Instructions

Contents

1. Download and install Python (1/4)

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

If you already have them installed, .

1. Download and install Python (2/4)
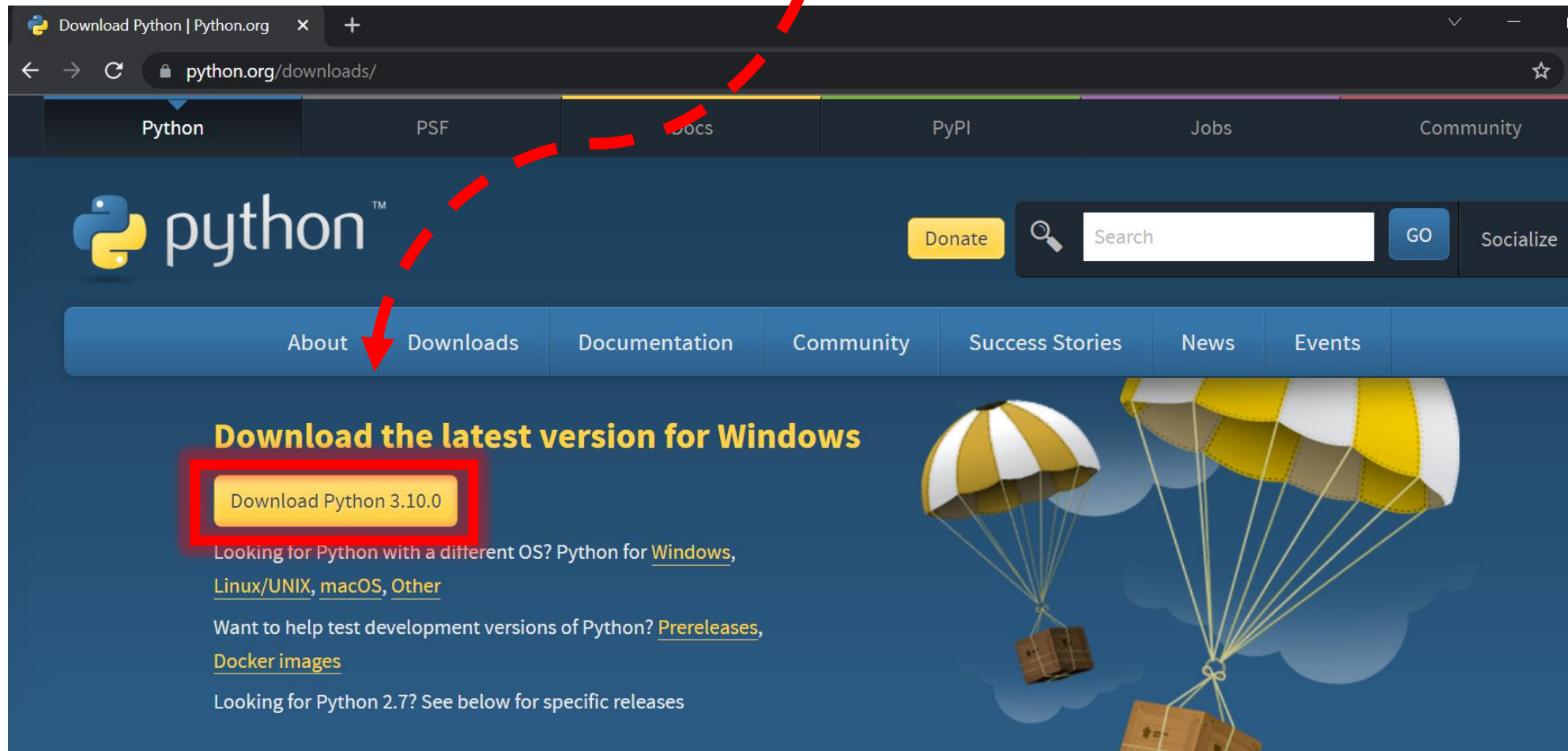
Go to **https://www.python.org/downloads/**

(or google "python download") to reach this page:
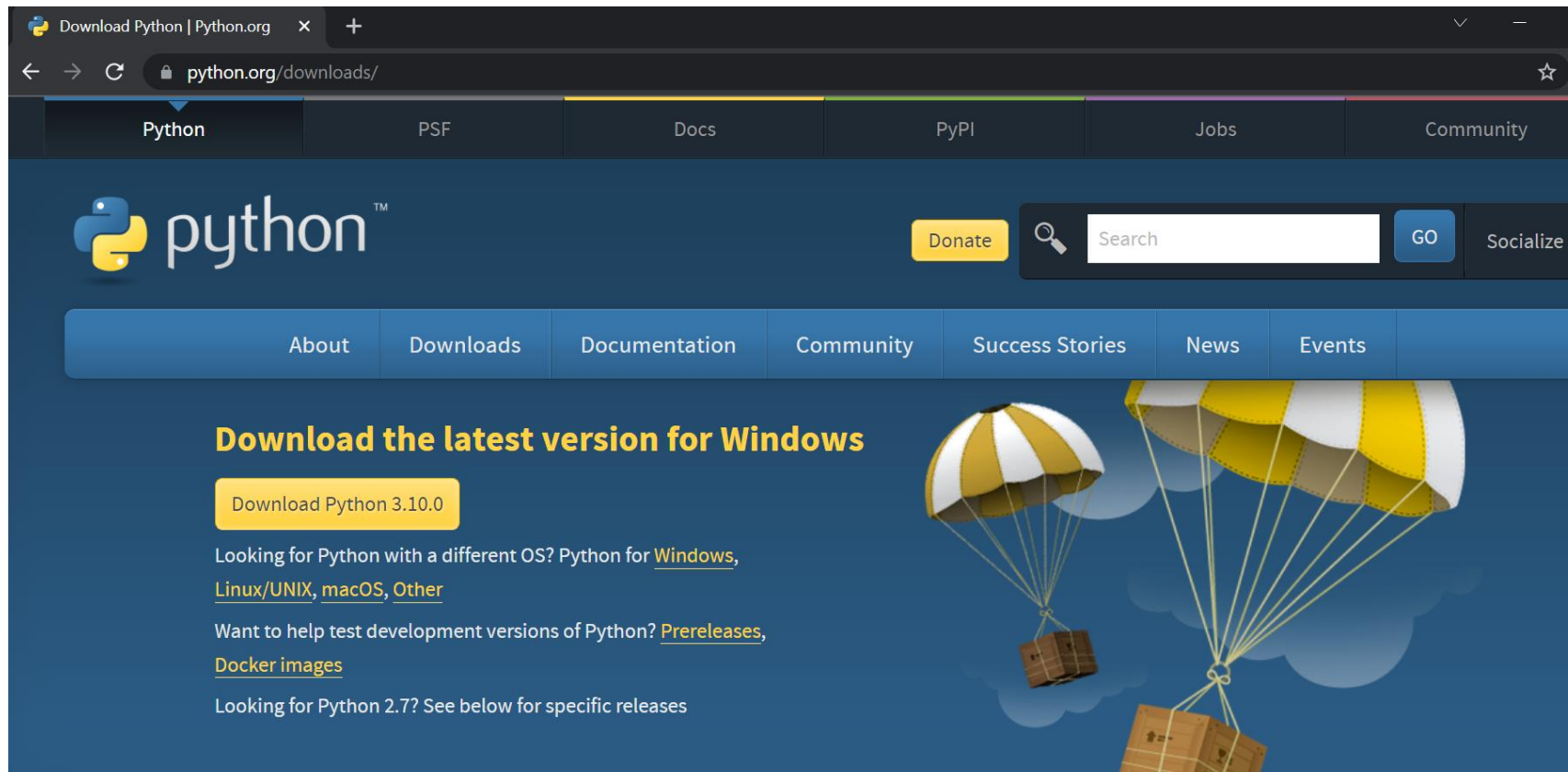
1. Download and install Python (3/4)

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)

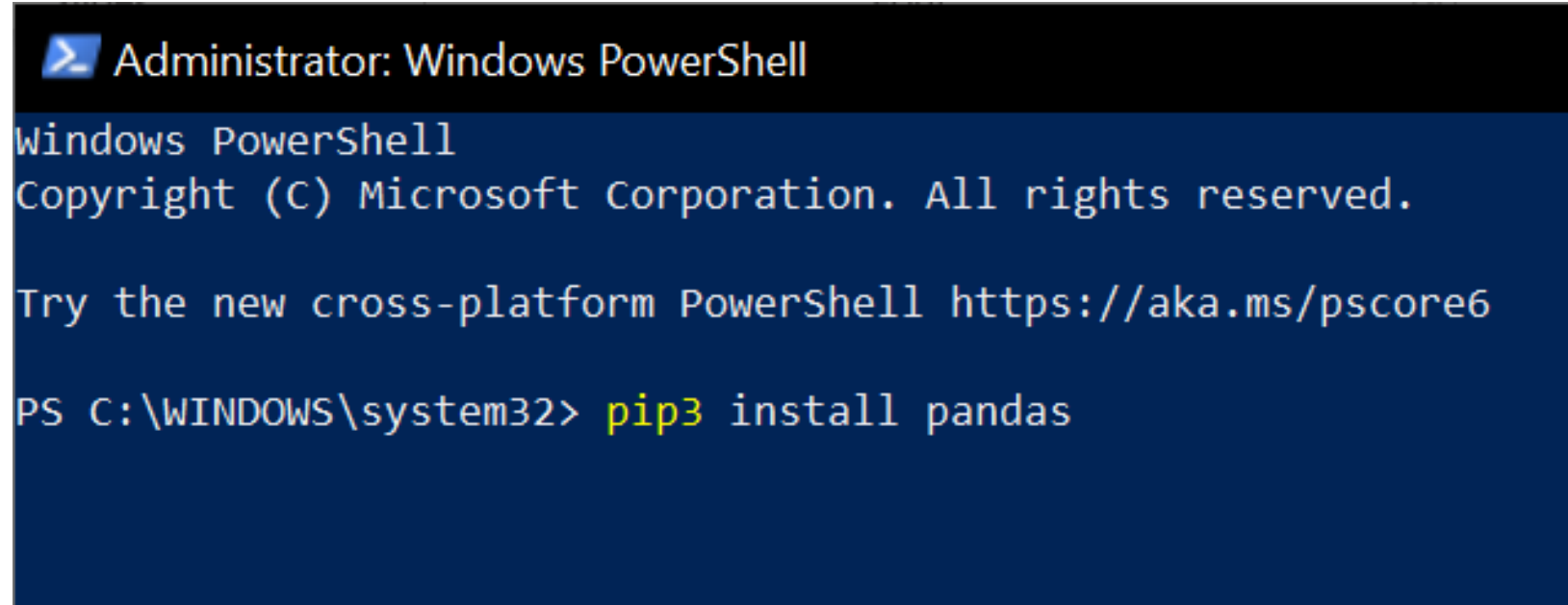Press Windows key on your keyboard together with

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)

Task Manager

Settings

File Explorer

Search

Run

2. Installing Pandas – Windows (2/2)

Type "pip3 install pandas" and press enter.

3. Download the python script

↑

Click the button above

(Download Python Script)
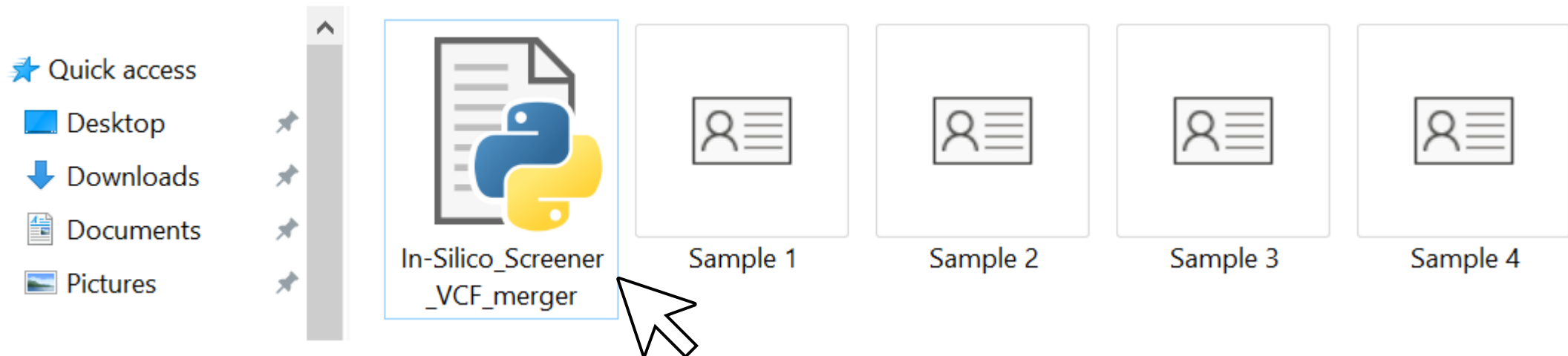
4. Preprocessing (1/5)

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).

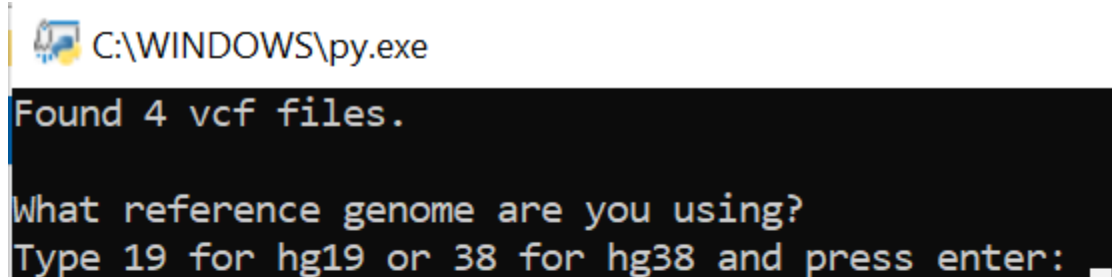VCF files can be directly in the same folder, or within its sub-folders.

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.
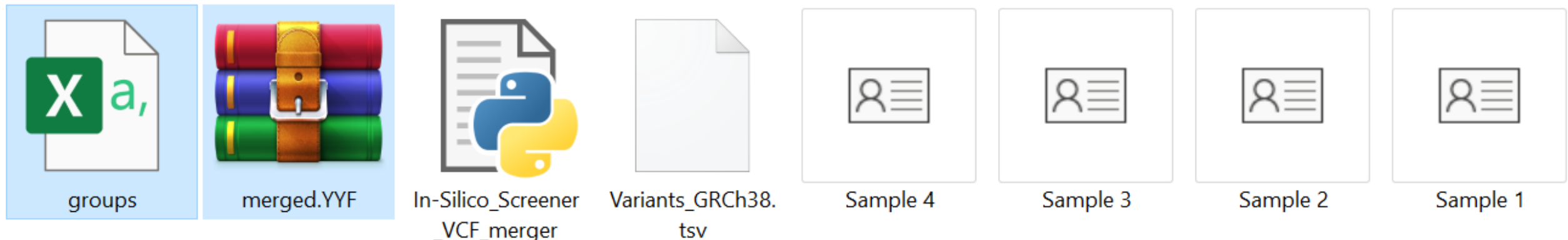
4. Preprocessing (4/5)

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:

| groups | merged.YYF | In-Silico_Screener_VCF_merger | Variants_GRCh38.tsv | Sample 4 | Sample 3 | Sample 2 | Sample 1 |

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.

	A	B
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>grouping 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	Phenotypes	Gene	Coordinates - hg38	Review Status
	filter data...			
	locus 1			
○ 1	Speech-language disorder 1	ZGRF1	4:112585555	no assertion criteria provided
○ 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 page and frequency to further assess its pathogenicity.
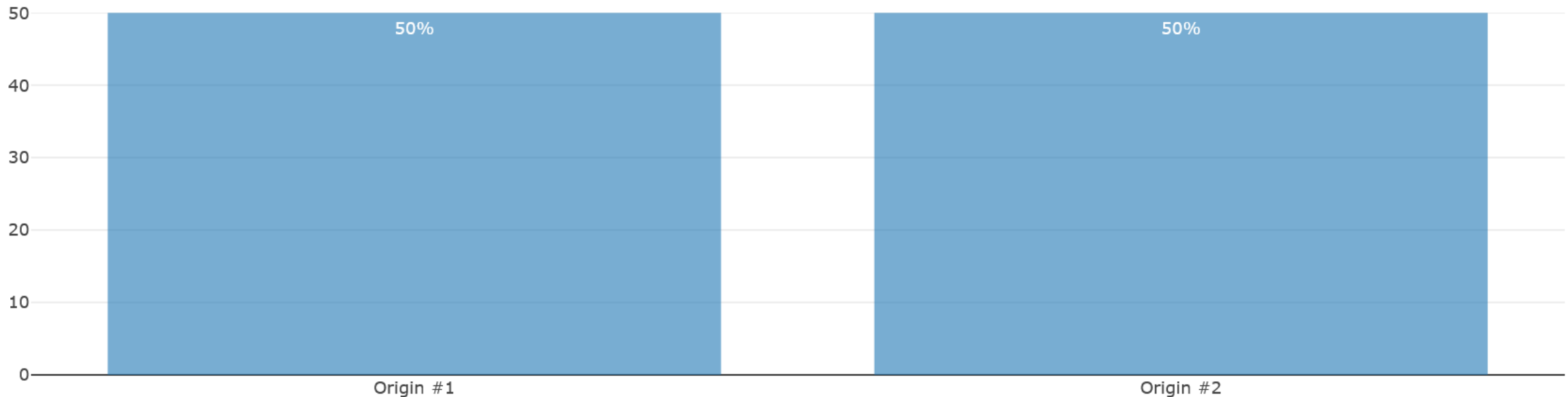
ClinVar Page

gnomAD frequency

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