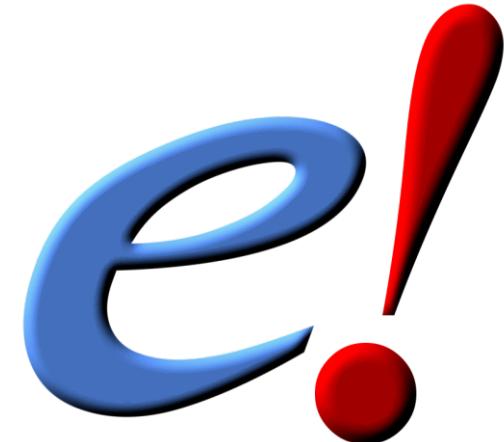
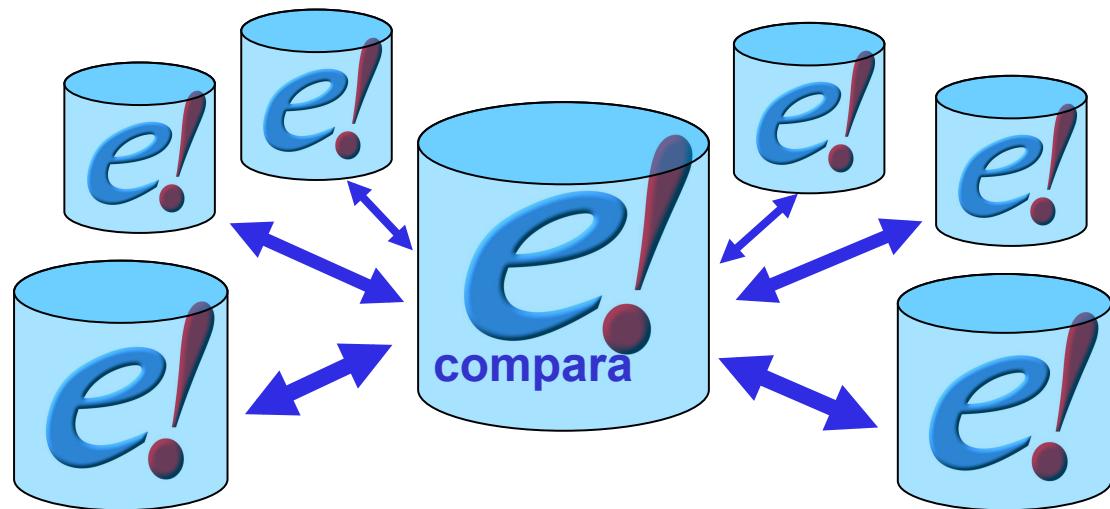




Ensembl Compara Perl API



What is Ensembl Compara?

A single database which contains precalculated comparative genomics data and which is linked to all the Ensembl Species databases.

Access via perl API and mysql

A production system for generating that database
(not in this presentation)

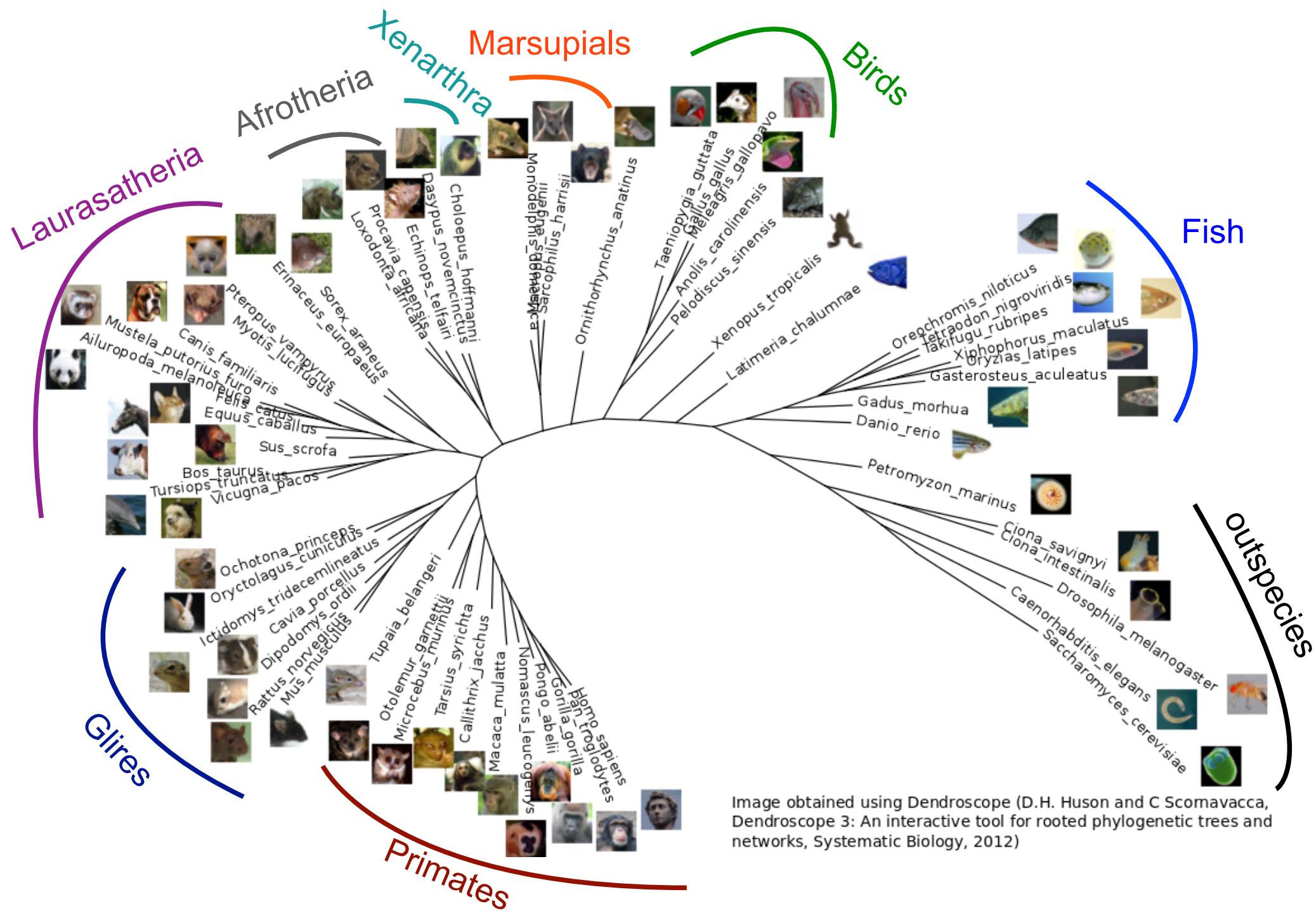
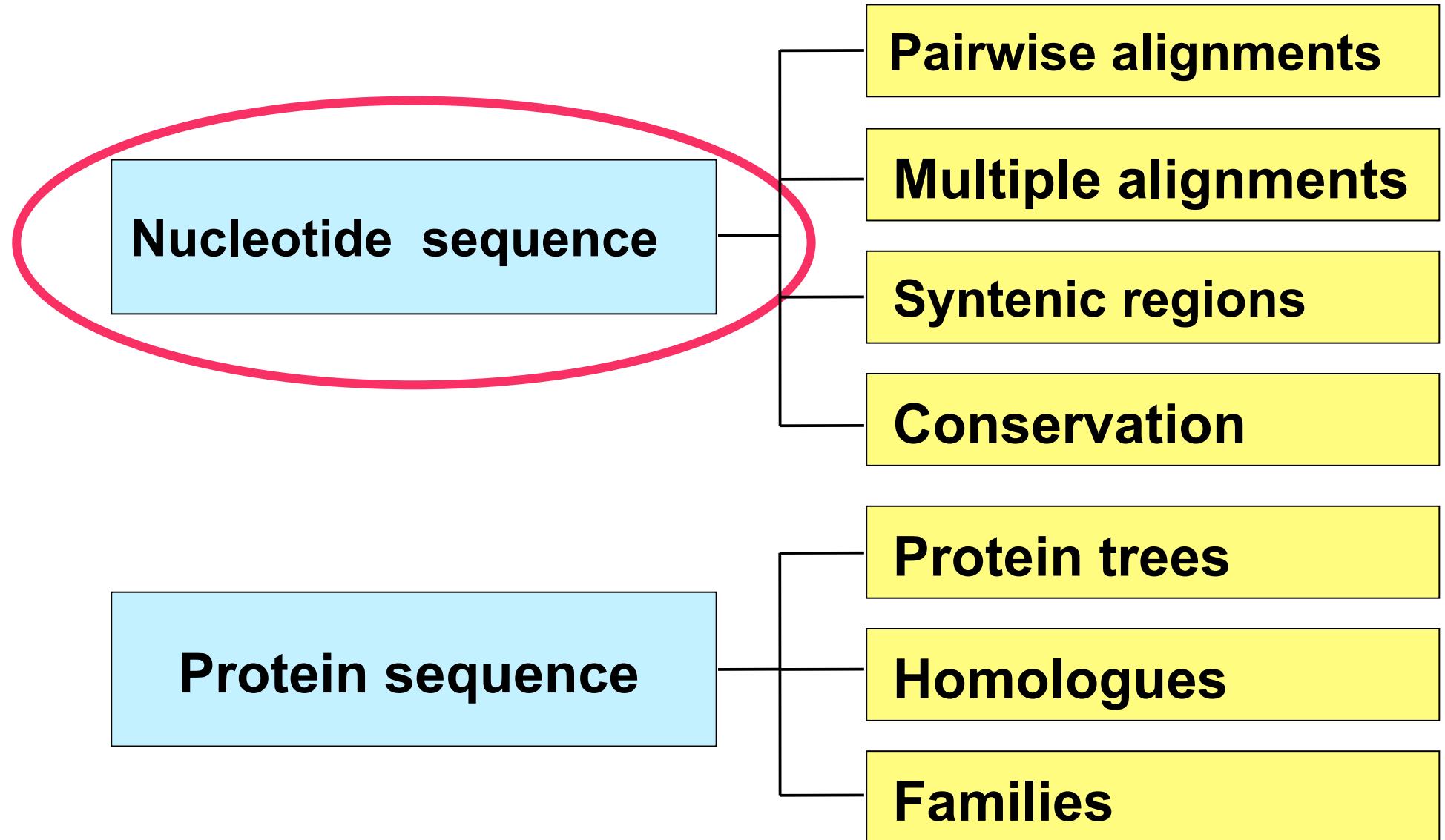


Image obtained using Dendroscope (D.H. Huson and C Scornavacca, Dendroscope 3: An interactive tool for rooted phylogenetic trees and networks, Systematic Biology, 2012)

Sequence types and outputs



Nucleotide sequence analyses

Pairwise Alignments

BLASTZ-net
LASTZ-net
t-BLAT-net

Syntenic regions

Only for species with chromosomal mappings

Multiple alignments

Mercator-Pecan
Enredo-Pecan-Ortheus

Conservation

GERP Cons. Scores
GERP Constr. Elements

Nucleotide sequence analyses

Pairwise Alignments

BLASTZ-net

LASTZ-net

t-BLAT-net

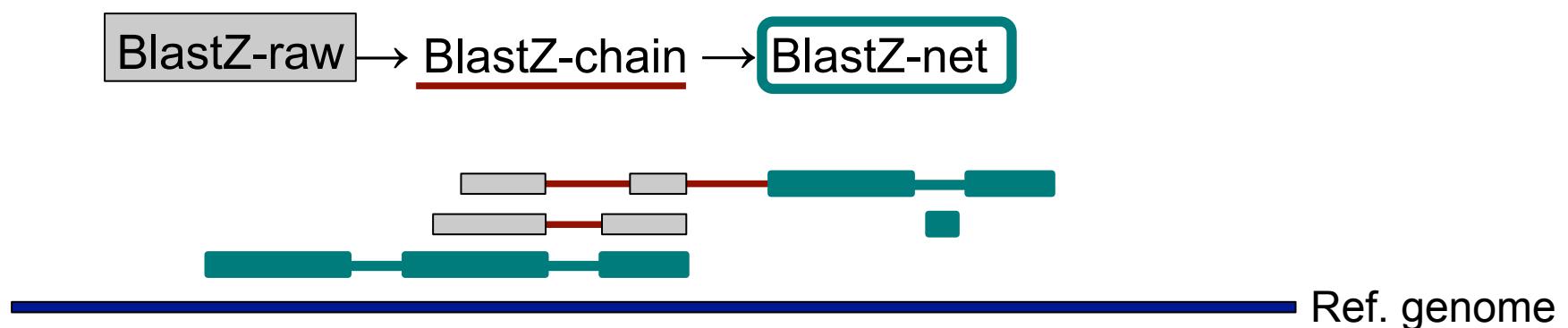
BLASTz-net / LASTz-net

- Closely related species
- LASTz is a replacement for BLASTz

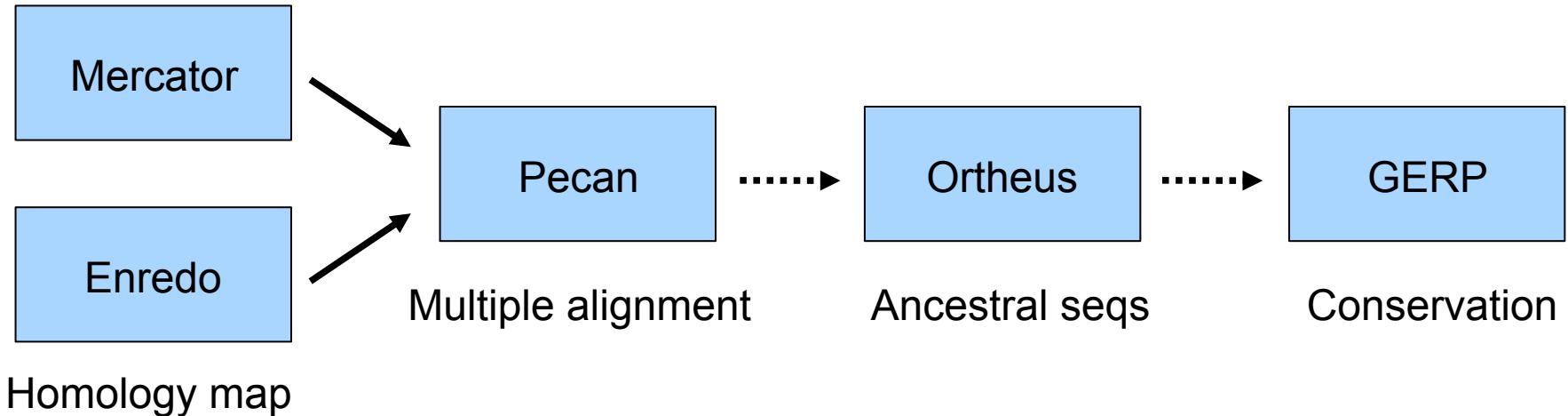
T-BLAT-net

- Distantly related species
- Coding + highly conserved

Chaining/Netting



Nucleotide sequence analyses



Multiple alignments

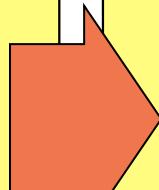
Mercator-Pecan

Enredo-Pecan-Ortheus

Conservation

GERP Cons. Scores

GERP Constr. Elements



Compara database is coupled to Ensembl core databases

Compara stores relationships between the genomes by loading references or ‘handles’ to external data.

Since there is minimal primary data inside Compara, to gain full access to the data these external links must be re-established

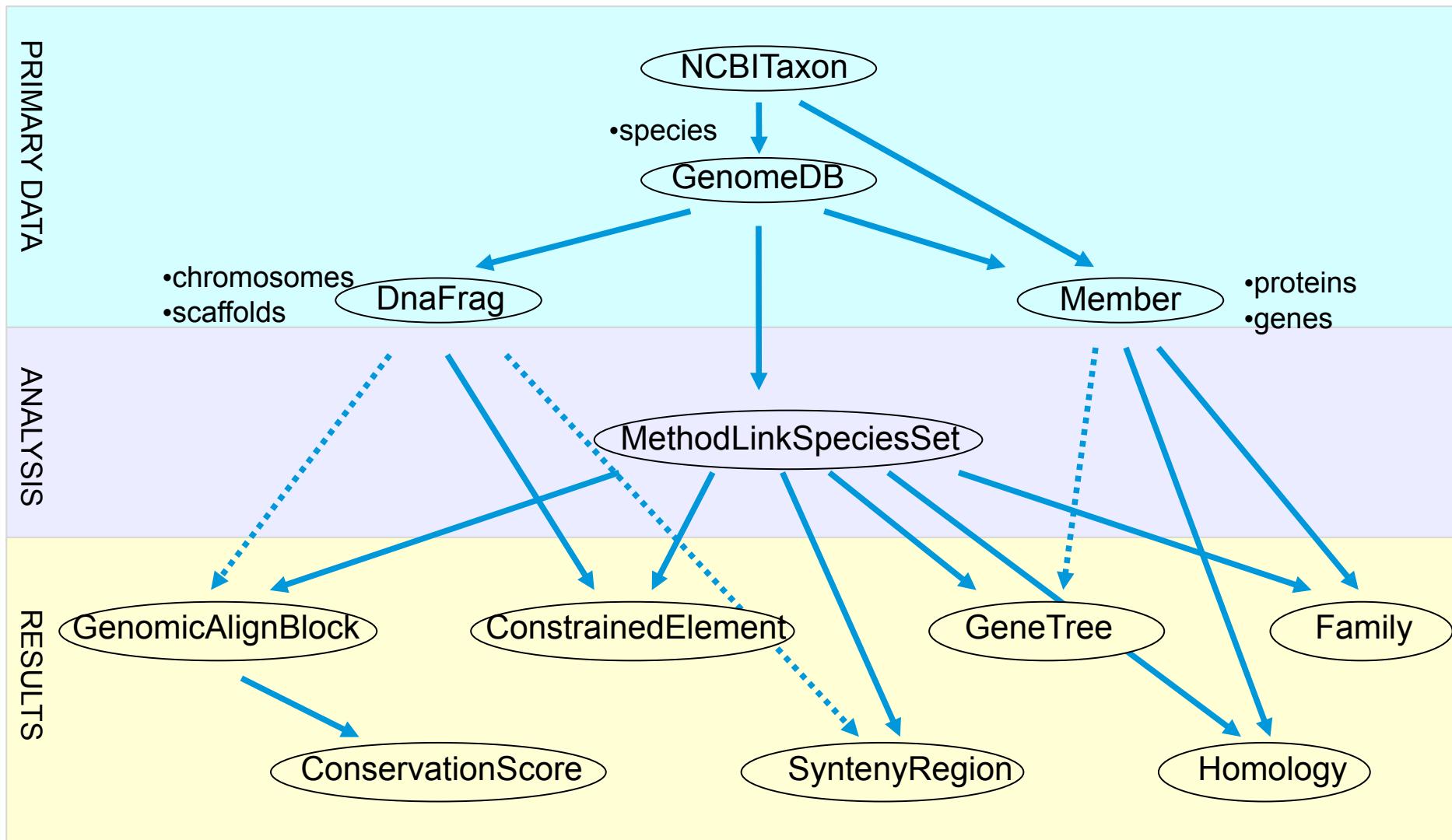
Example: `compara_73` must be linked with the `Ensembl core_73` databases

Proper REGISTRY configuration is critical (auto-loading is OK)

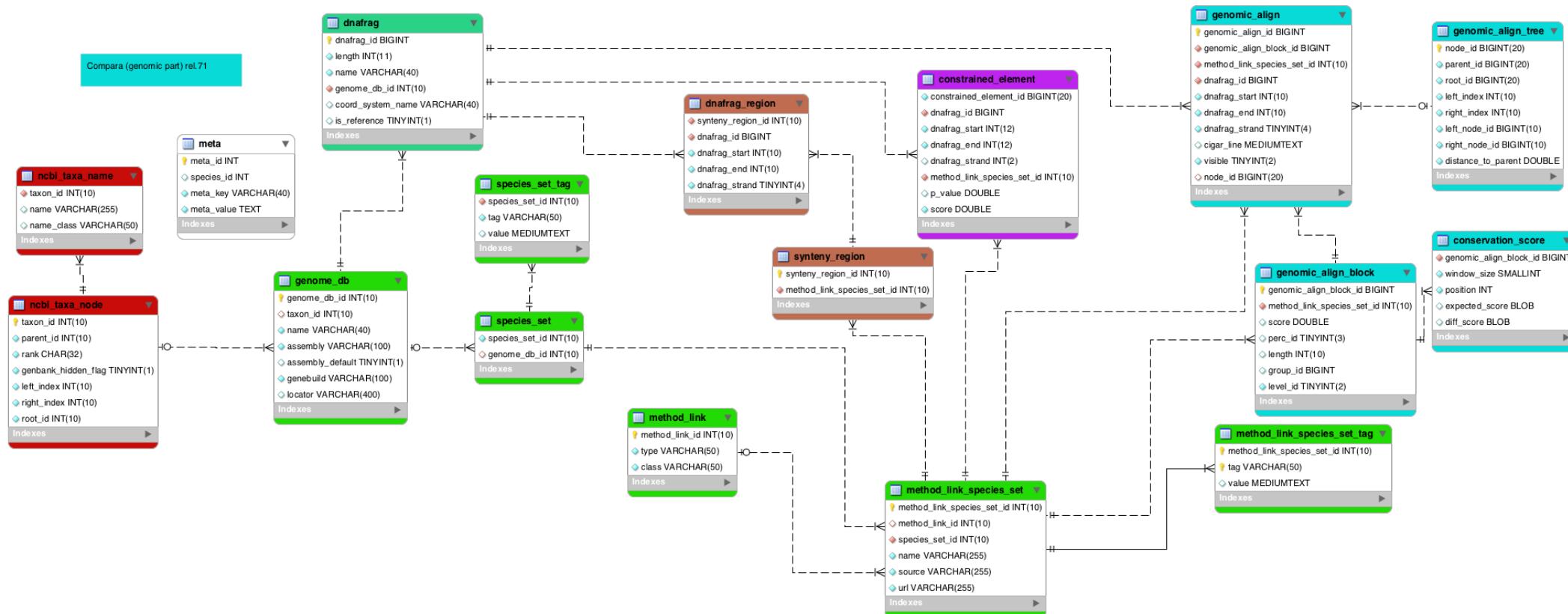
The Compara Perl API

- Written in Object-Oriented Perl
- Used to retrieve data from and store data into ensembl-compara database (only the production pipeline generates the alignments, trees, etc)
- Links species together for Ensembl website
- Generalized to extend to non-ensembl genomic data (Uniprot)
- Follows same 'Data Object', 'Object Adaptor' and 'DBAdaptor' design as the other Ensembl APIs

Compara object model overview



Database schema (genomic part)



[ensembl-compara/docs/schema/diagrams/genomics_schema.png](https://ensembl-compara.github.io/docs/schema/diagrams/genomics_schema.png)

Primary data

Conventions in these slides:

Methods returning values()

Methods returning objects()

Object Adaptor fetching method()

NCBITaxon: list of all species

- `taxon_id()`, `classification()`, `name()`

GenomeDB: relates to a particular Ensembl core DB

- `name()`, `assembly()`, `genebuild()`, `taxon()`
- `fetch_by_name_assembly()`, `fetch_by_registry_name()`,
`fetch_by_Slice()`, `fetch_all()`

DnaFrag: relates to all “top level” SeqRegions

- `name()`, `length()`, `genome_db()`, `slice()`, `coord_system_name()`
- `fetch_by_Slice()`, `fetch_all_by_GenomeDB_region`

Perl allows you to concatenate the calls:

```
$dnafrag->genome_db->taxon->classification()
```

GenomeDB example code

```
use strict;
use Bio::EnsEMBL::Registry;
my $reg = "Bio::EnsEMBL::Registry";

$reg->load_registry_from_db(
    -host=>"ensembldb.ensembl.org",
    -user => "anonymous");

my $genome_db_adaptor = $reg->get_adaptor("Multi", "compara", "GenomeDB");

my $genome_db = $genome_db_adaptor->fetch_by_registry_name("human");

print "Name: ", $genome_db->name, "\n";
print "Assembly: ", $genome_db->assembly, "\n";
print "GeneBuild: ", $genome_db->genebuild, "\n";
```

DnaFrag example code

```
use strict;
use Bio::EnsEMBL::Registry;
my $reg = "Bio::EnsEMBL::Registry";

$reg->load_registry_from_db(
    -host=>"ensembldb.ensembl.org",
    -user => "anonymous");

my $genome_db_adaptor = $reg->get_adaptor("Multi", "compara", "GenomeDB");

my $genome_db = $genome_db_adaptor->fetch_by_registry_name("human");

my $dnafrag_adaptor = $reg->get_adaptor("Multi", "compara", "DnaFrag");

my $dnafrag = $dnafrag_adaptor->fetch_by_GenomeDB_region(
    $genome_db, "chromosome", "13");

print "Name: ", $dnafrag->name, "\n";
print "Length: ", $dnafrag->length, "\n";
print "CoordSystem: ", $dnafrag->coord_system_name, "\n";
```

API documentation & Help

- **perldoc** – Viewer for inline API documentation.
 - shell> perldoc Bio::EnsEMBL::Compara::GenomeDB
 - shell> perldoc Bio::EnsEMBL::Compara::DBSQL::MemberAdaptor
 - online at: <http://www.ensembl.org/info/software/Pdoc/>
- Tutorial document:
cvs: ensembl-compara/docs/ComparaTutorial.pdf
- ensembl-dev mailing list:
<dev@ensembl.org>

Exercises – GenomeDB & DnaFrag

GenomeDB:

- Print the name, assembly version and genebuild version for the pig genome.
- Do the same for all the GenomeDBs in the compara DB

DnaFrag

- Print the name and length of the pig chromosome 15
- Print the name and length of all the DnaFrgs for chimp

Analysis

Conventions in these slides:

Methods returning values()
Methods returning objects()
Object Adaptor fetching method()

Method: type of analysis

- `type()`
- Possible values for the type are: BLASTZ_NET, LASTZ_NET, TRANSLATED_BLAT_NET, PECAN, EPO, EPO_LOW_COVERAGE, SYNTENY, FAMILY, ENSEMBL_ORTHOLOGUES, ENSEMBL_PARALOGUES, PROTEIN TREES, etc.

SpeciesSet: group of species/genomes involved in an analysis

- `genome_dbs()`

MethodLinkSpeciesSet: one particular analysis set

- `method()`, `species_set_obj()`, `name()`, `source()`, `url()`
- `fetch_all()`, `fetch_by_method_link_type_species_set_name()`,
`fetch_by_method_link_type_registry_aliases`,
`fetch_all_by_method_link_type`, etc.



MethodLinkSpeciesSet example code

```
use strict;
use Bio::EnsEMBL::Registry;
my $reg = "Bio::EnsEMBL::Registry";

$reg->load_registry_from_db(
    -host=>"ensembldb.ensembl.org",
    -user => "anonymous");

my $mlss = $reg->get_adaptor("Multi", "compara", "MethodLinkSpeciesSet");

my $mlss = $mlss->fetch_by_method_link_type_registry_aliases(
    "LASTZ_NET", ["human", "mouse"]);

print $mlss->name, "\n";

print "type: ", $mlss->method->type, "\n";

my $species_set = $mlss->species_set_obj();

foreach my $this_genome_db (@{$species_set->genome_dbs}) {
    print $this_genome_db->name(), "\n";
}
```

Exercises – MethodLinkSpeciesSet

- Print the name of the MethodLinkSpeciesSet for the pig-cow LASTZ-NET alignments.
- Print the list of all MethodLinkSpeciesSet entries stored in the database
- Print a list of the species and their internal IDs (dbIDs) for the 12 eutherian mammal EPO alignments
HINT: the species_set_name for the eutherian mammals is “mammals”.

GenomicAlignBlock

GenomicAlignBlock

- represents a genomic alignment
- contains 1 GenomicAlign per sequence
- `method_link_species_set()`, `score()`, `length()`, `perc_id()`,
`get_all_GenomicAligns()`, `get_SimpleAlign()`
- `fetch_all_by_MethodLinkSpeciesSet_Slice()`

Conventions in these slides:

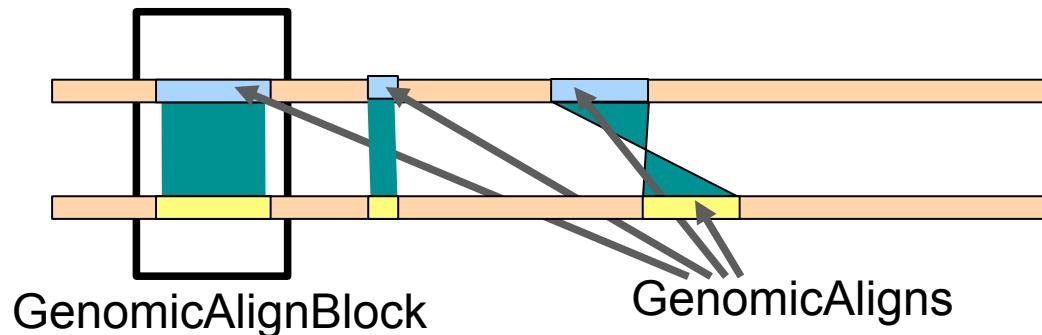
Methods returning values()

Methods returning objects()

Object Adaptor fetching method()

GenomicAlign

- `dnafrag()`, `genome_db()`, `get_Slice()`, `dnafrag_start`,
`dnafrag_end()`, `dnafrag_strand()`, `aligned_sequence()`



DnaFrag A from Genome 1

DnaFrag B from Genome 2

Alignments are stored in the genomic_align and genomic_align_block tables

For example:

gorilla_gorilla/MT/935-953
macaca_mulatta/MT/1469-1488
pan_troglodytes/MT/934-953
pongo_pygmaeus/MT/940-958
homo_sapiens/MT/1516-1534

gacat-ttaactaaaac-ccc
aacatcttaactaaacg-ccc
gatac-ttaacttaaaccccc
actac-ctaactaaaac-ccc
gacat-ttaactaaaac-ccc
* ***** ** ***

GACATTTAACTAAAACCCC
AACATCTTAACTAAACGCC
GATACTTTAACTTAAACCCCC
ACTACCTTAACTAAAACCCC
GACATTTAACTAAAACCCC

5MD11MD3M
17MD3M
5MD15M
5MD11MD3M
5MD11MD3M

5 genomic_align entries
1 genomic_align_block

Sequences from core

cigar lines

Multiple sequence alignments

Mercator-Pecan

- 19-way amniota vertebrates Pecan

EPO

- 6 primates EPO
- 12 eutherian mammals EPO
- 3 neognath birds EPO
- 5 teleost fish EPO

EPO-2X (EPO_LOW_COVERAGE)

- 35 eutherian mammals EPO_LOW_COVERAGE

Adding low-coverage (2X) genomes

Low coverage genomes cannot be fully assembled

Resulting assembly is too scattered to be used with Enredo

Run EPO on high-coverage genomes only

Map 2X genomes using pairwise alignments

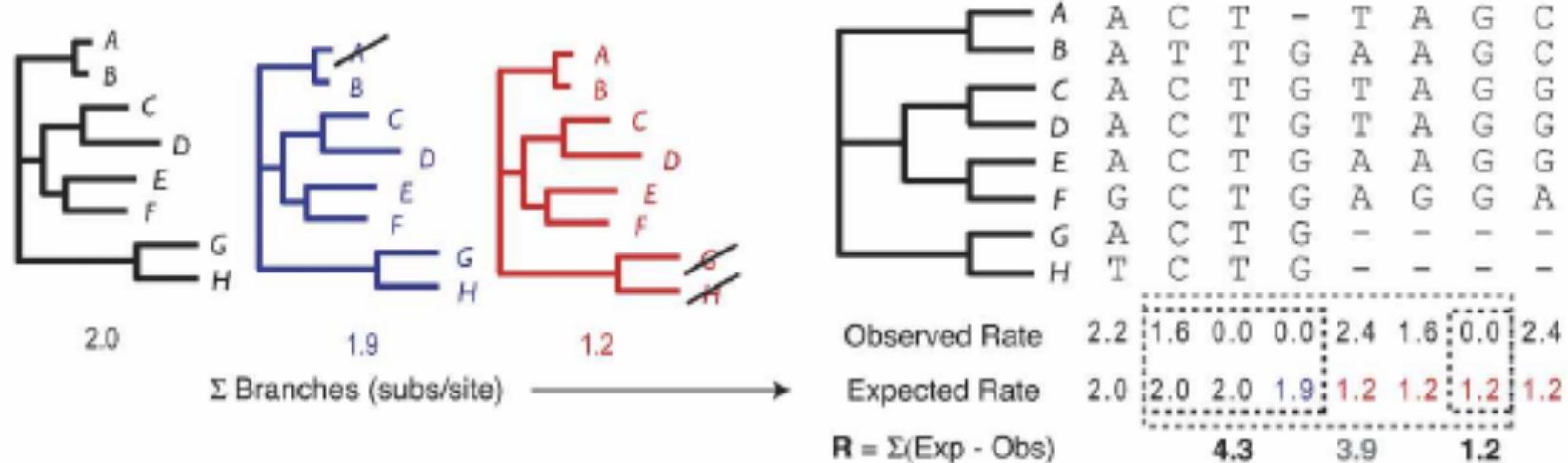


Exercises – GenomicAlignBlock

- Print the LASTZ_NET alignments for pig chromosome 15 with cow
Use pig coordinates 15 : 89151597 - 89157190
- Change the above example so that it prints the alignments for the 12 eutherian mammals EPO

Gerp Constrained Elements

Stretches of the alignment with a high conservation



Cooper et al. Genome Research, 2005

Constrained elements and coding exons

74% of coding exons are associated with constr. elem.

22% of constr. elem. are associated with coding exons

Constrained elements

Conventions in these slides:

Methods returning values()

Methods returning objects()

Object Adaptor fetching method()

ConstrainedElement: a constrained element

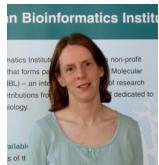
- slice, start, end, strand, seq_region_start, seq_region_end
- **get_SimpleAlign()**: this method gets the alignment from the corresponding GenomicAlignBlock and returns a Bio::SimpleAlign object.
- fetch_all_by_MethodLinkSpeciesSet_Slice

Exercises – ConstrainedElements

- Print the constrained element alignments from the previous pig locus (use the Constrained elements generated from the EPO_LOW_COVERGAGE mammals alignments)

Acknowledgements

Compara Team



Kathryn



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Matthieu

Ensembl 2014

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Framework Programme 7



Quantomics
From Sequence to Consequence :
Tools for the Exploitation of Livestock Genomes

