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  ensembl.org/info/about/publications.html

Mining e!Ensembl data with BioMart and VEP

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This workshop

1. Introduction to Ensembl
2. BioMart
   - Introduction
   - Demo
3. Variant Effect Predictor (VEP)
   - Introduction
   - Demo

e!Ensembl's BioMart

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What is BioMart?

A tool in your browser to:

- Export data with no programming required
- Build queries with a few mouse clicks
- Generate custom data tables and sequence files

Why use BioMart?

Why use BioMart?

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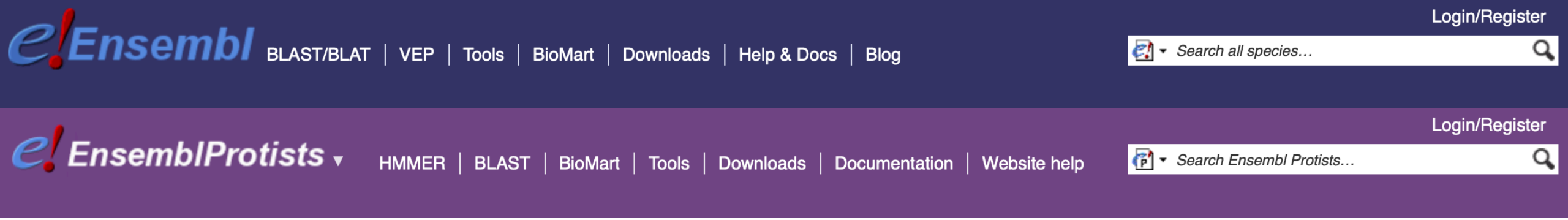
Why use BioMart?

For things that would be time consuming/difficult with the Ensembl browser:

- Query multiple things at once:
  - ID conversions
  - Gene locations
  - Download sequences
- Export large amounts of data



Where can I find BioMart?

ensembl.org/biomart/martview

protists.ensembl.org/biomart/martview

For which genomes is BioMart available?

- Ensembl
  44,048 genomes
- EnsemblFungi
  (some exceptions)
- EnsemblMetazoa
  78 genomes
- EnsemblPlants
  67 genomes
- EnsemblProtists
  (some exceptions)

How do I use BioMart?

The four steps

Dataset	Filters	Attributes	Results
Choose database & species	Narrow down the dataset	Specify your output	View & export

How do I use BioMart?
1. Dataset

Dataset

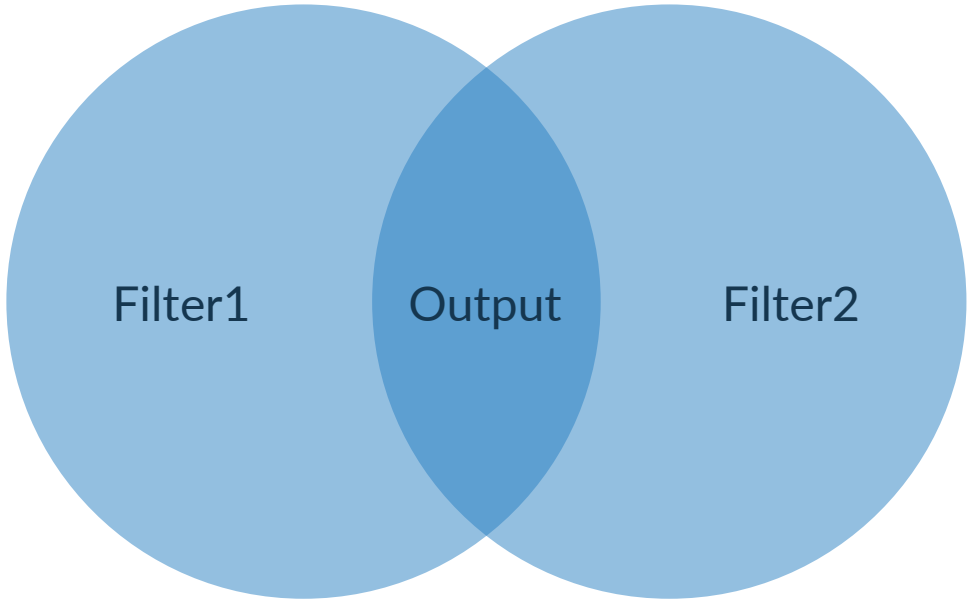
- Define the database you want to search with your filters:
  - Genes
  - Variation
  - Regulation
  - Mouse strains (genes)
- Define the species

How do I use BioMart?
2. Filters

Define a (large) set of genes/variants by combination of filters, e.g.:

- Region
- List of IDs
- Function (GO term)
- Phenotype

How do I use BioMart?
2. Filters



How do I use BioMart?
3. Attributes

Define the data you want to export (your output), e.g.:

- IDs
- Features
- Variants
- Orthologues/paralogues
- Sequences

How do I use BioMart?
4. Results

View and export data table/sequence in a number of formats:

- html
- csv
- tsv
- xls
- fasta

biomaRt: Bioconductor package for BioMart

Bioconductor provides tools for the analysis and comprehension of high-throughput genomic data using the R statistical programming language

- Easy installation:

```
source("http://bioconductor.org/biocLite.R")
biocLite("biomaRt")
```

More information

Kinsella *et al.*

Ensembl BioMarts: a hub for data retrieval across taxonomic space

Database: the Journal of Biological Databases and Curation (2011)

europepmc.org/abstract/MED/21785142

Smedley *et al.*

BioMart – biological queries made easy

BMC Genomics (2009) 10:22

europepmc.org/abstract/MED/19144180

Hands on

We're going to look at a set of six human genes, *ESPN*, *MYH9*, *USH1C*, *CISD2*, *THRB* and *WHRN*, and find out:

- Their NCBI gene IDs
- Their function via GO terms
- Their cDNA sequences

Dataset	Filters	Attributes	Results
Genes *Homo sapiens*	Gene names	NCBI IDs GO terms cDNA seq Gene names!	View & export

Variant Effect Predictor VeP

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What does the VEP do?

A tool to predict and annotate the functional consequences of variants
(SNPs, insertions, deletions, structural variants)

Input:

- Variant coordinates
- VCF
- Variant IDs
- HGVS
- SPDI

VeP
e!Ensembl

Output:

- Affected gene, transcript and protein sequence
- Pathogenicity
- Frequency data
- Regulatory consequences
- Splicing consequences
- Literature citations

Variant coordinates (Ensembl default)

```
1 182712 182712 A/C 1
2 265023 265023 C/T 1
3 319781 319781 A/- 1
19 110748 110747 -/T 1
```

VCF

```
#CHROM POS     ID        REF ALT
20     14370   rs6054257 G     A
20     17330   .         T     A
20     1110696 rs6040355 A     G,T
20     1230237 .         T     .
```

Variant IDs

```
rs41293501
COSM327779
FANCD1:c.475G>A
rs373400041
```

HGVS notation

```
AGT:c.803T>C
9:g.22125504G>C
ENST00000003084:c.1431_1433delTTC
19:g.110747_110748insT
```

SPDI

```
NC_000001.11:65567:A:C
NC_000002.12:265022:C:T
NC_000003.12:319780:A:
```

VEP features

Transcript consequence predictions:

- Ensembl / GENCODE
- GENCODE basic
- RefSeq
- Merged

Overlap with regulatory regions:

- ENCODE
- BLUEPRINT
- NIH Epigenomics Roadmap
- Can be limited to specific cell types

Known variants:

- dbSNP
- COSMIC
- ClinVar
- ESP
- HGMD-Public
- PhenCode

Allele frequencies:

- 1000 Genomes
- ESP
- gnomAD

Pathogenicity predictions:

- SIFT
- PolyPhen
- dbNSFP
- CADD
- Condel
- LoFTool
- FATHMM
- Mutation-Taster
- Many more!

Phenotype, disease, clinical significance:

- OMIM
- Orphanet
- GWAS catalog
- ClinVar

VEP plugins

- Add extra functionality
- Can extend, filter or manipulate the output
- May make use of external data or code
- Available on the web tool and with the script
- Many plugins for pathogenicity predictions

https://github.com/Ensembl/VEP_plugins
https://www.ensembl.org/info/docs/tools/vep/script/vep_plugins.html#plugins_existing

Using the VEP

- Clinical diagnostics
- Industry
- International consortia

SickKids illumina FABRIC GENOMICS CANCER RESEARCH UK Personalis NHS CONGENICA GENOME BASED MEDICINE

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 DockerHub

REST API

- Language-independent API
- Simple URL-based queries

Documentation

VEP REST API

Set up a cache

- Speed up your VEP script with an offline cache
- Keep your data private
- Use prebuilt caches for Ensembl species
- Or make your own cache from GTF and FASTA files – even for genomes not in Ensembl!

More information

McLaren *et al.*

The Ensembl Variant Effect Predictor

Genome Biology (2016) 17:122

europepmc.org/abstract/MED/27268795

Hands on

We're going to look at a set of four variants to find out what genes they hit and what effect they have on them:

```
9 128328461 128328461 A/- + var1
9 128322349 128322349 C/A + var2
9 128323079 128323079 C/G + var3
9 128322917 128322917 G/A + var4
```

Help and docs

Courses online:
www.ebi.ac.uk/training/online/subjects/11

Tutorials:
www.ensembl.org/info/website/tutorials

Animations:
www.youtube.com/user/EnsemblHelpdesk
u.youku.com/Ensemblhelpdesk

Email us: helpdesk@ensembl.org

Public mailing lists: dev@ensembl.org, announce@ensembl.org

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www.ensembl.info

Publications

List of publications:

ensembl.org/info/about/publications.html

Yates *et al.*

Ensembl 2020

Nucleic Acids Research (2020) 48(D1):D682-D688

europepmc.org/abstract/MED/31691826

Ensembl 2019

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Open Targets

TRANSFORMING GENETIC MEDICINE INITIATIVE

SAVE THE TASMANIAN DEVIL PROGRAM

National Human Genome Research Institute

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