FUNCTIONAL PREDICTION AT THE (META-)GENOMIC SCALE BY EVOLUTIONARY ANALYSIS

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1. PHYLOGENOMIC APPROACHES FOR ORTHOLOGY DETECTION AND FUNCTIONAL PREDICTION

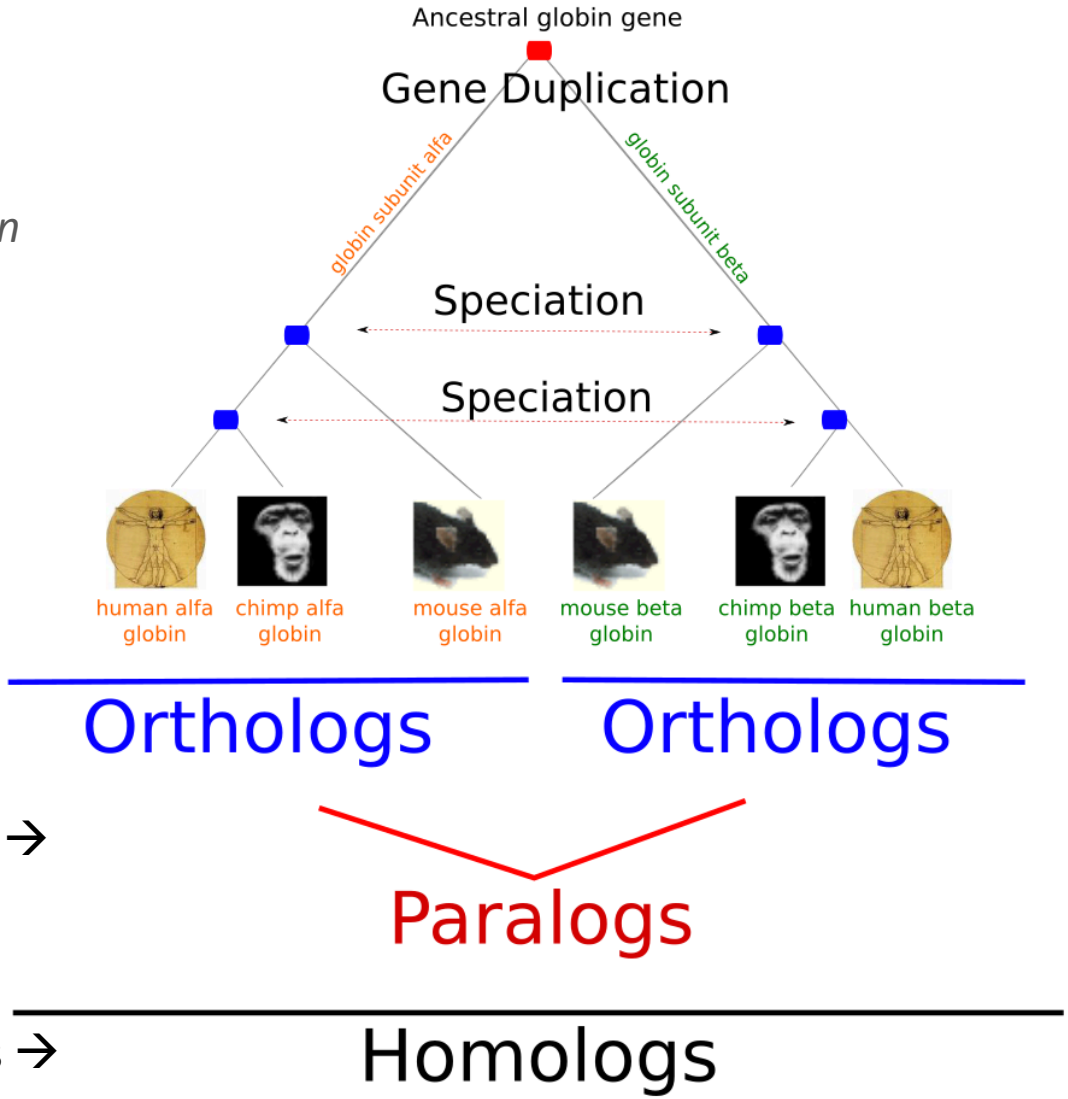
ORTHOLOGY AND FUNCTIONAL PREDICTION

Ortholog conjecture:

Function is more conserved between orthologs than between paralogs

↓

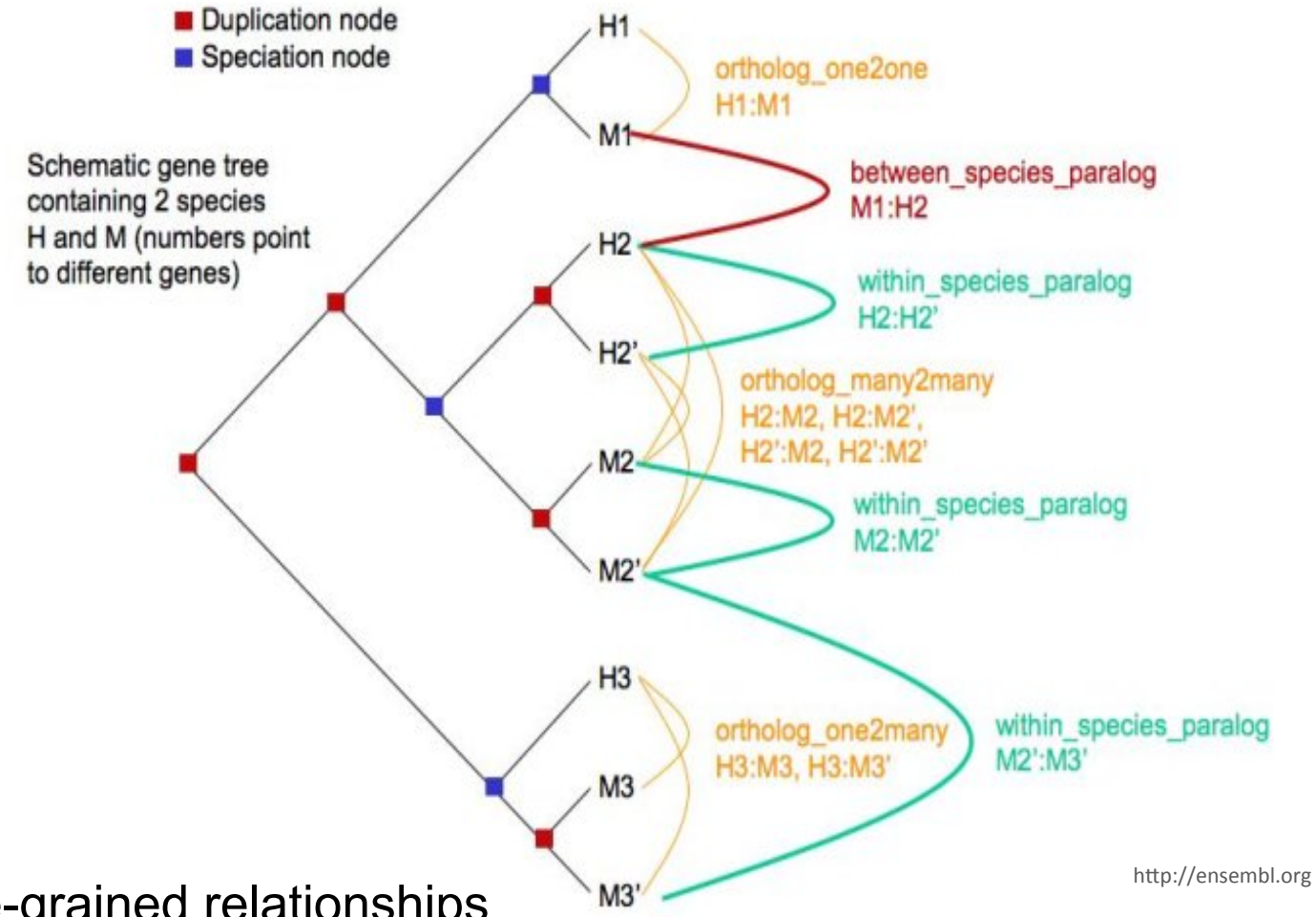
Predicting gene function turns into an orthology prediction problem



Deeper Evolutionary → analysis

BLAST results →

ORTHOLOGY DETECTION METHODS (PHYLOGENY)

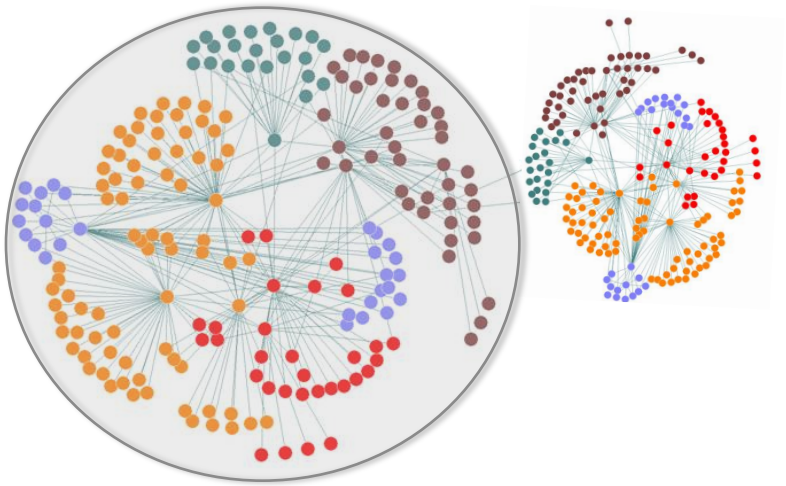


http://ensembl.org

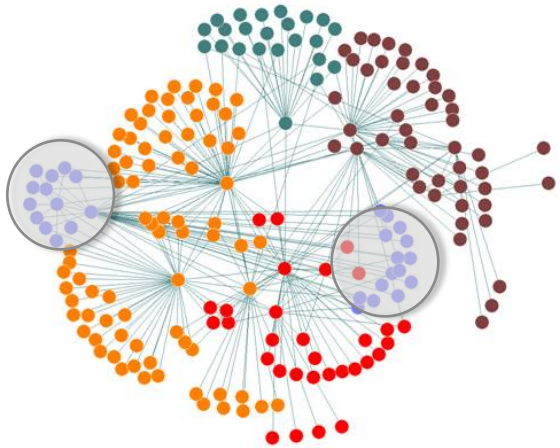
- Infer fine-grained relationships
- Allows tracing the origin of duplication and speciation events

ORTHOLOGY DETECTION METHODS (CLUSTERING)

- Build Clusters of Orthologous Groups (COGs) based on sequence similarity network
- Tend to be faster and cope for larger amounts of species/ sequences
- No co-orthology disambiguation and requires taxonomic constraints



1 COG (all species)

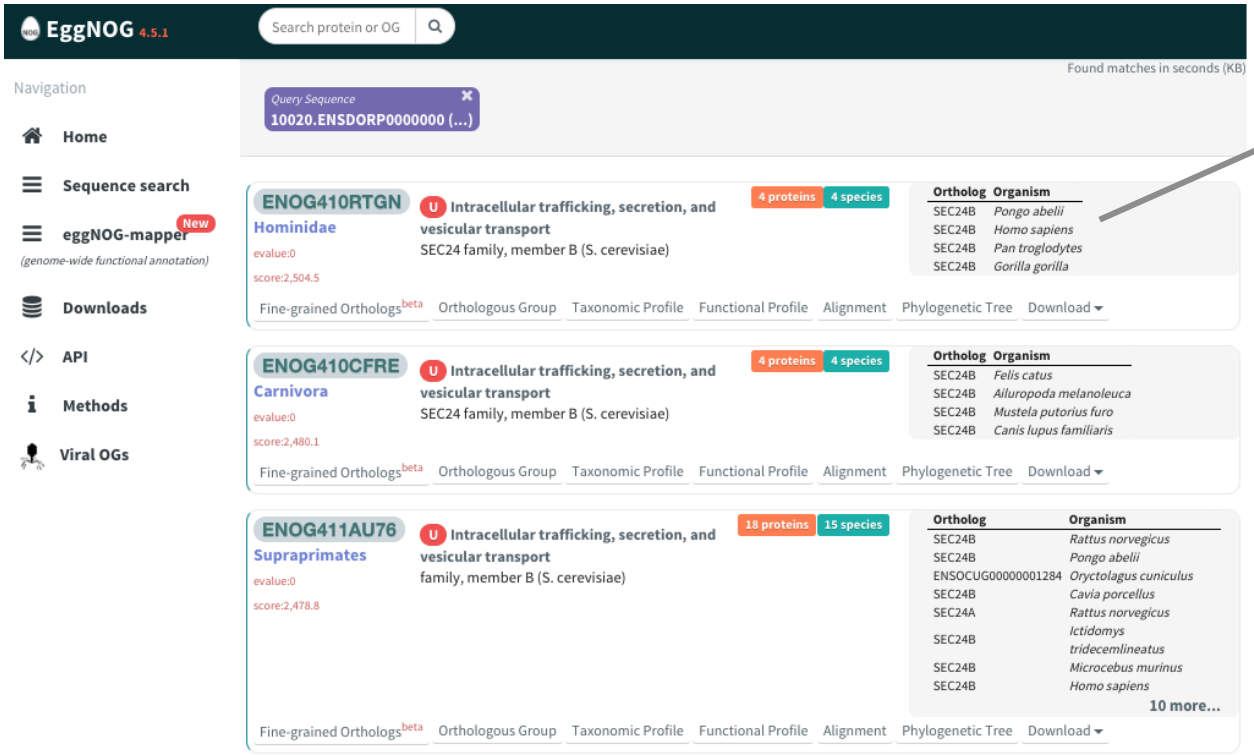


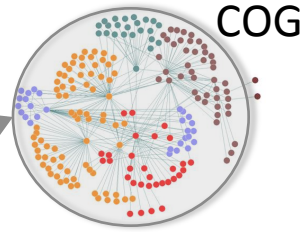
2 COGs (mammal species)

EggNOG 4.5.1

A database of orthologous groups and functional annotation

Organisms	Viruses	Orthologous Groups	Trees & Algs.
2,031	352	190k	1.9M



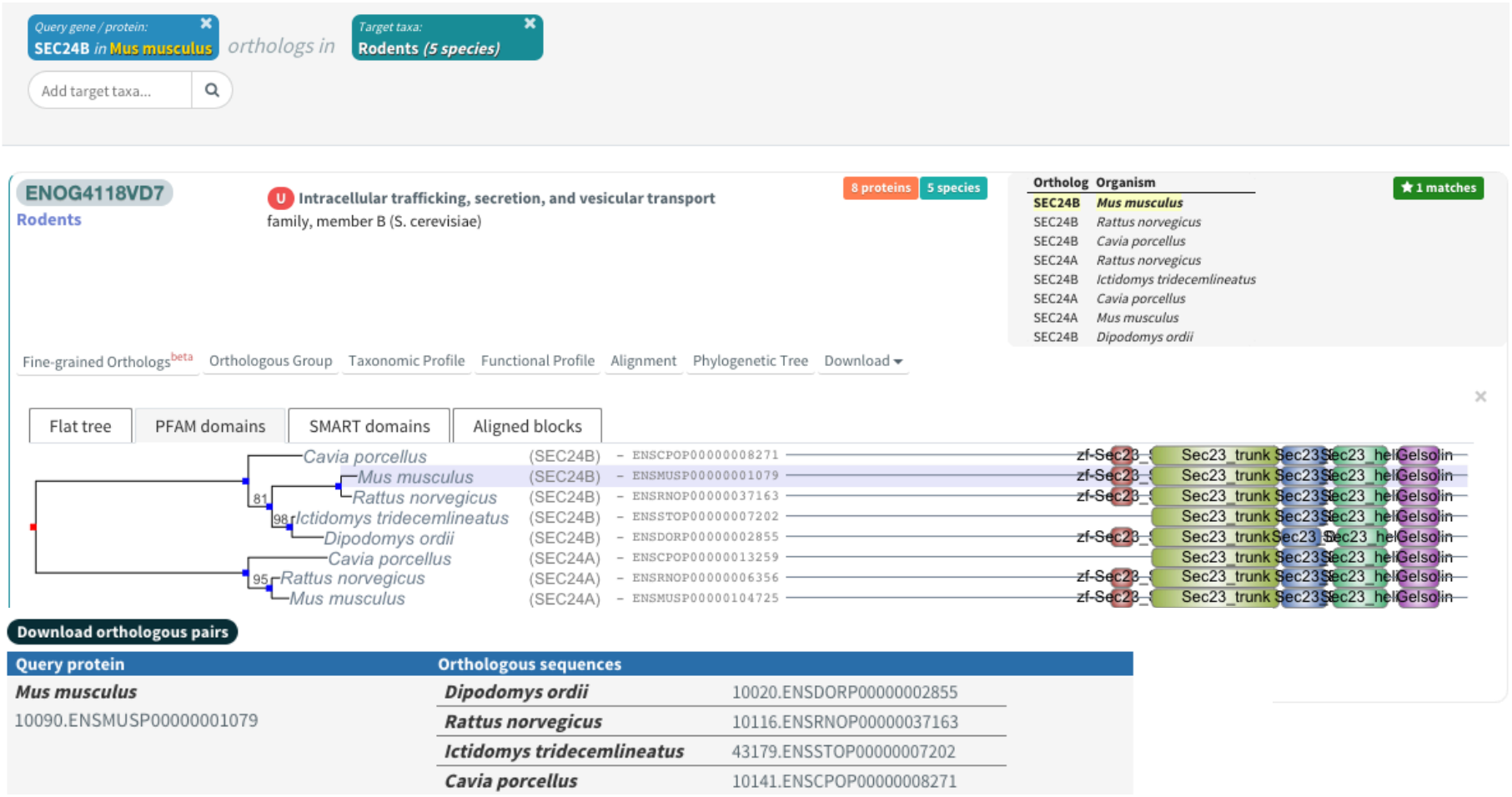


- Rapid sequence search
- Find orthologous groups
- Functional annotations
  - Domains
  - Gene Ontology
  - KEGG
  - Taxonomic distribution

http://eggnog.embl.de

Huerta-Cepas, et al. 2016 (Nucleic Acid Research)

FINE GRAINED ORTHOLOGY PREDICTIONS



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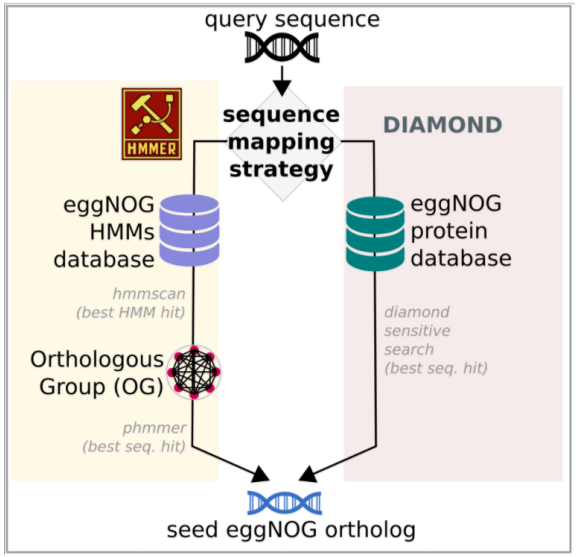
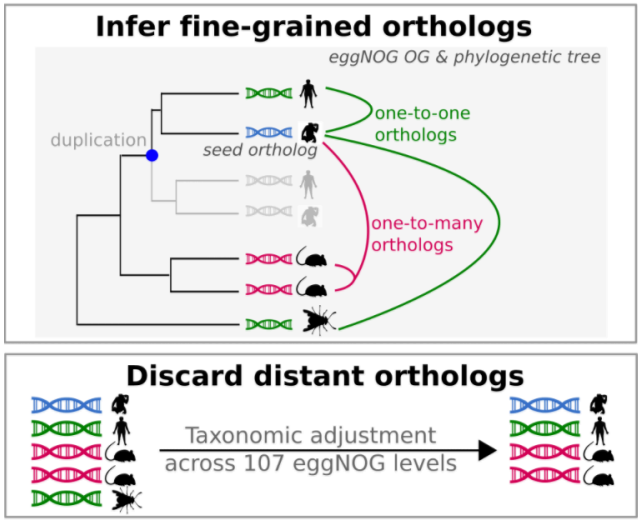
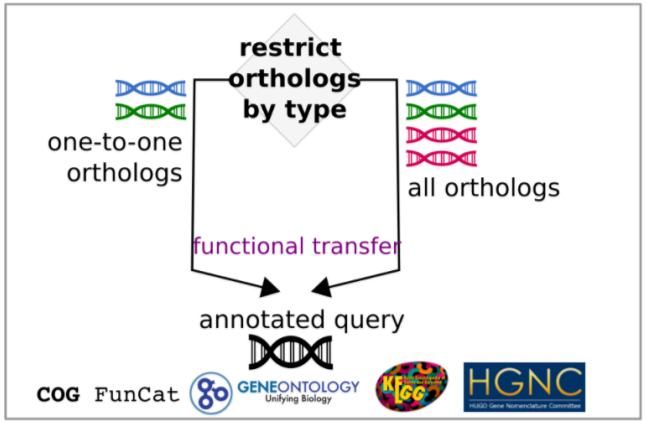
Huerta-Cepas, et al. 2016 (Nucleic Acid Research)

EFFICIENT ANNOTATION BY ORTHOLOGY MAPPING







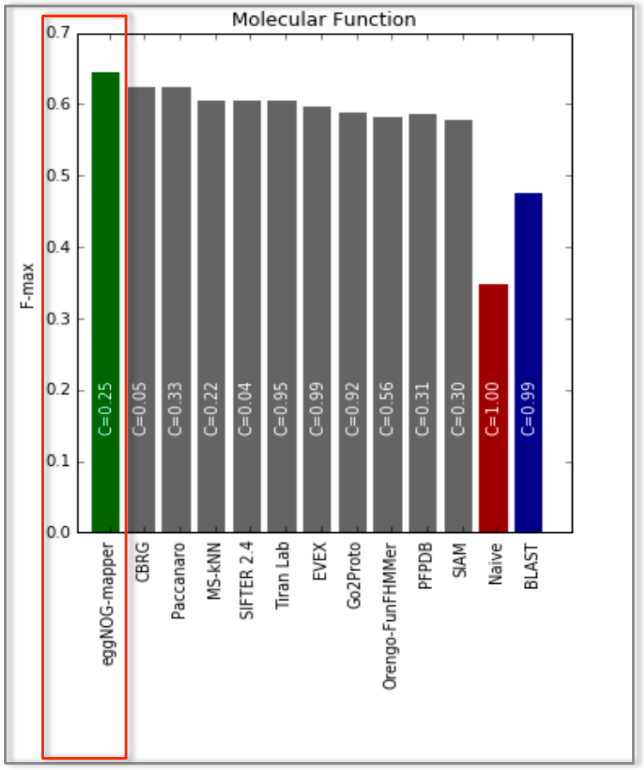
Find query's best match *Place it in tree* *Transfer terms from orthologs*

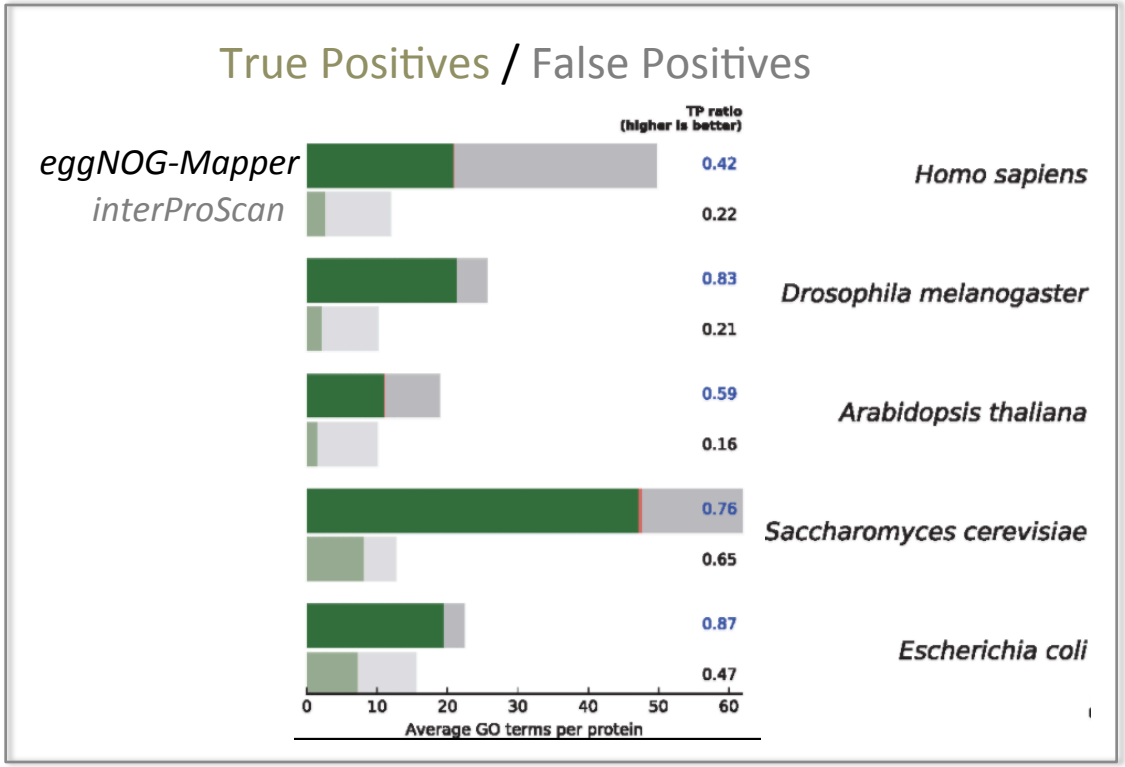
http://eggnog-mapper.embl.de

Huerta-Cepas et al. 2016 (submitted)

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 686070

EGGNOG-MAPPER PERFORMANCE





CAFA2: Jiang et al. Genome Biology (2016)

CAFA2 Challenge:

- *eggNOG-mapper ranked **top 5 out of 126 methods** in the 3 GO categories*

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3. FUNCTIONAL EXPLORATION OF METAGENOMIC DATASETS

FUNCTIONAL ANNOTATION OF METAGENOMIC DATA

Objective: "develop cutting edge methods for using large scale data to design cell factories and bacterial communities for biotechnological applications" http://dd-decaf.eu

@EMBL

- Mining new enzymes out from genomic and metagenomic data
- Building metabolic models based on functional annotation of bacterial communities

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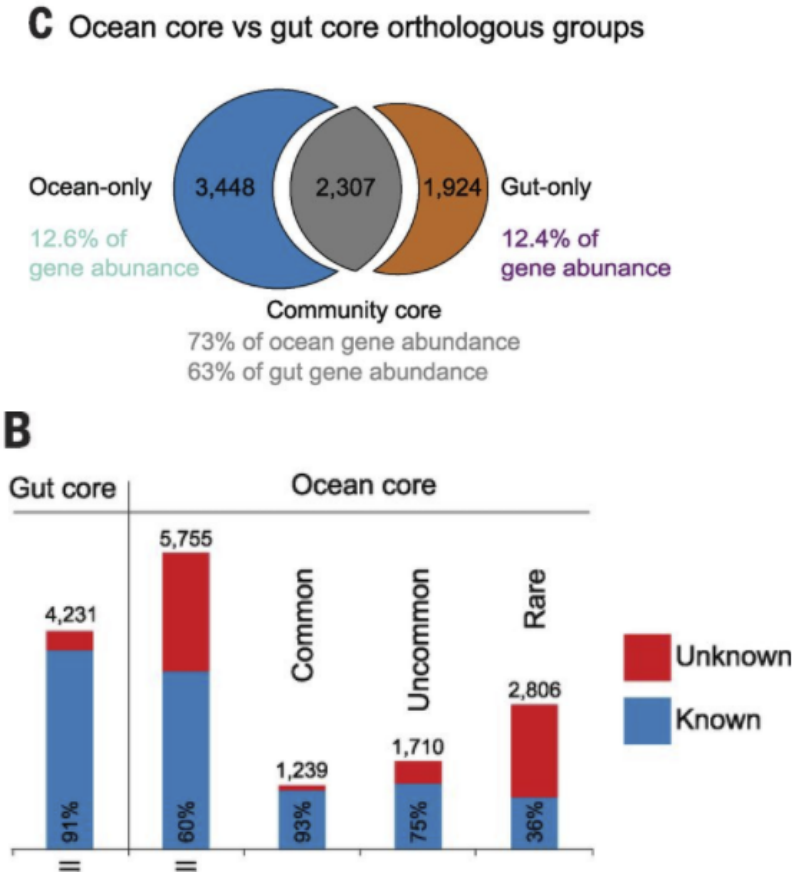
EXPLORING METAGENOMICS UNKNOWN FRACTION



Structure and function of the global ocean microbiome
Sunagawa el al. Science 348 (6237), 1261359

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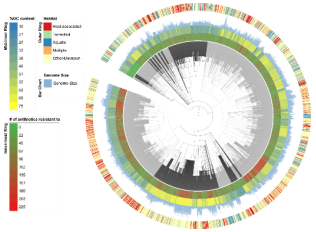
3. TOOLS

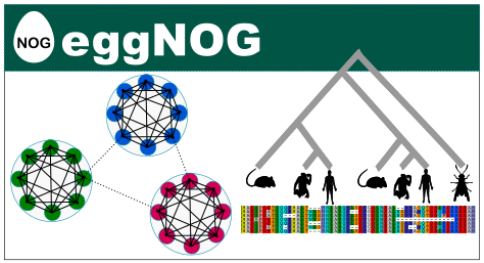
PROGENOMES



Consistently annotated prokaryotic genomes

http://progenomes.embl.de

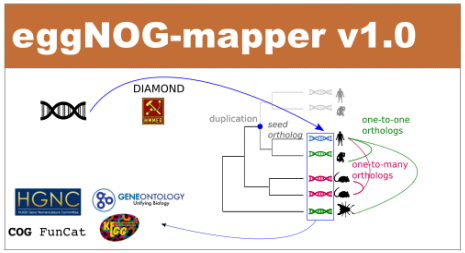
Mende et al. NAR 45 (2017) D286



Orthologous groups and functional information

http://eggnog.embl.de

Huerta-Cepas et al. NAR (2016)



Fast accurate functional annotation

http://eggnog-mapper.embl.de

Huerta-Cepas et al. MBE (2017)

ETE Toolkit

A Python framework to work with trees

```
from ete3 import Tree
tree = Tree('((A,B), D);')

print tree
#       /-A
#    /-|
# --|   \-B
#    \-D

A = tree & "A"
A.up.show()
```

Phylogenetic reconstruction and analysis

http://etetoolkit.org

Huerta-Cepas et al. MBE (2016)