**SUPPLEMENTARY DATA**

**GENEASE: Real time bioinformatics tool for multi-omics and disease ontology exploration, analysis and visualization**

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**Supplementary Table S1: SNP explore databases:** List of the annotation databases used in GENEASE exploration module for “SNP” Input category.

|  |  |  |
| --- | --- | --- |
| **Database/Tool Name** | **Group in Tool** | **URL** |
| **Exome Variant Server** | Genome Variation | <http://evs.gs.washington.edu/EVS/> |
| **GWAS Catalog** | Genome Variation | <https://www.ebi.ac.uk/gwas/home> |
| **Genome Variant Server** | Genome Variation | <http://gvs.gs.washington.edu/GVS144/> |
| **UCSC** | Genome Variation | <https://genome.ucsc.edu/> |
| **Ensembl** | Genome Variation | <http://useast.ensembl.org/index.html> |
| **dbSNP** | Genome Variation | <https://www.ncbi.nlm.nih.gov/projects/SNP/index.html> |
| **Geno2MP** | Genome Variation | <http://geno2mp.gs.washington.edu/Geno2MP/#/> |
| **DGV(Database of Genomic Variants)** | Genome Variation | <http://dgv.tcag.ca/dgv/app/home> |
| **VarSome** | Genome Variation | <https://varsome.com/> |
| **RegulomeDB** | Variant Annotation | <http://www.regulomedb.org/index> |
| **HaploReg** | Variant Annotation | <https://archive.broadinstitute.org/mammals/haploreg/haploreg.php> |
| **GWAVA** | Variant Annotation | <https://www.sanger.ac.uk/sanger/StatGen_Gwava> |
| **GTEx** | Variant Annotation | <https://gtexportal.org/home/> |
| **SNPeffect** | Variant Annotation | <http://snpeffect.switchlab.org/menu> |
| **Spliceman 2** | Variant Annotation | <http://fairbrother.biomed.brown.edu/spliceman2/upload> |
| **Varian Effect Predictor** | Variant Annotation | <http://www.ensembl.org/Tools/VEP/> |
| **PubMed** | Other Information | <https://www.ncbi.nlm.nih.gov/pubmed> |
| **SNPedia** | Other Information | <https://www.snpedia.com/index.php/SNPedia> |

**Supplementary Table S2: GENE explore databases:** List of databases used in GENEASE exploration module for “gene” input category.

|  |  |  |
| --- | --- | --- |
| **Database/Tool Name** | **Group in Tool** | **URL** |
| **UCSC** | Gene Information | <https://genome.ucsc.edu/> |
| **Ensembl** | Gene Information | <http://useast.ensembl.org/index.html> |
| **HGNC** | Gene Information | <http://www.genenames.org/> |
| **OMIM** | Gene Information | <https://omim.org/> |
| **HAVANA** | Gene Information | <http://vega.archive.ensembl.org/index.html> |
| **Illumina** | CpG Information | <https://www.illumina.com/> |
| **GWAS Catalog** | Genome & Variation | <https://www.ebi.ac.uk/gwas/home> |
| **ENCODE** | Genome & Variation | <https://www.encodeproject.org/> |
| **Exome Variant Server** | Genome & Variation | <http://evs.gs.washington.edu/EVS/> |
| **Genome Variant Server** | Genome & Variation | <http://gvs.gs.washington.edu/GVS144/> |
| **SNPeffect** | Genome & variation | <http://snpeffect.switchlab.org/menu> |
| **dbVar** | Genome & Variation | <https://www.ncbi.nlm.nih.gov/dbvar> |
| **ClinVar** | Genome & Variation | <https://www.ncbi.nlm.nih.gov/clinvar/> |
| **Geno2MP** | Genome & Variation | <http://geno2mp.gs.washington.edu/Geno2MP/#/> |
| **DGV(Database of Genomic Variants)** | Genome & Variation | <http://dgv.tcag.ca/dgv/app/home> |
| **GEO Profiles** | Gene Expression | <https://www.ncbi.nlm.nih.gov/geoprofiles> |
| **ArrayExpress** | Gene Expression | <https://www.ebi.ac.uk/arrayexpress/> |
| **GTEx** | Gene Expression | <https://gtexportal.org/home/> |
| **TargetScan** | Gene Expression | <http://www.targetscan.org/vert_71/> |
| **Encode Promoter** | Gene Expression | <http://promoter.bx.psu.edu/ENCODE/index.html> |
| **KEGG** | Pathways | <http://www.kegg.jp/kegg/kegg2.html> |
| **Reactome** | Pathways | <http://www.reactome.org/> |
| **BioCarta** | Pathways | <https://cgap.nci.nih.gov/> |
| **Protein Atlas** | Protein Information | <http://www.proteinatlas.org/> |
| **UniProt** | Protein Information | <http://www.uniprot.org/> |
| **Pfam** | Protein Information | <http://pfam.xfam.org/> |
| **SMART** | Protein Information | <http://smart.embl.de/> |
| **MGI (Mouse genome)** | Ortholog Information | <http://www.informatics.jax.org/> |
| **RGD (Rat genome)** | Ortholog Information | <http://rgd.mcw.edu/wg/home> |
| **ZFIN (zebrafish information)** | Ortholog Information | <http://zfin.org/> |
| **FlyBase** | Ortholog Information | <http://flybase.org/> |
| **WormBase** | Ortholog Information | <http://www.wormbase.org/#012-34-5> |
| **PomBase** | Ortholog Information | <https://www.pombase.org/> |
| **SGD (Yeast genome)** | Ortholog Information | <https://www.yeastgenome.org/> |
| **NCBI Map** | Other Information | <https://www.ncbi.nlm.nih.gov/> |
| **GeneCards** | Other Information | <http://www.genecards.org/> |
| **Vega** | Other Information | <http://vega.archive.ensembl.org/index.html> |
| **DECIPHER** | Other Information | <https://decipher.sanger.ac.uk/> |
| **PubMed** | Other Information | <https://www.ncbi.nlm.nih.gov/pubmed> |
| **NCBI Gene** | Other Information | <https://www.ncbi.nlm.nih.gov/gene/> |

**Supplementary Table S3: Disease explore databases:** List of databases used in GENEASE exploration module for “disease” input category.

|  |  |  |
| --- | --- | --- |
| **Database/Tool Name** | **Group in Tool** | **URL** |
| **GWAS Catalog** | Genome-wide Association/Gene Expression | <https://www.ebi.ac.uk/gwas/home> |
| **dbGaP** | Genome-wide Association/Gene Expression | <https://www.ncbi.nlm.nih.gov/gap> |
| **Geo DataSets** | Genome-wide Association/Gene Expression | <https://www.ncbi.nlm.nih.gov/gds> |
| **PhenX Toolkit** | Phenotype Genotype | <https://www.phenxtoolkit.org/index.php> |
| **DECIPHER** | Phenotype Genotype | <https://decipher.sanger.ac.uk/> |
| **ENCODE** | Variation Information | <https://www.encodeproject.org/> |
| **ClinVar** | Variation Information | <https://www.ncbi.nlm.nih.gov/clinvar/> |
| **OMIM** | Variation Information | <https://omim.org/> |
| **GeneCards** | Variation Information | <http://www.genecards.org/> |
| **Swissvar** | Variation Information | <http://www.expasy.org/> |

**Supplementary Table S4:** Execution times of bulk input requests of both SNP and gene lists (in cache and not in cache scenarios).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Gene** | | |  | **SNP** | | |
| **Number of Genes** | **Runtime(not in cache)** | **Runtime(in cache)** |  | **Number of SNPs** | **Runtime(not in cache)** | **Runtime(in cache)** |
| 100 | 28 secs | 2.5 secs |  | 100 | 67 secs | 1.7 secs |
| 500 | 144 secs | 14 secs |  | 200 | 123 secs | 2.5 secs |
| 1000 | 290 secs | 30 secs |  | 500 | 300 secs | 9.7 secs |

**Supplementary Table S5:** List of annotation databases used in “Enrichment Analysis” module. Annotation terms download and parsed in real-time for each request.

|  |  |  |
| --- | --- | --- |
| **Annotation Type** | **Database/Project Name** | **URL(s)/File(s)** |
| **Biological Pathways** | KEGG(Kyoto Encyclopaedia of Genes and Genomes) | <http://rest.kegg.jp/list/pathway/hsa>  <http://rest.kegg.jp/link/hsa/pathway> |
| **Gene Ontologies** | GOC(Gene Ontology Consortium) | <http://geneontology.org/ontology/go.obo>  <http://geneontology.org/gene-associations/goa_human.gaf.gz> |
| **Phenotype Ontologies** | HPO(Human Phenotype Ontology) | <http://compbio.charite.de/jenkins/job/hpo.annotations.monthly/lastStableBuild/artifact/annotation/ALL_SOURCES_ALL_FREQUENCIES_genes_to_phenotype.txt> |

**Supplementary Table S6:** Gene coverage in the ontology terms used in GENEASE in comparison with other tools.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Gene Counts** | | | | |
|  | **KEGG Pathways** | **GO Biological Process** | **GO Cellular Component** | **GO Molecular Function** | **Human Phenotype Ontologies** |
| **Actual Counts** | 7320 | 17783 | 18932 | 17758 | 3699 |
| **DAVID** | 6910 | 16792 | 18224 | 16881 | Unsupported |
| **Enrichr** | 7010 | 13822 | 10427 | 10601 | 3096 |
| **GENEASE** | 7320 | 17257 | 18631 | 17505 | 3699 |

**Supplementary Figure S1**: Exploring proxy variants: SNP explore result for **rs9272346** with LD option to find its proxy variants in CEU (European) population (r2>0.8). A particular proxy variant can be further explored by selecting the particular row in the result table.

