

Introduction to Ensembl REST and EnsemblLite

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Overview of the day

11am-11:15am	Quick introductions
11:15-11:50am	EnsEMBL REST introduction
11:50am-12pm	Break
12-12:50pm	EnsEMBL REST exercises
12:50-1pm	Break
1-1:50pm	EnsEMBL REST exercises
1:50-2pm	Break
2-2:15pm	EnsemblLite: motivation and introduction
2:15-2:50pm	Demonstration of EnsemblLite capabilities and Cogent3
2:50-3pm	Break
3-4pm	Hacking of EnsemblLite code

Quick introductions!

In about 30 seconds, please tell us:

- Your name
- Where you work
- What you're interested in
- What you expect from this mini-course

Ensembl REST introduction: Accessing genome data programmatically

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Based on slides from the Ensembl Project



Course materials

- This course:

[https://github.com/cogent3/SMBE2024Workshop/tree/main/EnsEMBL REST API](https://github.com/cogent3/SMBE2024Workshop/tree/main/EnsEMBL%20REST%20API)

- EnsEMBL Project:

<http://training.ensembl.org/events/>

- Slides
- Jupyter notebooks

What is Ensembl?

Ensembl is an **open source** genome browser with a large amount of data available to explore and a number of biological annotations:

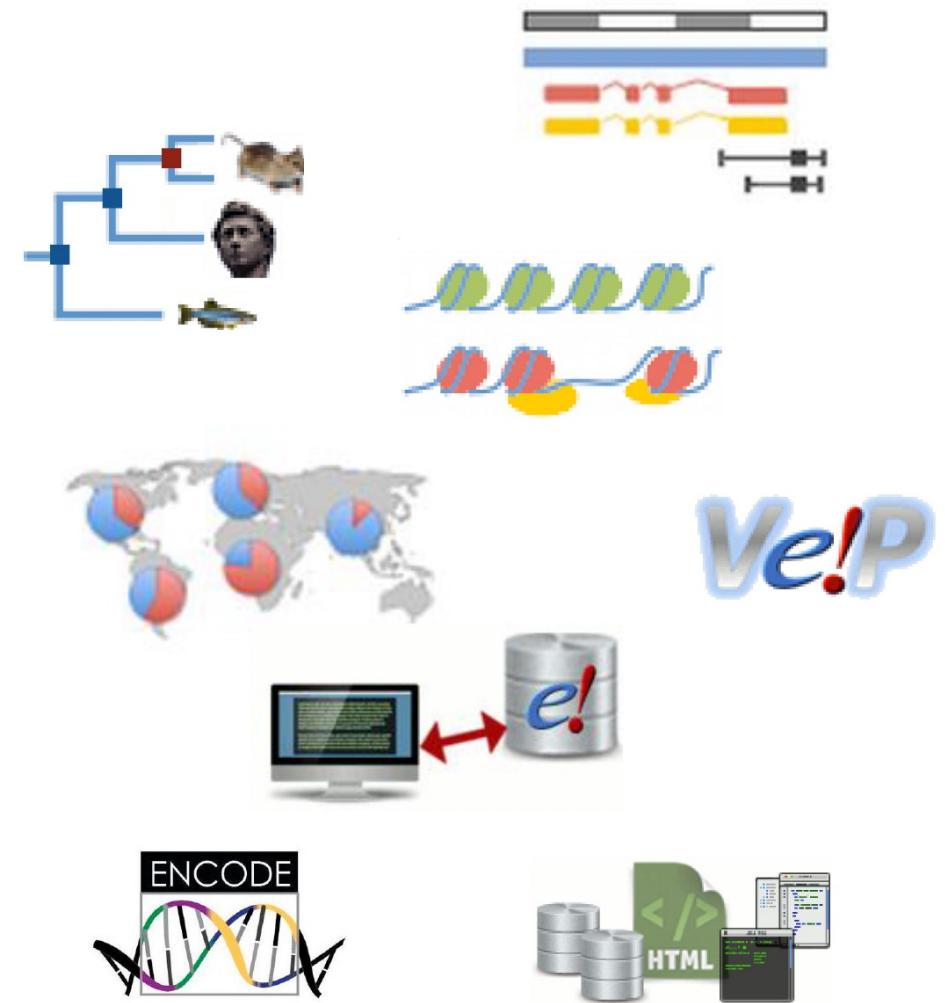
www.ensembl.org

- **Genomic assemblies:** automated gene annotation
- **Variation:** Small and large-scale sequence variation with phenotype associations
- **Comparative genomics:** Whole genome alignments, gene trees
- **Regulation:** Potential promoters and enhancers, DNA regulation



Ensembl Features

- Gene builds for >300 species
- Gene trees
- Regulatory build (ENCODE)
- Variation display and VEP
- Display of user data
- BioMart (data export)
- Programmatic access via the APIs
- Completely open source



Ensembl sites

- Ensembl (vertebrates)
- Ensembl Genomes (non-vertebrates)

Ensembl Rapid Release

Portals:

- Ensembl GRCh37
- Ensembl COVID-19



EnsemblPlants

The screenshot shows the EnsemblPlants homepage. It features a search bar at the top with "All species" selected. Below the search bar are sections for "All genomes" and "Favourite genomes", which include icons for *Arabidopsis thaliana* (TAIR10), *Oryza sativa* (Japonica Group) (IRGSP 1.0), and *Triticum aestivum* (IWGSC). A sidebar on the right is titled "Wheat assemblies" and lists various wheat cultivars and their assembly details.

EnsemblMetazoa

The screenshot shows the EnsemblMetazoa homepage. It features a search bar at the top with "All species" selected. Below the search bar are sections for "All genomes" and "Favourite genomes", which include icons for *Anopheles gambiae* (AgamP4), *Drosophila melanogaster* (BDGP8.32), and *Apis mellifera* (DH4). A sidebar on the right is titled "What's New in Release 53" and lists new assemblies and gene sets.

EnsemblProtists

The screenshot shows the EnsemblProtists homepage. It features a search bar at the top with "All species" selected. Below the search bar are sections for "All genomes" and "Favourite genomes", which include icons for *Plasmodium falciparum* 3D7 (ASM276v2), *Dicyostelium discoideum* d7, *Phytophthora infestans* (ASM1429v1), and *Lishmania major* (ASM272v2). A sidebar on the right is titled "What's New in Release 53" and lists new genomes and protein features.

EnsemblFungi

The screenshot shows the EnsemblFungi homepage. It features a search bar at the top with "All species" selected. Below the search bar are sections for "All genomes" and "Favourite genomes", which include icons for *Saccharomyces cerevisiae* (R64-1-1), *Schizosaccharomyces pombe* (ASM500v4), *Aspergillus nidulans* (ASM1142v1), and *Puccinia graminis* (ASM1495v1). A sidebar on the right is titled "What's New in Release 53" and lists updated data and protein features.

EnsemblBacteria

The screenshot shows the EnsemblBacteria homepage. It features a search bar at the top with "Search for a gene" and "Search for a genome". Below the search bars are sections for "Archive sites" and "Ensembl Bacteria". A sidebar on the right is titled "What's New in Release 53" and lists recent releases.

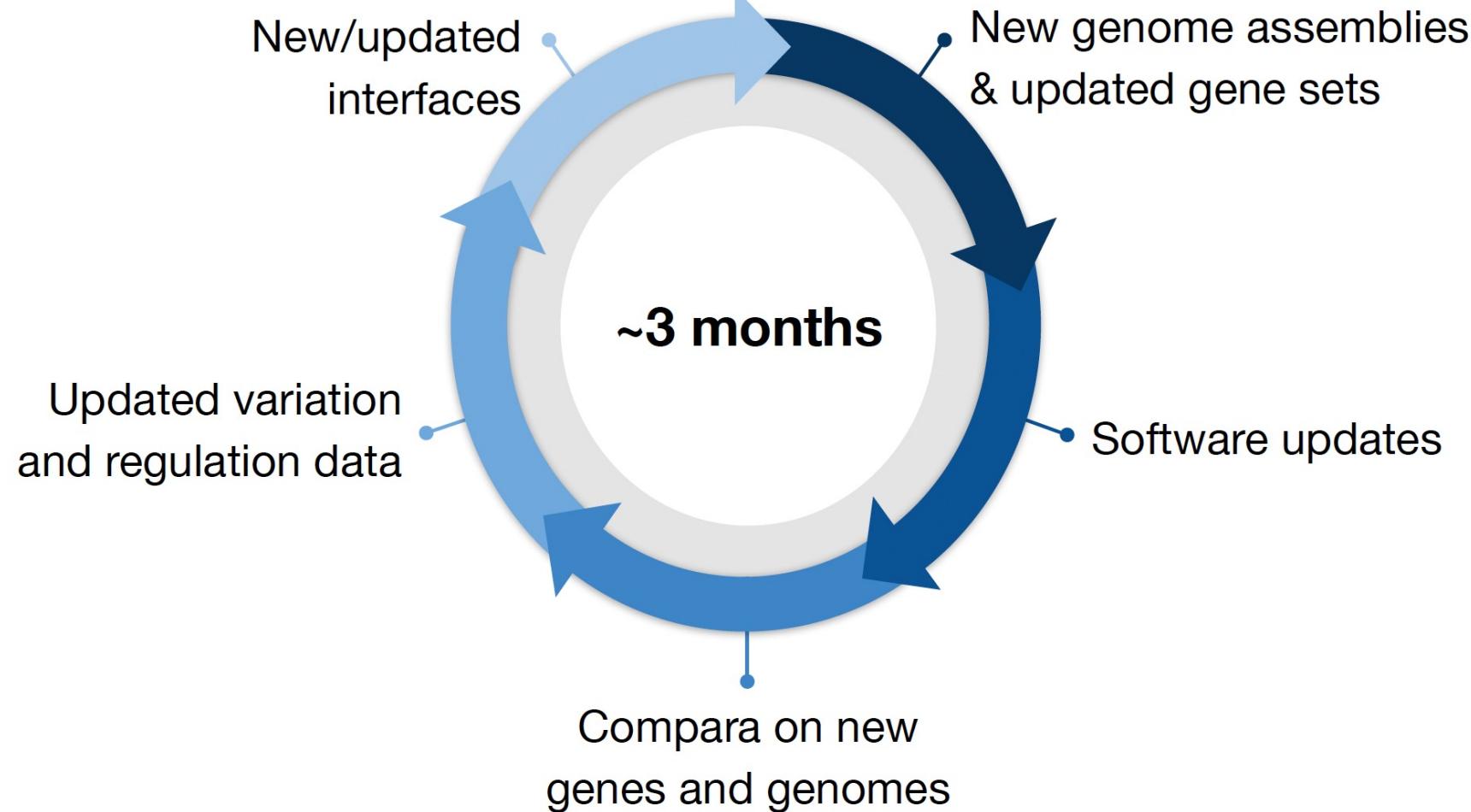
EnsemblCOVID-19

The screenshot shows the EnsemblCOVID-19 homepage. It features a search bar at the top with "SARS-CoV-2" selected. Below the search bar are sections for "Reference Genome", "COVID-19 resources", and "Sequence and annotation data". A sidebar on the right is titled "View in Genome browser" and "Download data".

Release cycle

112

May 2024



REST archives

The Ensembl project provides archive services for up to five years, to match the Ensembl website archives.

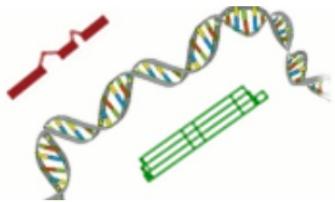
<http://e97.rest.ensembl.org>



How Ensembl is organised - Schemas

Core

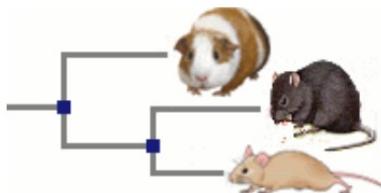
Sequence, genes and other [automated annotation](#)



- [Perl API](#)
- [Database schema](#)
- [Tutorial](#)

Comparative genomics

Gene trees, homologies, multiple and pairwise genomic alignments



- [Perl API](#)
- [Database schema](#)
- [Tutorial](#)

Variation

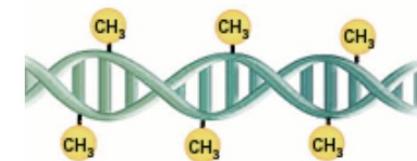
SNPs, somatic mutations and structural variants



- [Perl API](#)
- [Database schema](#)
- [Tutorial](#)

Regulation

Regulatory features, motifs and oligoprobes

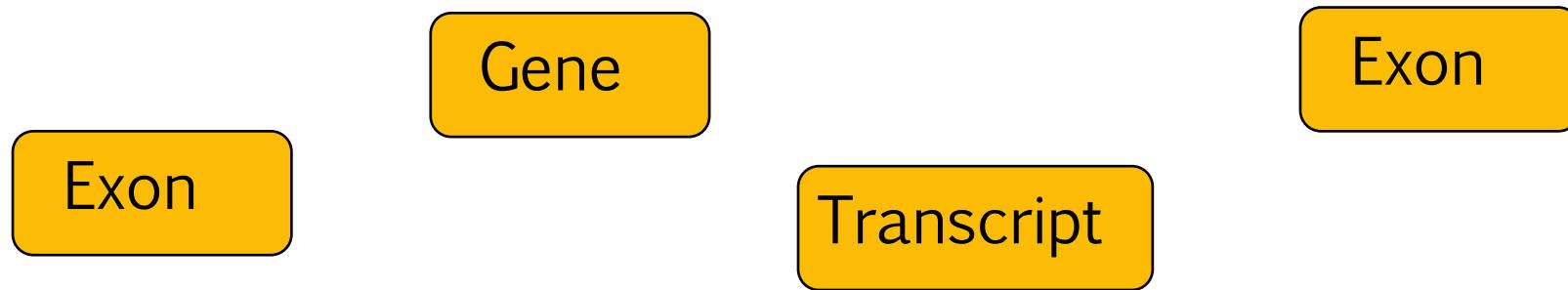


- [Perl API](#)
- [Database schema](#)
- [Tutorial](#)

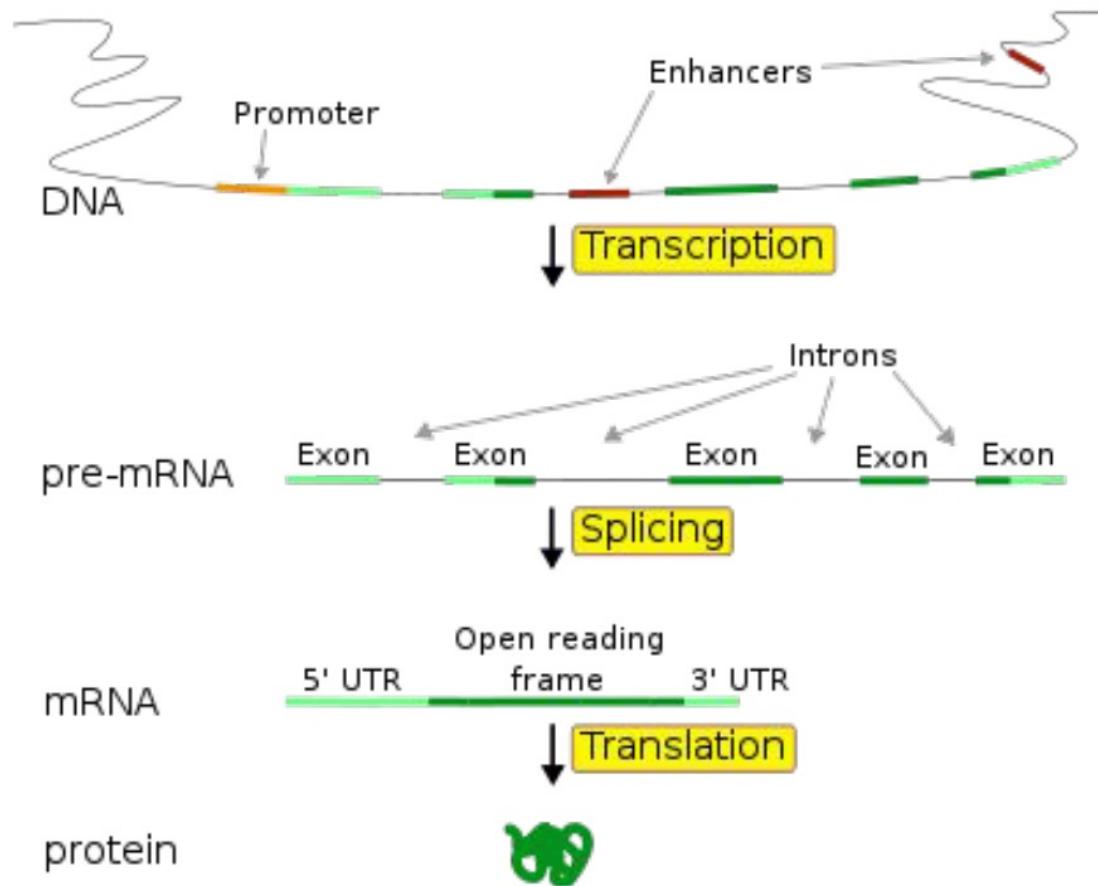
Data objects

These model biological entities, e.g., genes, transcripts, exons, etc.

A data object represents a piece of data that is (or can be) stored in the database.



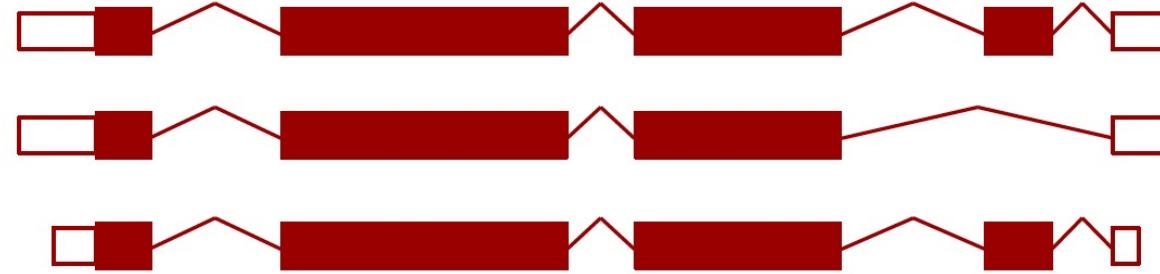
Ensembl data model



*e!*Ensembl

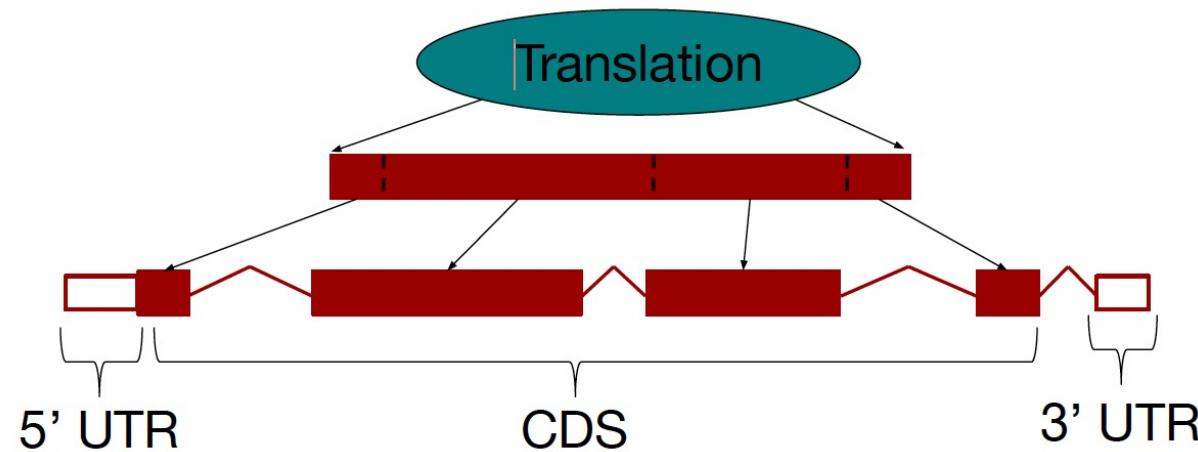
Ensembl data model

- Primary Feature types are Genes, Transcripts, and Exons
- A Gene is a set of alternatively spliced Transcripts
- A Transcript is a set of Exons



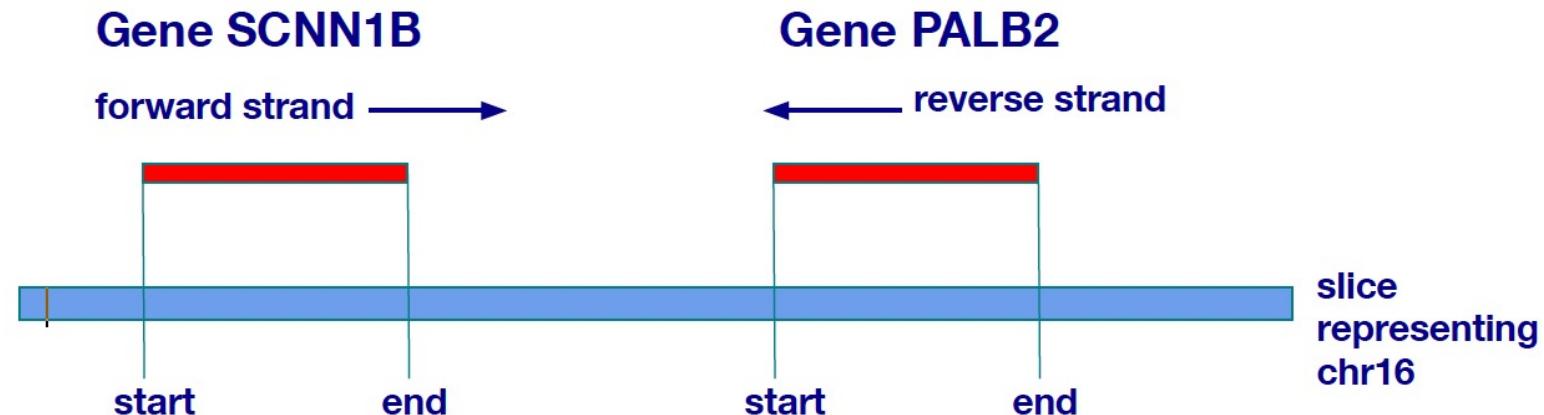
Ensembl data model

- Translations are not Features
- Peptides are not stored in the database, they are computed on the fly using Transcript objects
- Not all transcripts have a translation (e.g., ncRNAs)



Features

- Features have a defined location on the genome
- Start and end are always plotted on the forward strand. Start < end
- Genes and exons are examples of Features



What is a REST API?

Representational State Transfer. It describes how one system can communicate state with another.

Typically over HTTP(s), providing a machine readable, language agnostic method to access remote data or services.



Ensembl REST

- Language agnostic access to Ensembl datasets
- Only a fraction of the functionality of the Perl API is exposed

<http://rest.ensembl.org>



Ensembl REST API Endpoints

Archive

Resource	Description
<code>GET archive/id:id</code>	Uses the given identifier to return the archived sequence
<code>POST archive:id</code>	Retrieve the archived sequence for a set of identifiers

Comparative Genomics

Resource	Description
<code>GET genetree:id:id</code>	Retrieves a gene tree for a gene tree stable identifier
<code>GET genetree/member:id:id</code>	Retrieves the gene tree that contains the gene / transcript / translation stable identifier
<code>GET genetree/member/symbol/:species:/symbol</code>	Retrieves the gene tree that contains the gene identified by a symbol
<code>GET alignment/region/:species/:region</code>	Retrieves genomic alignments as separate blocks based on a region and species
<code>GET homology:id:id</code>	Retrieves homology information (orthologs) by Ensembl gene id
<code>GET homology/symbol/:species:/symbol</code>	Retrieves homology information (orthologs) by symbol

Cross References

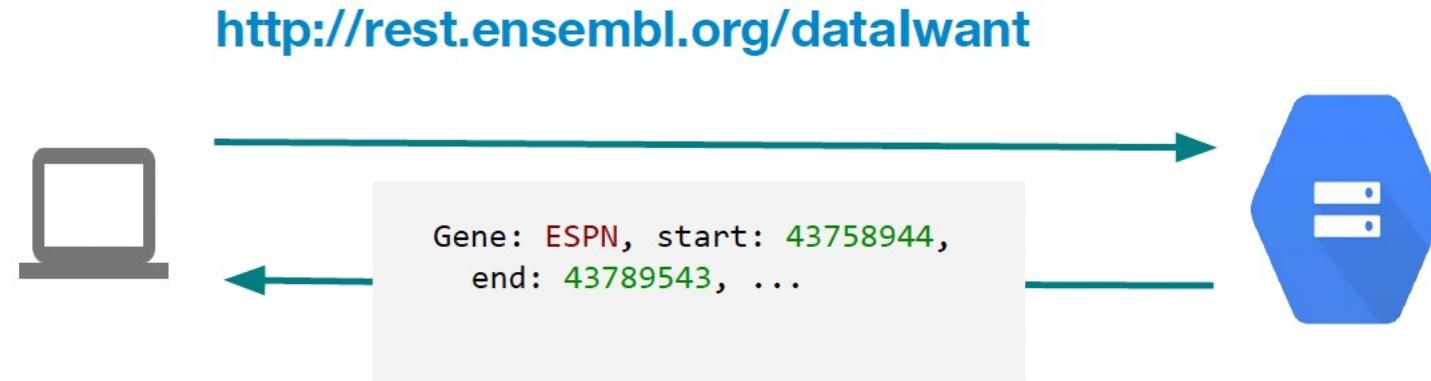
Resource	Description
<code>GET xrefs/symbol/:species:/symbol</code>	Looks up an external symbol and returns all Ensembl objects linked to it. This can be a display name for a gene/transcript/translation, a synonym or an externally linked reference. If a gene's transcript is linked to the supplied symbol the service will return both gene and transcript (it supports transient links).
<code>GET xrefs/id:id</code>	Perform lookups of Ensembl identifiers and retrieve their external references in other databases
<code>GET xrefs/name/:species:/name</code>	Performs a lookup based upon the primary accession or display label of an external reference and returning the information



What is an endpoint?

An endpoint is a particular output that you can get given a particular input.

It is a function that interacts with the Ensembl database.



Endpoint documentation

Full documentation of all the endpoints is found at:

<http://rest.ensembl.org>

The documentation lists:

- All the endpoints grouped by function
- The required parameters for each endpoint
- Optional parameters
- Example code for using the endpoints



Functional groupings

- Archive
- Comparative genomics
- Cross references
- Information
- Lookup
- Mapping
- Ontology and Taxonomy
- Sequence variation
- ...

e!Ensembl Endpoints User Guide Change Log About the Ensembl Project Contact Ensembl

Ensembl REST API Endpoints

Archive

Resource	Description
GET archive/id/:id	Uses the given identifier to return the archived sequence
POST archive/:id	Retrieve the archived sequence for a set of identifiers

Comparative Genomics

Resource	Description
GET genetree/:id/:id	Retrieves a gene tree for a gene tree stable identifier
GET genetree/member/:id/:id	Retrieves the gene tree that contains the gene / transcript / translation stable identifier
GET genetree/member/:symbol/:species/:symbol	Retrieves the gene tree that contains the gene identified by a symbol
GET alignment/:region/:species/:region	Retrieves genomic alignments as separate blocks based on a region and species
GET homology/:id/:id	Retrieves homology information (orthologs) by Ensembl gene id
GET homology/:symbol/:species/:symbol	Retrieves homology information (orthologs) by symbol

Cross References

Resource	Description
GET xrefs/:symbol/:species/:symbol	Looks up an external symbol and returns all Ensembl objects linked to it. This can be a display name for a gene/transcript/translation, a synonym or an externally linked reference. If a gene's transcript is linked to the supplied symbol the service will return both gene and transcript (it supports transient links).
GET xrefs/:id/:id	Perform lookups of Ensembl Identifiers and retrieve their external references in other databases
GET xrefs/:name/:species/:name	Performs a lookup based upon the primary accession or display label of an external reference and returning the information

Archive

- Fetch latest versions of archive Ensembl IDs

Archive

Resource	Description
GET archive/id/:id	Uses the given identifier to return its latest version
POST archive/id	Retrieve the latest version for a set of identifiers



*e!*Ensembl

Comparative genomics

- Gene trees, homologues, and alignments

Comparative Genomics

Resource	Description
GET cafe/genetree/id/:id	Retrieves a cafe tree of the gene tree using the gene tree stable identifier
GET cafe/genetree/member/id/:id	Retrieves the cafe tree of the gene tree that contains the gene / transcript / translation stable identifier
GET cafe/genetree/member/symbol/:species/:symbol	Retrieves the cafe tree of the gene tree that contains the gene identified by a symbol
GET family/id/:id	Retrieves a family information using the family stable identifier
GET family/member/id/:id	Retrieves the information for all the families that contains the gene / transcript / translation stable identifier
GET family/member/symbol/:species/:symbol	Retrieves the information for all the families that contains the gene identified by a symbol
GET genetree/id/:id	Retrieves a gene tree for a gene tree stable identifier
GET genetree/member/id/:id	Retrieves the gene tree that contains the gene / transcript / translation stable identifier
GET genetree/member/symbol/:species/:symbol	Retrieves the gene tree that contains the gene identified by a symbol
GET alignment/region/:species/:region	Retrieves genomic alignments as separate blocks based on a region and species
GET homology/id/:id	Retrieves homology information (orthologs) by Ensembl gene id
GET homology/symbol/:species/:symbol	Retrieves homology information (orthologs) by symbol

Cross references

- Look up other IDs in Ensembl and find other IDs attached to Ensembl objects

Cross References

Resource	Description
GET xrefs/symbol/:species/:symbol	Looks up an external symbol and returns all Ensembl objects linked to it. This can be a display name for a gene/transcript/translation, a synonym or an externally linked reference. If a gene's transcript is linked to the supplied symbol the service will return both gene and transcript (it supports transient links).
GET xrefs/id/:id	Perform lookups of Ensembl Identifiers and retrieve their external references in other databases
GET xrefs/name/:species/:name	Performs a lookup based upon the primary accession or display label of an external reference and returning the information we hold about the entry

Information

- Get current release information and data available

Information

Resource	Description
GET info/analysis/:species	List the names of analyses involved in generating Ensembl data.
GET info/assembly/:species	List the currently available assemblies for a species, along with toplevel sequences, chromosomes and cytogenetic bands.
GET info/assembly/:species/:region_name	Returns information about the specified toplevel sequence region for the given species.
GET info/biotypes/:species	List the functional classifications of gene models that Ensembl associates with a particular species. Useful for restricting the type of genes/transcripts retrieved by other endpoints.
GET info/biotypes/groups/:group/:object_type	Without argument the list of available biotype groups is returned. With :group argument provided, list the properties of biotypes within that group. Object type (gene or transcript) can be provided for filtering.
GET info/biotypes/name/:name/:object_type	List the properties of biotypes with a given name. Object type (gene or transcript) can be provided for filtering.

Linkage disequilibrium

- Find variants in LD across a locus or to a known variant

Linkage Disequilibrium

Resource	Description
GET /ld/:species/:id/:population_name	Computes and returns LD values between the given variant and all other variants in a window centered around the given variant. The window size is set to 500 kb.
GET /ld/:species/pairwise/:id1/:id2	Computes and returns LD values between the given variants.
GET /ld/:species/region/:region/:population_name	Computes and returns LD values between all pairs of variants in the defined region.

Lookup

- Find Ensembl objects in the database

Lookup

Resource	Description
GET lookup/id/:id	Find the species and database for a single identifier e.g. gene, transcript, protein
POST lookup/id	Find the species and database for several identifiers. IDs that are not found are returned with no data.
GET lookup/symbol/:species/:symbol	Find the species and database for a symbol in a linked external database
POST lookup/symbol/:species/:symbol	Find the species and database for a set of symbols in a linked external database. Unknown symbols are omitted from the response.

Mapping

- Map between coordinates

Lookup

Resource	Description
GET lookup/id/:id	Find the species and database for a single identifier e.g. gene, transcript, protein
POST lookup/id	Find the species and database for several identifiers. IDs that are not found are returned with no data.
GET lookup/symbol/:species/:symbol	Find the species and database for a symbol in a linked external database
POST lookup/symbol/:species/:symbol	Find the species and database for a set of symbols in a linked external database. Unknown symbols are omitted from the response.

Ontologies and Taxonomy

- Map hierarchical relationships

Ontologies and Taxonomy

Resource	Description
GET ontology/ancestors/:id	Reconstruct the entire ancestry of a term from is_a and part_of relationships
GET ontology/ancestors/chart/:id	Reconstruct the entire ancestry of a term from is_a and part_of relationships.
GET ontology/descendants/:id	Find all the terms descended from a given term. By default searches are conducted within the namespace of the given identifier
GET ontology/id/:id	Search for an ontological term by its namespaced identifier
GET ontology/name/:name	Search for a list of ontological terms by their name
GET taxonomy/classification/:id	Return the taxonomic classification of a taxon node
GET taxonomy/id/:id	Search for a taxonomic term by its identifier or name
GET taxonomy/name/:name	Search for a taxonomic id by a non-scientific name

Overlap

Find features that overlaps regions or other features, e.g.,

- Genes in a region
- Variants in a gene or protein
- Domains in a protein

Overlap

Resource	Description
GET overlap/id/:id	Retrieves features (e.g. genes, transcripts, variants and more) that overlap a region defined by the given identifier.
GET overlap/region/:species/:region	Retrieves features (e.g. genes, transcripts, variants and more) that overlap a given region.
GET overlap/translation/:id	Retrieve features related to a specific Translation as described by its stable ID (e.g. domains, variants).

Phenotype associations

- Get genes/variants linked to phenotypes
- Get phenotypes linked to genes

Phenotype annotations

Resource	Description
GET /phenotype/accession/:species/:accession	Return phenotype annotations for genomic features given a phenotype ontology accession
GET /phenotype/gene/:species/:gene	Return phenotype annotations for a given gene.
GET /phenotype/region/:species/:region	Return phenotype annotations that overlap a given genomic region.
GET /phenotype/term/:species/:term	Return phenotype annotations for genomic features given a phenotype ontology term

Regulation

- Find details of microarrays
- Find details of epigenomes and regulatory features

Regulation

Resource	Description
GET regulatory/species/:species/microarray/:microarray/vendor/:vendor	Returns information about a specific microarray
GET regulatory/species/:species/epigenome	Returns information about all epigenomes available for the given species
GET species/:species/binding_matrix/:binding_matrix_stable_id/	Return the specified binding matrix
GET regulatory/species/:species/microarray	Returns information about all microarrays available for the given species
GET regulatory/species/:species/microarray/:microarray/probe/:probe	Returns information about a specific probe from a microarray
GET regulatory/species/:species/microarray/:microarray/probe_set/:probe_set	Returns information about a specific probe_set from a microarray
GET regulatory/species/:species/id/:id	Returns a RegulatoryFeature given its stable ID (e.g. ENSR00000082023)

Sequences

- Fetch nucleotide and amino acid sequences

Sequence

Resource	Description
GET sequence/:id/:id	Request multiple types of sequence by stable identifier. Supports feature masking and expand options.
POST sequence/:id	Request multiple types of sequence by a stable identifier list.
GET sequence/region/:species/:region	Returns the genomic sequence of the specified region of the given species. Supports feature masking and expand options.
POST sequence/region/:species	Request multiple types of sequence by a list of regions.

Transcript haplotypes

- Get haplotypes from real individuals

Transcript Haplotypes

Resource	Description
GET transcript_haplotypes/:species/:id	Computes observed transcript haplotype sequences based on phased genotype data

VEP

- Get variant consequences on genes and transcripts

VEP

Resource	Description
GET vep/:species/hgvs/:hgvs_notation	Fetch variant consequences based on a HGVS notation
POST vep/:species/hgvs	Fetch variant consequences for multiple HGVS notations
GET vep/:species/id/:id	Fetch variant consequences based on a variant identifier
POST vep/:species/id	Fetch variant consequences for multiple ids
GET vep/:species/region/:region/:allele/	Fetch variant consequences
POST vep/:species/region	Fetch variant consequences for multiple regions

Variation

- Get information about Ensembl variants

Variation

Resource	Description
GET variant_recoder/:species/:id	Translate a variant identifier, HGVS notation or genomic SPDI notation to all possible variant IDs, HGVS and genomic SPDI
POST variant_recoder/:species	Translate a list of variant identifiers, HGVS notations or genomic SPDI notations to all possible variant IDs, HGVS and genomic SPDI
GET variation/:species/:id	Uses a variant identifier (e.g. rsID) to return the variation features including optional genotype, phenotype and population data
GET variation/:species/pmcid/:pmcid	Fetch variants by publication using PubMed Central reference number (PMCID)
GET variation/:species/pmid/:pmid	Fetch variants by publication using PubMed reference number (PMID)
POST variation/:species/	Uses a list of variant identifiers (e.g. rsID) to return the variation features including optional genotype, phenotype and population data

Endpoint Documentation

GET lookup/id/:id

Find the species and database for a single identifier e.g. gene, transcript, protein

Parameters

Required

Name	Type	Description	Default	Example Values
id	String	An Ensembl stable ID	-	ENSG00000157764

Optional

Name	Type	Description	Default	Example Values
callback	String	Name of the callback subroutine to be returned by the requested JSONP response. Required ONLY when using JSONP as the serialisation method. Please see the user guide .	-	randomlygeneratedname
db_type	String	Restrict the search to a database other than the default. Useful if you need to use a DB other than core	-	core otherfeatures
expand	Boolean(0,1)	Expands the search to include any connected features. e.g. If the object is a gene, its transcripts, translations and exons will be returned as well.	0	-

You must include the id in the URL in this position

Resource

Information

Methods	GET
Response formats	json xml jsonp

You can choose to include these in the URL in the format:
parameter=option

Sample code

[Example output](#)[Perl](#)[Python2](#)[Python3](#)[Ruby](#)[Java](#)[Curl](#)[Wget](#)

```
1. use strict;
2. use warnings;
3.
4. use HTTP::Tiny;
5.
6. my $http = HTTP::Tiny->new();
7.
8. my $server = 'http://rest.ensembl.org';
9. my $ext = '/lookup/id/ENSG00000157764?expand=1';
10. my $response = $http->get($server.$ext, {
11.     headers => { 'Content-type' => 'application/json' }
12. });
13.
14. die "Failed!\n" unless $response->{success};
15.
16.
17. use JSON;
18. use Data::Dumper;
19. if(length $response->{content}) {
```

Making a REST call in the browser

- The easiest way to make REST calls is to put URLs into the browser
- This can be used as a quick look-up
- This can help you to test the URLs in your scripts to see:
 - If they work
 - If you've included the correct parameters
 - What the output looks like

Pinging the database

Ping confirms that you have a connection to the database

`http://rest.ensembl.org/info/ping?content-type=application/json`

```
{  
  ping: 1  
}
```

Requesting a gene by ID

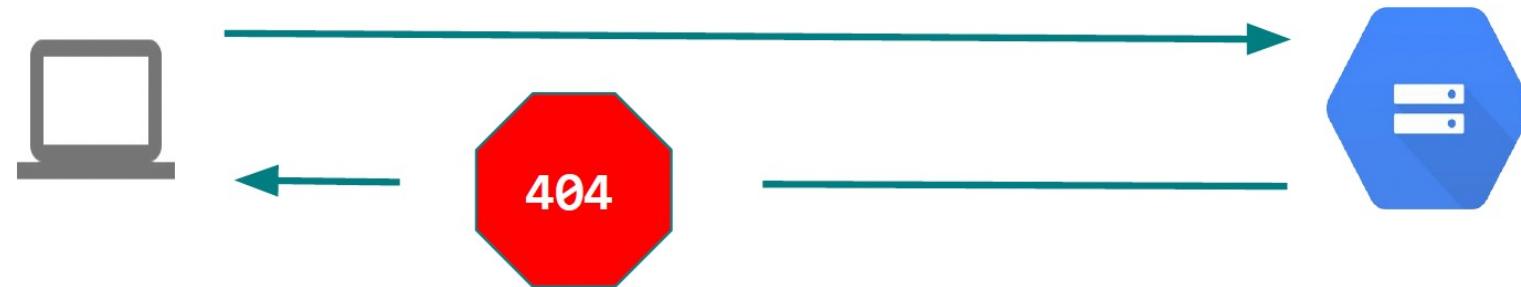
[http://rest.ensembl.org/lookup/id/ENSG00000157764
?content-type=application/json](http://rest.ensembl.org/lookup/id/ENSG00000157764?content-type=application/json)

```
{  
    "source": "ensembl_havana",  
    "object_type": "Gene",  
    "logic_name": "ensembl_havana_gene",  
    "version": 12,  
    "species": "homo_sapiens",  
    "description": "B-Raf proto-oncogene, serine/threonine kinase [Source:HGNC  
Symbol;Acc:HGNC:1097]",  
    "display_name": "BRAF",  
    "assembly_name": "GRCh38",  
    "biotype": "protein_coding",  
    "end": 140924764,  
    "seq_region_name": "7",  
    "db_type": "core",  
    "strand": -1,  
    "id": "ENSG00000157764",  
    "start": 140719327  
}
```

HTTP Status Codes

The server uses HTTP status codes to signal the request outcome

`http://rest.ensembl.org/thisdoesntexist`



HTTP Status Codes

Code	Name	Notes
200	OK	Request was a success
400	Bad Request	Occurs during exceptional circumstances such as the service is unable to find an ID. Check if the response Content-type or Accept was JSON. If so the JSON object is an exception hash with the message keyed under error
403	Forbidden	You are submitting far too many requests and have been temporarily forbidden access to the service. Wait and retry with a maximum of 15 requests per second.
404	Not Found	Indicates a badly formatted request. Check your URL

HTTP Status Codes (cont.)

Code	Name	Notes
408	Timeout	The request was not processed in time. Wait and retry later
429	Too Many Requests	You have been rate-limited; wait and retry. The headers X-RateLimit-Reset, X-RateLimit-Limit and x-RateLimit-Remaining will inform you of how long you have until your limit is reset and what that limit was. If you get this response and have not exceeded your limit then check if you have made too many requests per second.
503	Service Unavailable	The service is temporarily down; retry after a pause
418	I'm a teapot	An April Fools joke added in 1998, who said computer scientists don't have a sense of humour?

Scripting around REST API calls

Scripting around calls allows you to:

- Extract specific bits of data from your REST call
- Output in your preferred format
- Link together calls for more complicated queries
- Integrate your queries into a larger pipeline

Language agnostic access

- REST APIs are designed to be accessed using any programming language
- Calls can be made and decoded within any script
- The Ensembl project has examples in Python, Perl and R

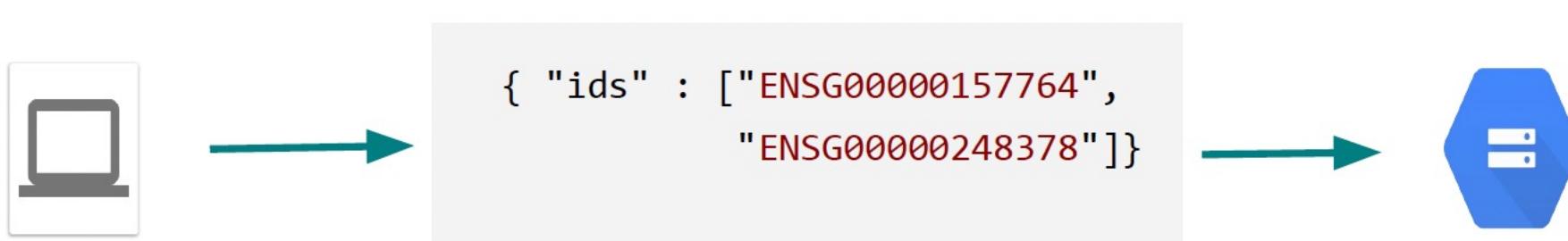


HTTP Methods – GET vs POST

GET <http://rest.ensembl.org/lookup/ENSG00000157764>



POST <http://rest.ensembl.org/lookup/>



Rate limiting

- Requests are rate limited to prevent a single user from monopolising the resources
- Limits are per IP address
- You are allowed 55,000 requests over an hour (3,600 seconds – an average of 15 requests per second)

X-RateLimit-Limit: 55000

X-RateLimit-Reset: 892

X-RateLimit-Period: 3600

X-RateLimit-Remaining: 54999

~15 min
until reset

1 request used

Want more? Full REST API training course

- On-demand training – Learn online in your own time

[https://www.ebi.ac.uk/training/online/courses/
ensembl-rest-api/](https://www.ebi.ac.uk/training/online/courses/ensembl-rest-api/)

- Live courses: Work with a trainer (virtually or in-person)

Trainers from the Ensembl Project can teach at any institute for free
(plus trainers' expenses in high-income countries)

Email: helpdesk@ensembl.org

training.ensembl.org/hosting

Getting help

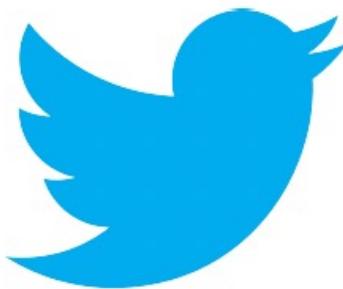
- Ensembl outreach team: helpdesk@ensembl.org
- Developer mailing list: dev@ensembl.org
- The REST API release notes:

<https://github.com/Ensembl/ensembl-rest/wiki/Change-log>

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Training materials

- Gavin and Stefano – thanks for joining this effort!
- Ensembl team
- SMBE organisers – thanks for the space
- You guys – thanks for your attention!



Time for exercises!

➤ go to

Python: <https://shorturl.at/SsPDw>

Or R: <https://shorturl.at/zR6I2>

Click on File > Save a copy in Drive

Start the exercises in your copy!

