

Instructions





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1. Download and install Python (1/4)

You need Python 3 and Pandas to run In-Silico Screener.

If you already have them installed, jump to page 10.

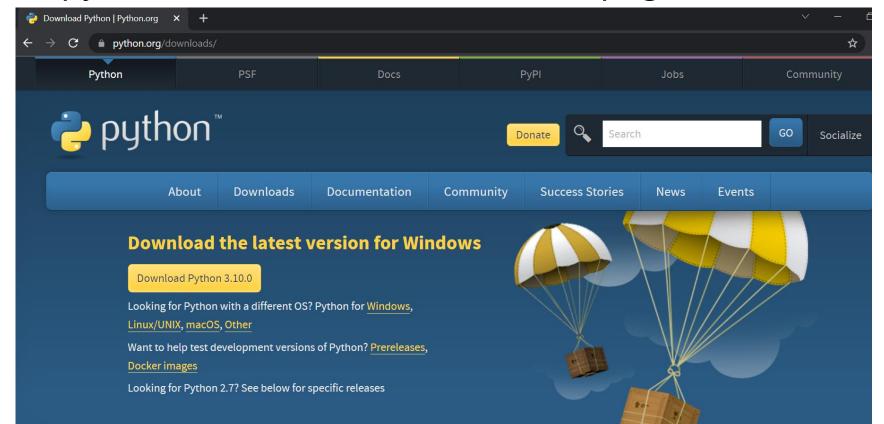




1. Download and install Python (2/4)

Go to https://www.python.org/downloads/

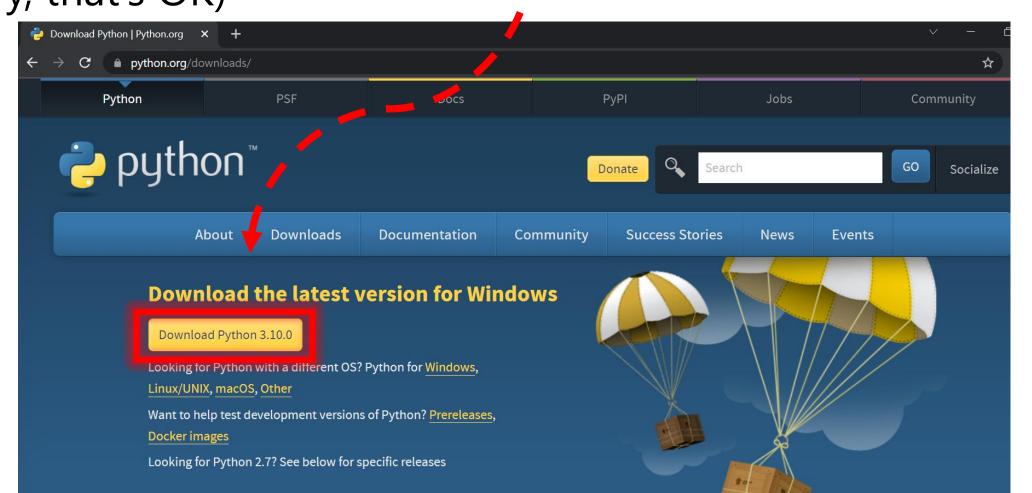
(or google "python download") to reach this page:





1. Download and install Python (3/4)

Download the installation file using this button: (version may vary, that's OK)





1. Download and install Python (4/4)

Run the downloaded installation file, be sure to check this checkbox:





2. Installing Pandas – MacOS/Linux

Via terminal, install pandas using the command line:

pip3 install pandas



2. Installing Pandas – Windows (1/2)

Press Windows key on your keyboard together with

the X key:



Select "Windows PowerShell (Admin)".

This will open "PowerShell" in a new blue window.

Apps and Features

Mobility Center

Power Options

Event Viewer

System

Device Manager

Network Connections

Disk Management

Computer Management

Windows PowerShell

Windows PowerShell (Admin)

<u>T</u>ask Manager

Setti<u>ng</u>s

File Explorer

Search

<u>R</u>un



2. Installing Pandas – Windows (2/2)

Type "pip3 install pandas" and press enter.

```
Administrator: Windows PowerShell
Windows PowerShell
Copyright (C) Microsoft Corporation. All rights reserved.

Try the new cross-platform PowerShell https://aka.ms/pscore6

PS C:\WINDOWS\system32> pip3 install pandas
```



3. Download the python script using this button (on the website, not the one on this slide)

Download Python Script



4. Preprocessing (1/5)

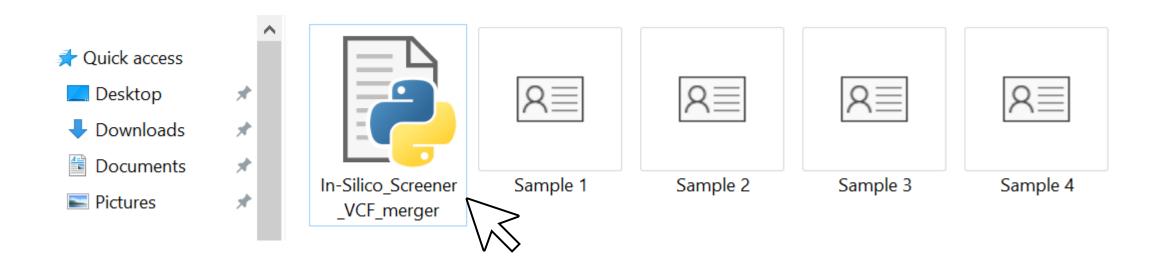
Place the python script from page 10 within a directory containing your whole-exome or whole-genome sequencing files in VCF formats (ending with either .vcf or .vcf.gz).

VCF files can be directly in the same folder, or within its sub-folders.



4. Preprocessing (2/5)

Activate the python script.





4. Preprocessing (3/5)

Follow the instructions, type "19" if you are using GRCh19/hg19 as reference genome, or "38" for GRCh38/hg38. Then press enter.

```
C:\WINDOWS\py.exe

Found 4 vcf files.

What reference genome are you using?

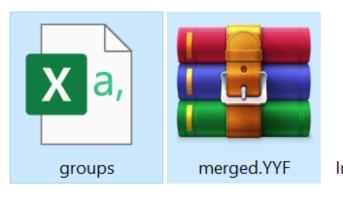
Type 19 for hg19 or 38 for hg38 and press enter: __
```



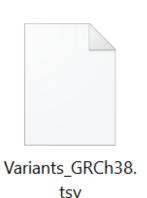
4. Preprocessing (4/5)

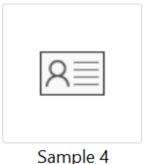
A variant database file will be downloaded. You can edit it and rerun to add additional variants.

Once the process is done, you will be provided with new files:



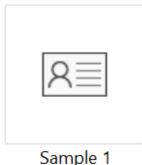














4. Preprocessing (5/5)

You can upload *merged.YYF* right away to begin an analysis, or tag samples by group name using the

groups file.

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F5	- i ×	✓ fx
	Α	В
1	Sample	Group
2	Sample 1	Origin #1
3	Sample 2	Origin #1
4	Sample 3	Origin #2
5	Sample 4	Origin #2



5. Analysis (1/4)

Upload *merged.YYF* alone or with the groups file to the web-application:

```
Drag or <u>select YYF file here</u>

Optional: add <u>groups file</u>
```

Then press the Analyze button.



5. Analysis (2/4)

Pick a variant for further information (heterozygotes, homozygotes and links)



In-Silico Screener

	\$Alleles	<pre>Phenotypes</pre>	\$ Gene	\$Coordinates - hg38	Review Status
	filter data	LOCUS I			
0		Speech-language disorder 1	ZGRF1	4:112585555	no assertion criteria provided
0	1	Recombinase activating gene 2 deficiency; Primary immunodeficiency; Histiocy medullary reticulosis	RAG2	11:36592849	criteria provided, single submitter
•	1	not provided Retinal dystrophy Vitelliform macular dystrophy type 2	BEST1	11:61958159	criteria provided, multiple submitters, no conflicts



5. Analysis (3/4)

Be sure to review the variant's ClinVar, gnomAD and GeniePool page and frequency to further assess its pathogenicity.

<u>ClinVar Page</u>

gnomAD frequency

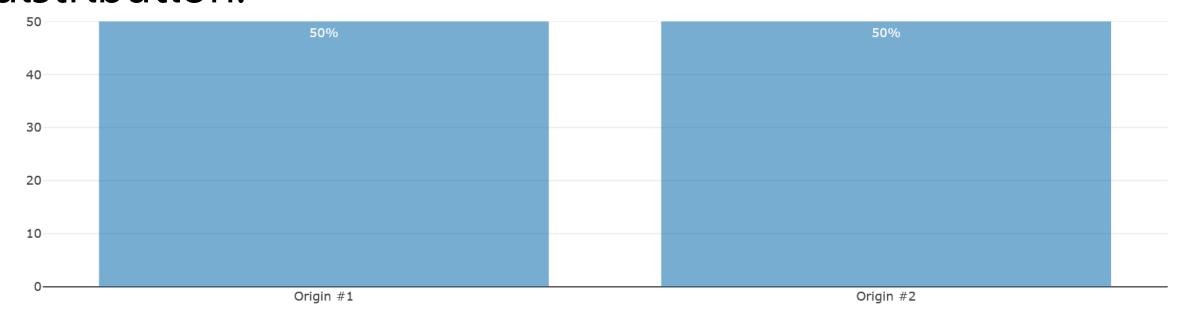
<u>GeniePool</u>





5. Analysis (4/4)

If you uploaded a *groups* file, you will be provided with additional information regarding variants' population distribution.





This is it.

Good luck!

In-Silico Screener