Transcriptome Functional Annotation

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657.001 Transcriptomics (WS 2018/2019)

Why functional annotation

- Get biological understanding from features (transcripts)
- Validate experiments (RNA-seq expectations)
- Generate new hypotheses (unexpected findings)
- Limitations
  - Only as good as published or known information about genes and proteins in known species
  - Reliable annotation difficult to achieve for novel or mixed species

Transcriptome functional annotation

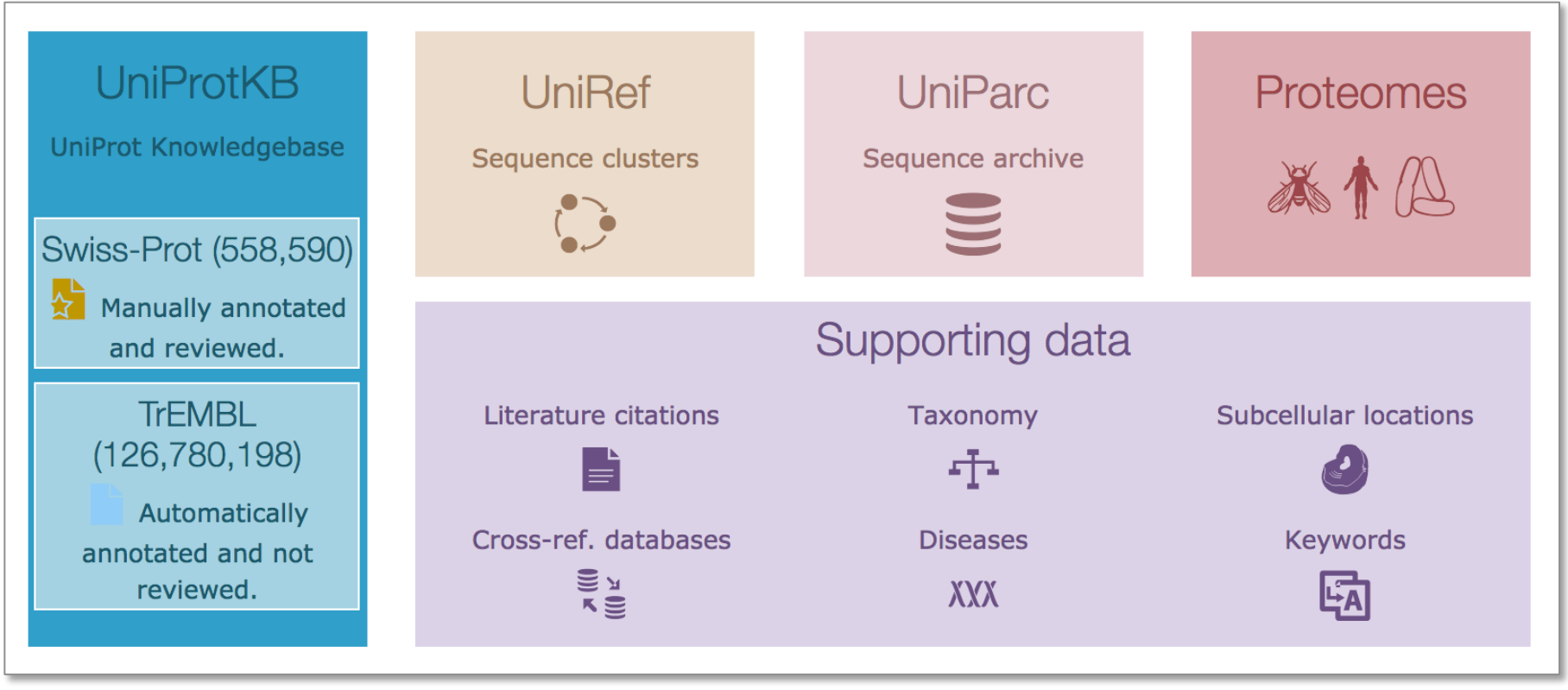
- Coding region prediction
  - ORF (open reading frame) identification
  - Likely coding region prediction
- Protein search
  - Search transcripts and predicted proteins against reliable protein databases (e.g. Swiss-Prot)
- Functional information collection
  - Use various annotation sources

Sources of annotation

- Proteins and protein domains
  - Swiss-Prot, Pfam, InterPro
- Gene Ontology
  - Most popular, but can be too general
- Pathways
  - KEGG, Reactome, BioCata, PANTHER
- Other databases
  - Orthologous groups, diseases

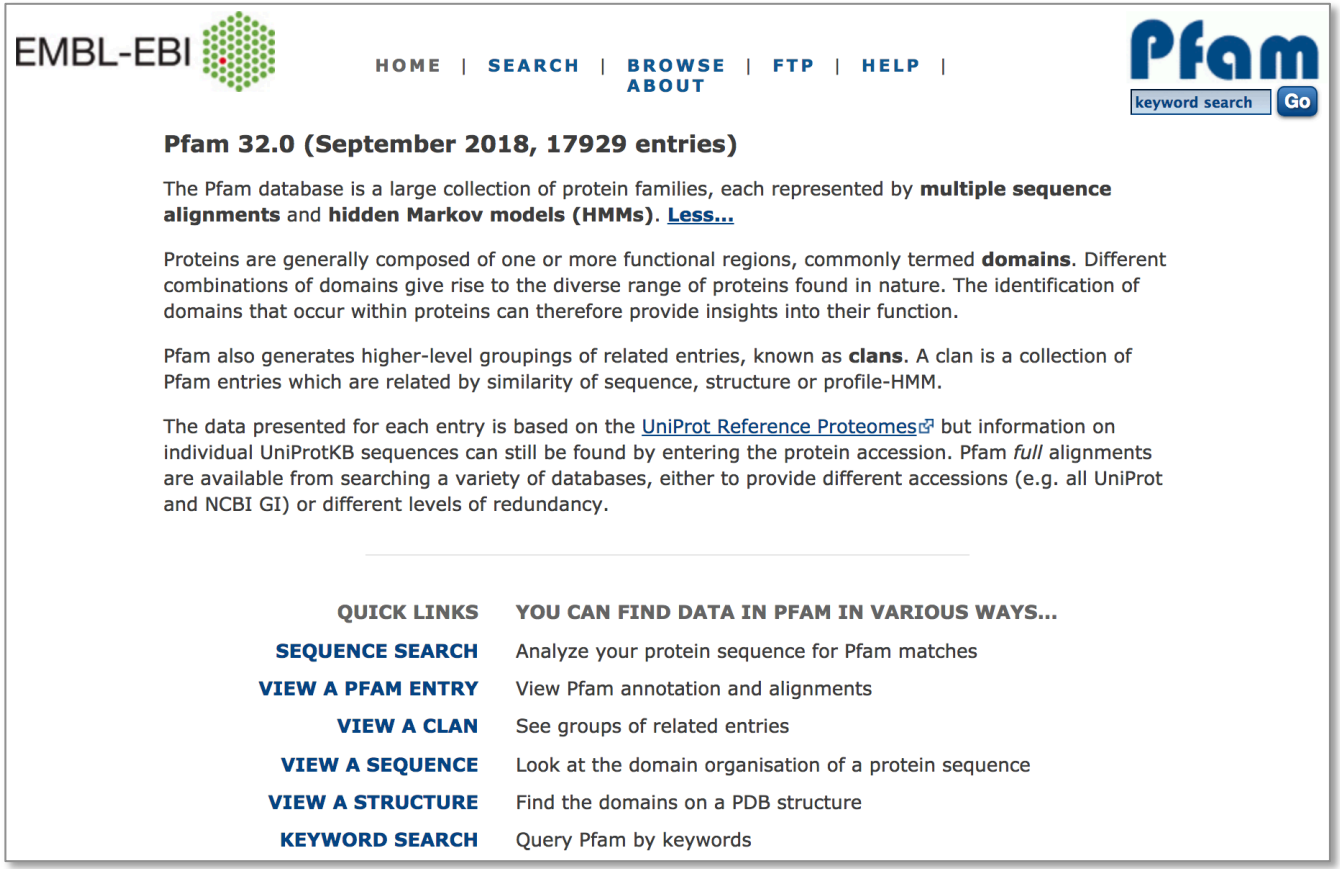
Protein database: Swiss-Prot

- Most reliable, manually annotated protein database



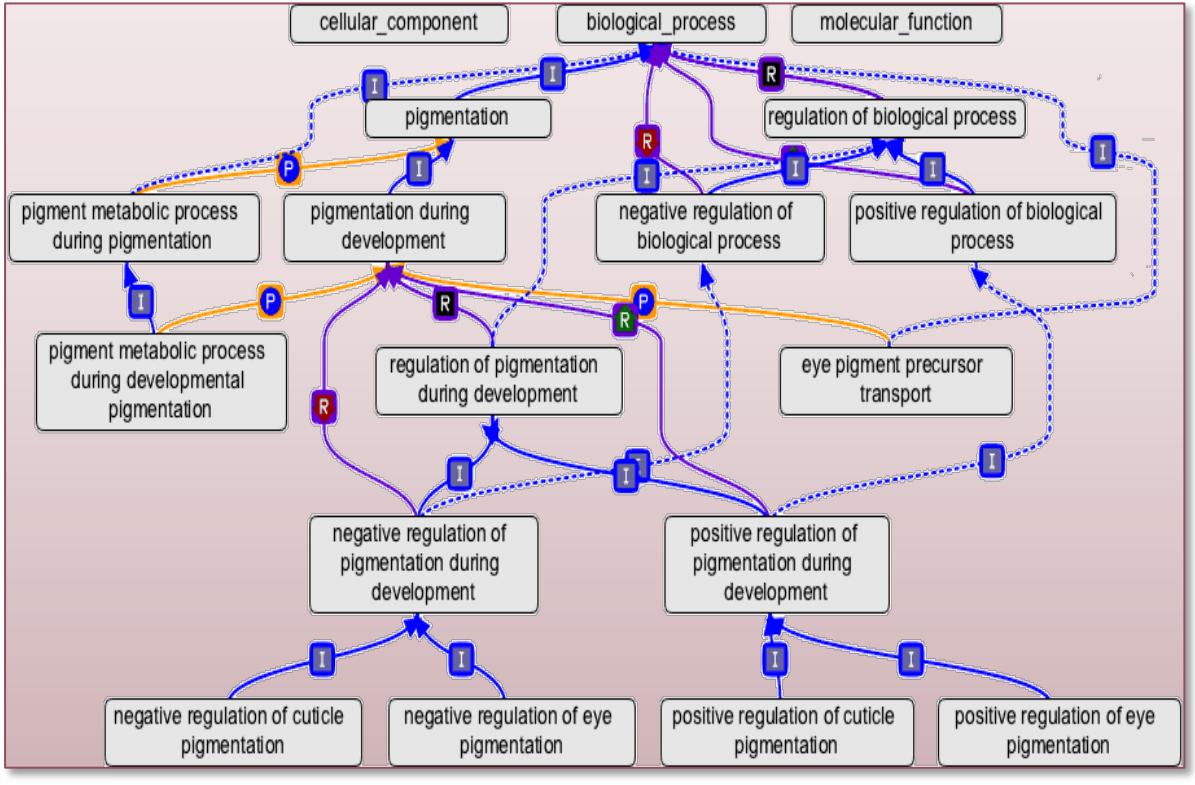
Protein database: Pfam

- Protein families and domains



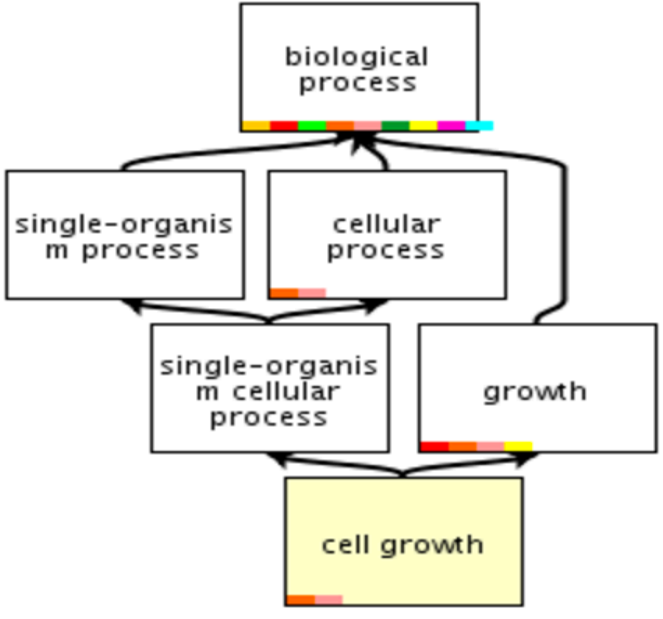
Gene Ontology (GO)

- GO project provides
  - Controlled vocabularies of terms representing gene product properties
- 3 ontologies
  - Cellular Component (CC)
  - Biological Process (BP)
  - Molecular Function (MF)



GO term example

- id: GO:0016049
- name: cell growth
- namespace: biological_process
- def: "The process in which a cell irreversibly increases in size over time by accretion and biosynthetic production of matter similar to that already present." [GOC:ai]
- subset: goslim_generic
- subset: goslim_plant
- subset: gosubset_prok
- synonym: "cell expansion" RELATED []
- synonym: "cellular growth" EXACT []
- synonym: "growth of cell" EXACT []
- is_a: GO:0009987 ! cellular process
- is_a: GO:0040007 ! growth
- relationship: part_of GO:0008361 ! regulation of cell size

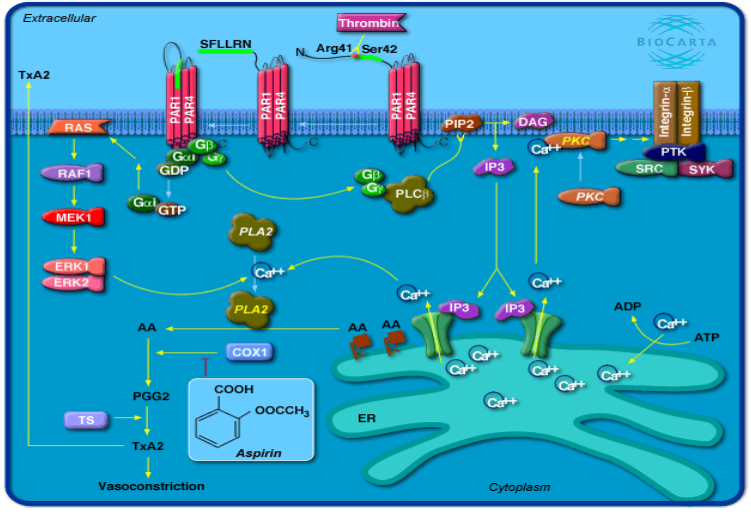


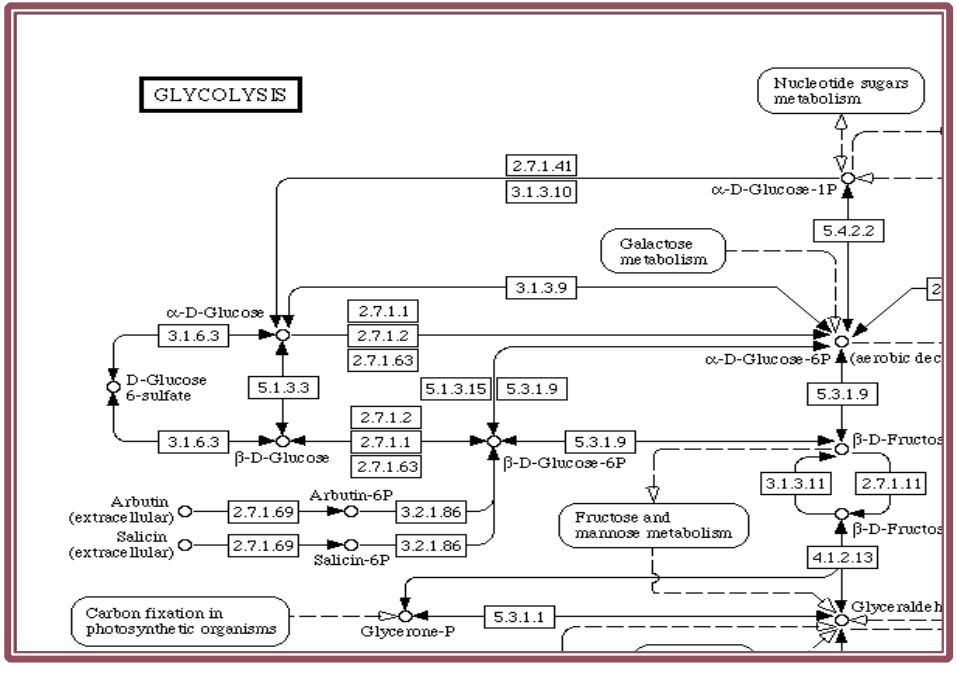
GO annotation

- Which biological processes or molecular functions are enriched in my gene list?
- Results given as a set of enriched or over-represented GO terms
  - Degrees of enrichment somtimes available
  - Interpretation is important
  - Often need more information from other annotation sources

Pathways

- KEGG pathways most popular
- Many others exist
  - BioCarta
  - MetaCyc
  - Reactome



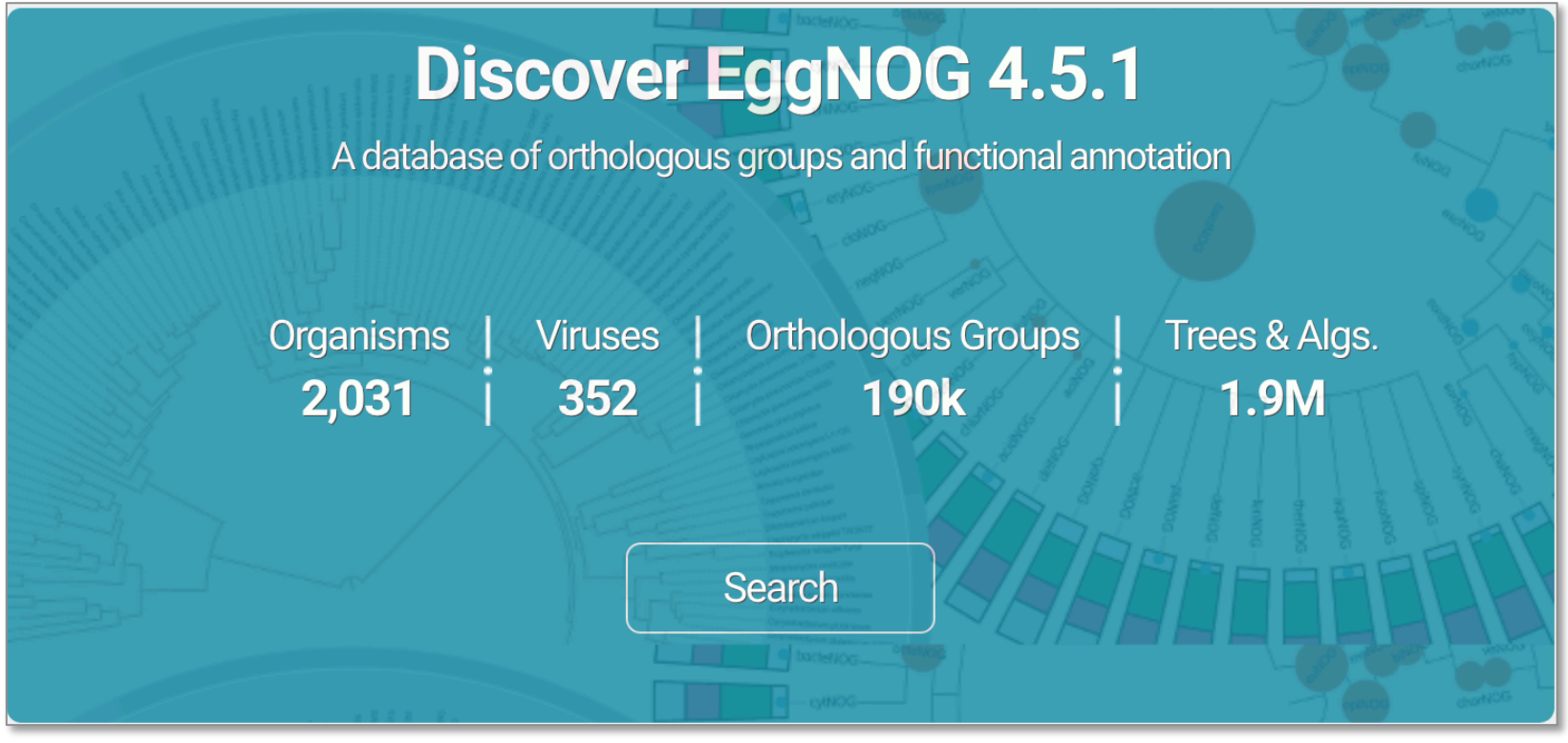


Pathway annotation

- Are there specific pathways enriched in my gene list?
- What are other genes involved in those pathways?
- Results given as a set of pathways
  - More than simple terms (enzymes, involved genes, reactions)
  - Interpretation and cross-check with other sources of annotation necessary

Orthologous groups: EggNOG

- Orthologous groups of genes



Lab overview