

# High-throughput Sequencing course 2019

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# OMICS ERA

What is ‘OMICS’: derived from Latin suffix “ome” meaning mass or many.

Thus OMICS involve a mass (large number) of measurements per endpoint. (Jackson et al. 2006)

- Genomics
- Transcriptomics
- Proteomics
- Reactomics
- Metabonomics
- Phenomics

# APPLICATION OF DIFFERENT OMICS

Genomics	Transcriptomics	Proteomics	Metabolomics	Protein–DNA interactions	Protein–protein interactions	Fluxomics	Phenomics
Genomics (sequence annotation)	<ul style="list-style-type: none"> <li>• ORF validation</li> <li>• Regulatory element identification<sup>76</sup></li> </ul>	<ul style="list-style-type: none"> <li>• SNP effect on protein activity or abundance</li> </ul>	• Enzyme annotation	<ul style="list-style-type: none"> <li>• Binding-site identification<sup>75</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Functional annotation<sup>78</sup></li> </ul>	• Functional annotation	<ul style="list-style-type: none"> <li>• Functional annotation<sup>75, 90</sup></li> <li>• Biomarkers<sup>125</sup></li> </ul>
Transcriptomics (microarray, SAGE)		<ul style="list-style-type: none"> <li>• Protein: transcript correlation<sup>78</sup></li> </ul>	• Enzyme annotation <sup>104</sup>	<ul style="list-style-type: none"> <li>• Gene-regulatory networks<sup>76</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Functional annotation<sup>88</sup></li> <li>• Protein complex identification<sup>87</sup></li> </ul>		• Functional annotation <sup>102</sup>
Proteomics (abundance, post-translational modification)			<ul style="list-style-type: none"> <li>• Enzyme annotation<sup>94</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Regulatory complex identification</li> </ul>	<ul style="list-style-type: none"> <li>• Differential complex formation</li> </ul>	• Enzyme capacity	• Functional annotation
			Metabolomics (metabolite abundance)	<ul style="list-style-type: none"> <li>• Metabolic-transcriptional response</li> </ul>		<ul style="list-style-type: none"> <li>• Metabolic pathway bottlenecks</li> </ul>	<ul style="list-style-type: none"> <li>• Metabolic flexibility</li> <li>• Metabolic engineering<sup>104</sup></li> </ul>
				Protein–DNA interactions (ChIP-chip)	<ul style="list-style-type: none"> <li>• Signalling cascades<sup>99, 102</sup></li> </ul>		<ul style="list-style-type: none"> <li>• Dynamic network responses<sup>84</sup></li> </ul>
					Protein–protein interactions (yeast 2H, coAP-MS)		<ul style="list-style-type: none"> <li>• Pathway identification activity<sup>88</sup></li> </ul>
						Fluxomics (isotopic tracing)	<ul style="list-style-type: none"> <li>• Metabolic engineering</li> </ul>

Phenomics (phenotype arrays, RNAi screens, synthetic lethals)

# Genomics

Refer to the use of computational and statistical analysis to decipher biology from genome sequences including both DNA and RNA sequences as other post-genomic data (i.e. Genomic microarrays)

# Functional Genomics

Is a field of molecular biology that attempts to make use of the vast wealth of data produced by genomics (i.e. genomic sequences) to describe function and interactions. Unlike Genomics, functional genomics focuses on the dynamic aspects such as transcription, translation, protein-protein interactions. Is a more high-throughput methods rather than a gene by gene approach.

# Confusion with the word ontology ?



## Controlled Vocabulary:

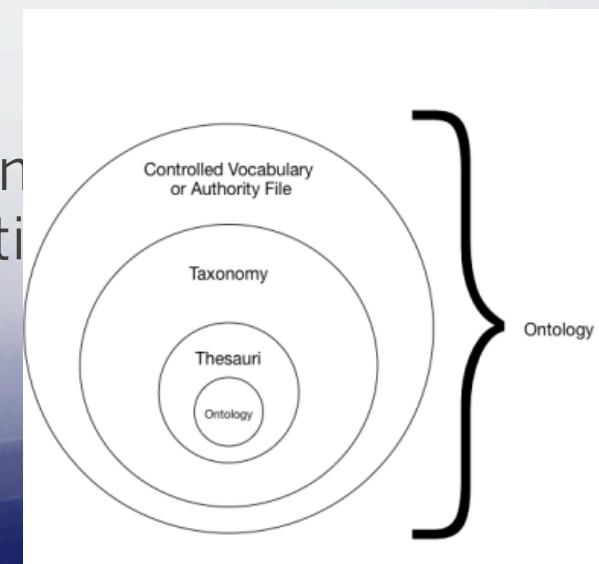
Is a restricted list of words used for labeling, indexing or categorizing

## Taxonomy:

Is a classification system. The taxonomy in a controlled vocabulary indicates a hierarchical structure based on an IsA relationship

## Ontology:

Is a controlled vocabulary with a taxonomy more complex than just IsA relationships



# Using Ontology for data analysis

- Standard identifiers for classes and relations that represent the phenomena within a domain;
- Vocabulary for a domain;
- Metadata that describes the intended meaning of the classes and relations in ontologies;
- Machine-readable axioms and definitions that enable computational access to some aspects of the meaning of classes and relations

The use of standard identifiers for classes and relations in ontologies is a key component in enabling data integration across multiple databases, because the same identifiers can be used across multiple, disconnected databases, files or web sites

These identifiers are widely used in structured file formats, in knowledge bases and data repositories.

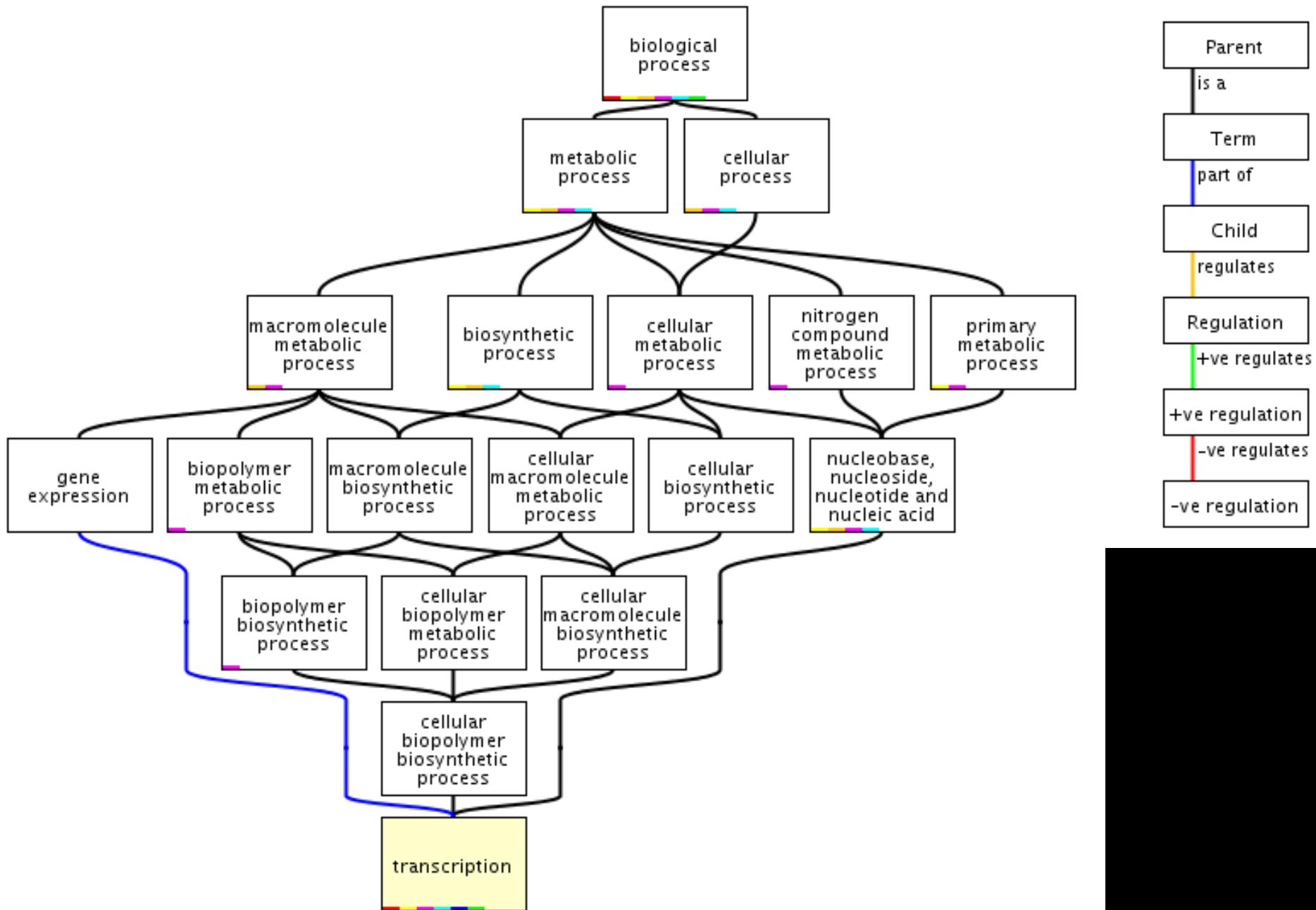
# Most successful ontology thus far

\$200 mill. invested in literature and database curation using the Gene Ontology (GO) since 1999

over 11 million annotations relating gene products (proteins) described in the UniProt, Ensembl and other databases to terms in the GO

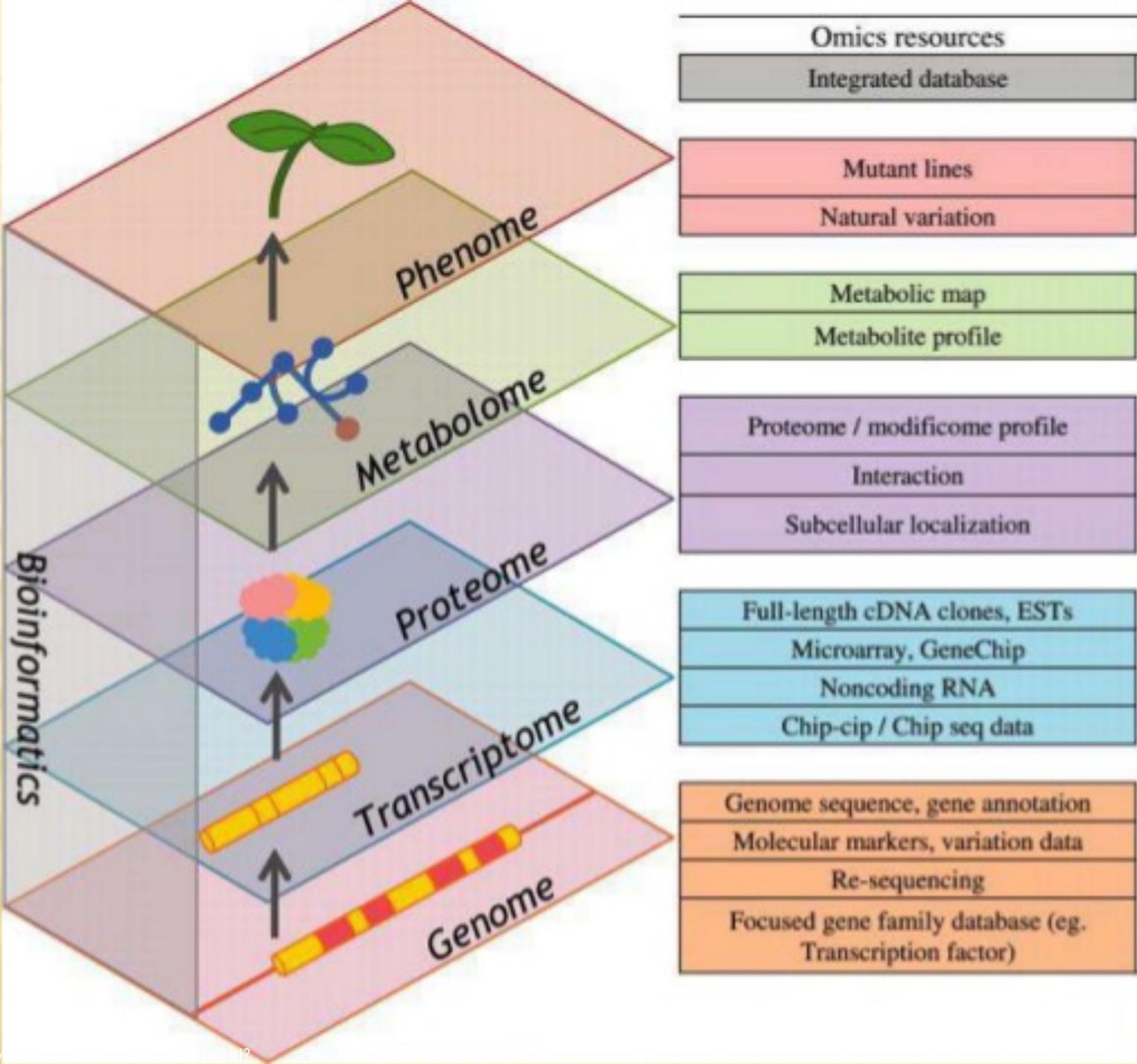
GO provides a controlled system of representations for use in annotating data and literature that is

- multi-species
- multi-disciplinary
- multi-granularity, from molecules to population



# Gene ontology structure

- |   |                      |
|---|----------------------|
| GO MF   | molecular functions  |
| Molecular activities of a gene product                                    |                      |
| GO BP   | biological processes |
| Specific Objective that the organism is genetically programmed to achieve |                      |
| GO CC   | cellular components  |
| Where gene products are active  |                      |



High-throughput technologies generated data sets of often thousands of genes, which needed to be interpreted in terms of biological roles.

This provided the impetus behind the ongoing functional and structural annotation of gene products, which is now available through the GO database ([AMIGO](#)) and is a mainstay of modern bioinformatics.

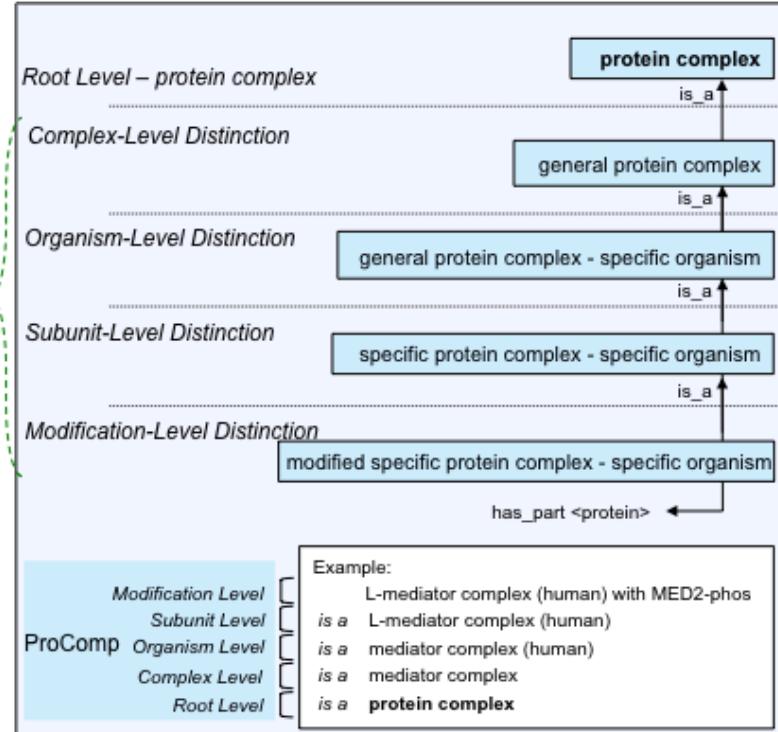
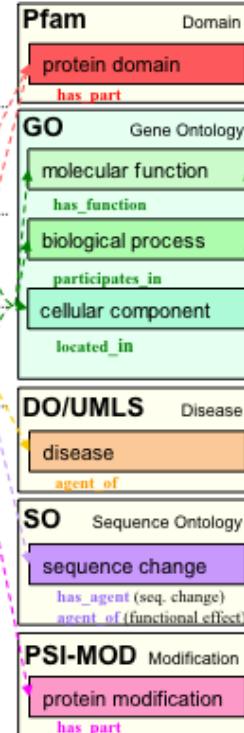
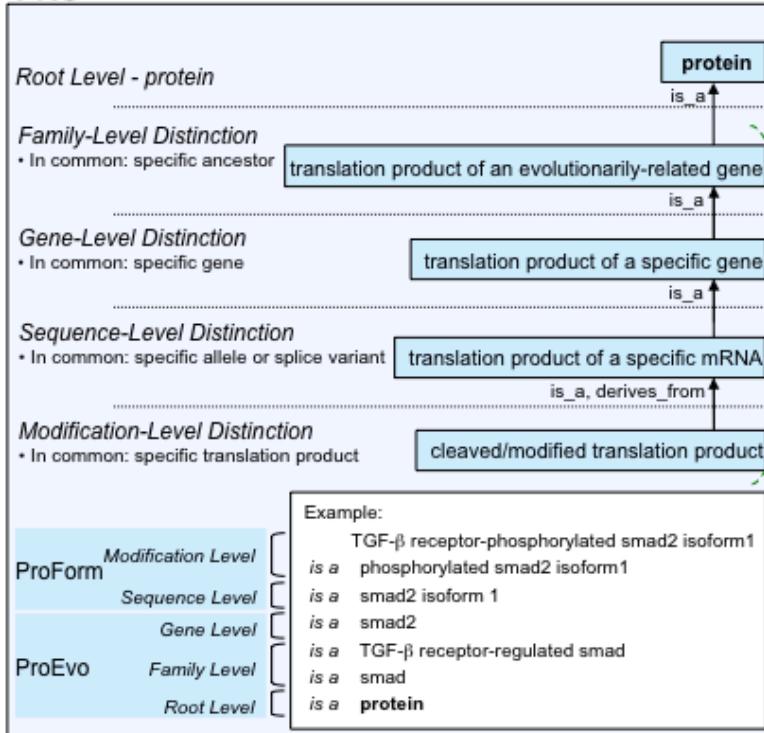
# Protein Ontology

<https://proconsortium.org/>

PRO encompasses three sub-ontologies: proteins based on evolutionary relatedness (ProEvo); protein forms produced from a given gene locus (ProForm); and protein-containing complexes (ProComp).

(Explanation of the figure)

## PRO



Go to the AMIGO database and describe it

AmiGO 2 Home Search ▾ Browse Tools & Resources Help Feedback About AmiGO 1.8

AmiGO 2

More information on quick search [?](#)

Quick search  Search

You can click here to use the gene ontology tools

**Search Templates**  
  
Use predefined **templates** to explore Gene Ontology data.  
[Go »](#)

**Advanced Search**  
  
Interactively **search** the Gene Ontology data for annotations, gene products, and terms using a powerful search syntax and filters.  
[Search ▾](#)

**Browse the Ontology**  
  
Use the drill-down **browser** to view the ontology structure with annotation counts.  
[Go »](#)

**GOOSE**  
  
Use **GOOSE** to query the legacy GO database with **SQL**.  
[Go »](#)

**Term Enrichment Service**  
  
Your genes here...  
  
  
biological process  
  
Homo sapiens  
  
[Submit](#)  
Powered by [PANTHER](#)  
[Advanced »](#)

**Statistics**  
  
View the most recent **statistics** about the Gene Ontology data in AmiGO.  
[Go »](#)

**And Much More...**  
  
Many **more tools** are available from the software list, such as alternate searching modes, Visualize, non-JavaScript pages.  
[Go »](#)



## Explore GO data

[Home](#) allows simple quick searches using autocomplete and the new GOIr backend.

**Interactively search** and filter the GO data as you type. These pages allow you to use a powerful search syntax (including boolean operators).

**Annotations:** Associations between GO terms and genes or gene products.

**Ontology:** Gene Ontology Term, Synonym, or Definition.

**Genes and gene products:** Genes and gene products associated with GO terms.

**Search templates** (a search "wizard") can be used to quickly answer common questions using a fill-in-the-blank approach.

**Visualization** creator for GO graph. Freely make your own ontology graph, including label and color changes. Please see the documentation for more [details](#).

**Drill-down browser** can be used to explore the ontologies and annotation from the top levels by opening direct descendant terms individually to create a custom view.

**Base statistics** can give a high-level view of what kind of data is available in AmiGO.

**PubMed ID search** takes you to a page with summary information and all GO annotations using the inputted ID.

E.g. PMID:123456

Search

**Medial search** returns match counts for the different search personalities and allows users to select which one they wish to continue with.

Quick search

Search

## Analysis of GO data

**Term enrichment services** offers access to term enrichment analysis, finding significant shared GO terms or parents of those GO terms to help discover what input genes may have in common.

**Term enrichment** **AmiGO 1.8** finds significant shared GO terms or parents of those GO terms, used to describe the genes in the query/input set to help discover what those genes may have in common.

**GO slimmer** **AmiGO 1.8** allows you to map the granular annotations of the query set of genes to one or more high-level, broader parent terms referred to as GO Slim terms.

**BLAST** **AmiGO 1.8** search for gene products. The sequence search is performed using either BLASTP or BLASTX (from the WU-BLAST package), depending on the type of the input sequence.

**Term matrix** for exploring gene product (biolentity) co-annotation information.

## Directly query GO data

**GOOSE** is the GO Online SQL Environment. Using this, users may query the a GO SQL database directly using SQL, or edit one of the already made templates.

**Gannet** is the Solr analog to GOOSE.

You can click here for the  
gene ontology enrichment  
analysis

## Instance information

**Schema details** what fields are recognized by AmiGO 2 on the Solr server.

**Load details** about which files are being used in this instance of AmiGO 2 and when they were loaded.

**OWLTools information** for the bundled version with this instance of AmiGO.

**Yeast** lists the species references currently understood by AmiGO.



UPL14.1 New! PANTHER14.1 is generated from the 2018\_04 release of [ReferenceProteome dataset](#)

Search

All

Quick links

[Whole genome function views](#)

[Genome statistics](#)

[Data Version](#)

[How to cite PANTHER](#)

**NEW!** [Recent publication describing PANTHER](#)

News

PANTHER 14.1 Released

[Click for additional info.](#)

Newsletter subscription

Enter your Email:



Gene List Analysis      Browse      Sequence Search      cSNP Scoring      Keyword Search

Please refer to our article in [Nature Protocols](#) for detailed instructions on how to use this page.

*Error parsing request, no input specified*

**Help Tips**

**Steps:**

1. Enter ids and or select file for batch upload. Else enter ids or select file or list from workspace for comparing to a reference list.

Enter IDs: **Supported IDs**

Upload IDs: **File format**

Choose File **no file selected**

Please [login](#) to be able to select lists from your workspace.

Select List Type:

ID List  
 Previously exported text search results  
 Workspace list  
 PANTHER Generic Mapping  
 ID's from Reference Proteome Genome

Organism for id list: **Absidia glauca (ABSGL)**

VCF File      Flanking region: **20 Kb**

2. Select organism.

Homo sapiens  
Mus musculus  
Rattus norvegicus  
Gallus gallus  
Danio rerio

3. Select Analysis.

Functional classification viewed in gene list  
 Functional classification viewed in graphic charts  
 Statistical overrepresentation test  
 Statistical enrichment test

Bar chart  
 Pie chart  
 Use default settings  
 Use default settings

Paste your gene list or upload your file

Choose the species

Choose the analysis type

UPL14.1 New! PANTHER14.1 is generated from the 2018\_04 release of [ReferenceProteome dataset](#)

 PANTHER BAR CHART  
[Pie Chart](#) [Export](#)

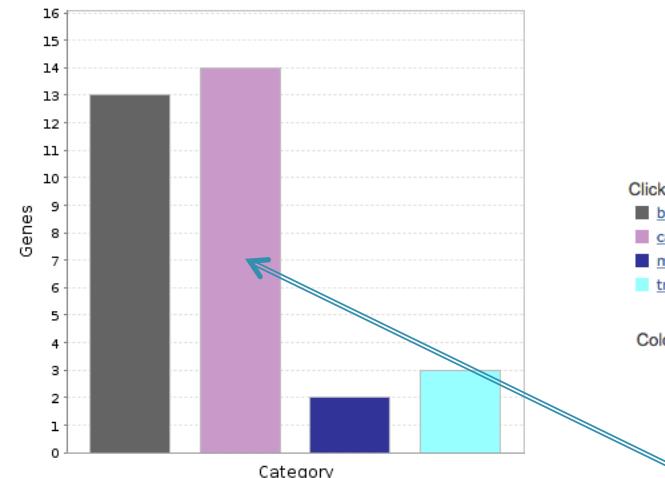
## Features:

- Mouse-over bar chart category to see category name and statistics
- Click on a bar chart category to drill down to child categories
- Click on chart legend link to retrieve gene list for each category
- Click on a color key in chart legend to choose your favorite color for the category **NEW!**

Select Ontology:  View: 

## PANTHER GO-Slim Molecular Function

Total # Genes: 22 Total # function hits: 32



Click to get gene list for a category:

- [binding \(GO:0005488\)](#)
- [catalytic activity \(GO:0003824\)](#)
- [molecular function regulator \(GO:0098772\)](#)
- [translation regulator activity \(GO:0045182\)](#)

Color picker powered by  Web Colors by ViziBone

\*\*Chart tooltips are read as: Category name (Accession # genes) in percent  
against total # genes; Percent of gene hit against total # Function hits

Click on the bar to see more specific terms

# Fungi Databases

Eupath DB

FungiDB

YeastMine

Select gene ids and paste your gene list than  
Get Answer

You will get a list of the Gene Id; organism;  
transcript IDs; location etc.

You can

Add Step

Transform to pathway

# Find Orthologous

Go to

<https://yeastmine.yeastgenome.org/yeastmine/begin.do>

## **Homolog**

A gene related to a second gene by descent from a common ancestral DNA sequence. The term, homolog, may apply to the relationship between genes separated by the event of speciation (see Ortholog) or to the relationship between genes separated by the event of genetic duplication.

## **Ortholog**

Orthologs are genes in different species that evolved from a common ancestral gene by speciation. Normally, orthologs retain the same function in the course of evolution. Identification of orthologs is critical for reliable prediction of gene function in newly sequenced genomes.

## **Paralog**

Paralogs are genes related by duplication within a genome. Orthologs retain the same function in the course of evolution, whereas paralogs evolve new functions, even if these are related to the original one.

# STEPS 1

1. Search for genes and organism  
*Cryptococcus neoformans* var. *grubii* H99
2. Paste the list of the all *Cryptococcus*  
*neoformans* var. *grubii* H99 and **RUN**
3. You will find genes that are present in the  
database
4. Than do save list a new page will open

## STEPS 2

5. Than under Orthologous click S.cerevisiae and you will get a list of orthologous
6. Than under Orthologous you can click on human or mouse orthologous of S.cerevisiae
7. Than you can use that list for search Gene Ontology or other human or mouse databases.

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# Thank you

Any questions contact me:  
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