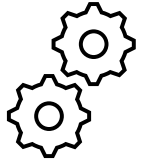


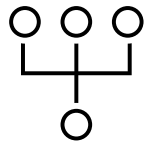
# Instructions



# Contents



[Installing prerequisites \(pages 3-10\)](#)



[Preprocessing your data \(pages 11-15\)](#)



[Analysis \(Page 16-20\)](#)

# 1. Download and install Python (1/4)

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

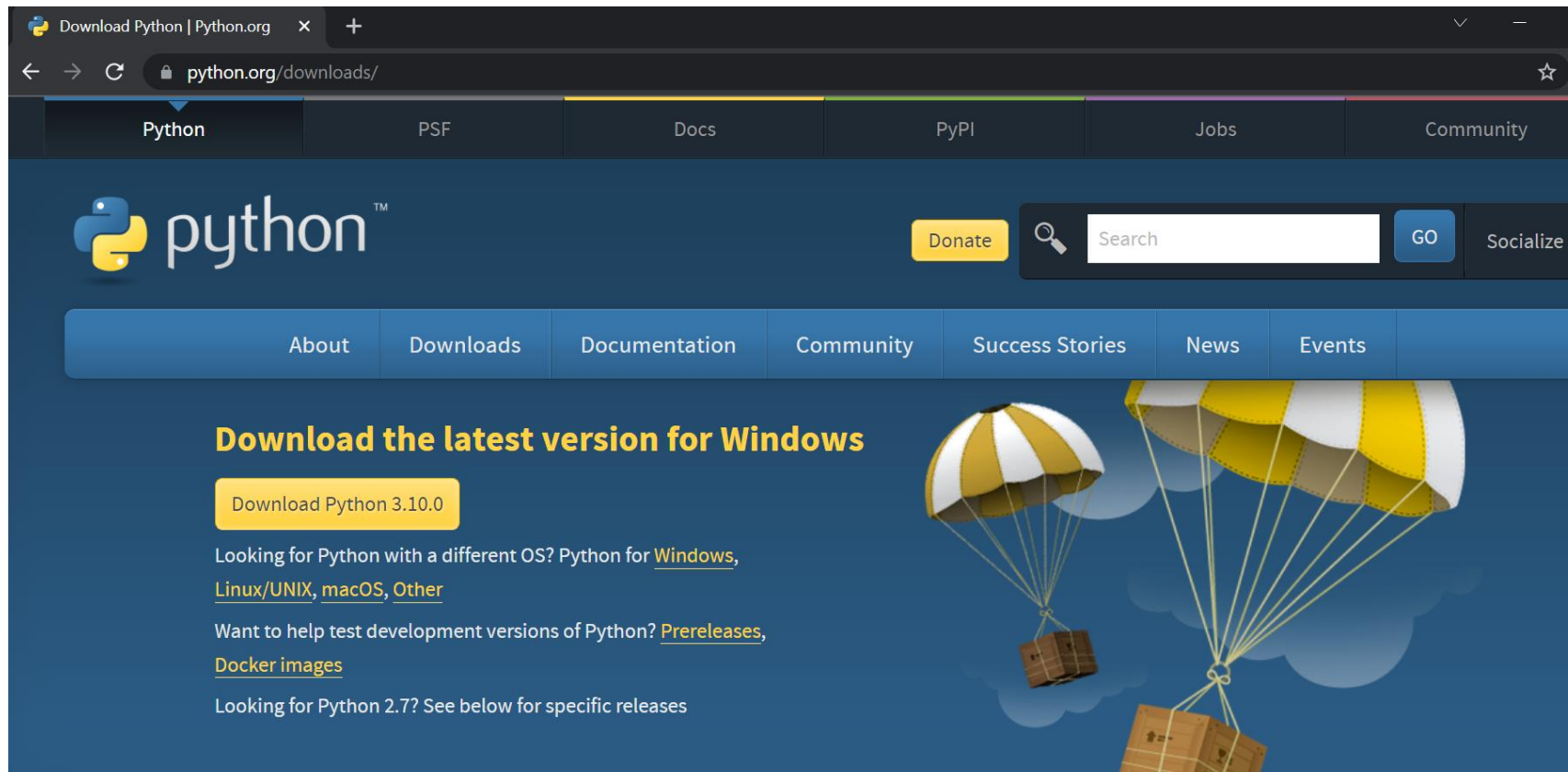
If you already have them installed, [jump to page 10](#).



# 1. Download and install Python (2/4)

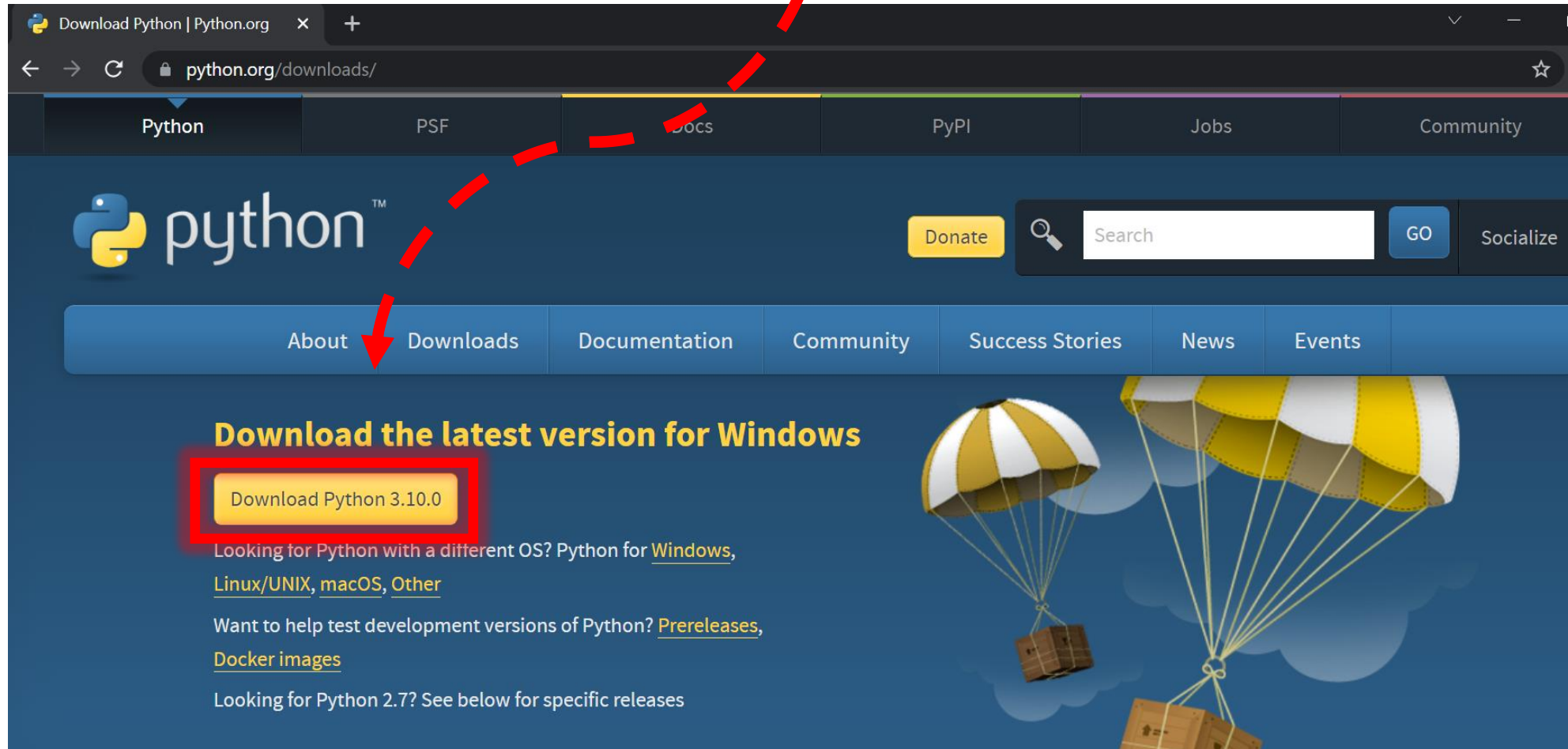
Go to <https://www.python.org/downloads/>

(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)



The screenshot shows the Python.org website. A red dashed arrow points from the text above to the 'Downloads' button in the navigation bar. Another red dashed arrow points from the 'Downloads' button to a yellow button labeled 'Download Python 3.10.0', which is highlighted with a red rectangular box. Below this button, there are links for other operating systems and versions.

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Want to help test development versions of Python? [Prereleases](#), [Docker images](#)

Looking for Python 2.7? See below for specific releases

# 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)".

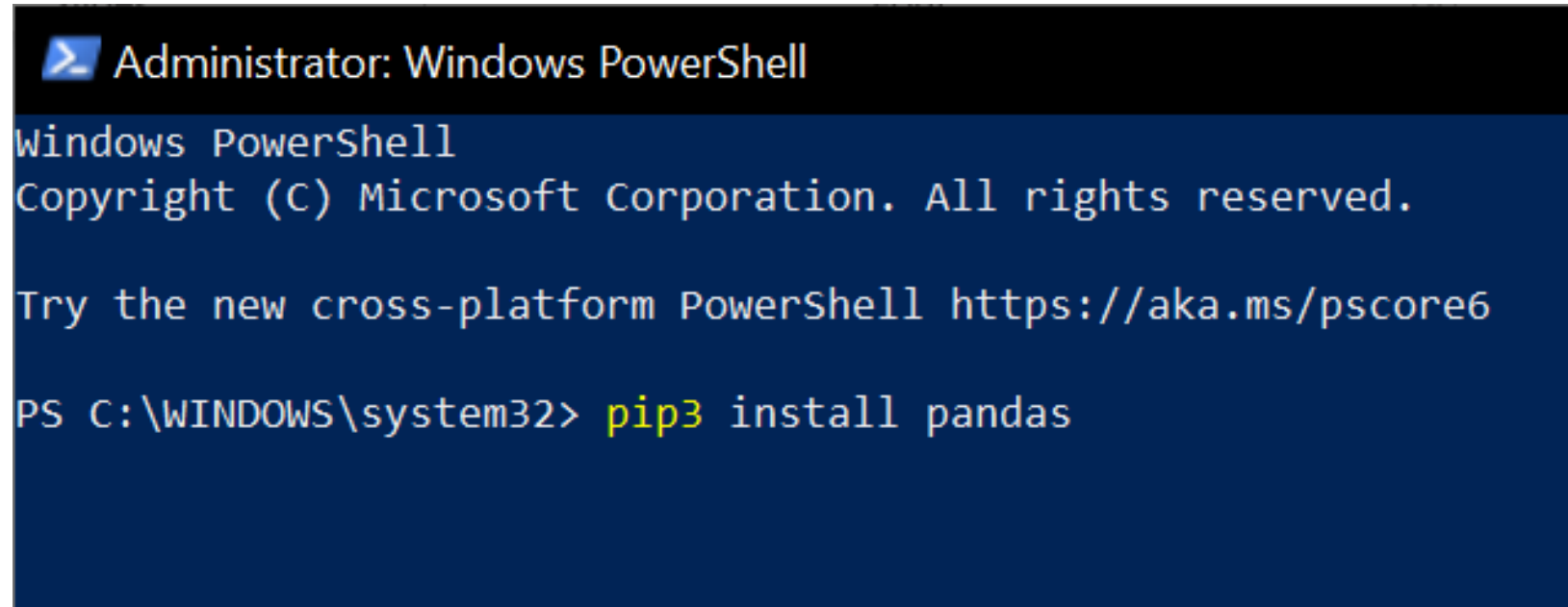
This will open "PowerShell" in a new blue window.





## 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/powershell

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)

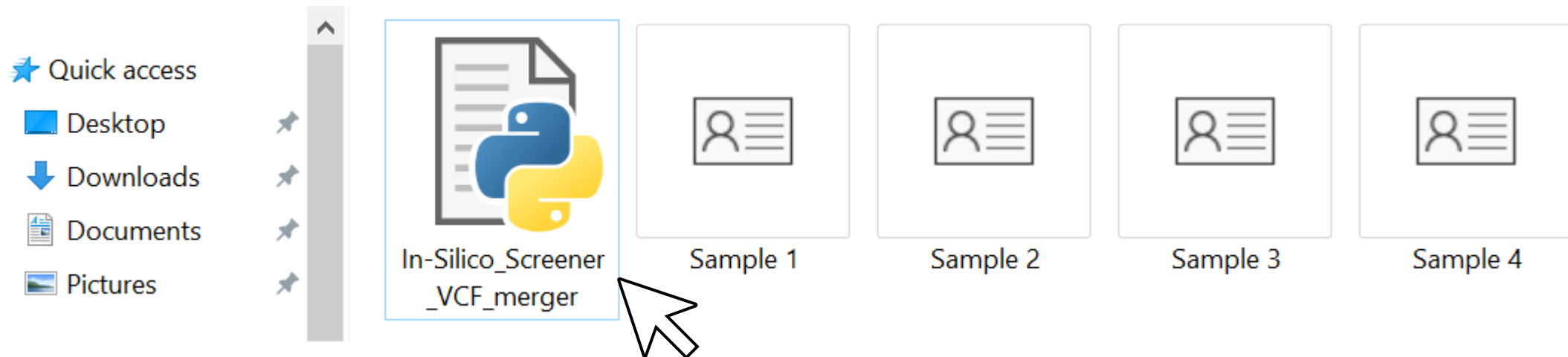
Place the python script from page 10 within a directory containing your whole-exome or whole-genome sequencing files in VCF formats (ending with either .vcf or .vcf.gz).

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



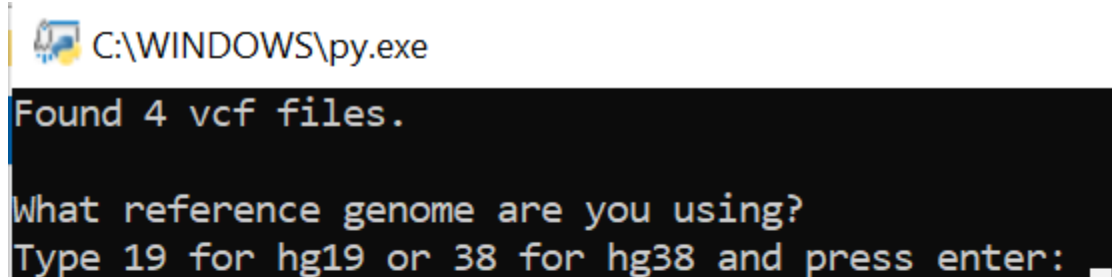
## 4. Preprocessing (2/5)

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.



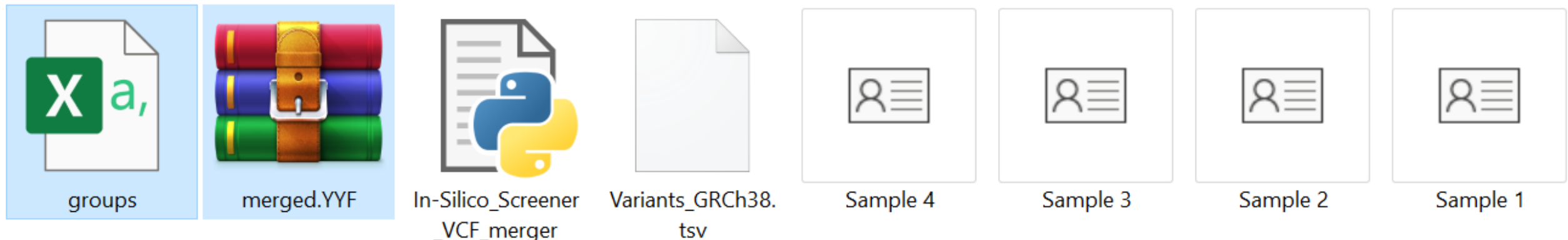
```
C:\WINDOWS\py.exe
Found 4 vcf files.

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.

Clipboard		Font	
F5		✕	✓ <i>fx</i>
	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 [select YYF file here](#)

Optional: add [groups file](#)






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			
<input type="radio"/>	1	Speech-language disorder 1	ZGRF1	4:112585555	no assertion criteria provided
<input type="radio"/>	1	Recombinase activating gene 2 deficiency;Primary immunodeficiency;Histiocytosis;medullary reticulosis	RAG2	11:36592849	criteria provided, single submitter
<input checked="" type="radio"/>	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](#)

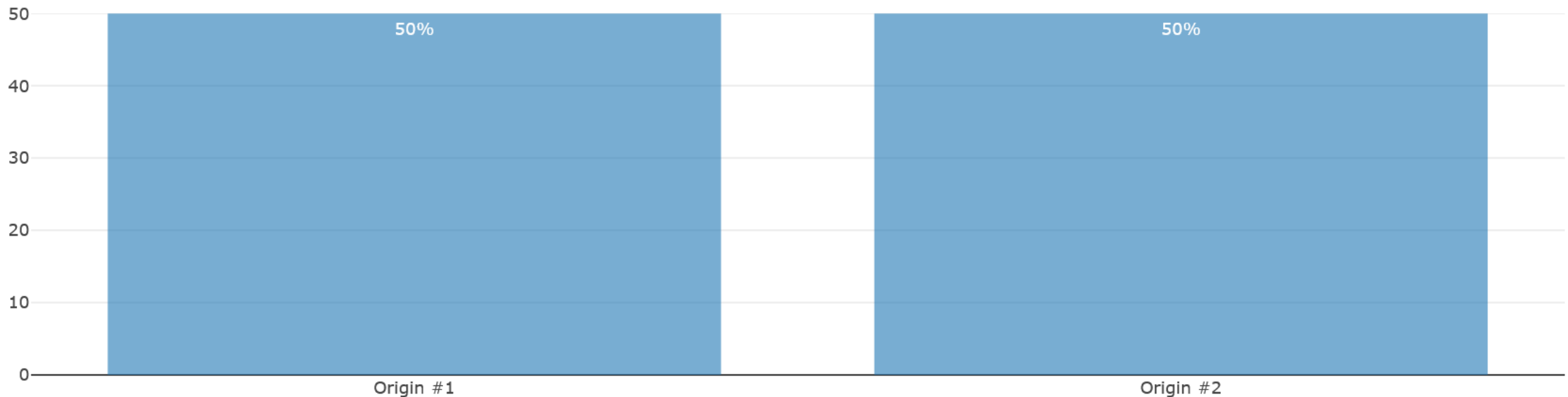


[gnomAD frequency](#)



## 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**