

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

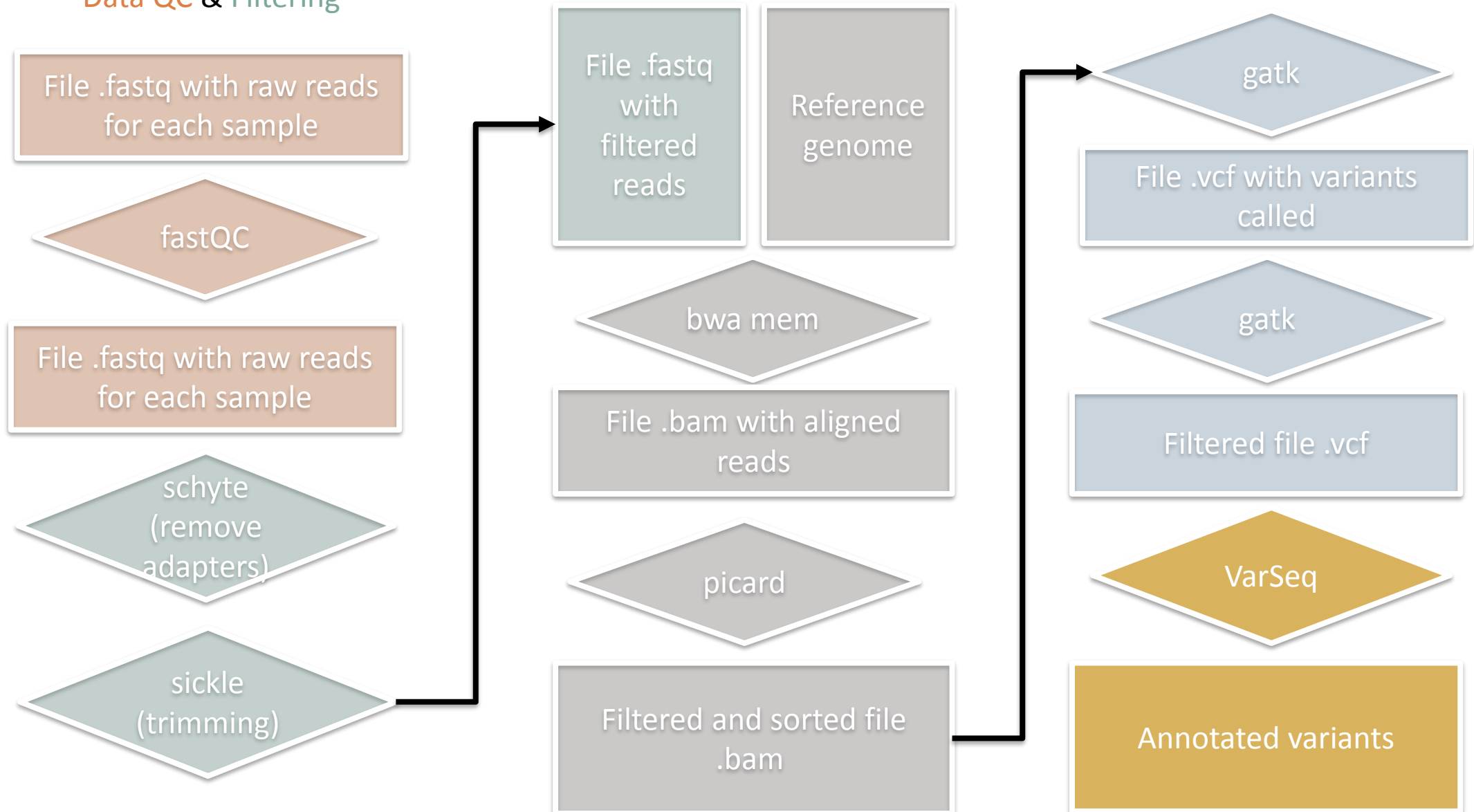
File .vcf with variants
called

gatk

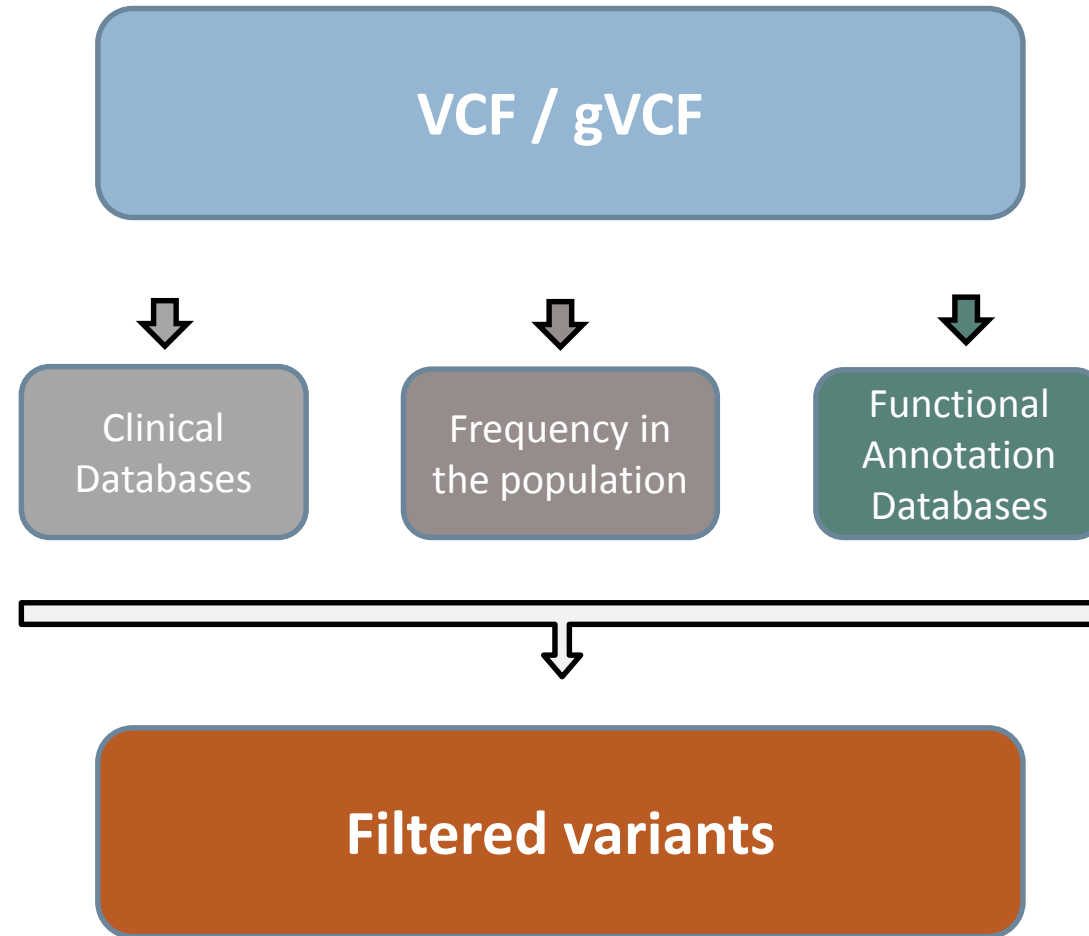
Filtered file .vcf

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



Mendel,MD

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[1-Click](#)

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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.

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Mendel,MD - Walkthrough www.mendelmd.org
from Raony Guimaraes

Individuals

#	ID	Name	Options	Uploaded By	# Lines	Created on	Modified on	Annotation Time	ScanTime	Status	Operations
10	101	sample 1001	+ 0:01 + Details	raony	None	June 14, 2017, 9:19 p.m.	June 14, 2017, 9:19 p.m.	None	None	new	Reupload Reupload
10	100	sample 1000	+ 0:01 + Details	raony	348	June 14, 2017, 9:12 p.m.	June 14, 2017, 9:12 p.m.	0:01:37.726440	0:00:00.204747	uploaded	Reupload Reupload
10	179	ref2019 download	+ 0:01 + Details		10140	June 14, 2017, 8:10 p.m.	June 14, 2017, 8:21 p.m.	0:00:00.760706	0:01:57.042401	uploaded	Reupload Reupload
10	100	sample1001	+ 0:01 + Details	pernigla	72005	June 14, 2017, 5:50 p.m.	June 14, 2017, 5:50 p.m.	0:16:27.606607	0:00:47.881066	uploaded	Reupload Reupload
10	100	sample1001	+ 0:01 + Details	pernigla	72006	June 14, 2017, 2:22 p.m.	June 14, 2017, 2:40 p.m.	0:15:00.000001	0:00:58.614000	uploaded	Reupload Reupload
10	107	ref2019 download	+ 0:01 + Details	raony	10140	June 14, 2017, 12:42 p.m.	June 14, 2017, 2:03 p.m.	0:05:25.710004	0:01:55.890000	uploaded	Reupload Reupload
10	101	sample 1001	+ 0:01 + Details	raony	10140	June 14, 2017, 12:37 p.m.	June 14, 2017, 12:52 p.m.	0:07:00.070706	0:01:50.000000	uploaded	Reupload Reupload
10	101	sample 1001	+ 0:01 + Details	pernigla	10140	June 14, 2017, 9:00 p.m.	June 14, 2017, 9:00 p.m.	0:00:00.000000	0:00:00.000000	uploaded	Reupload Reupload
10	101	sample 1001	+ 0:01 + Details	raony	10140	June 14, 2017, 8:24 p.m.	June 14, 2017, 8:24 p.m.	0:04:21.400706	0:12:11.201000	uploaded	Reupload Reupload

01:45



<https://mendelmd.org/>

Mendel,MD



Mendel,MD

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Individuals

#	ID	Name	Options	Uploaded By	# Lines	Created on	Modified on	Annotation Time	Insertion Time	Status	Operations
101	sample 1001		+ Edit + Delete	raony	None	June 14, 2017, 9:19 p.m.	June 14, 2017, 9:19 p.m.	None	None	new	Reupload Reupload
102	sample 1002		+ Edit + Delete	raony	348	June 14, 2017, 9:10 p.m.	June 14, 2017, 9:12 p.m.	0:01:37.729445	0:00:00.294747	uploaded	Reupload Reupload
103	na12878 individual		+ Edit + Delete	raony	19140	June 14, 2017, 8:10 p.m.	June 14, 2017, 8:21 p.m.	0:06:00.780788	0:01:57.042451	uploaded	Reupload Reupload
104	sample 1004		+ Edit + Delete	raony	72005	June 14, 2017, 5:50 p.m.	June 14, 2017, 5:50 p.m.	0:16:27.609607	0:00:47.891588	uploaded	Reupload Reupload
105	sample 1005		+ Edit + Delete	raony	73888	June 14, 2017, 2:22 p.m.	June 14, 2017, 2:40 p.m.	0:16:00.000001	0:00:58.614889	uploaded	Reupload Reupload
106	na12878 individual		+ Edit + Delete	raony	19140	June 14, 2017, 12:42 p.m.	June 14, 2017, 2:03 p.m.	0:05:25.710084	0:01:58.890538	uploaded	Reupload Reupload
107	na12878 individual		+ Edit + Delete	raony	19140	June 14, 2017, 12:37 p.m.	June 14, 2017, 12:52 p.m.	0:07:00.670708	0:01:58.006175	uploaded	Reupload Reupload
108	sample 1008		+ Edit + Delete	raony	19140	June 14, 2017, 9:40 p.m.	June 14, 2017, 9:40 p.m.	0:00:00.000000	0:00:00.000000	uploaded	Reupload Reupload
109	sample 1009		+ Edit + Delete	raony	80157	June 15, 2017, 9:37 p.m.	June 15, 2017, 9:38 p.m.	0:24:21.440708	0:12:11.221142	uploaded	Reupload Reupload

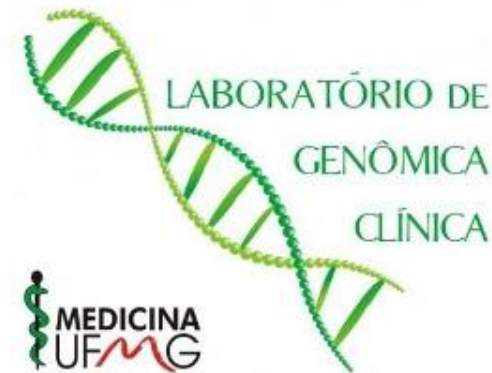
01:45

Upload your VCF Files

You will receive an e-mail as soon this process finishes with the link to start analysing your individuals.
You can take this time to read our [Documentation](#) about how to filter your variants.

[+ Please, select your VCF files...](#)

[Click here when your files have finished uploading!](#)



<https://mendelmd.org/>

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1-Click

Filter Analysis

Family Analysis

Comparison

Analysis selection

Mendel,MD - Walkthrough www.mendelmd.org from Raony Guimaraes

Individuals

#	ID	Name	Options	Uploaded By	#P Lines	Created on	Modified on	Annotation Time	Insertion Time	Status	Operations
1	181	sample1000	+ 0:01 + Details	Henry	None	June 14, 2017, 9:19 p.m.	June 14, 2017, 9:19 p.m.			new	Download Upload
2	182	sample1000	+ 0:01 + Details	Henry	344	June 14, 2017, 9:10 p.m.	June 14, 2017, 9:12 p.m.	0:01:37.728440	0:00:00.258747	uploaded	Download Upload
3	179	sample1000	+ 0:01 + Details	Henry	10140	June 14, 2017, 9:10 p.m.	June 14, 2017, 9:21 p.m.	0:00:00.700780	0:01:57.042401	uploaded	Download Upload
4	188	sample1000	+ 0:01 + Details	perceira	72006	June 14, 2017, 9:50 p.m.	June 14, 2017, 9:50 p.m.	0:18:27.608867	0:00:47.881888	uploaded	Download Upload
5	188	sample1000	+ 0:01 + Details	perceira	72006	June 14, 2017, 2:22 p.m.	June 14, 2017, 2:40 p.m.	0:18:00.008891	0:00:58.014800	uploaded	Download Upload
6	187	sample1000	+ 0:01 + Details	Henry	10140	June 14, 2017, 12:42 p.m.	June 14, 2017, 2:03 p.m.	0:00:25.702084	0:01:55.840036	uploaded	Download Upload
7	181	sample1000	+ 0:01 + Details	Henry	10140	June 14, 2017, 12:27 p.m.	June 14, 2017, 12:52 p.m.	0:07:00.870708	0:01:58.098175	uploaded	Download Upload
8	181	sample1000	+ 0:01 + Details	Henry	10140	June 14, 2017, 12:27 p.m.	June 14, 2017, 12:52 p.m.	0:07:00.870708	0:01:58.098175	uploaded	Download Upload

01:45

vimeo



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The screenshot shows the 'Family Analysis' tool interface. The top navigation bar includes links for 'Upload', 'Dashboard', '1-Click', 'Tools', 'Docs', and 'Forum', along with a 'Donate' button. The main header area contains the title 'Family Analysis' and a '+ Filter Options' button. Below the header, there are tabs for 'Main', 'Variants', 'Databases', 'Diseases', 'Saved Configs', 'Saved Analysis', and 'FAQ'. The interface is split into two columns: 'FATHER' and 'MOTHER'. Each column has a 'Main' tab and a 'Variants' tab. The 'FATHER' column shows a list of variants (1351s, 1352s, 1353s) and a 'SELECT VARIANTS FROM INDIVIDUALS:' section. The 'MOTHER' column shows a list of variants (1351s, 1352s, 1353s) and a 'GROUPS:' section. At the bottom, there is a 'SUBMIT' button and a 'RESET FILTER' link.

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INHERITANCE



Autosomal Recessive

Autosomal Dominant

Autosomal Compound Heterozygous

X-linked Recessive

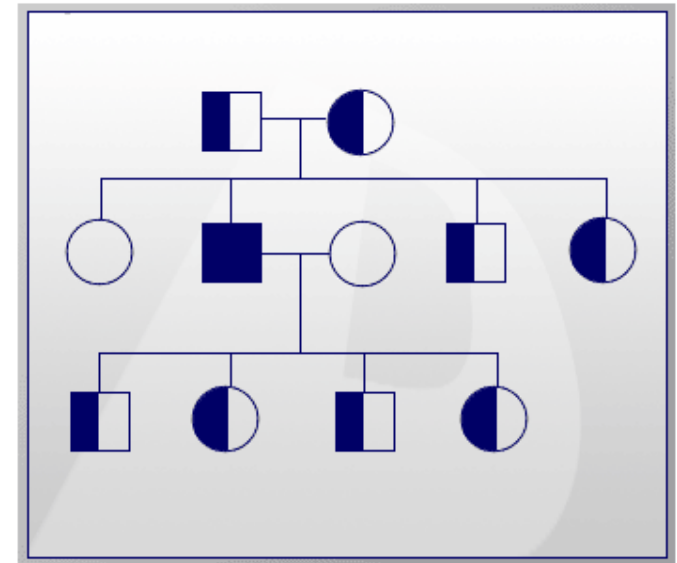
X-linked Dominant

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.



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or

Upload a VCF

1-Click

Filter Analysis

Family Analysis

Comparison

Mendel,MD - Walkthrough www.mendelmd.org from Raony Guimaraes

Individuals

#	ID	Name	Options	Uploaded By	MP Lines	Created on	Modified on	Annotation Time	Insertion Time	Status	Operations
1	101	sample1001	• 0:01 • Details	Henry	None	June 14, 2017, 8:19 p.m.	June 14, 2017, 8:19 p.m.		None	view	Download Upload
2	102	sample1002	• 0:01 • Details	Henry	344	June 14, 2017, 8:10 p.m.	June 14, 2017, 8:12 p.m.	0:01:37.728440	0:00:00.296747	preloaded	Download Upload
3	179	hap12019 download	• 0:01 • Details		19146	June 14, 2017, 8:10 p.m.	June 14, 2017, 8:21 p.m.	0:00:00.702786	0:01:57.042401	preloaded	Download Upload
4	188	sample1004	• 0:01 • Details	peragala	72036	June 14, 2017, 5:50 p.m.	June 14, 2017, 5:50 p.m.	0:18:27.620667	0:00:47.891066	preloaded	Download Upload
5	189	sample1014	• 0:01 • Details	peragala	73908	June 14, 2017, 2:22 p.m.	June 14, 2017, 2:40 p.m.	0:19:00.000841	0:00:58.614809	preloaded	Download Upload
6	187	hap12019 download	• 0:01 • Details	Henry	19146	June 14, 2017, 12:42 p.m.	June 14, 2017, 2:03 p.m.	0:05:25.752084	0:01:55.940536	preloaded	Download Upload
7	188	sample1004	• 0:01 • Details	Henry	19146	June 14, 2017, 12:37 p.m.	June 14, 2017, 12:42 p.m.	0:07:00.876706	0:01:59.090179	preloaded	Download Upload
8	187	hap12019 download	• 0:01 • Details	Henry	19146	June 14, 2017, 7:46 p.m.	June 14, 2017, 8:10 p.m.	0:00:00.000000			
9	188	sample1004	• 0:01 • Details	Henry	19146	June 14, 2017, 7:57 p.m.	June 14, 2017, 8:24 p.m.	0:04:21.840700	0:12:11.201360	preloaded	Download Upload

01:45

vimeo

Analysis selection



Recessive Homozygous Analysis

The screenshot shows the 'Filter Analysis' tool interface. At the top, there is a navigation bar with a profile icon, a menu icon, and links for Upload, Dashboard, 1-Click, Tools, Docs, Forum, and a Donate button. On the right, there are Login and Password input fields. Below the navigation bar, there is a '+ Filter Options' section. This section contains three tabs: 'Main', 'Variants', and 'Databases'. The 'Main' and 'Variants' tabs are circled in red, and a red arrow points from the 'Variants' tab to the 'SELECT VARIANTS FROM' section. The 'SELECT VARIANTS FROM' section has four sub-sections: 'INDIVIDUALS:' with buttons for '× 1351s', '× 1352s', and '× 1353s'; 'GROUPS:' with a 'SELECT YOUR GROUPS' button; 'SNP LIST:' with a text area; and 'GENE LIST:' with a text area. To the right of these is the 'EXCLUDE VARIANTS FROM' section, which also has four sub-sections: 'INDIVIDUALS:' with a 'SELECT YOUR CONTROLS' button; 'EXCLUDE GROUPS:' with a 'SELECT YOUR GROUPS' button; 'EXCLUDE SNP LIST:' with a text area; and 'EXCLUDE GENE LIST:' with a text area. At the bottom, there is a 'SELECT INHERITANCE:' section with five buttons: 'RECESSIVE HOMOZYGOUS' (highlighted in red), 'RECESSIVE COMPOUND HETEROZYGOUS', 'DOMINANT HETEROZYGOUS', 'X-LINKED RECESSIVE HEMIZYGOUS', and 'X-LINKED DOMINANT HETEROZYGOUS'. A red arrow points from the 'RECESSIVE HOMOZYGOUS' button to the text at the bottom right.

Available filters

Main Variants Databases

SELECT VARIANTS FROM

INDIVIDUALS:

× 1351s × 1352s × 1353s

GROUPS:

SELECT YOUR GROUPS

SNP LIST:

GENE LIST:

EXCLUDE VARIANTS FROM

INDIVIDUALS:

SELECT YOUR CONTROLS

EXCLUDE GROUPS:

SELECT YOUR GROUPS

EXCLUDE SNP LIST:

EXCLUDE GENE LIST:

SELECT INHERITANCE:

RECESSIVE HOMOZYGOUS RECESSIVE COMPOUND HETEROZYGOUS DOMINANT HETEROZYGOUS X-LINKED RECESSIVE HEMIZYGOUS X-LINKED DOMINANT HETEROZYGOUS

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

Filters (Variants)

Main

Variants

Databases

MUTATION TYPE: HOMOZYGOUS (Ex. 1/1, 2/1, 1/2) ▼	CHR: <input type="text"/> POS: <input type="text"/>	<div>PASS</div>
VARIANT EFFECT	FUNCTIONAL CLASS	IMPACT
<div>CDS CHROMOSOME LARGE DELETION CODON CHANGE CODON INSERTION</div>	<div>NONE SILENT MISSENSE NONSENSE</div>	<div>HIGH MODERATE MODIFIER LOW</div>
DBSNP BUILD: <= ▼ <input type="text"/>	READ DEPTH: >= ▼ 10 QUAL: <= ▼ <input type="text"/>	VARIANTS PER GENE: <= ▼ <input type="text"/>
<div><input type="checkbox"/> EXCLUDE VARIANTS AT VARISNP</div> <div><input type="checkbox"/> SHOW ONLY VARIANTS PRESENT IN COMMON GENES BETWEEN ALL THE INDIVIDUALS SELECTED</div> <div><input type="checkbox"/> SHOW ONLY VARIANTS AT EXACTLY SAME POSITION BETWEEN ALL THE INDIVIDUALS SELECTED</div> <div><input type="checkbox"/> EXCLUDE ALL VARIANTS PRESENT IN LATEST DBSNP BUILD</div> <div><input type="checkbox"/> SHOW ONLY VARIANTS PRESENT AT HGMD</div>		

☒ OPEN RESULT IN A NEW WINDOW

SUBMIT

RESET FILTER

Filters (Databases)

Main

Variants

Databases

FREQUENCIES

1000 GENOMES
FREQUENCY

0 - 0.01

☐ EXCLUDE ALL VARIANTS PRESENT IN
1000GENOMES

DBSNP
FREQUENCY

0 - 0.01

☐ EXCLUDE ALL VARIANTS PRESENT IN
DBSNP

ESP6500
FREQUENCY

0 - 0.01

☐ EXCLUDE ALL VARIANTS PRESENT IN EXOME
SEQUENCING PROJECT

SCORES

SIFT SCORE

0 - 0.05

☐ EXCLUDE VARIANTS WITHOUT SIFT SCORE

CADD

☐ EXCLUDE VARIANTS WITHOUT CADD SCORE

POLYPHEN2 SCORE

0.8 - 1

☐ EXCLUDE VARIANTS WITHOUT POLYPHEN SCORE

MCAP

☐ EXCLUDE VARIANTS WITHOUT M-CAP SCORE

☒ OPEN RESULT IN A NEW WINDOW

SUBMIT

Mendel,MD



+ 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	ESPe500	Sift	PP2	CADD	M-CAP	CLINVAR	HI Score
<input type="checkbox"/>	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 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	ESPe500	Sift	PP2	CADD	M-CAP	CLINVAR	HI Score
<input type="checkbox"/>	View	1351s	6	.	16327384	10929.9	A	G	PASS	1/1	101	SYNONYMOUS_CODING	LOW							None None None None	None None 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
		▲▼	▲▼	▲▼	▲▼	▲▼	▲▼		▲▼					▲▼								
<input type="checkbox"/> 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	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

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wANNOVAR

ANNOVAR is a rapid, efficient tool to annotate functional consequences of genetic variation from high-throughput sequencing data. wANNOVAR provides easy and intuitive web-based access to the most popular functionalities of the ANNOVAR software

[Get Started](#)[About](#)[Contact](#)[Share](#)

19 people like this. [Click here](#) to see what your friends like.

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

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Example

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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_annotvar). 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

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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!



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

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Chr	Start	End	Ref	Alt	Func	Gene	GeneDetail	ExonicFunc	AACChange
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

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Sort by:

Filter by:

1000G_ALL:	<input type="text" value="<="/> <input type="text" value="0.01"/>	1000G_AFR:	<input type="text"/>	1000G_EUR:	<input type="text" value="<="/> <input type="text" value="0.01"/>
ExAC_Freq:	<input type="text" value="<="/> <input type="text" value="0.01"/>	ExAC_AMR:	<input type="text"/>	ExAC_NFE:	<input type="text"/>
ESP6500si_ALL:	<input type="text" value="<="/> <input type="text" value="0.01"/>	CG46:	<input type="text"/>	COSMIC_ID:	<input type="text"/>
ClinVar_DIS:	<input type="text"/>	ClinVar_DB:	<input type="text"/>	GWAS_DIS:	<input type="text"/>
GWAS_OR:	<input type="text"/>	GWAS_BETA:	<input type="text"/>		

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
- ☒ nonsynonymous SNV
- ☐ synonymous SNV
- ☒ stopgain SNV
- ☒ stoploss SNV
- ☐ unknown

Go

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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,DTNBP1:NM_001271666:exon10:c.C708T:p.D236D
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.D475D
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_001293217:exon4:c.C333T:p.Y111Y
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?

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Genome

Human

GRCh38/hg38

GRCh37/hg19

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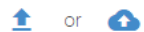
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Upload to submit

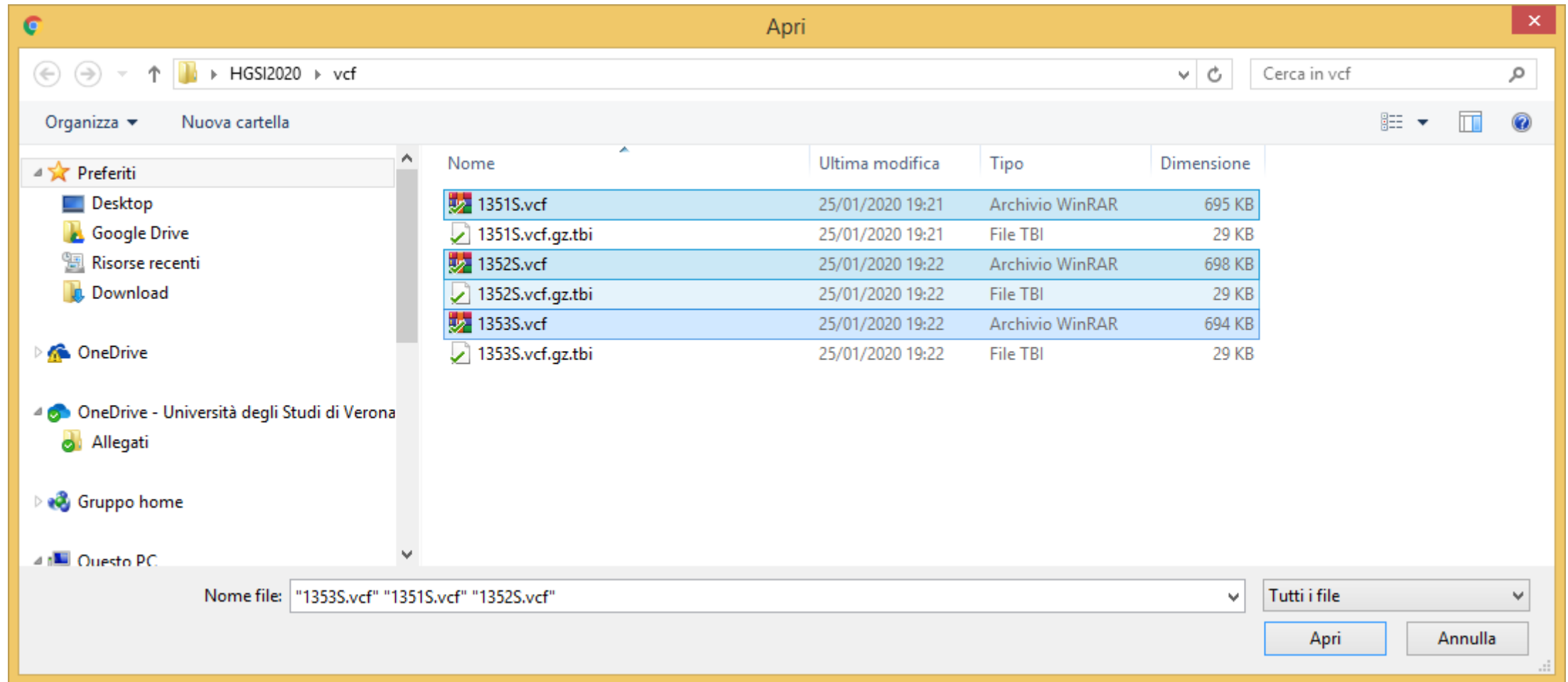
Accepts [vcf](#) and [snp](#) files

Annotations will be deleted after 1 month of inactivity



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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)



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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

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B Submit Incomplete Failed Results Public Shared Guide

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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 : 1879

heterozygotes/homozygotes median : 1879

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:

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



pathogenic

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



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 ;

splID: 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»

dbSNPfunc

dbSNPalleles

dbSNPalleleNs

dbSNPalleleFreqs

clinvaralleleID

clinvarphenotypeList

clinvar.clinicalSignificance

benign	4	<input checked="" type="checkbox"/>	<input type="checkbox"/>
conflicting interpretations of pathogenicity	4	<input checked="" type="checkbox"/>	<input type="checkbox"/>
pathogenic	2	<input checked="" type="checkbox"/>	<input type="checkbox"/>
conflicting interpretations of pathogenicity, other, risk factor	1	<input checked="" type="checkbox"/>	<input type="checkbox"/>
likely benign	1	<input checked="" type="checkbox"/>	<input type="checkbox"/>
likely pathogenic	1	<input checked="" type="checkbox"/>	<input type="checkbox"/>

Less ^ Detail

RefSeq Transcripts ⓘ

Name: [NM_001024630](#) ; [NM_001015051](#) ; [NM_001278478](#)
spDisplayID: [RUNX2_HUMAN](#) ; [RUNX2_HUMAN](#) ;
spID: [Q13950](#) ; [Q13950](#) ; [A0A0D9SEN7](#)
mRNA: [NM_001024630](#) ; [NM_001015051](#) ; [NM_001278478](#)
protAcc: [NM_001024630](#) ; [NM_001015051](#) ; [NM_001278478](#)

Site Type: [exonic](#)
Strand: +

Description: Homo sapiens runt related transcription factor 2 (RUNX2), transcript variant 1, mRNA. (from RefSeq NM_001024630) ; Homo sapiens runt related transcription factor 2 (RUNX2), transcript variant 2, mRNA. (from RefSeq NM_001015051) ; Homo sapiens runt related transcription factor 2 (RUNX2), transcript variant 4, mRNA. (from RefSeq NM_001278478)

Exonic impact: ⓘ

Function: [synonymous](#)
Codon Number: [80](#) ; [80](#) ; [66](#)
Codon Position: [3](#)
Reference Codon: [GCG](#)
Alternate Codon: [GCA](#)
Reference Amino Acid: [A](#)
Alternate Amino Acid: [A](#)

Clinvar x RefSeq: ⓘ

No Clinvar records > 32bp overlap these RefSeq transcripts

RefSeq Nearest Transcripts ⓘ

Nearest Gene Symbol: [RUNX2](#)
Nearest Name: [NM_001024630](#) ; [NM_001015051](#) ; [NM_001278478](#)


ClinVar ⓘ

Allele ID: [24336](#) ; [193462](#)

Bystro

pathogenic



Sort ▾ Tools ▾ Size ▾ Filter Pipeline ▾ 

Searched: *pathogenic*

+pathogenic X

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

☐ Expand all

LAMA2

chr6 : 129,250,185

R619H

More ▾ Detail

Cadd 0.77

PhyloP -1.57

PhastCons 0

Filters & Aggregations

Explore your data by specific field

chrom ▾

pos ▾

type ▾

discordant ▾

alt ▾

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](#) ; [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](#)
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: [ACGTGTTCCACGTGTTTC](#) ; [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](#)