf4
Reference_genome=hg38
Disease_model=no filtering
Processed variants=11627

Basic Information

exome summary results	view	CSV file	TXT file
genome summary results	view	CSV file	TXT file

wAnnovar

100 results per page

back to HOME

Page: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

Chr	Start	End	Ref	Alt	Func	Gene	GeneDetail	ExonicFunc	AAChange
chr6	348906	348906	G	A	exonic	DUSP22		synonymous SNV	DUSP22:NM_001286555:exon7:c.G573A:p.P191P
chr6	656143	656143	C	A	exonic	HUS1B		nonsynonymous SNV	HUS1B:NM_148959:exon1:c.G802T:p.D268Y
chr6	656343	656343	T	C	exonic	HUS1B		nonsynonymous SNV	HUS1B:NM_148959:exon1:c.A602G:p.Q201R
chr6	1312882	1312882	A	C	exonic	FOXQ1		nonsynonymous SNV	FOXQ1:NM_033260:exon1:c.A178C:p.T60P
chr6	1312886	1312886	A	C	exonic	FOXQ1		nonsynonymous SNV	FOXQ1:NM_033260:exon1:c.A182C:p.Q61P
chr6	1313717	1313717	A	G	exonic	FOXQ1		nonsynonymous SNV	FOXQ1:NM_033260:exon1:c.A1013G:p.E338G
chr6	1394808	1394808	T	C	exonic	FOXF2		synonymous SNV	FOXF2:NM_001452:exon2:c.T1284C:p.Y428Y
chr6	1742560	1742560	A	G	exonic	GMDS		synonymous SNV	GMDS:NM_001253846:exon8:c.T708C:p.D236D,GMDS:NM_001500:exon8:c.T798C:p.D266D
chr6	2749147	2749147	C	T	exonic	MYLK4		nonsynonymous SNV	MYLK4:NM_001012418:exon2:c.G148A:p.G50R,MYLK4:NM_001347872:exon2:c.G316A:p.G106R
chr6	2765910	2765910	T	C	exonic	WRNIP1		synonymous SNV	WRNIP1:NM_020135:exon1:c.T288C:p.G96G,WRNIP1:NM_130395:exon1:c.T288C:p.G96G
chr6	2766231	2766231	T	C	exonic	WRNIP1		synonymous SNV	WRNIP1:NM_020135:exon1:c.T609C:p.S203S,WRNIP1:NM_130395:exon1:c.T609C:p.S203S
chr6	2784337	2784337	G	A	exonic	WRNIP1		synonymous SNV	WRNIP1:NM_020135:exon6:c.G1656A:p.P552P,WRNIP1:NM_130395:exon6:c.G1581A:p.P527P

wAnnovar

Sort by:

Filter by:

1000G_ALL:	<=	0.01	1000G_AFR:			1000G_EUR:	<=	0.01
ExAC_Freq:	<=	0.01	ExAC_AMR:			ExAC_NFE:		
ESP6500si_ALL:	<=	0.01	CG46:			COSMIC_ID:		
ClinVar_DIS:			ClinVar_DB:			GWAS_DIS:		
GWAS_OR:			GWAS_BETA:					

Chr:

Start:

End:

Gene:

1000G_ALL:

1000G_EAS:

1000G_AFR:

Func:

- [ ] exonic
- [ ] exonic;splicing
- [ ] splicing
- [ ] UTR3
- [ ] UTR5
- [ ] intronic
- [ ] intergenic
- [ ] upstream
- [ ] downstream
- [ ] upstream;downstream
- [ ] ncRNA_exonic
- [ ] ncRNA_intronic
- [ ] ncRNA_UTR3
- [ ] ncRNA_UTR5

ExonicFunc:

- [ ] frameshift insertion
- [ ] frameshift deletion
- [ ] nonframeshift deletion
- [ ] nonframeshift insertion
- [x] nonsynonymous SNV
- [ ] synonymous SNV
- [x] stopgain SNV
- [x] stoploss SNV
- [ ] unknown

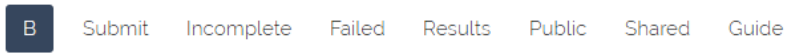
Go

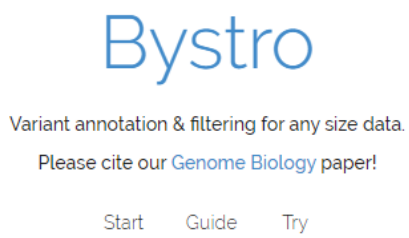
wAnnovar

Chr	Start	End	Ref	Alt	Func	Gene	GeneDetail	ExonicFunc	AAChange
chr6	3273220	3273220	G	A	exonic	SLC22A23		synonymous SNV	SLC22A23:NM_001286455:exon10:c.C1053T:p.N351N,SLC22A23:NM_015482:exon10:c.C1896T:p.N632N,SLC22A23:NM_021945:exon11:c.C1053T:p.N351N
chr6	4031690	4031690	A	G	exonic	PRPF4B		nonsynonymous SNV	PRPF4B:NM_003913:exon2:c.A173G:p.K58R
chr6	6174635	6174635	G	A	exonic	F13A1		synonymous SNV	F13A1:NM_000129:exon12:c.C1692T:p.V564V
chr6	15524578	15524578	G	A	exonic	DTNBP1		synonymous SNV	DTNBP1:NM_001271669:exon7:c.C654T:p.D218D,DTNBP1:NM_001271668:exon8:c.C708T:p.D236D,DTNBP1:NM_001271667:exon9:c.C516T:p.D172D,DTNBP1:NM_032122:exon9:c.C759T:p.D253D,DT
chr6	16129381	16129381	A	C	exonic	MYLIP		nonsynonymous SNV	MYLIP:NM_013262:exon1:c.A59C:p.K20T
chr6	17616571	17616571	C	T	exonic	NUP153		synonymous SNV	NUP153:NM_001278210:exon20:c.G4173A:p.S1391S,NUP153:NM_005124:exon21:c.G4299A:p.S1433S,NUP153:NM_001278209:exon22:c.G4392A:p.S1464S
chr6	17828347	17828347	A	G	exonic	KIF13A		synonymous SNV	KIF13A:NM_001105566:exon14:c.T1425C:p.D475D,KIF13A:NM_001105567:exon14:c.T1425C:p.D475D,KIF13A:NM_001105568:exon14:c.T1425C:p.D475D,KIF13A:NM_022113:exon14:c.T1425C:p.
chr6	18121617	18121617	C	T	exonic	NHLRC1		synonymous SNV	NHLRC1:NM_198586:exon1:c.G990A:p.Q330Q
chr6	20546466	20546466	G	A	exonic	CDKAL1		nonsynonymous SNV	CDKAL1:NM_017774:exon3:c.G116A:p.R39Q
chr6	25610111	25610111	A	G	exonic	CARMIL1		synonymous SNV	CARMIL1:NM_001173977:exon36:c.A3891G:p.K1297K,CARMIL1:NM_017640:exon36:c.A3909G:p.K1303K
chr6	27911949	27911949	A	G	exonic	OR2B2		nonsynonymous SNV	OR2B2:NM_033057:exon1:c.T371C:p.V124A
chr6	30146010	30146010	G	A	exonic	TRIM40		nonsynonymous SNV	TRIM40:NM_138700:exon2:c.G362A:p.R121Q,TRIM40:NM_001286633:exon3:c.G362A:p.R121Q
chr6	30340333	30340333	C	T	exonic	TRIM39		nonsynonymous SNV	TRIM39:NM_021253:exon7:c.C865T:p.L289F
chr6	30547202	30547202	T	A	exonic	GNL1		nonsynonymous SNV	GNL1:NM_005275:exon10:c.A1351T:p.I451F
chr6	30619578	30619578	C	T	exonic	MRPS18B		nonsynonymous SNV	MRPS18B:NM_014046:exon2:c.C164T:p.P55L
chr6	30723611	30723611	C	T	exonic	TUBB		synonymous SNV	TUBB:NM_001293214:exon3:c.C417T:p.Y139Y,TUBB:NM_001293212:exon4:c.C609T:p.Y203Y,TUBB:NM_001293215:exon4:c.C333T:p.Y111Y,TUBB:NM_001293216:exon4:c.C333T:p.Y111Y,TUBB:NM
chr6	30950414	30950414	C	T	exonic	DPCR1		synonymous SNV	DPCR1:NM_080870:exon2:c.C1950T:p.N650N
chr6	31027301	31027301	G	A	exonic	MUC22		nonsynonymous SNV	MUC22:NM_001198815:exon3:c.G1870A:p.E624K,MUC22:NM_001318484:exon3:c.G1879A:p.E627K,MUC22:NM_001322469:exon3:c.G1879A:p.E627K
chr6	31027303	31027303	G	C	exonic	MUC22		nonsynonymous SNV	MUC22:NM_001198815:exon3:c.G1872C:p.E624D,MUC22:NM_001318484:exon3:c.G1881C:p.E627D,MUC22:NM_001322469:exon3:c.G1881C:p.E627D
chr6	31535469	31535469	G	C	exonic	DDX39B		synonymous SNV	DDX39B:NM_004640:exon6:c.C633G:p.V211V,DDX39B:NM_080598:exon6:c.C633G:p.V211V
chr6	31624305	31624305	C	A	exonic	PRRC2A		nonsynonymous SNV	PRRC2A:NM_004638:exon4:c.C335A:p.P112Q,PRRC2A:NM_080686:exon4:c.C335A:p.P112Q
chr6	31773029	31773029	G	A	exonic	VWA7		nonsynonymous SNV	VWA7:NM_025258:exon7:c.C1012T:p.R338C
chr6	31774590	31774590	C	T	exonic	VWA7		nonsynonymous SNV	VWA7:NM_025258:exon5:c.G647A:p.S216N
chr6	32213706	32213706	T	C	exonic	NOTCH4		nonsynonymous SNV	NOTCH4:NM_004557:exon14:c.A2302G:p.T768A

How are these genes classified in ClinVar?

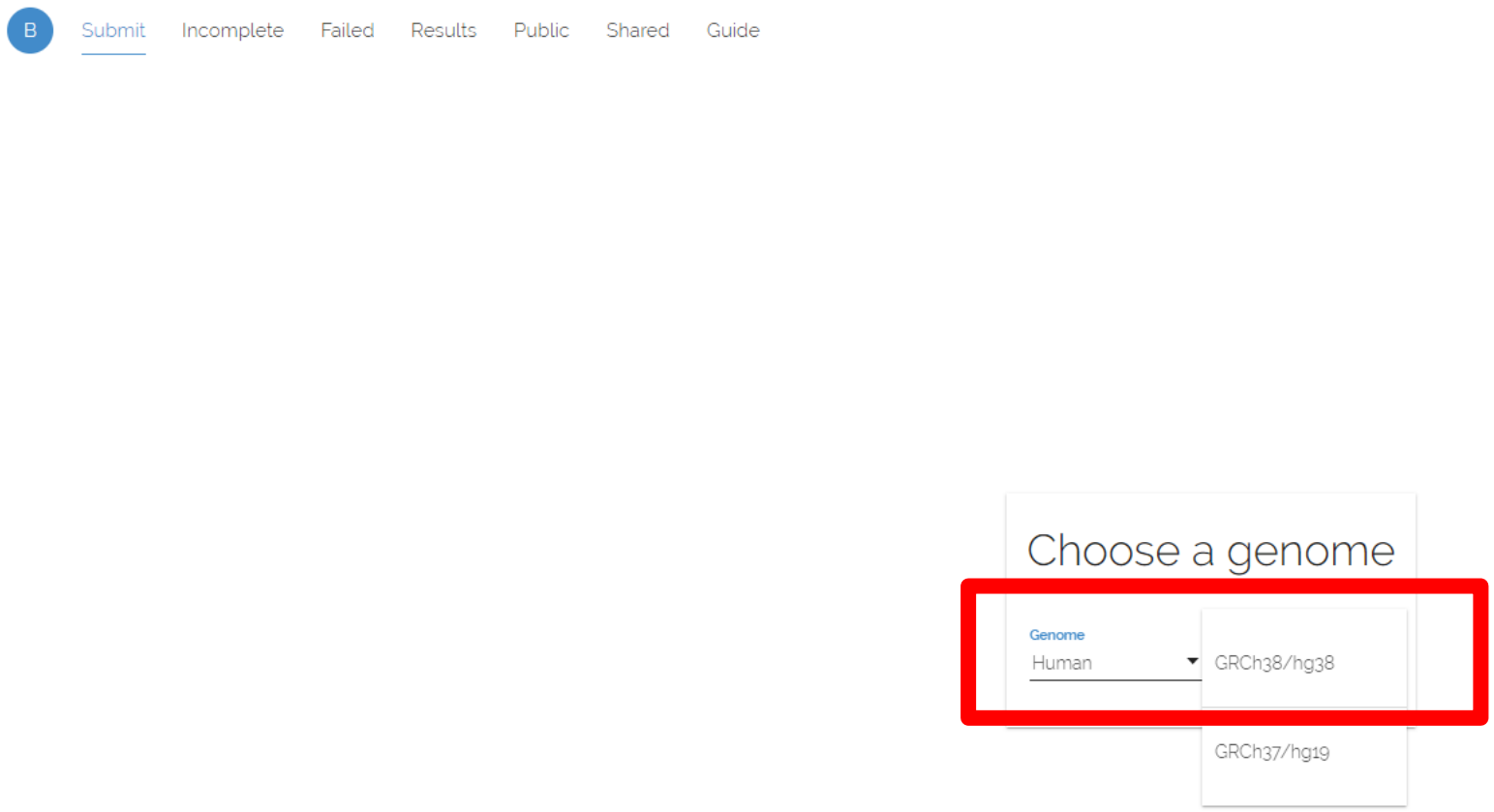
Bystro





https://bystro.io/

Bystro


B
Submit
Incomplete
Failed
Results
Public
Shared
Guide
Denise Lavezzari
Log out
Choose a genome
Genome
Human
GRCh38/hg38
GRCh37/hg19

Bystro

B Submit Incomplete Failed Results Public Shared Guide

Denise Lavezzari Log out

Upload to submit

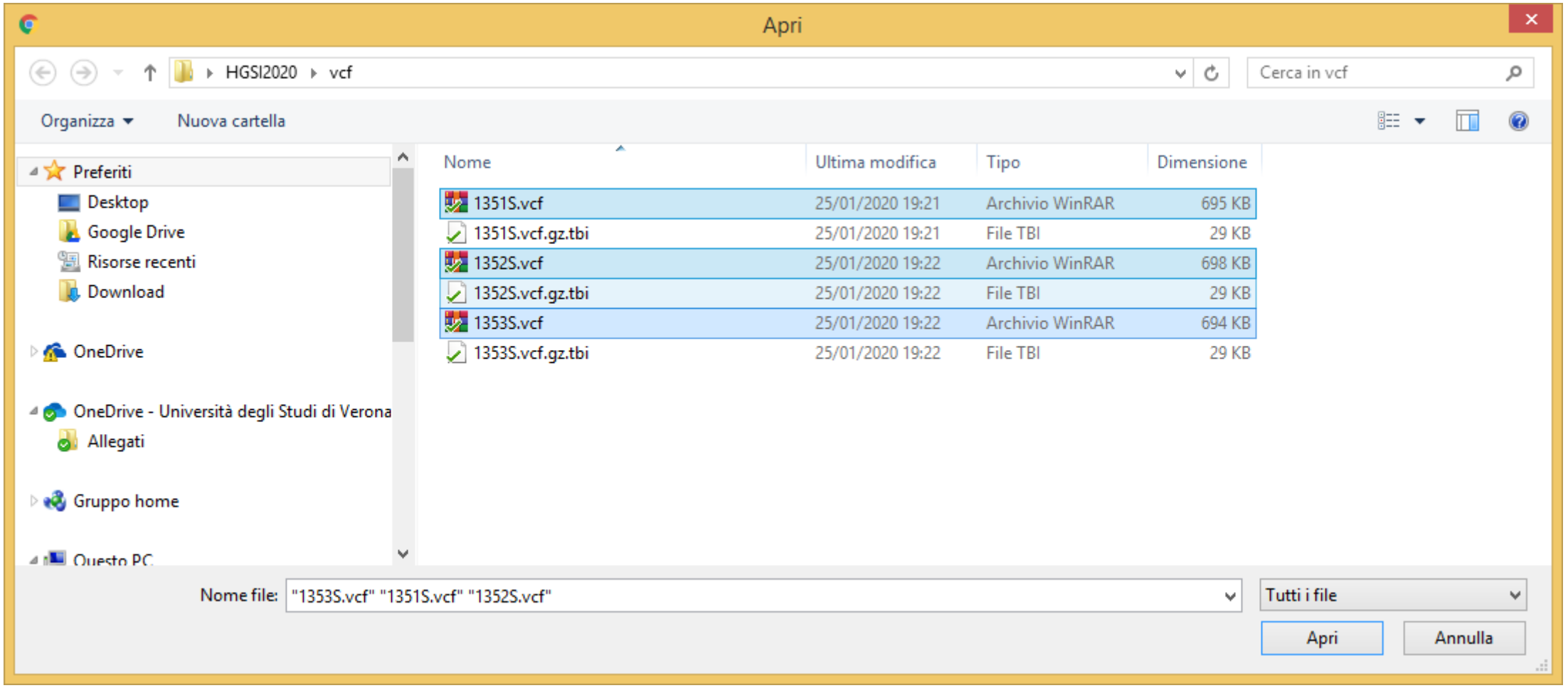
Accepts .vcf and .snp files

Annotations will be deleted **after 1 month of inactivity**

or

Back Start

Bystro


Apri
HGSI2020 ▸ vcf
Cerca in vcf
Organizza
Nuova cartella
Preferiti
Desktop
Google Drive
Risorse recenti
Download
OneDrive
OneDrive - Università degli Studi di Verona
Allegati
Gruppo home
Questo PC
Nome
Ultima modifica
Tipo
Dimensione
1351S.vcf 25/01/2020 19:21 Archivio WinRAR 695 KB
1351S.vcf.gz.tbi 25/01/2020 19:21 File TBI 29 KB
1352S.vcf 25/01/2020 19:22 Archivio WinRAR 698 KB
1352S.vcf.gz.tbi 25/01/2020 19:22 File TBI 29 KB
1353S.vcf 25/01/2020 19:22 Archivio WinRAR 694 KB
1353S.vcf.gz.tbi 25/01/2020 19:22 File TBI 29 KB
Nome file: "1353S.vcf" "1351S.vcf" "1352S.vcf"
Tutti i file
Apri
Annulla

Bystro

Upload to submit

Accepts .vcf and .snp files

Annotations will be deleted after 1 month of inactivity

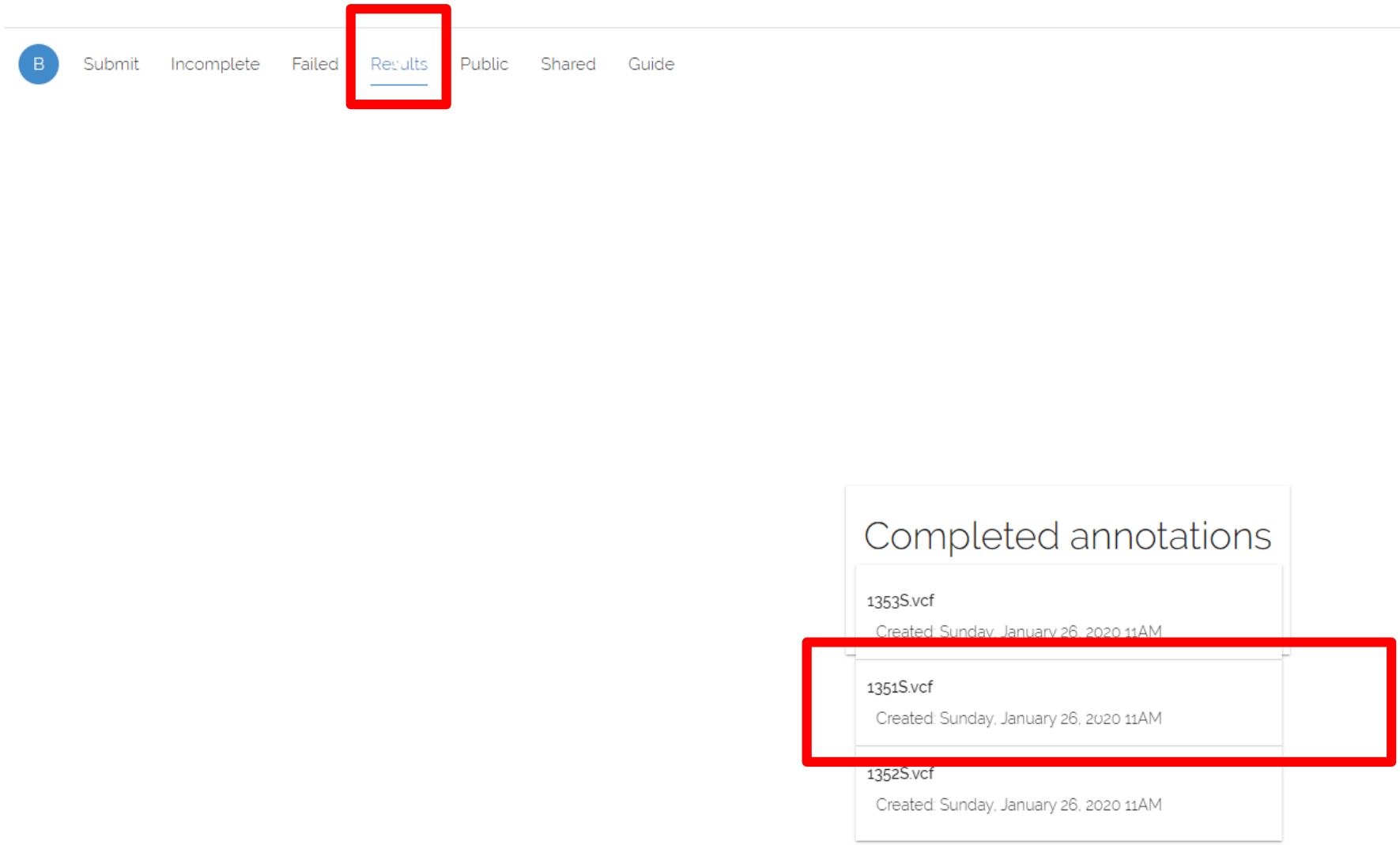
1351S.vcf.gz (Size: 694.1 kB)

1352S.vcf.gz (Size: 697.4 kB)

1353S.vcf.gz (Size: 693.7 kB)

Back Start

Bystro


B
Submit
Incomplete
Failed
Results
Public
Shared
Guide
Completed annotations
1353S.vcf
Created: Sunday, January 26, 2020 11AM
1351S.vcf
Created: Sunday, January 26, 2020 11AM
1352S.vcf
Created: Sunday, January 26, 2020 11AM

Bystro

B Submit Incomplete Failed Results Public Shared Guide Denise Lavezzari Log ou

1351S.vcf (completed)
Created on: Jan 26, 2020 11:46:40 AM
Notes: (Click to add a note)

Search this file
Ex: * (all results) , exonic , pathogenic missense cadd > 15

Sample Summary

View

1351S

Experiment

Statistical details

Sample Summary Statistics

heterozygotes/homozygotes mean : 1.879
heterozygotes/homozygotes median : 1.879
heterozygotes/homozygotes sd : NA

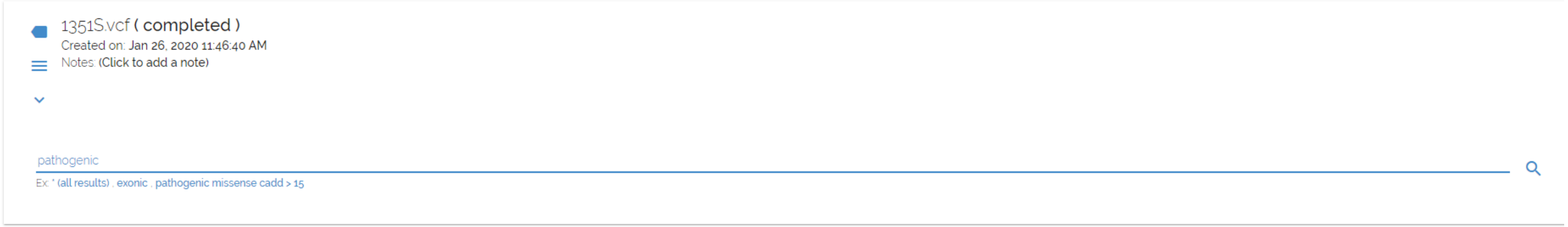
samples : 1

samples_bad : 0

silent/replacement mean : 0.923
silent/replacement median : 0.923
silent/replacement sd : NA

Bystro

Search for pathogenic variants:



Bystro

pathogenic

Sort Tools Size Filter Pipeline

Searched: ***pathogenic***

Search Results Summary

Found 8 results in 0.002s

Showing page 1 (10 results per page)

Ts/Tv Ratio

Tr:Tv Ratio: 3
Transitions: 6
Transversions: 2

Filters & Aggregations

Explore your data by specific field

Expand all

LAMA2

chr6 : 129,250,185

R619H

Less Detail

RefSeq Transcripts

Name: NM_001079823 ; NM_000426
spDisplayID: LAMA2_HUMAN ;
spID: P24043 ;
mRNA: NM_001079823 ;
protAcc: NM_001079823 ;

Site Type: exonic
Strand: +

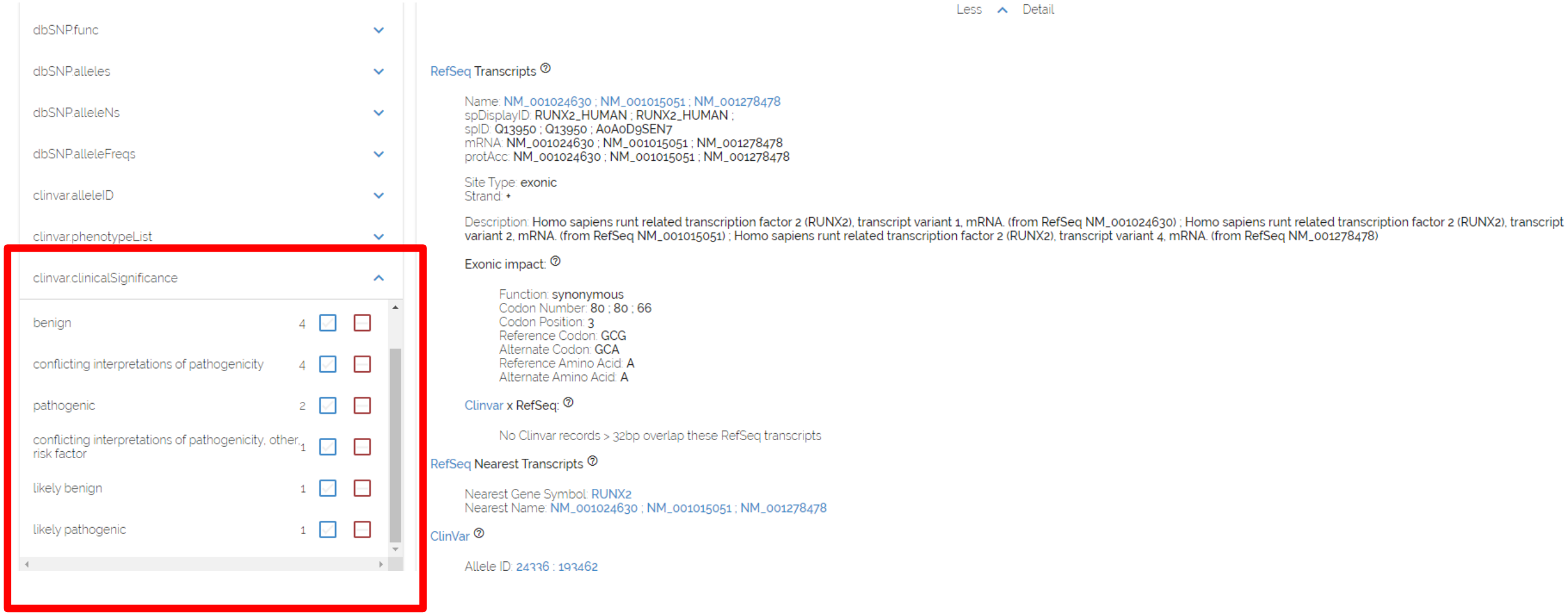
Description: Homo sapiens laminin subunit alpha 2 (LAMA2), transcript variant 2, mRNA. (from RefSeq NM_001079823) ;

Exonic impact:

Function: nonSynonymous
Codon Number: 619

Bystro

Select Clinvar significance: «pathogenic variants»



Bystro

pathogenic

Sort Tools Size Filter Pipeline

Searched: ***pathogenic***

+pathogenic ✕

Search Results Summary

Found 2 results in 0.001s

Showing page 1 (10 results per page)

Ts/Tv Ratio

Tr:Tv Ratio: ∞

Transitions: 2

Transversions: 0

Filters & Aggregations

Explore your data by specific field

chrom

pos

type

discordant

alt

Expand all

LAMA2

chr6 : 129,250,185

R619H

More Detail

Cadd: 0.77 PhyloP: -1.57 PhastCons: 0

RUNX2

chr6 : 45,422,774

A80A

A66A

More Detail

Cadd: 19.2 PhyloP: 0.76 PhastCons: 1

Bystro

RefSeq Transcripts

Name: NM_001079823 ; NM_000426
spDisplayID: LAMA2_HUMAN ;
spID: P24043 ;
mRNA: NM_001079823 ;
protAcc: NM_001079823 ;

Site Type: exonic
Strand: +

Description: Homo sapiens laminin subunit alpha 2 (LAMA2), transcript variant 2, mRNA. (from RefSeq NM_001079823) ;

Exonic impact:

Function: nonSynonymous
Codon Number: 619
Codon Position: 2
Reference Codon: CGT
Alternate Codon: CAT
Reference Amino Acid: R
Alternate Amino Acid: H

Clinvar x RefSeq:

Allele ID: 29342 ; 73040 ; 158994 ; 164020 ; 260937 ; 430992 ; 443868 ; 455103 ; 455104 ; 455109 ; 455110
Clinical Significance: Pathogenic ; Pathogenic ; Uncertain significance ; Likely pathogenic ; Likely pathogenic ; Pathogenic ; Likely pathogenic ; Pathogenic ; Pathogenic ; Pathogenic ; Likely pathogenic
Phenotypes: Merosin deficient congenital muscular dystrophy ; See cases ; See cases ; See cases ; Merosin deficient congenital muscular dystrophy ; Merosin deficient congenital muscular dystrophy ; not provided ; Laminin alpha 2-related dystrophy ; Laminin alpha 2-related dystrophy ; Laminin alpha 2-related dystrophy ; Laminin alpha 2-related dystrophy
Origin: germline ; not provided ; not provided ; de novo ; unknown ; inherited ; germline ; germline ; germline ; germline ; germline
Number of Submitters: 2 ; 1 ; 1 ; 1 ; 1 ; 1 ; 1 ; 1 ; 1 ; 1 ; 1
Review Status: no assertion criteria provided ; criteria provided, single submitter ; no assertion criteria provided ; no assertion criteria provided ; criteria provided, single submitter ; criteria provided, single submitter ; criteria provided, single submitter ; criteria provided, single submitter ; criteria provided, single submitter ; criteria provided, single submitter ; criteria provided, single submitter
Type: deletion ; copy number loss ; copy number loss ; copy number loss ; deletion ; deletion ; deletion ; deletion ; deletion ; deletion ; deletion
Clinvar Record Size (computed) : 4.987 bp ; 3.176.172 bp ; 296.255 bp ; 2.940.307 bp ; 162 bp ; 85 bp ; 35 bp ; 251 bp ; 1.536 bp ; 148 bp ; 11.976 bp

RefSeq Nearest Transcripts

Nearest Gene Symbol: LAMA2
Nearest Name: NM_001079823 ; NM_000426

ClinVar

Allele ID: 46903 ; 98850 ; 191335
Clinical Significance: Pathogenic ; Benign ; Pathogenic
Phenotypes: Laminin alpha 2-related dystrophy ; Merosin deficient congenital muscular dystrophy ; not provided ; Congenital Muscular Dystrophy, LAMA2-related ; Merosin deficient congenital muscular dystrophy ; not specified ; Merosin deficient congenital muscular dystrophy
Origin: germline
Number of Submitters: 4 ; 6 ; 1
Review Status: criteria provided, multiple submitters, no conflicts ; criteria provided, multiple submitters, no conflicts ; criteria provided, single submitter
Type: duplication ; single nucleotide variant ; insertion
Reference Allele : ACGTGTTC ; G ; -
Alternate Allele: : ACGTGTTCACGTGTTC ; A ; ATGTTCAC

dbSNP

Name: rs3816665 ; rs797044643
Alleles: C ; T ;

Strand: - ; +
Class: single ; insertion
Function: missense ; untranslated-5 ; frameshift ; untranslated-5

Allele frequencies: 0.813745975494385 ; 0.186253994703293 ;
Allele sample sizes: 102768 ; 23522 ;
Observed alleles: C ; T ; - ; ATGTTCAC

gnomAD whole-genome matches

Alternate Allele: A
ID: rs3816665

Allele Frequency

Overall: 0.253026992082596
AMR: 0.108851999044418
ASJ: 0.149006992578506
EAS: 0.080323800444603
FIN: 0.186927005648613
NFE: 0.137412995100021
OTH: 0.176171004772186
Male: 0.256035000085831
Female: 0.249311998486519

Allele Number

Overall: 30886
AMR: 836
ASJ: 302
EAS: 1606
FIN: 3488
NFE: 14984
OTH: 982
Male: 17068
Female: 13818

gnomAD whole-exome matches

Alternate Allele: A
ID: rs3816665

Allele Frequency

Overall: 0.173500001430511
AMR: 0.11913999915123
ASJ: 0.157323002815247
EAS: 0.0780306980013847
FIN: 0.189890995621681
NFE: 0.135849997401237
SAS: 0.234662994742393
OTH: 0.157058998942375
Male: 0.172204002737999
Female: 0.175071001052856