

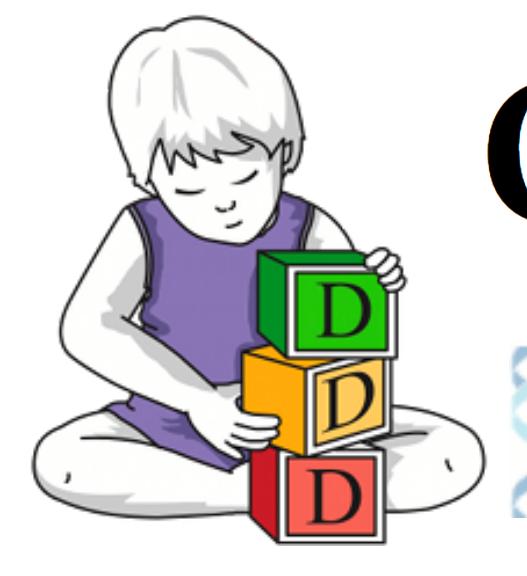
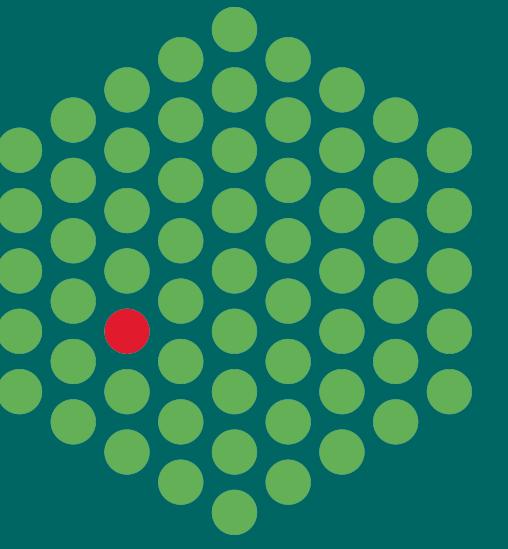
Enhanced access to extensive phenotype and disease annotation of genes and genetic variation in Ensembl

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EMBL-EBI



OMIM®

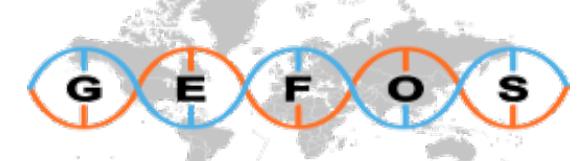
ClinVar

COSMIC
Catalogue of somatic mutations in cancer

IMPC
International Mouse Phenotyping Consortium

MAGIC
Mutagenesis and Insulin-related Trait Consortium

NHGRI-EBI
GWAS Catalog



Ensembl Variant Effect Predictor (VEP)

- Powerful open-source toolset for genomic variants interpretation and annotation
- Uses the extensive Ensembl transcriptomic, regulatory and variation data to predict consequences of variants
- Reports allele frequency data from reference projects and the results of multiple pathogenicity predictors
- Reports aggregated phenotypes for genes and variants from overlapping genes and variants

Interfaces

- Command line interface

```
./vep --cache -i input.vcf --plugin Phenotypes  
  
## PHENOTYPES : Phenotypes associated with overlapping genomic features
```

- Web tool: <https://www.ensembl.org/Tools/VEP>

Uploaded variant	Location	Allele	Consequence	Symbol	Feature	Protein position	Amino acids	SIFT	PolyPhen	AF	Clinical significance	Associated phenotypes
rs7412	19:44908822-	T	missense_variant	APOE	ENST00000434152	202	R/C	0	0.999	0.0751	41 Phenotype associations	Alzheimer disease 2 (ENSG00000130203,MIM morbid)
rs7412	19:44908822-	T	missense_variant	APOE	ENST00000252486	176	R/C	0	1	0.0751	41 Phenotype associations	ALZHEIMER DISEASE 4 (ENSG00000130203,MIM morbid)
rs7412	19:44908822-	T	missense_variant	APOE	ENST00000425718	176	R/C	0	1	0.0751	41 Phenotype associations	Alzheimer's disease late onset (rs7412,NHGRI-EBI GWAS catalog)

AF	Clinical significance	PubMed IDs	Associated phenotypes
0.0751	pathogenic, drug_response, other	114 PubMed IDs	41 Phenotype associations
0.0751	pathogenic, drug_response, other	114 PubMed IDs	41 Phenotype associations

41 Phenotype associations
• Alzheimer disease 2 (ENSG00000130203,MIM morbid)
• ALZHEIMER DISEASE 4 (ENSG00000130203,MIM morbid)
• Alzheimer's disease late onset (rs7412,NHGRI-EBI GWAS catalog)
• Alzheimer's disease or family history of Alzheimer's disease (rs7412,NHGRI-EBI GWAS catalog)
• Apolipoproteinemia E1 (rs7412,ClinVar)
• atorvastatin response - Efficacy (rs7412,ClinVar)
• Blood protein levels (rs7412,NHGRI-EBI GWAS catalog)
• Cardiovascular risk factors (rs7412,NHGRI-EBI GWAS catalog)
• Cholesterol total (rs7412,NHGRI-EBI GWAS catalog)

VEP is also available in REST

<https://www.ensembl.org/vep>

REST API

- Retrieval of phenotype annotations directly assigned or overlapping the variant or gene name/symbol or region of interest
- Search by ontology term to query across traits described differently in different resources

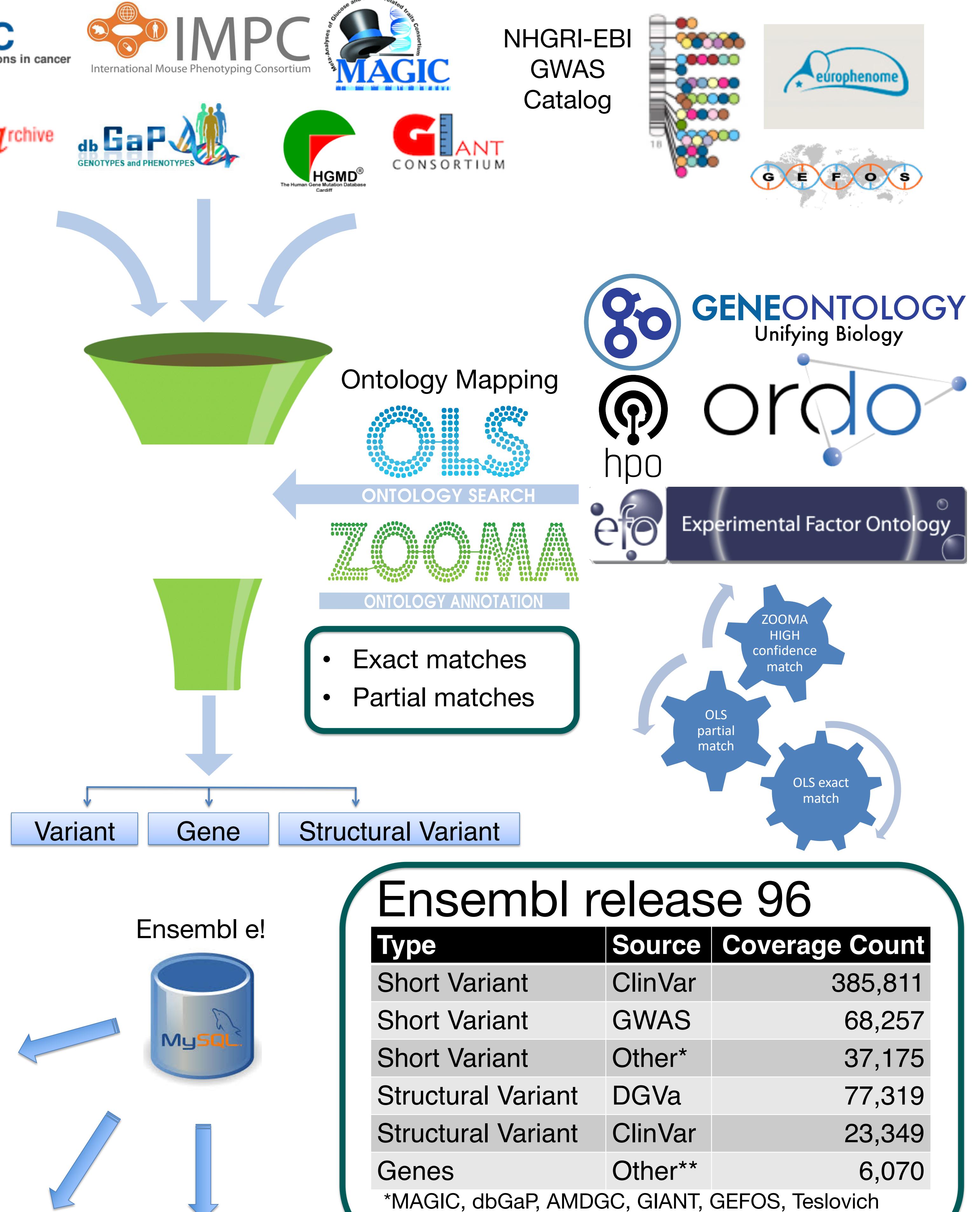
Phenotype annotations

Resource	Description
<code>GET /phenotype/accession/species/:accession</code>	Return phenotype annotations for genomic features given a phenotype ontology accession
<code>GET /phenotype/gene/species/:gene</code>	Return phenotype annotations for a given gene.
<code>GET /phenotype/region/species/:region</code>	Return phenotype annotations that overlap a given genomic region.
<code>GET /phenotype/term/species/:term</code>	Return phenotype annotations for genomic features given a phenotype ontology term
<code>include_associated Boolean(0,1)</code>	Include phenotypes associated with variants reporting this gene.
<code>include_overlap Boolean(0,1)</code>	Include phenotypes of features overlapping the gene.

re!st

```
{  
  "description": "PARKINSON DISEASE 8, AUTOSOMAL DOMINANT",  
  "Variation": "rs34637584",  
  "attributes": {  
    "risk_allele": "A",  
    "external_id": "RCV000002017.9",  
    "submitter_name": [  
      "Institute of Human Genetics,Klinikum rechts der Isar",  
      "OMIM",  
      "Courtagen Diagnostics Laboratory,Courtagen Life Sciences",  
      "GeneReviews",  
      "Invitae",  
    ],  
    "clinical_significance": "pathogenic",  
    "MIM": "609007",  
    "associated_gene": "LRRK2",  
    "review_status": "criteria provided, multiple submitters, no conflicts"  
  },  
  "location": "12:40340400-40340400",  
  "ontology_acceossions": [  
    "EFO:0002508"  
  ],  
  "source": "ClinVar"  
},
```

<https://rest.ensembl.org/>



Genome Browser

- View genes and variants for traits associated with the same ontology term
- Filter by a data source, feature type and original trait description

Loci associated with Bardet-Biedl syndrome (Orphanet:110) ↗

Filter Feature type: All Annotation source: All Phenotype/Disease/Trait: All

Name(s)	Type	Genomic location (strand)	Reported gene(s)	Phenotype/Disease/Trait	Annotation source	Submitter	External reference	Supporting evidence
rs1192652072	Variant	7:33388022 (+)	BBS9	BARDET-BIEDL SYNDROME 1	ClinVar	-	-	PMID:22190896, PMID:20835237
rs267607031	Variant	CHR_HSCHR1_3_CTG32	SDCCAG8	BARDET-BIEDL SYNDROME 16	ClinVar	-	-	MIM:613524, PMID:22190896, PMID:20835237
rs886049845	Variant	12:76345167-76345168 (+)	BBS10	Bardet-Biedl syndrome	ClinVar	-	-	-
rs141263993	Variant	1:32204044 (+)	CCDC28B	BARDET-BIEDL SYNDROME 1, MODIFIER OF	ClinVar	-	-	MIM:610162, PMID:12677559, PMID:16327777
rs137853921	Variant	2:169493769 (+)	BBS5	Bardet-Biedl syndrome	ClinVar	-	-	-
WDPBP	Gene	2:63119559-63827843 (-)	-	BARDET-BIEDL SYNDROME TYPE 15	DDG2P	-	-	-
rs61756571	Variant	7:33336435 (+)	BBS9	Bardet-Biedl syndrome	ClinVar	-	-	-
rs200817579	Variant	12:88084735 (+)	CEP290	Bardet-Biedl syndrome	ClinVar	-	-	-
rs758139447	Variant	11:66526151 (+)	BBS1, ZDHHC24	Bardet-Biedl syndrome	ClinVar	-	-	-

- View summary counts for related terms

Phenotype/Disease/Trait description	Mapped ontology Term	Relationship with Orphanet:110	Variant	Structural Variant	Gene	QTL
BARDET-BIEDL SYNDROME 5	Bardet-Biedl syndrome 5	4	-	1	-	-
BARDET-BIEDL SYNDROME 12	Bardet-Biedl syndrome 12	62	-	1	-	-
BARDET-BIEDL SYNDROME TYPE 15	Bardet-Biedl syndrome	-	-	1	-	-
Phenotype, disease and trait annotations associated with variants in this gene						
All variants with a phenotype annotation			258	Show details		
Annotated by HGMD but no phenotype description is publicly available			89	Show		
Bardet-Biedl syndrome	ClinVar	-	4	Show		
BARDET-BIEDL SYNDROME 10	ClinVar	-	92	Show		
BARDET-BIEDL SYNDROME 110, DISGENIC	ClinVar	-	1	Show		
Bardet-Biedl syndrome	ClinVar	-	65	Show		
Unknown diseases not specified	ClinVar	-	59	Show		
Retinal dystrophy	ClinVar	-	6	Show		
Retinitis pigmentosa	ClinVar	-	1	Show		
	ClinVar	-	2	Show		

Equivalent to the ontology term "Orphanet:110"
Child term of "Orphanet:110"
Term related to "Orphanet:110"

Phenotype, disease and trait annotations associated with variants in this gene

Phenotype, disease and trait annotations associated with variants in other species

<https://www.ensembl.org/>