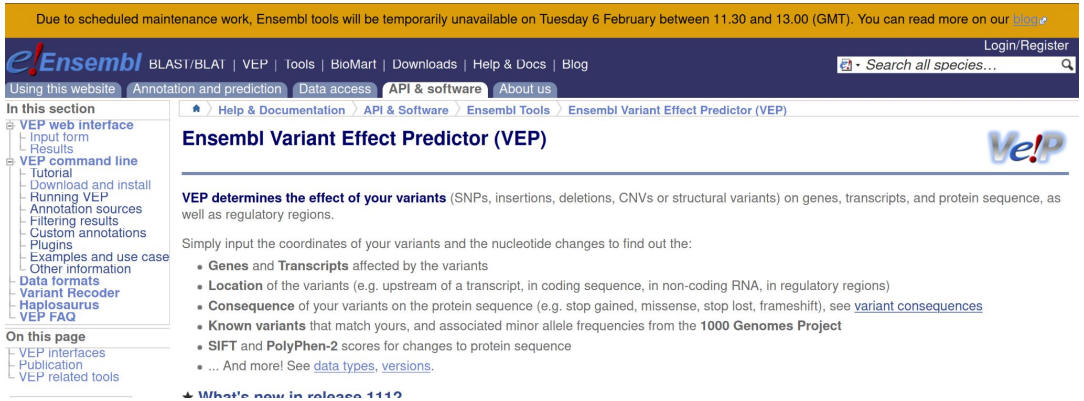
Anotação e Priorização de Variantes

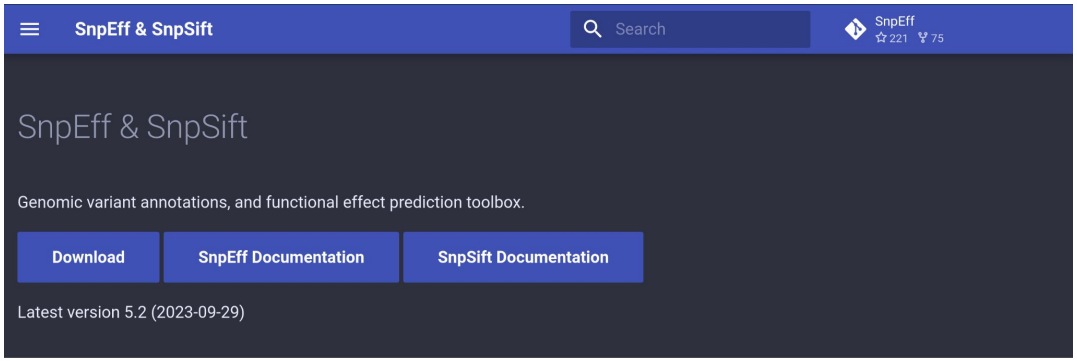
José Ferrão e Hugo Martiniano

Anotação

- Processo através do qual é feita a identificação do impacto das variantes e do seu significado funcional
- Existem várias ferramentas



https://www.ensembl.org/info/docs/tools/vep/index.html



http://pcingola.github.io/SnpEff/

VEP - Variant Effect Predictor

- Software para anotação de variantes (https://www.ensembl.org/info/docs/tools/vep/index.html)

- Desenvolvido pelo Ensembl (https://www.ensembl.org/index.html)

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Ensembl is a genome browser for vertebrate genomes that supports research in comparative genomics, evolution, sequence variation and transcriptional regulation. Ensembl annotate genes, computes multiple alignments, predicts regulatory function and collects disease data. Ensembl tools include BLAST, BLAT, BioMart and the Variant Effect Predictor (VEP) for all supported species.

Ensembl Release 111 (January 2024)

- MANE Select (v1.2) GRCh38.p14 patch annotation
- Human variation data updated to dbSNP156
- Updated genome assembly and annotation for sheep and cattle
- Regulatory annotation of open chromatin regions and promoters in common carp and rainbow trout (a collaboration with the AQUA-FAANG consortium)
- Updated regulatory annotation, including enhancers, for pig and chicken, Atlantic salmon, European seabass and turbot

Variant Effect Predictor

Web interface

- Point-and-click interface
- Suits smaller volumes of data

Documentation

Launch VeP

Command line tool

- More options and flexibility
- For large volumes of data

Documentation

Clone from GitHub

Download (zip)

Pull Docker image from

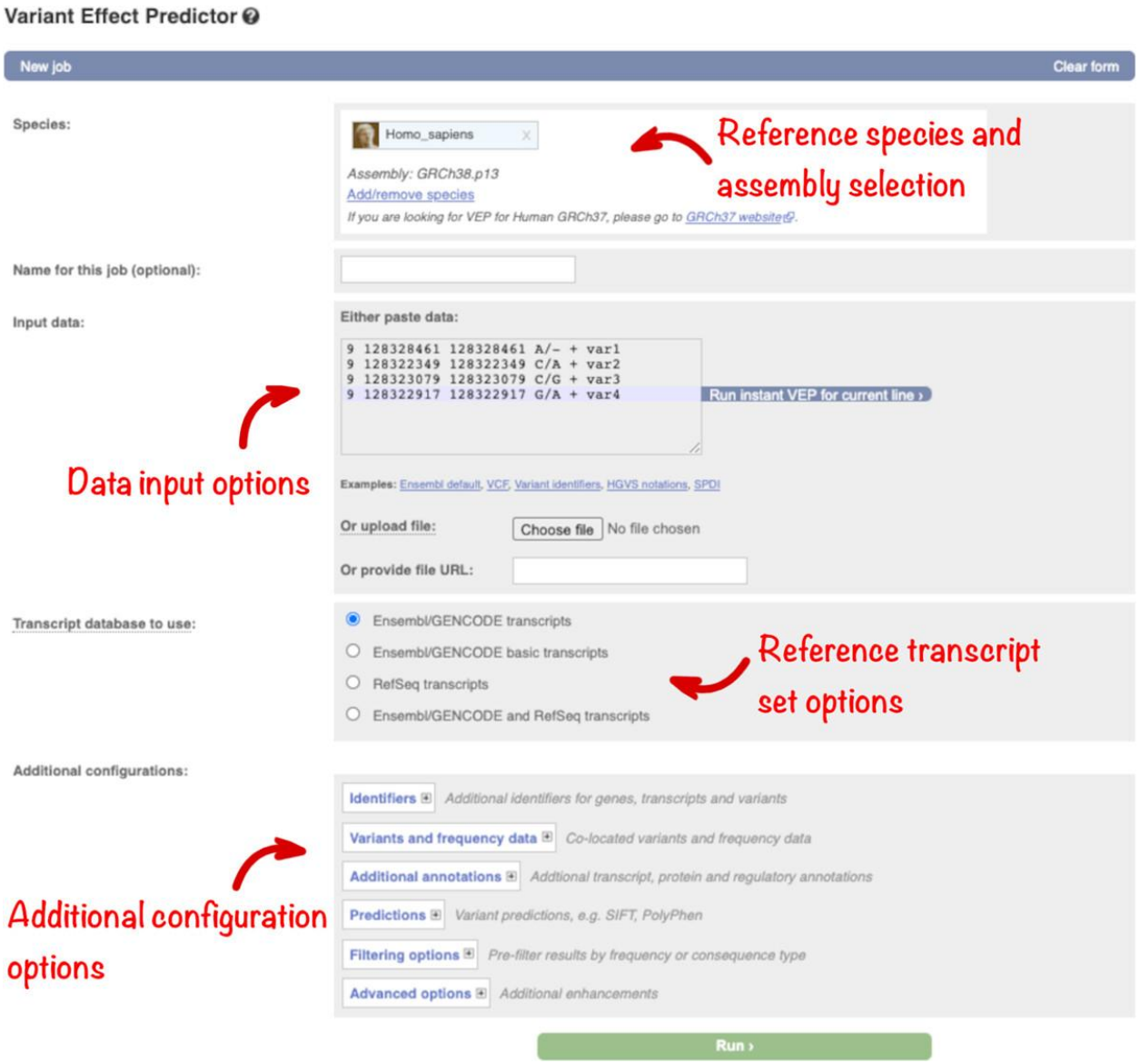
REST API

- Language-independent API
- Simple URL-based queries

Documentation

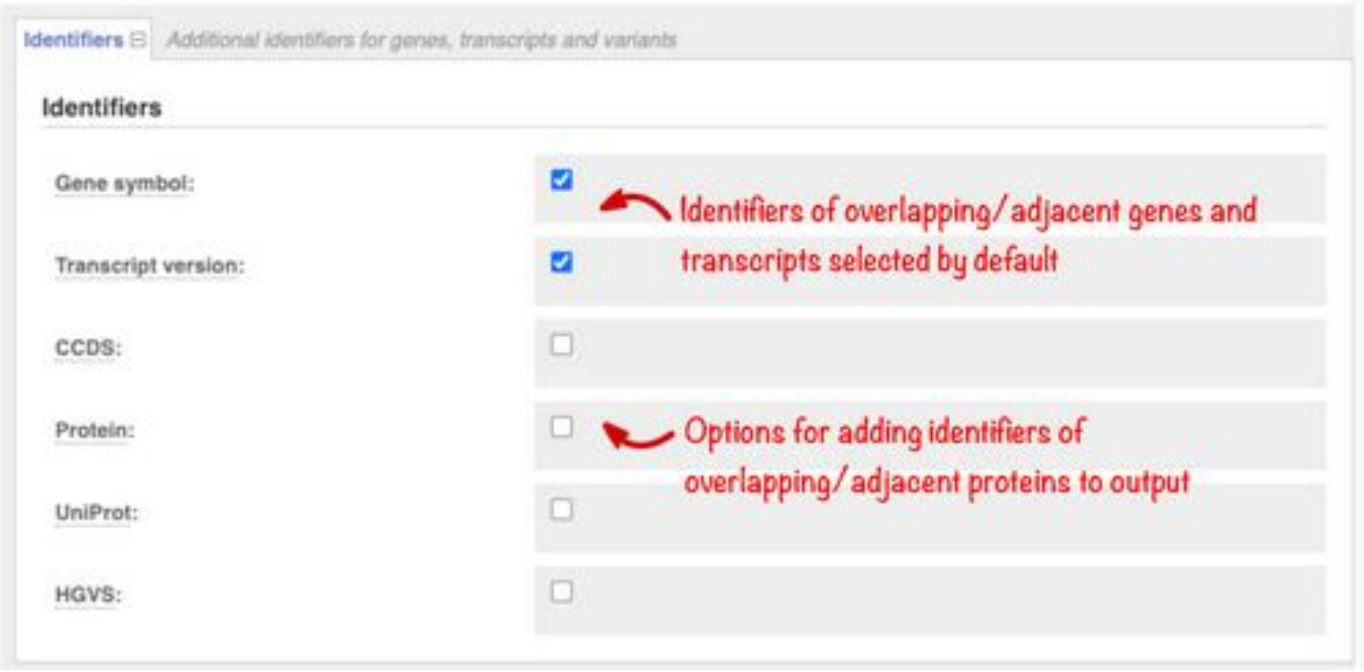
VEP REST API

https://www.ensembl.org/info/docs/tools/vep/index.html



https://doi.org/10.1002/humu.24298

Variant Effect Predictor



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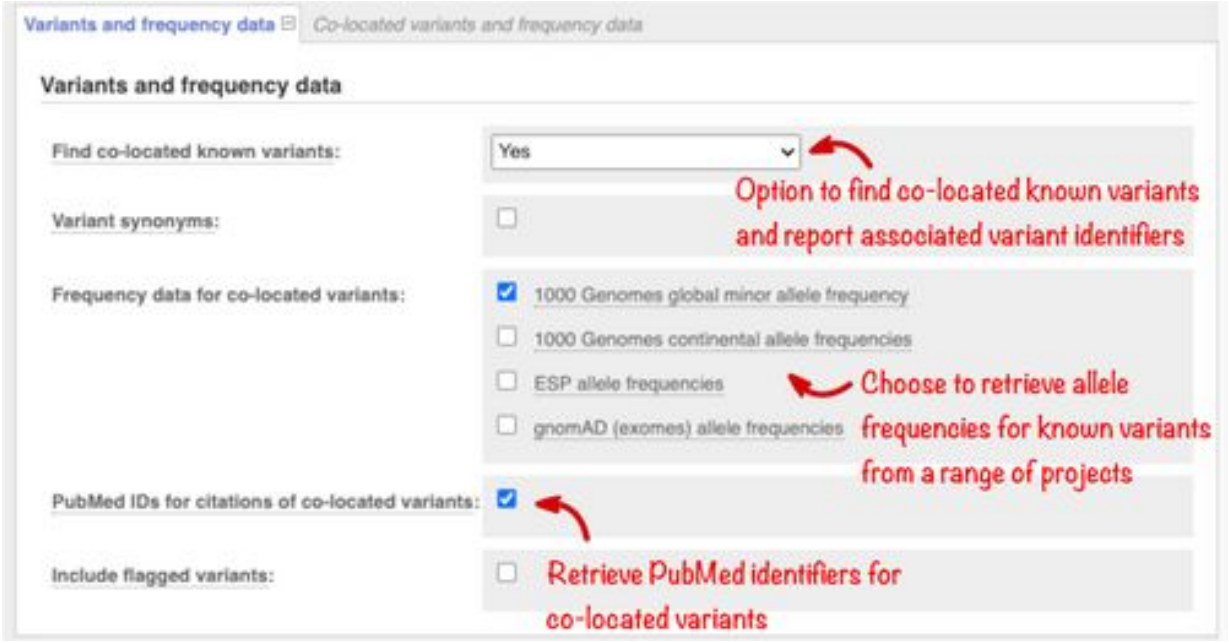
Variant Effect Predictor



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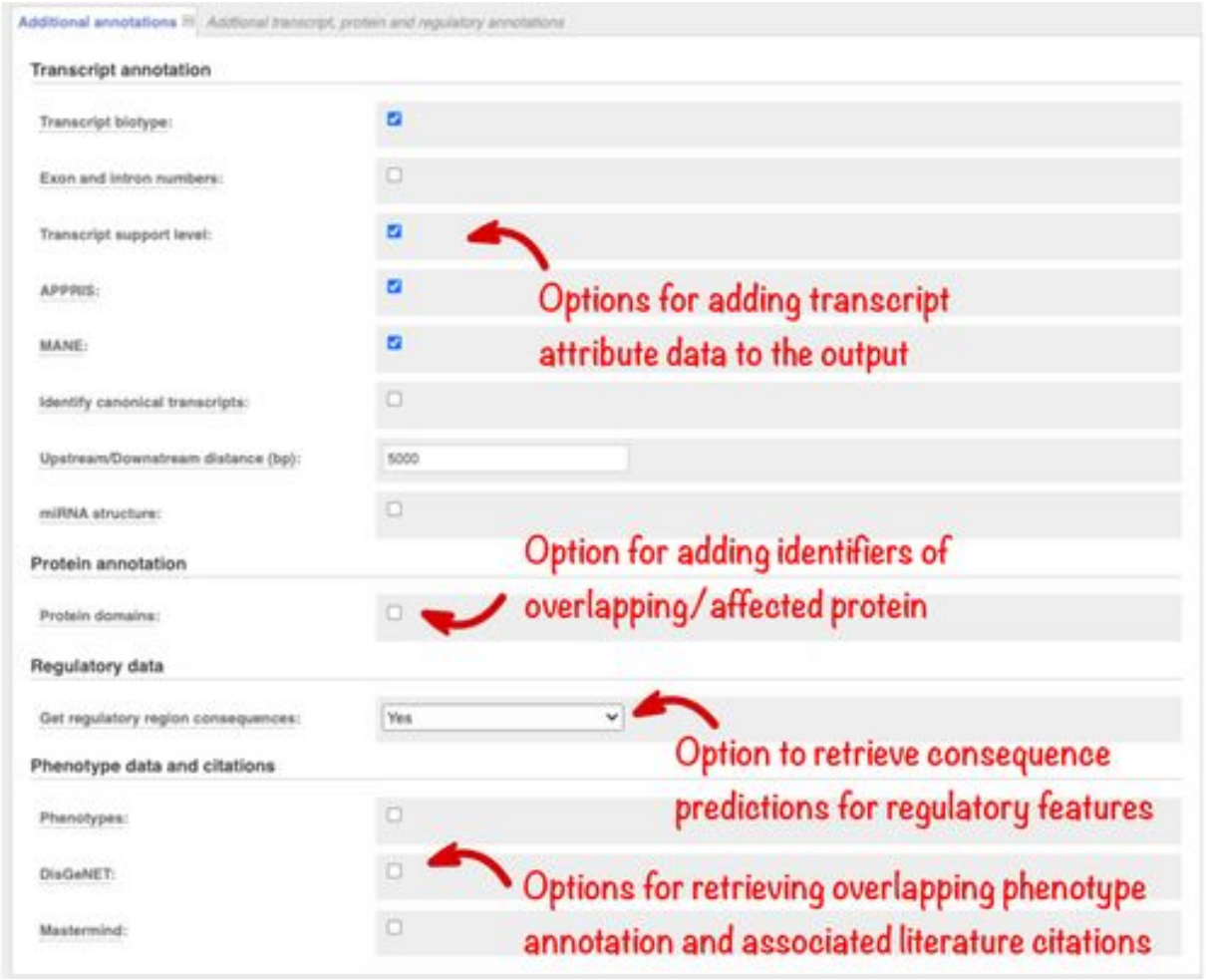

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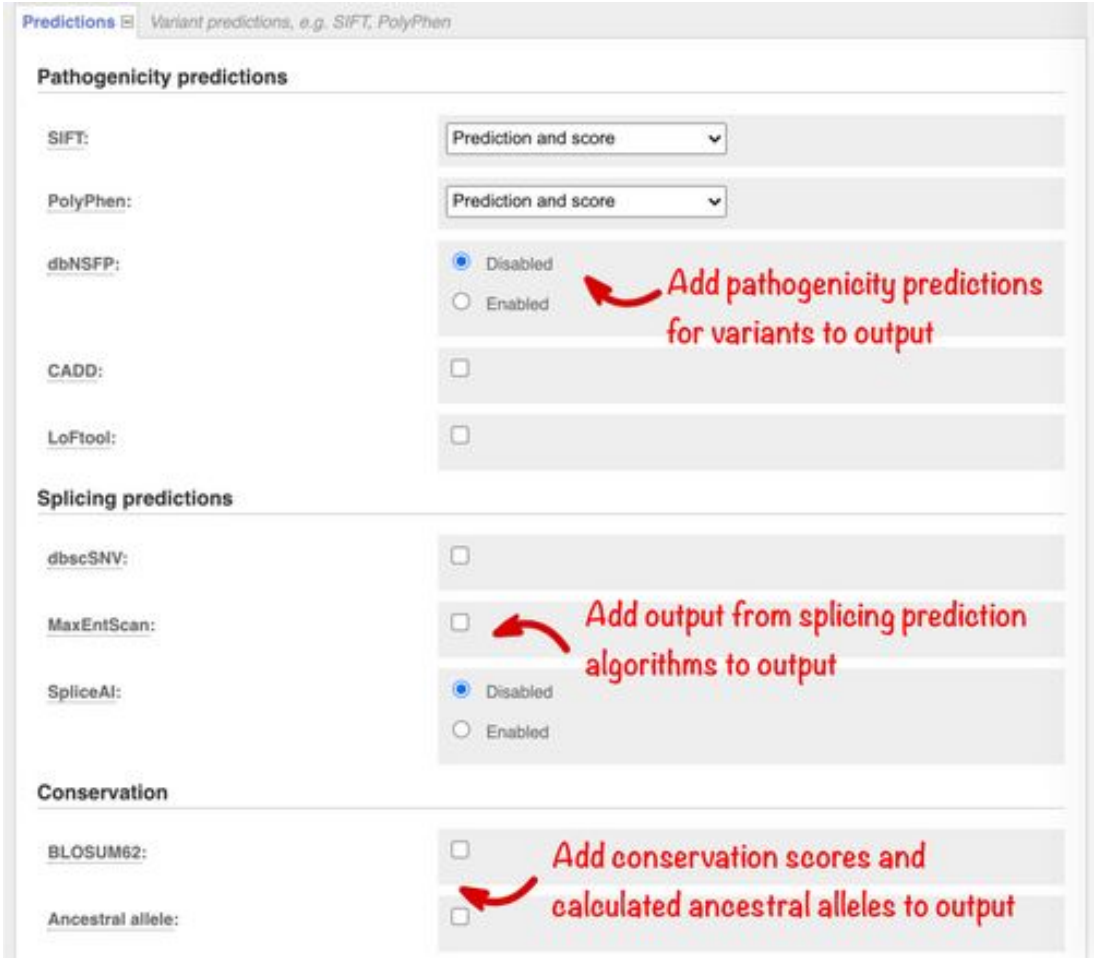

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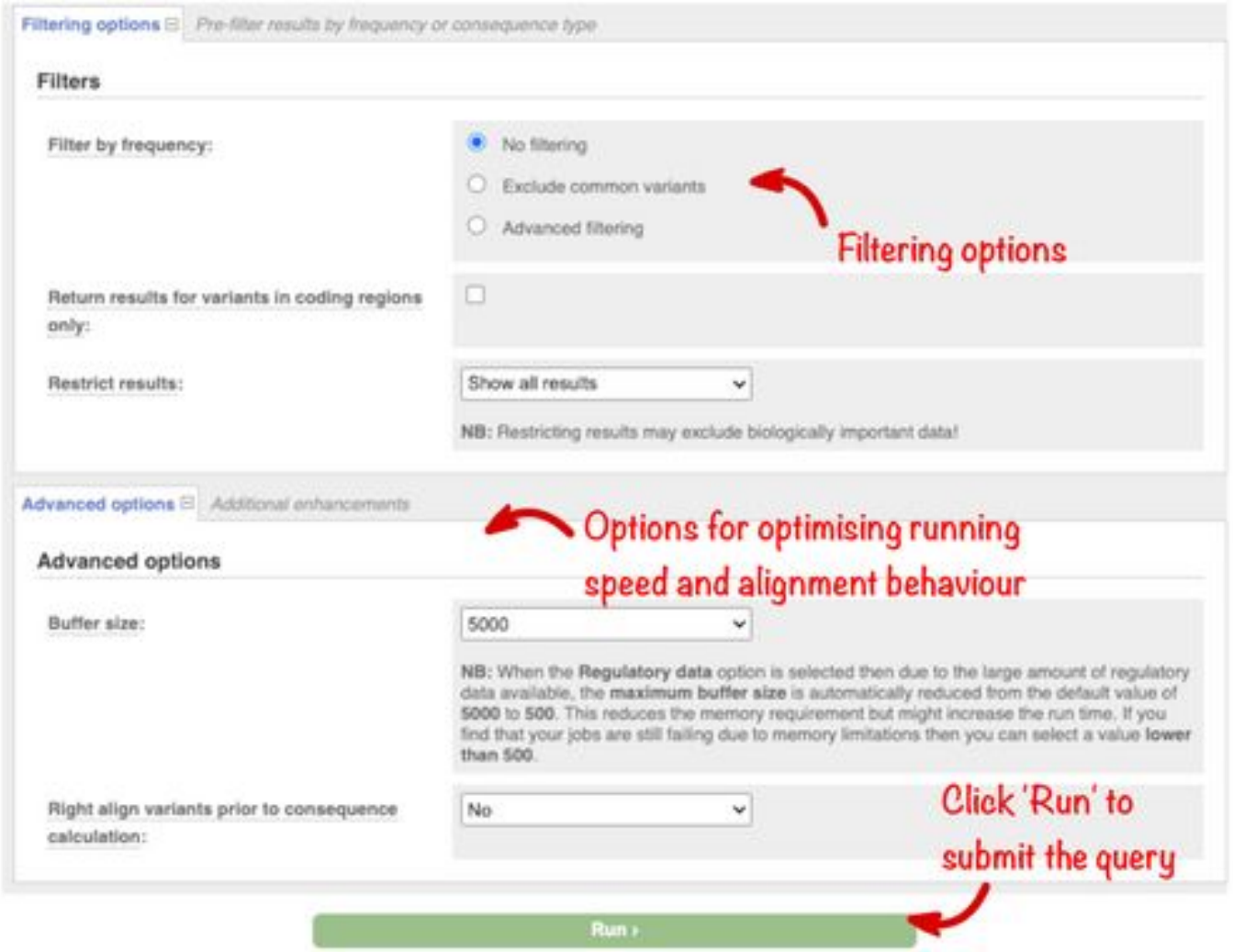

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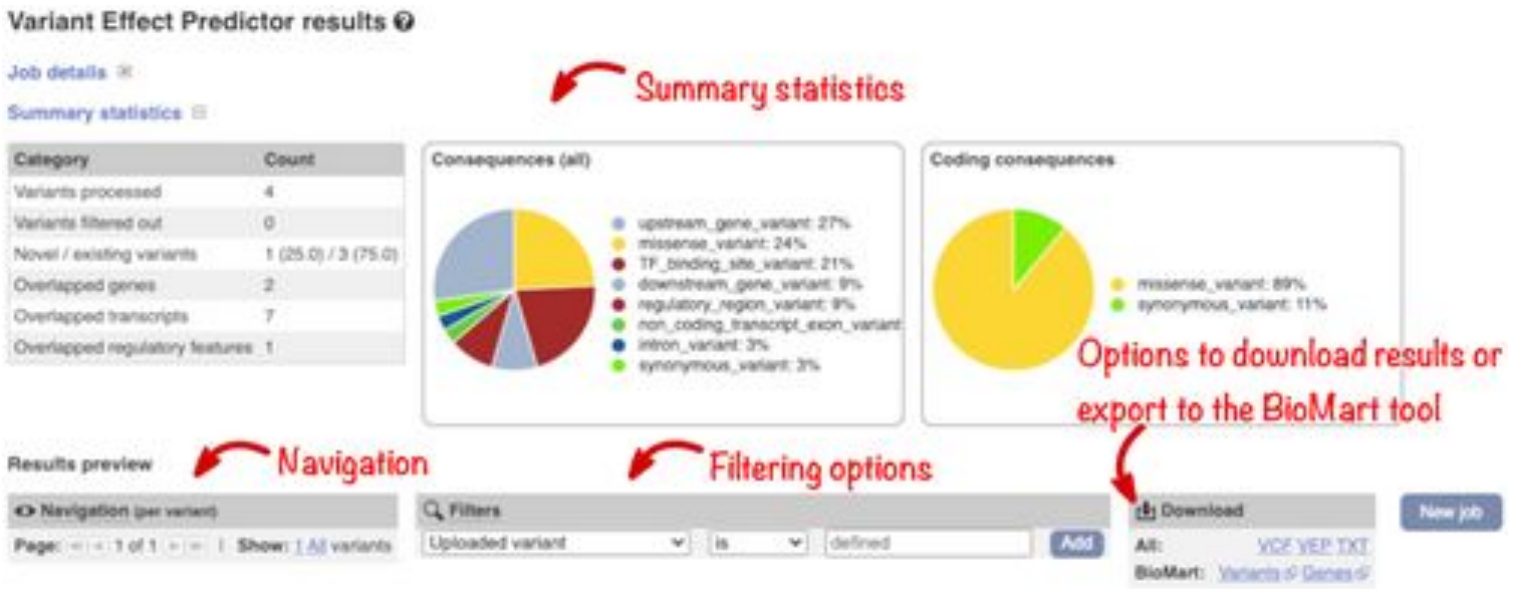

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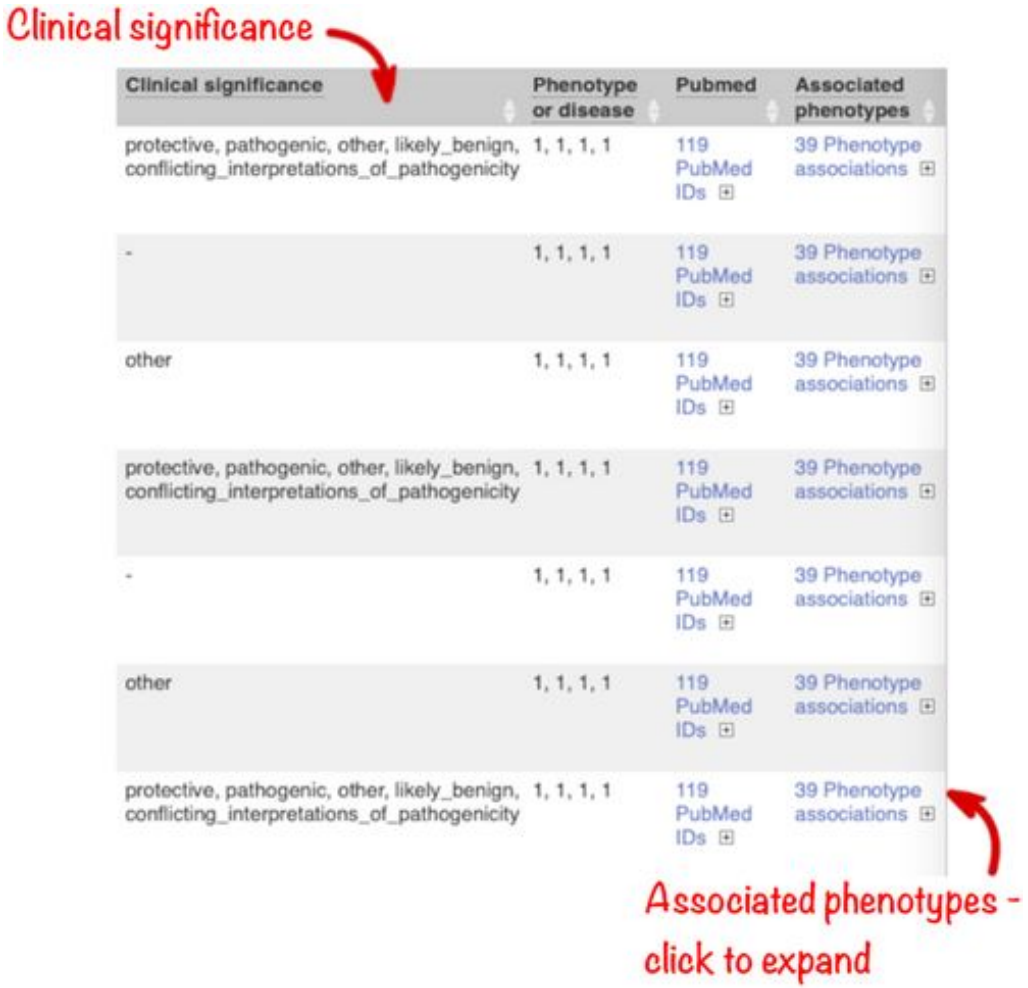

Clinical significance	Phenotype or disease	Pubmed	Associated phenotypes
protective, pathogenic, other, likely_benign, conflicting_interpretations_of_pathogenicity	1, 1, 1, 1	119 PubMed IDs	39 Phenotype associations
-	1, 1, 1, 1	119 PubMed IDs	39 Phenotype associations
other	1, 1, 1, 1	119 PubMed IDs	39 Phenotype associations
protective, pathogenic, other, likely_benign, conflicting_interpretations_of_pathogenicity	1, 1, 1, 1	119 PubMed IDs	39 Phenotype associations
-	1, 1, 1, 1	119 PubMed IDs	39 Phenotype associations
other	1, 1, 1, 1	119 PubMed IDs	39 Phenotype associations
protective, pathogenic, other, likely_benign, conflicting_interpretations_of_pathogenicity	1, 1, 1, 1	119 PubMed IDs	39 Phenotype associations

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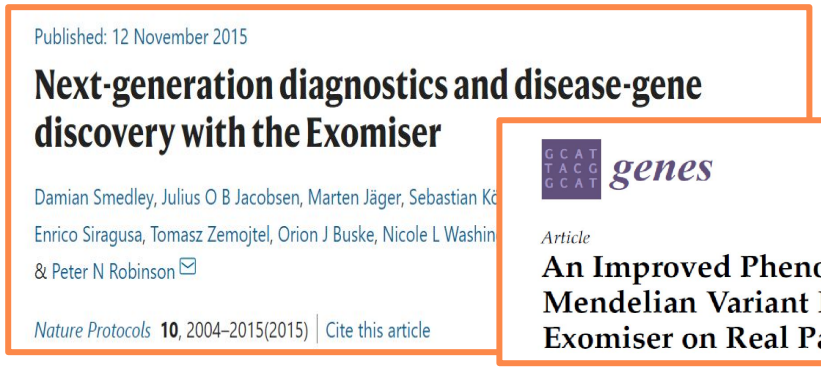
Priorização

- Processo através do qual é feito um ranking de variantes, de acordo com a sua patogenicidade e/ou relevância para o fenótipo em causa.

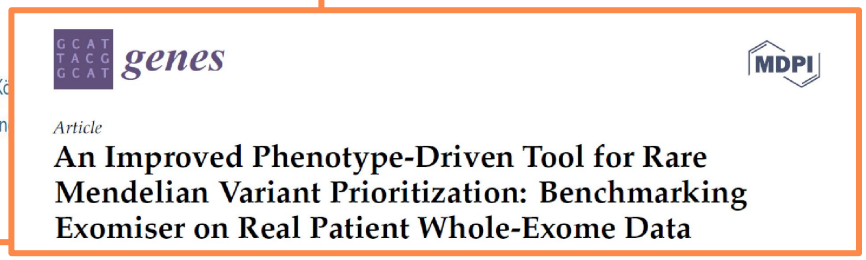
Exomiser


Published: 12 November 2015

Next-generation diagnostics and disease-gene discovery with the Exomiser

Damian Smedley, Julius O B Jacobsen, Marten Jäger, Sebastian Kö
Enrico Siragusa, Tomasz Zemojtel, Orion J Buske, Nicole L Washin
& Peter N Robinson

Nature Protocols 10, 2004–2015(2015) | Cite this article


genes

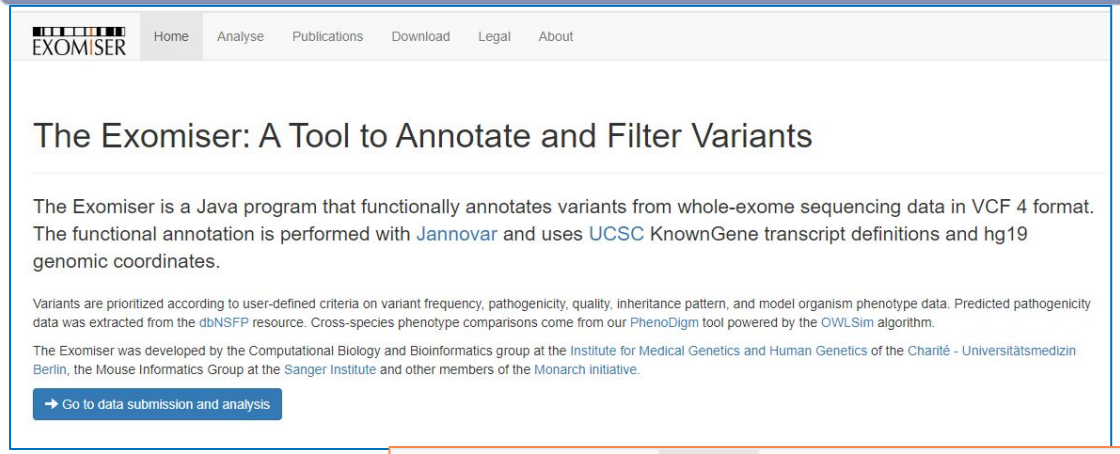
MDPI

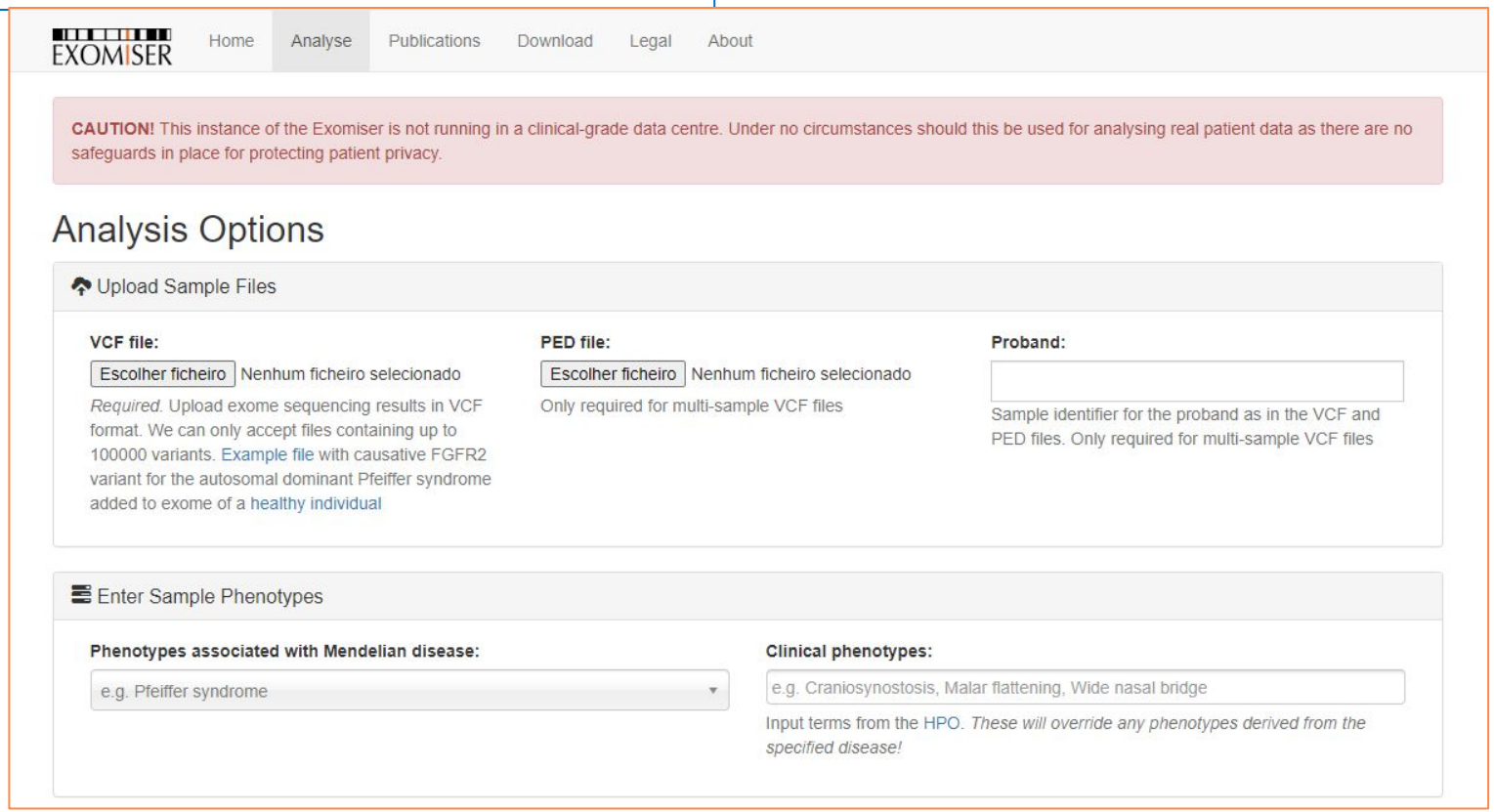
Article

An Improved Phenotype-Driven Tool for Rare Mendelian Variant Prioritization: Benchmarking Exomiser on Real Patient Whole-Exome Data

- **Priorização de variantes:**
  - Fenótipo/Termos HPO – Específicos; Representativos do diagnóstico clínico
  - **<u>Variantes + Termos HPO</u>**:
    - **74% dos casos** com variante causal na **1ª posição** do ranking
    - **94% no top 5**
    - Posição mais baixa foi a 42ª
  - Só Variantes (**sem termos HPO**):
    - **3% dos casos** com variante causal na **1ª posição**
    - **27% no top 5**

wellcome sanger institute

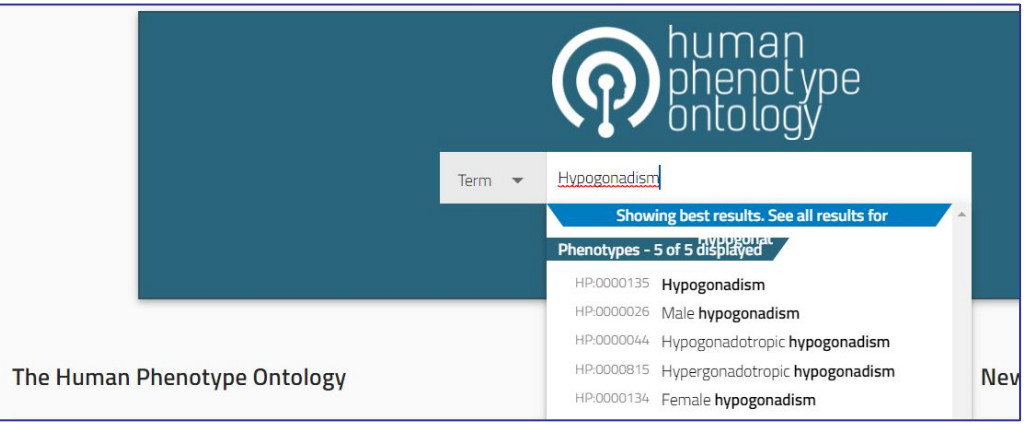


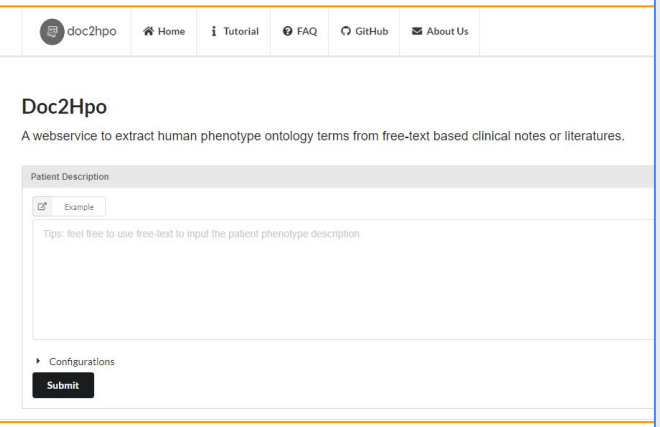


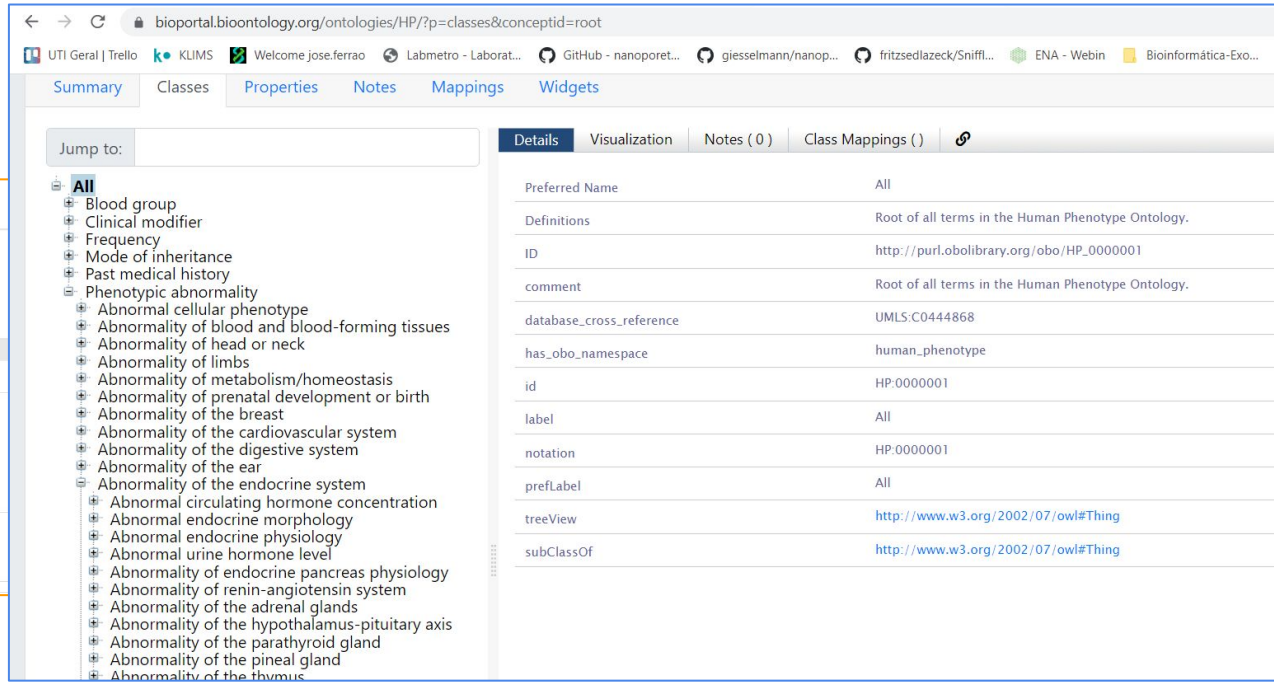
https://exomiser.monarchinitiative.org/exomiser/

HPO

https://hpo.jax.org/app/ https://doc2hpo.wglab.org/
https://bioportal.bioontology.org/ontologies/HP/?p=classes&conceptid=root







Phen2Gene - HPO´s to gene list