Nucleotide sequence alignments in Compara

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What is Ensembl Compara?

A single database which contains precalculated comparative genomics data

Access via perl API and mysql

A production system for generating that database

(not in this presentation)

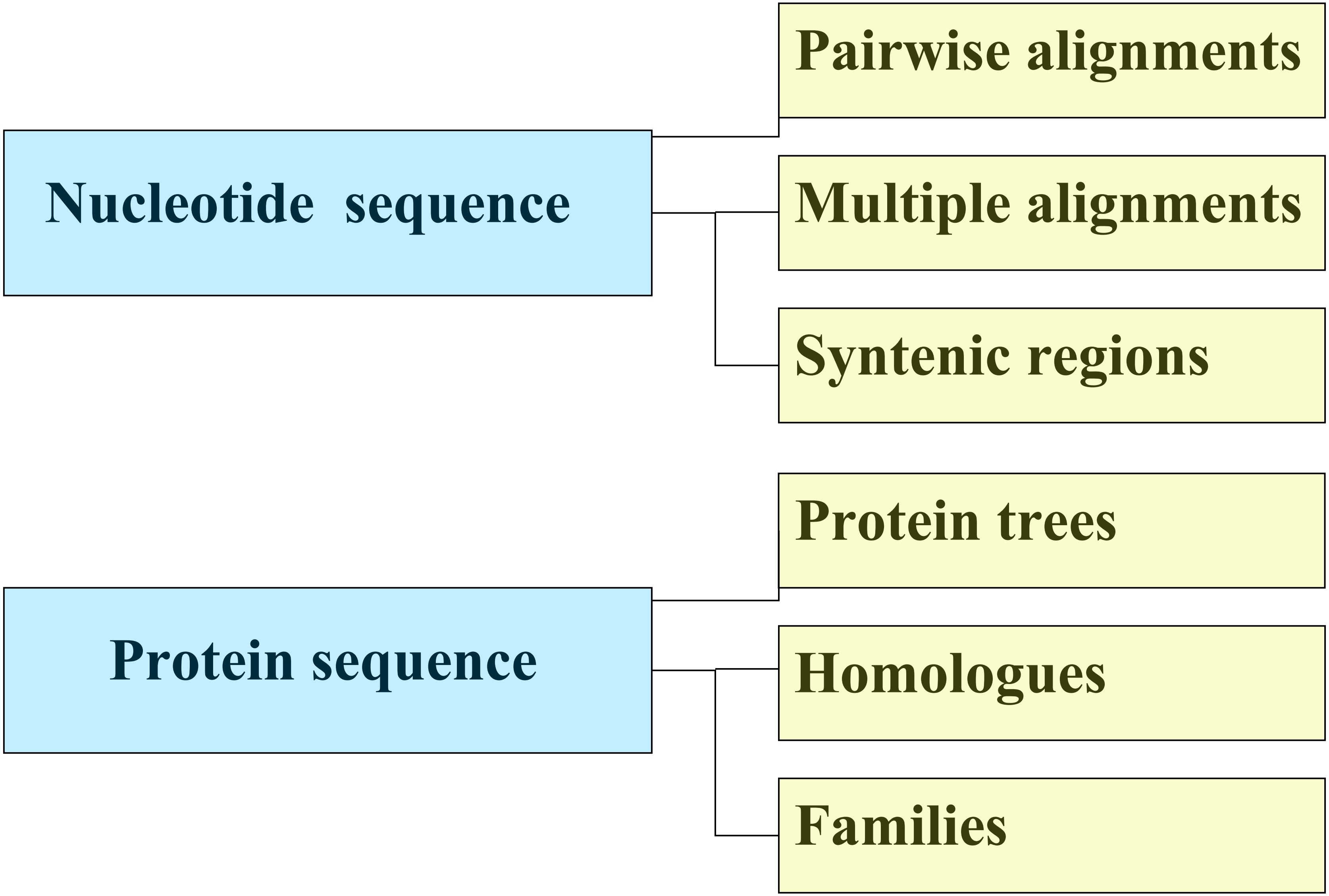
Compara database & the Ensembl core databases

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

Example: compara_63 must be linked with the
Ensembl core_63 databases

Proper REGISTRY configuration is critical.
load_registry_from_db is probably the best choice here

Sequence types and outputs


Nucleotide sequence

Pairwise alignments

Multiple alignments

Syntenic regions

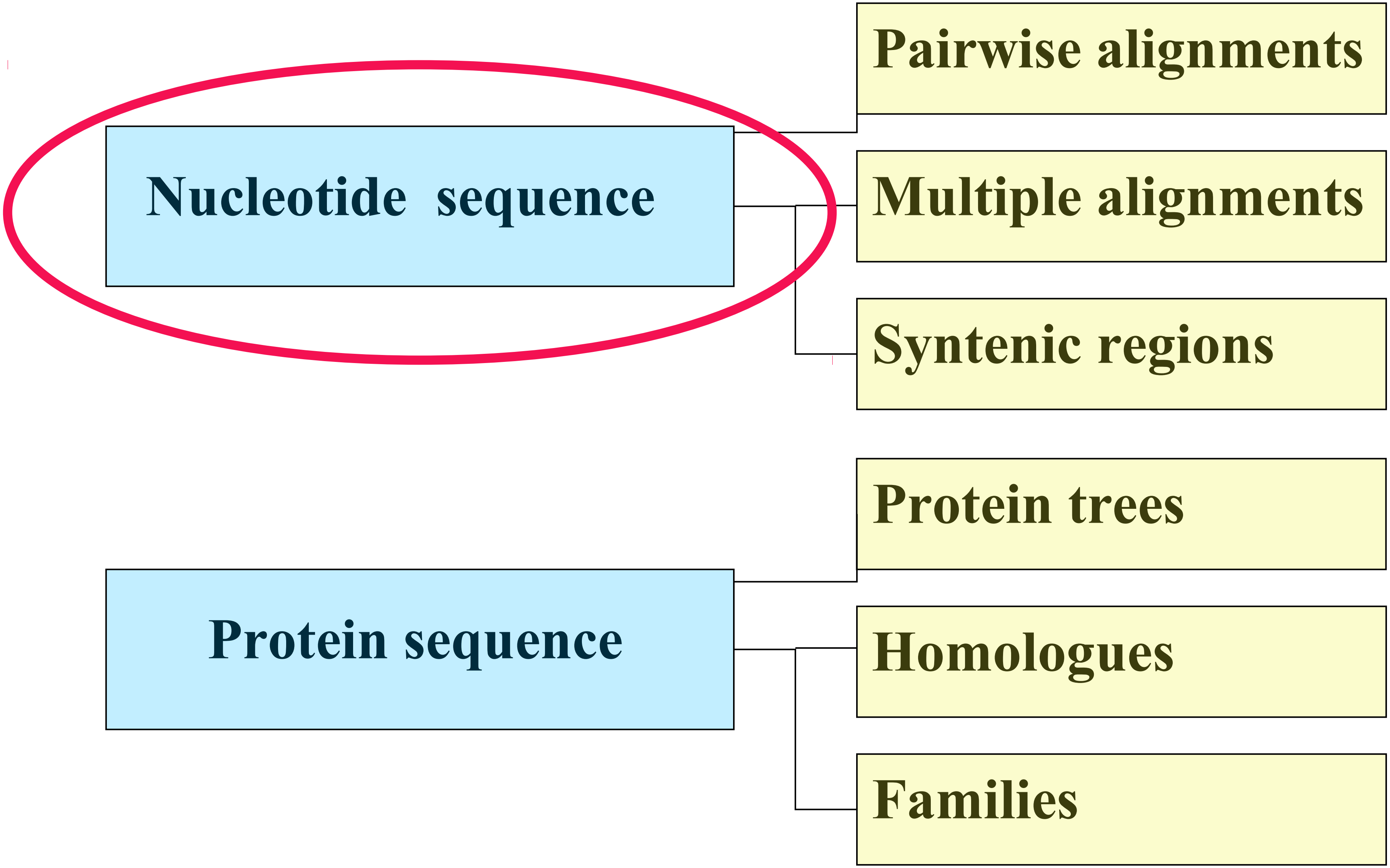
Protein sequence

Protein trees

Homologues

Families

Sequence types and outputs



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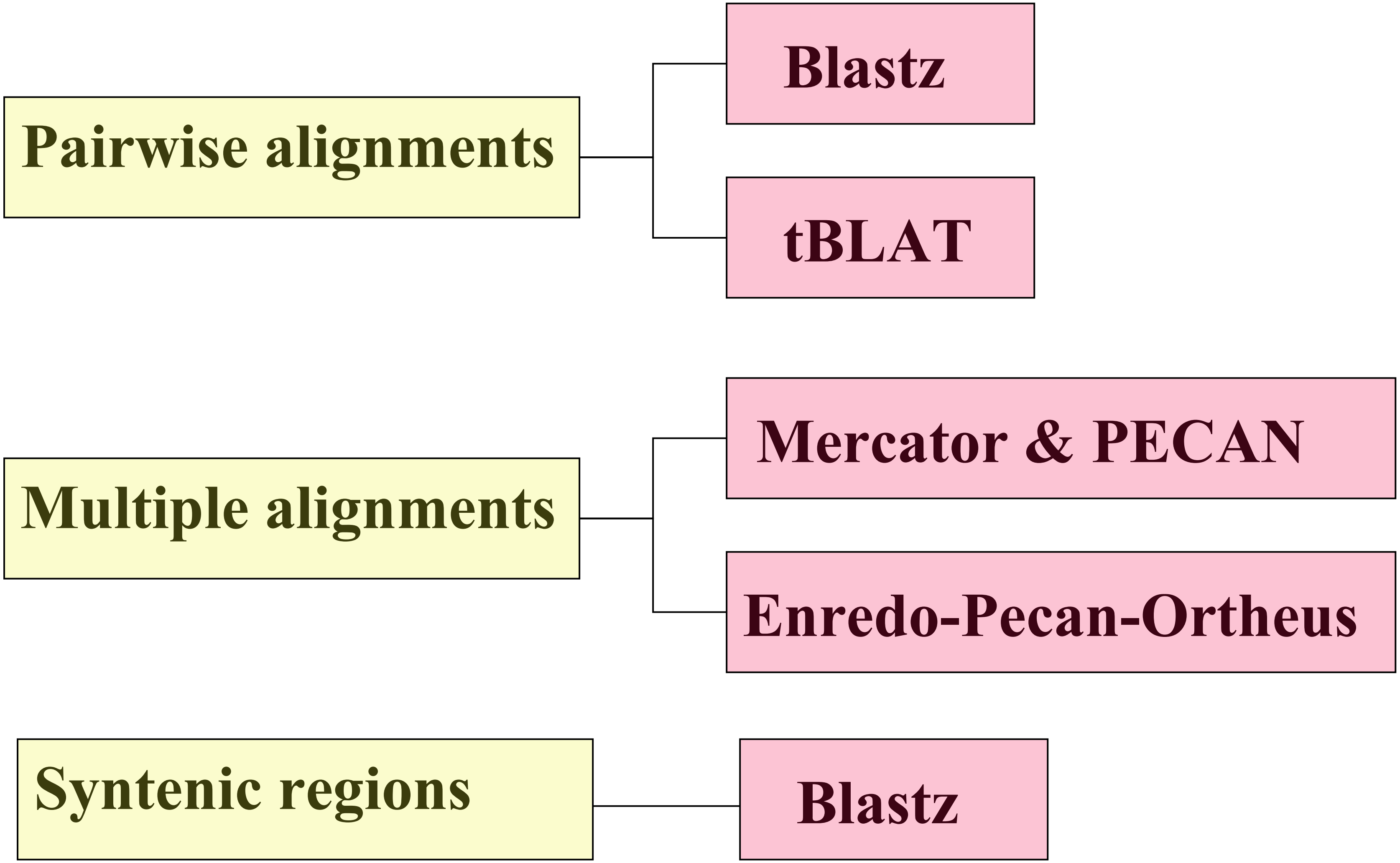
Pipelines and outputs for nucleotide sequence



Pairwise alignments

Blastz

tBLAT

Multiple alignments

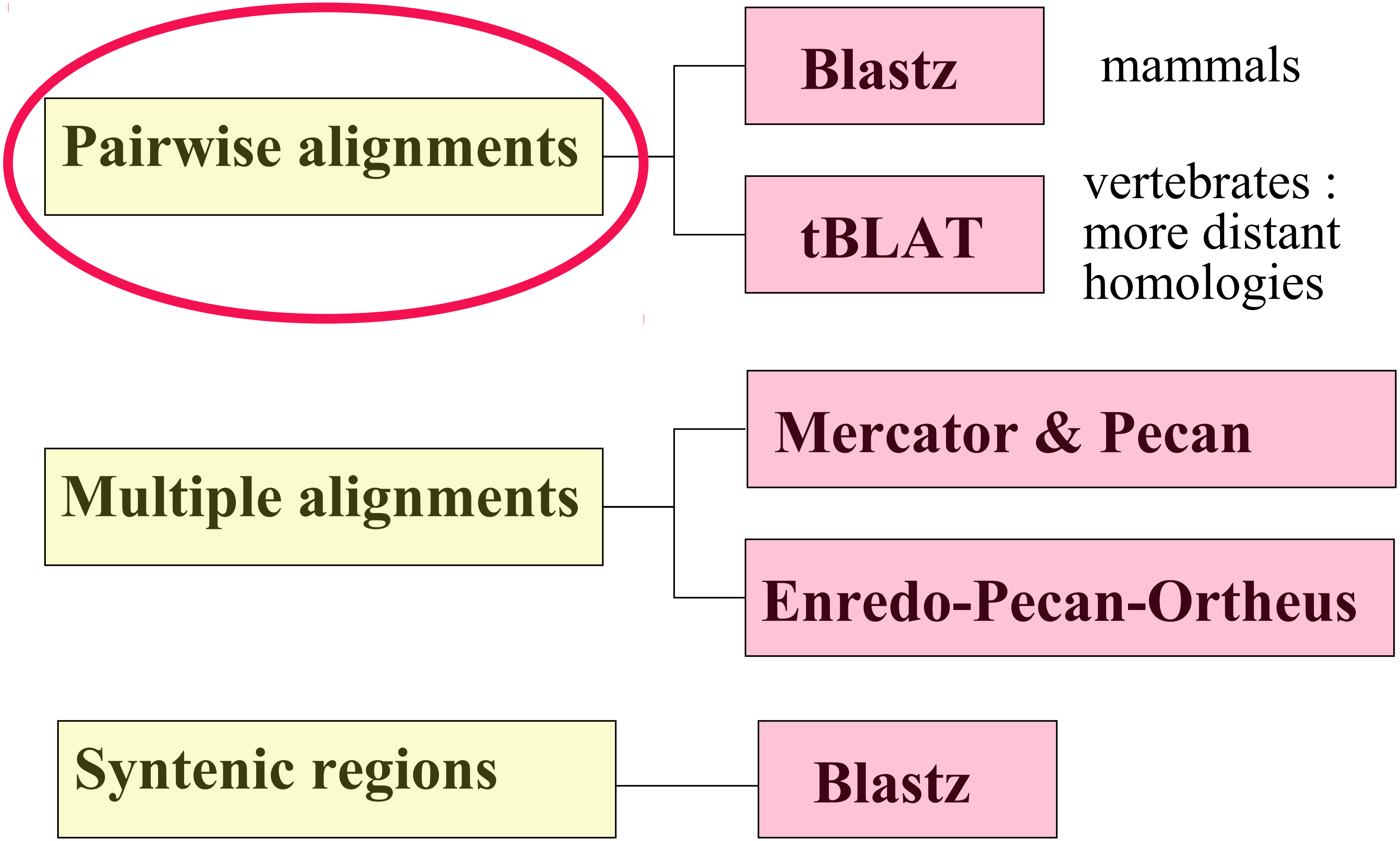
Mercator & PECAN

Enredo-Pecan-Ortheus

Syntenic regions

Blastz

Pipelines and outputs for nucleotide sequence



Pairwise alignments

Blastz

mammals

tBLAT

vertebrates : more distant homologies

Multiple alignments

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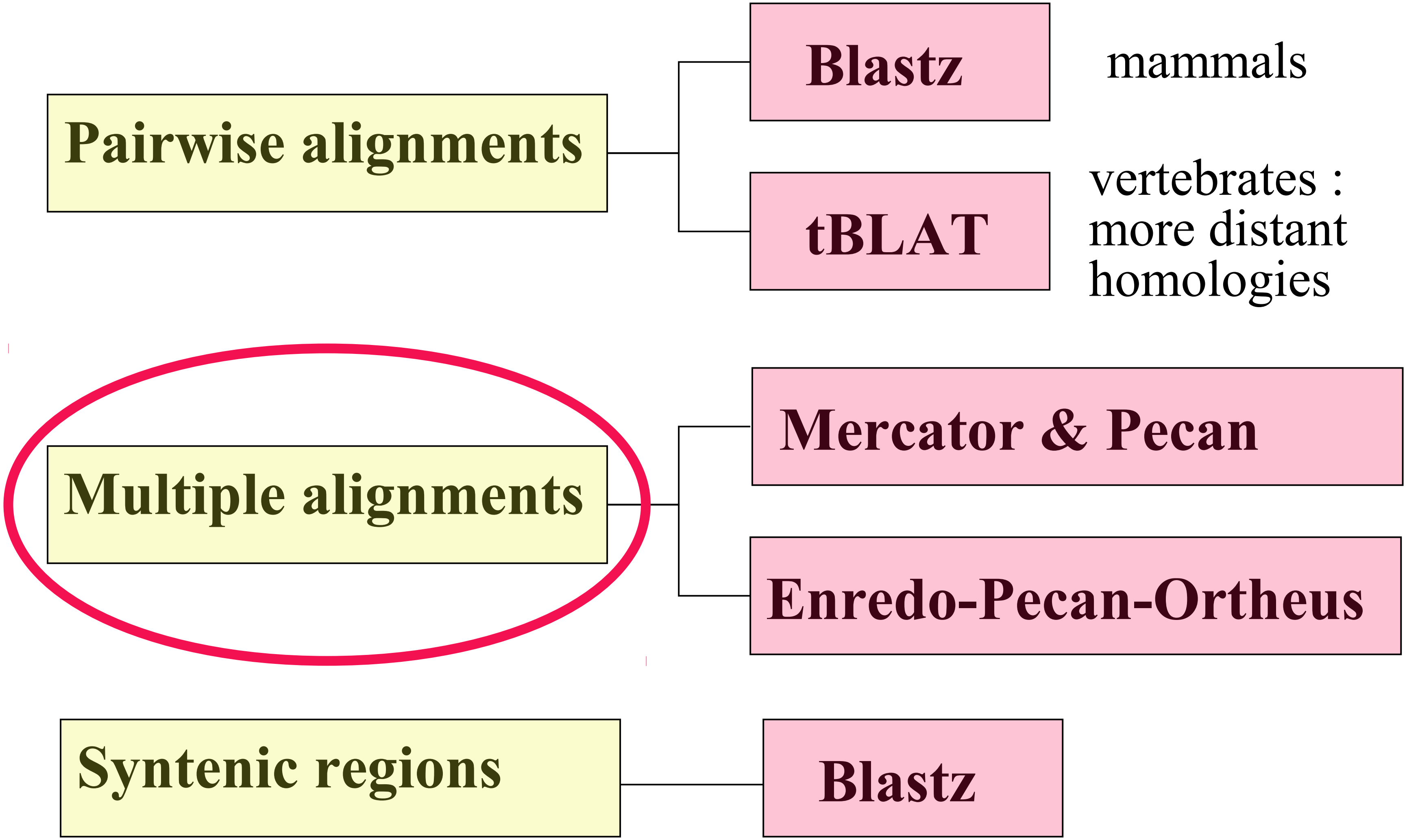
Pipelines and outputs for nucleotide sequence



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Syntenic regions

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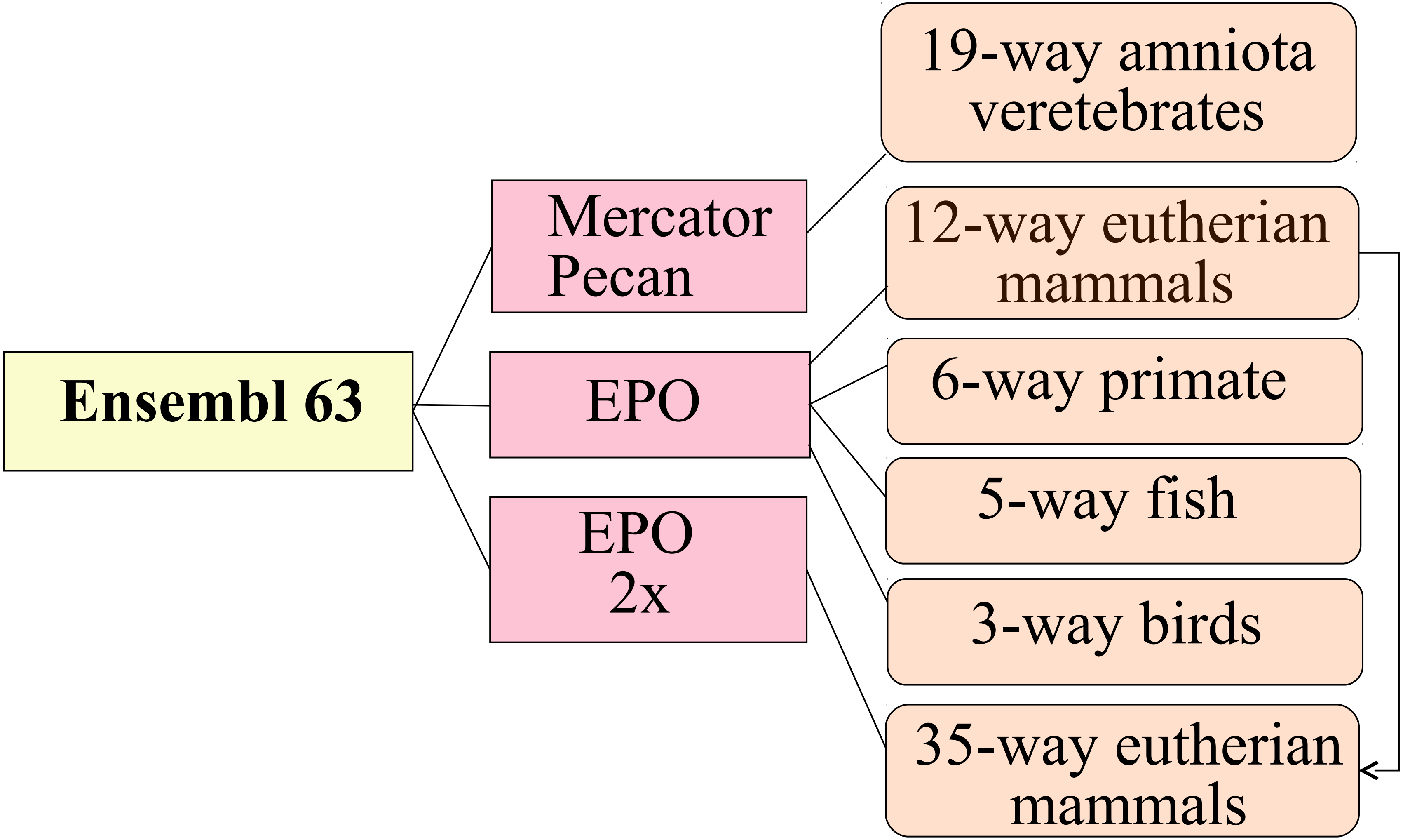
Generating multiple alignments

- **We build homology maps for multiple alignments using**
  - **Mercator** : A graph based program, which uses exon sequences as anchors. It does not allow for the alignment of duplicated regions in a genome.
  - **Enredo** : Also graph based. Use conserved regions from pairwise blastz alignments of whole genomes as anchors. It does allow for the alignment of duplicated regions.
- **Alignment is done using Pecan.**
- **Ancestral sequences are generated using Ortheus.**

MSA in Compara 63



Ensembl 63

Mercator Pecan

EPO

EPO 2x

19-way amniota veretebrates

12-way eutherian mammals

6-way primate

5-way fish

3-way birds

35-way eutherian mammals

Alignments are stored in the genomic_align and genomic_align_block tables

A small example :

```
gorilla_gorilla/MT/935-953   gacat-ttaactaaaac-ccc
macaca_mulatta/MT/1469-1488  aacatcttaactaaacg-ccc
pan_troglodytes/MT/934-953   gatac-ttaacttaaccccc
pongo_pygmaeus/MT/940-958    actac-ctaactaaaac-ccc
homo_sapiens/MT/1516-1534    gacat-ttaactaaaac-ccc
                                *   ***** **   ***
```

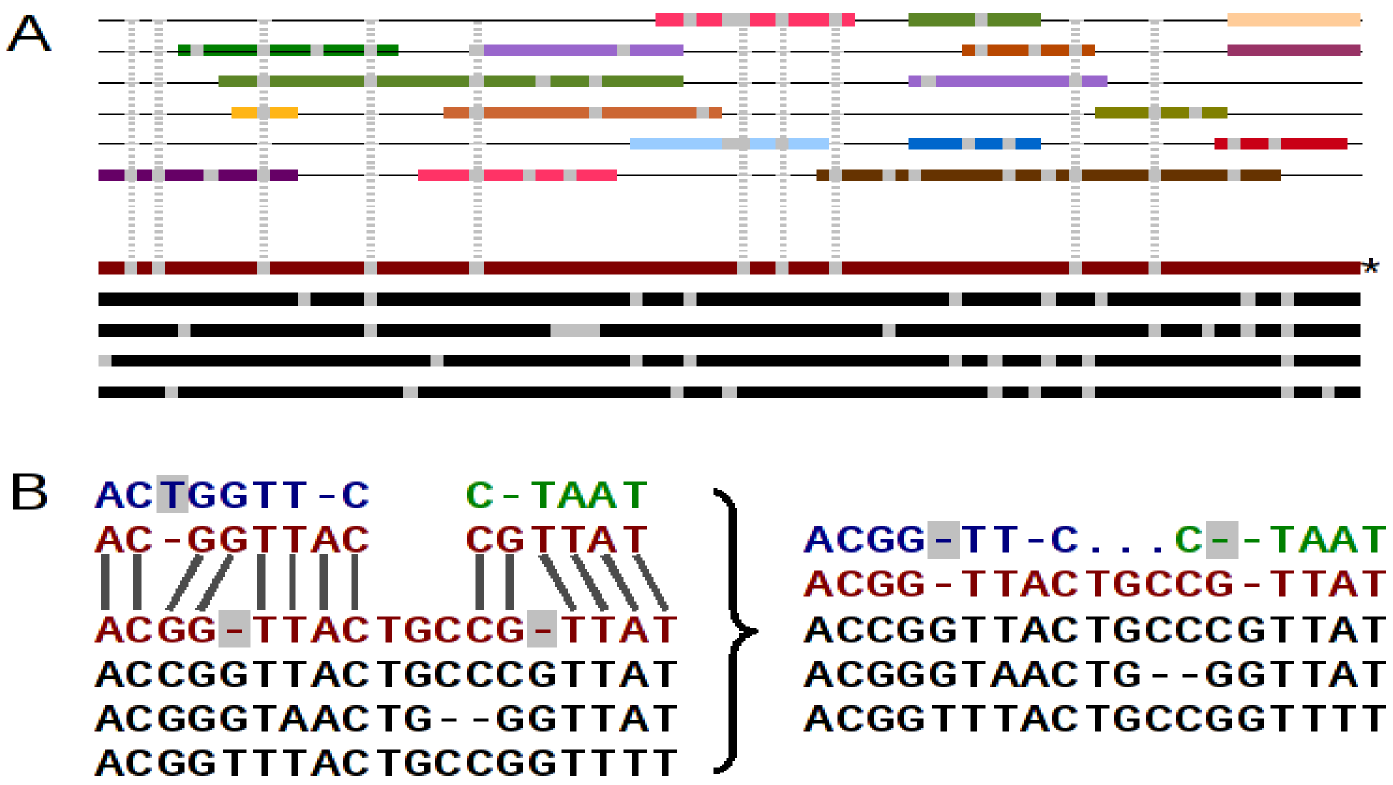
```
GACATTTAACTAAAACCCC     5MD11MD3M
AACATCTTAACTAAACGCCC    17MD3M
GATACTTAACTTAAACCCCC    5MD15M
ACTACCTAACTAAAACCCC     5MD11MD3M
GACATTTAACTAAAACCCC     5MD11MD3M
```

5 genomic_align entries
1 genomic_align_block

Sequences from core

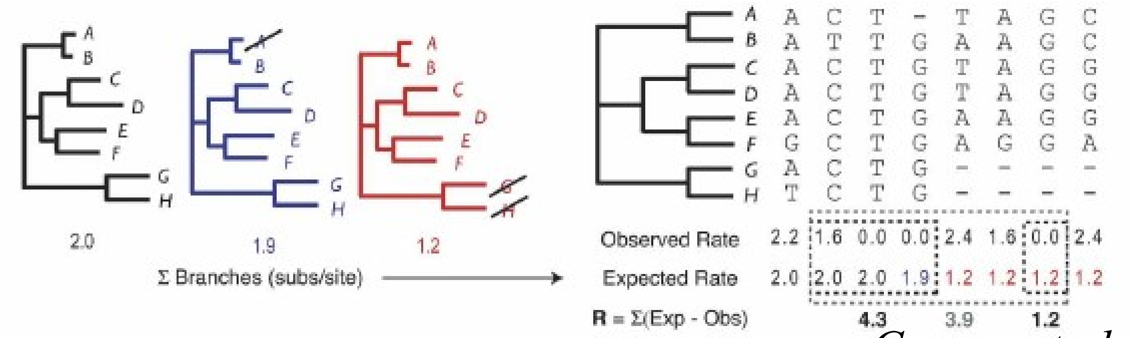
Adding low-coverage (2X) genomes

- 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



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

ensembl-dev mailing list and HelpDesk

- ensembl-dev mailing list is great for questions around the API and the DB (ensembl-dev@ebi.ac.uk)
- HelpDesk is very helpful
- Give detailed info on what you are trying to do
- Check that you have the modules installed ($PERL5LIB pointing to them)

- Ensembl Compara Team:
  - Javier
  - Kathryn
  - Matthieu
  - Leo
  - Stephen
  - Miguel