

# Introduction to the Gene Ontology

Midori A. Harris EBI & GO Consortium EMBRACE Workshop — Applied Gene Ontology 7–9 November 2007

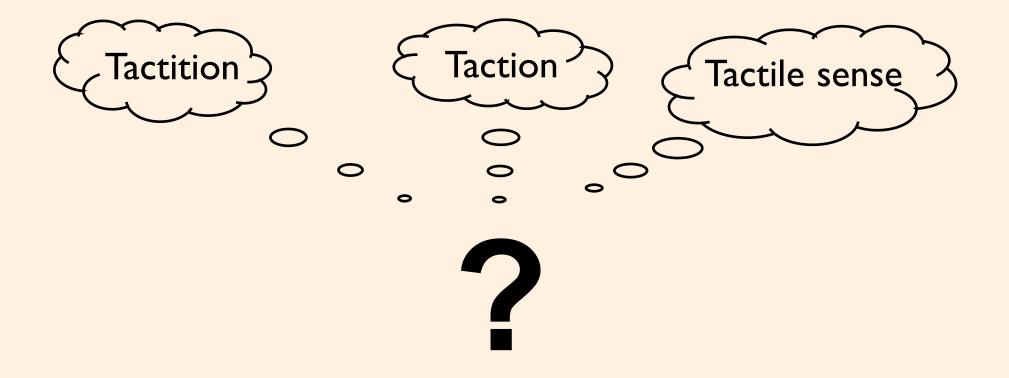


### Reasons for GO

- The problem: how to
  - ... communicate
  - … represent biological knowledge in databases
  - ... query databases find useful answers to biological questions like
    - What does the gene product do?
    - Where and when does it act?
    - Why does it perform these activities?



People call the same thing by different names





### A Common Vocabulary:

GO uses one term and many characterized synonyms





### GO project aims

- Compile structured vocabularies describing aspects of molecular biology
- Describe gene products using vocabulary terms (annotation)
- Provide public resource of data and tools:
  - to query and modify the vocabularies and annotations
  - annotation tools for curators

## GO Scope: 3 domains

- Molecular Function elemental activity or task
  - nuclease, DNA binding, transcription factor
- Biological Process broad objective or goal
   *mitosis, signal transduction, metabolism*
- Cellular Component location or complex
  - nucleus, ribosome, origin recognition complex
- \* 'Normal' functions and processes only:
  - No pathological processes
  - No experimental conditions



```
[Term]
id: GO:0046423
name: allene-oxide cyclase activity
namespace: molecular function
def: "Catalysis of the reaction: (9Z)-(13S)-12,13-
epoxyoctadeca-9, 11, 15-trienoate = (15Z)-12-
oxophyto-10,15-dienoate." [EC:5.3.99.6]
synonym: "(9Z)-(13S)-12,13-epoxyoctadeca-9,11,15-
trienoate isomerase (cyclizing)" EXACT [EC:5.3.99.6]
xref: EC:5.3.99.6
xref: MetaCyc:ALLENE-OXIDE-CYCLASE-RXN
is a: GO:0009975 ! cyclase activity
is a: GO:0016860 ! intramolecular oxidoreductase
activity
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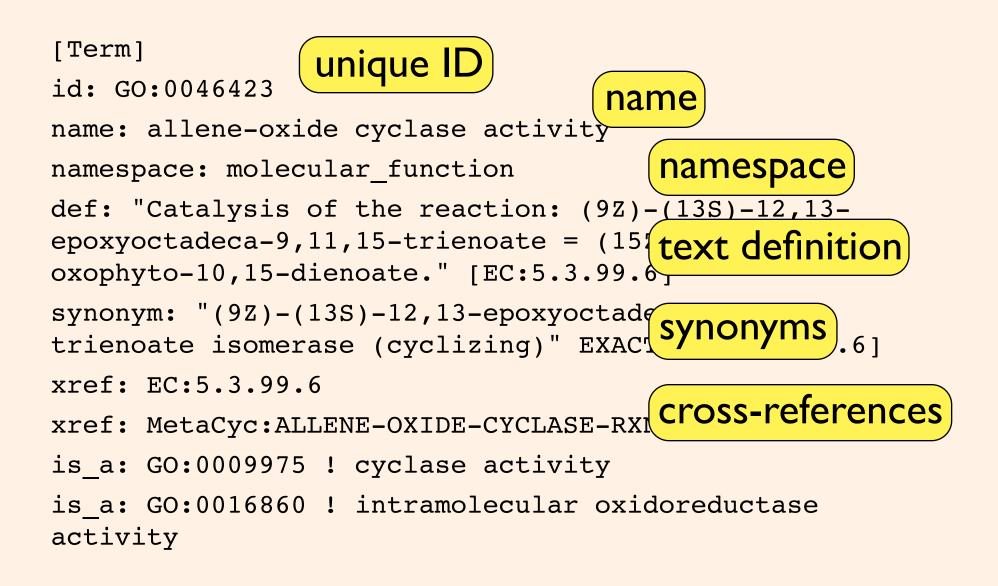
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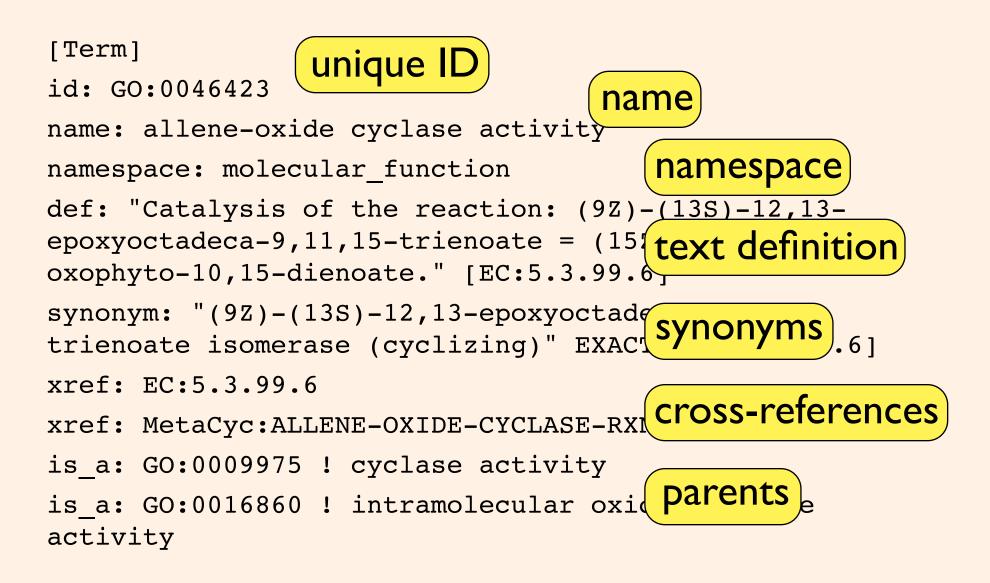
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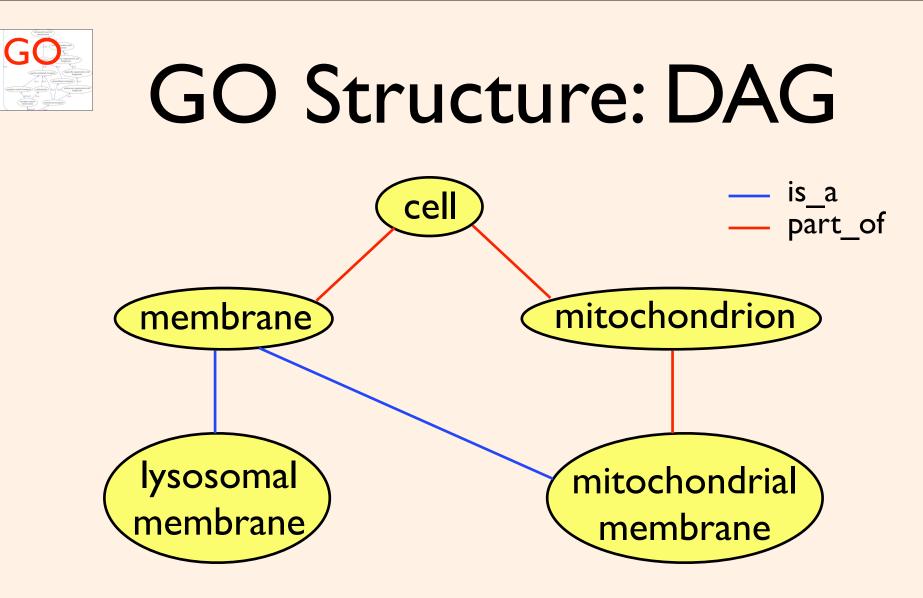


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GO is a directed acyclic graph (DAG): a term can have one or more parent(s)

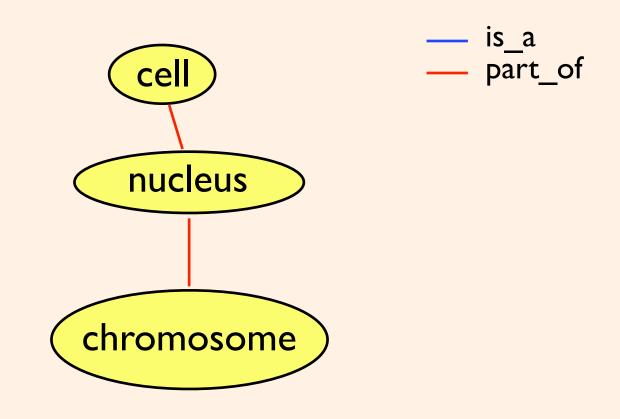


### GO relationships

- now in use:
  - is\_a subclass; a is a type of b
  - part\_of
    - physical part of (component)
    - subprocess of (process)
- to be added:
  - regulates



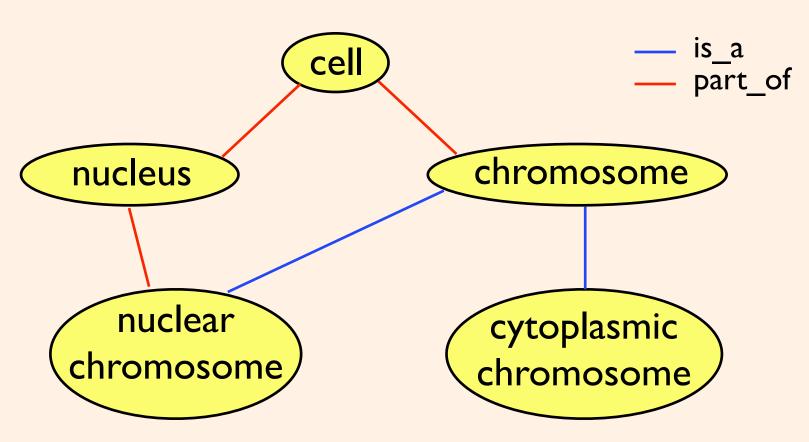
### True Path Rule



But what about bacteria??

### True Path Rule

GC



Resolved structure (some terms omitted for clarity)

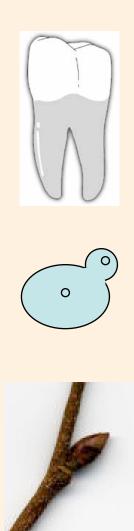


### Ontology Rules (examples)

- Univocity
  - A term (or relationship) should mean the same thing every time it's used
- Positivity
  - Complements of classes are not themselves classes; i.e., terms such as 'non-mammal' or 'nonmembrane' do not designate genuine classes
- Objectivity
  - Which classes exist does not depend on our biological knowledge; terms such as 'unknown', 'unclassified' or 'unlocalized' are thus unsuitable



People use the same words to describe different things

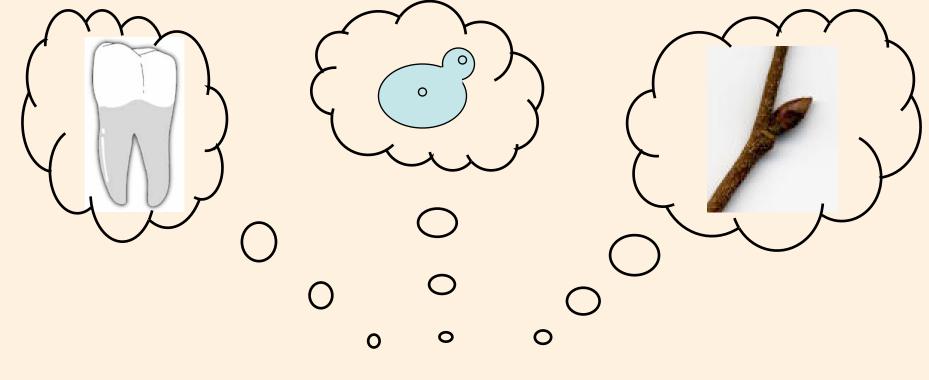


= bud initiation

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Bud initiation? How is a computer to know?

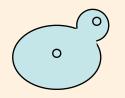


### Univocity:

#### GO adds descriptors to discriminate among organisms



= tooth bud initiation



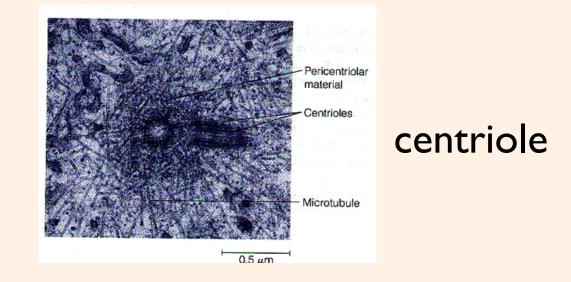
= cellular bud initiation



= leaf bud initiation

note: hypothetical examples

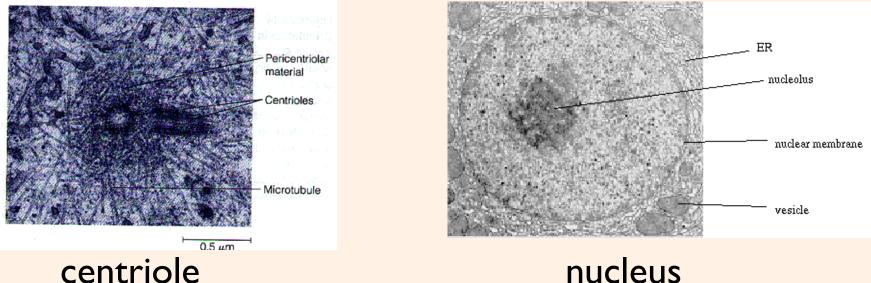




- Some organelles are membrane-bound.
- A centrosome is not a membrane bound organelle, but it still may be considered an organelle.



#### Sometimes absence is a distinction in a biologist's mind



#### nucleus

#### non-membrane-bound organelle GO:0043228

#### membrane-bound organelle GO:0043227



Sometimes absence is a distinction in a biologist's mind

Note the logical difference between "non-membrane-bound organelle" and "not a membrane-bound organelle"

nor orga The latter includes everything that is not a membrane bound organelle!

rane

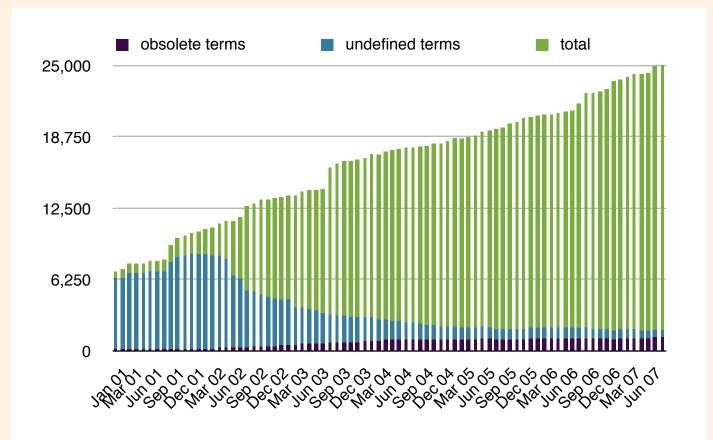
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ER



### GO Term History

#### Jan. 2001–August 2007





### Why GO Changes

- Advances in biology
- New groups join, requiring new terms or different relationships between terms
- Update legacy terms
- Improve logical consistency



### What kinds of changes?

#### Small or large scale

Biological or logical/structural motivation



### Small-scale Changes

- Individuals (e.g. annotators) request changes
  - Usually one or a few things at a time
  - New terms
  - Path corrections/additions
  - Improved definitions
- Closely coordinated with annotation



### Large-scale Changes

- Improve ontology for a biological topic all at once
  - Motivation: improve usefulness for biologists, especially annotators
  - Usually connected with content meeting
  - Expert biologists involved
- Apply a logical/structural improvement to entire ontology at once
  - Motivation: improve consistency; enhance "computability"
  - Software developers involved



### Applications of GO

- Gene product annotation
  - model organism databases
  - genome sequence analysis
- Expression data analysis
- Text mining
- More ...



- What is GO annotation?
  - An annotation is a statement that a gene product ...
    - ... has a particular molecular function
    - ... is involved in a particular biological process
    - ... is located within a certain cellular component
  - ... as determined by a particular method
  - ... as described in a particular reference



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gene

product

terms

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reference

gene

product

terms



- GO provides source vocabularies for text mining and NLP
- Text mining may be able to help GO annotators



 GO provides source vocabularies for text mining and NLP

### Text mining may be able to help GO annotators

The Journal of Biological Chemistry  $\otimes$  2003 by The American Society for Biochemistry and Molecular Biology, Inc.

Vol. 278, No. 10, Issue of March 7, pp. 8487–8493, 2003 Printed in U.S.A.

#### High Conservation of the Set1/Rad6 Axis of Histone 3 Lysine 4 Methylation in Budding and Fission Yeasts\*

Received for publication, September 18, 2002, and in revised form, December 17, 2002 Published, JBC Papers in Press, December 17, 2002, DOI 10.1074/jbc.M209562200

#### Assen Roguev‡§, Daniel Schaft‡§, Anna Shevchenko¶, Rein Aasland||\*\*, Andrej Shevchenko¶, and A. Francis Stewart‡ ‡‡

From *‡BIOTEC*, Technische Universitaet Dresden, c/o Max Planck Institute for Molecular Cell Biology and Genetics and the ¶Max Planck Institute for Molecular Cell Biology and Genetics, Pfotenhauerstrasse 108, D-01307 Dresden, Germany and the *¶Department of Molecular Biology*, University of Bergen, Thromoehlenstrasse 55, N-5020 Bergen, Norway

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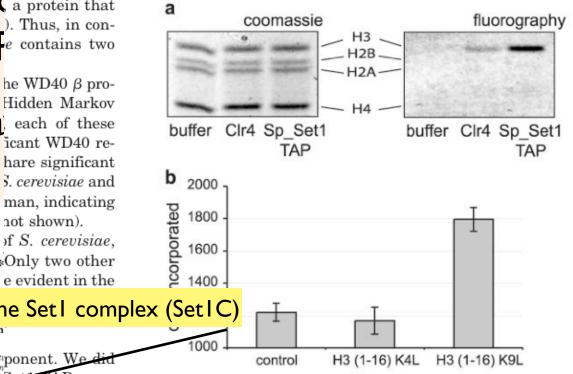
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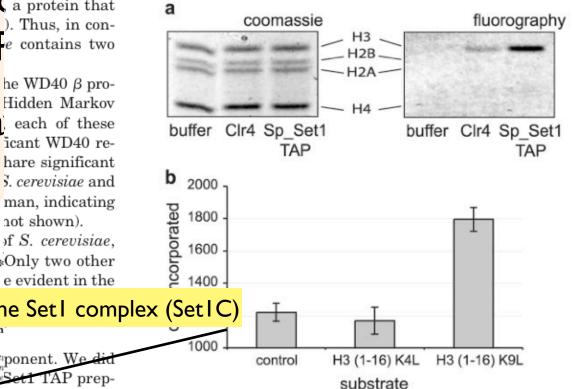
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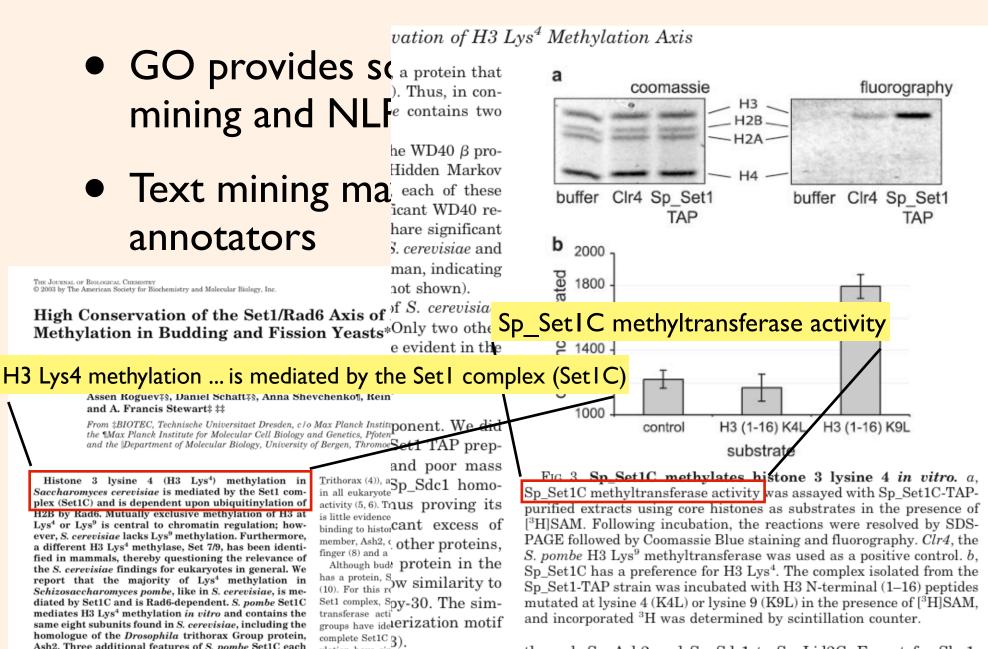
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# GO & gene expression

A	Section of the sectio	AD ST ST	* ( <sup>9</sup> )	В	Supervision of the second		
	Contraction of the second	An In Contraction of the second	S C C		Suppose of the solution of the	and the second	
IBA & LT			Fatty acid-binding protein, liver	IBA & LT			procerboxylate transporter 2 itty acid-binding protein, liver
			Peroxisomal carnitine octanoy/transferase Adipophilin (Adipose differentiation-related				doplasmin precursor
IBA			Acyl-coenzyme A cxidase 1, percxisomal	protein) IBA			D104
1			Putative RNA-binding protein 3				N29 gene product
			Fatty acid-binding protein, liver				JTR in Human DNA sequence from clone RP1-155G6
LT			ELOVL family member 6, elongation of ion	g chain fatty acids LT			CFZP564/C2062 protein
	the second s		Apolipoprotein C-II precursor	L1	and the second se		cuolar protein sorting 338
			Alpha-2-macroglobulin precursor				tative acid phosphatase F29C11.1 romosome 13 open reading frame 11; B230339H12Rik
			Hemopexin precursor (Beta-18-glycoprote				rosyl-DNA phosphotlesterase 1
			UDP-glucuronosyltransforase 2B15 pro	cursor			JTR in Homo sapiens FACLS mRNA for fatty acid openzyme A
			Hypothetical protein MOC54289				crosomal glutathione S-transferase 1
			Glutathione S-transferase alpha 1 Aldo-keto reductase family 1 member C3			Ā	ginane 1
			Argininosuccinate synthese				dehydrogenase family 7 member A1
			Carbamoyi-phosphate synthese		8.41		JTR in Homo sepiene, Similar to catalase
			Carbemoyi-phosphale synthese				ubsmoyl-phosphele synthese
		10.0	Catalase			Tr	yptophen 2,3-dioxygenase
			Aldehyde dehydrogenase 1A1				tochondriai 60S ribosomal protein L3
			Selenoprotein P precursor				asma retinol-binding protein precursor
			Carbamoyi-phosphate synthese				IP synthese a chain
			Cytochrome P450 2C21				collepoprotein C-III precursor
			Plasma retinol-binding protein precurse	*			ansthyretin precursor
			3'UTR in Homo aspiens SLC25A15 gene				snapecific lipid-transfer protein
			Cytochrome P450 2C10				systemylate-binding protein-interacting protein 2
1			Hypothetical protein ycbX	IBA & LT			pothetical protein MGC54289
			Phenylalanina-4-hydroxylase	IDA G EI			tochrome P450 1A2
			Gamma-glutamyl hydrolase precursor				OP-glucuronosyltransferase 2815 precursor
			Microsomal glutathione S-transforase 1				ulnone oxidoreductase yi-CoA dehydrogenase, shori/branched chain specific
IBA & LT			multiple coegulation factor deficiency 2				yi-Cox denyorogenase, anorionancheo chain apeciac IP synthese gamma chain
			Cytochrome P450 1A2				obable oxidoreductase ephD
			ARL-6 interacting protein-1				acylgiycerol cholinephosphotraneferase
			UDP-glucose 6-dehydrogenase Sodium/bile sold cotransporter				JTR in Homo septens C1ort22 mRNA
		100	Dial homolog subfamily B member 9				tenyialanine 4-hydroxylase
			Glutathione S-transferase Yc-1				4 methyl sterol oxidase
			ETS-related transcription factor EIf-1				giopoletin-related protein 3 precursor
	and the second se		Conserved oligometric Golgi complex comp	coart 6			dium/bile acid cotransporter
			Cytochrome P450 51A1			0	tochrome c oxidase polypeptide III
			Aryl hydrocarbon receptor precursor			A	gininosuccinate synthese
			Tryptophen 2,3-dioxygenase				tochrome P450 2C10
			Cysteine suffnic acid decarboxylase	-			S ribosomal protein S3a
			HMG-box transcription factor 1			Pr	envicysteine coldase precursor

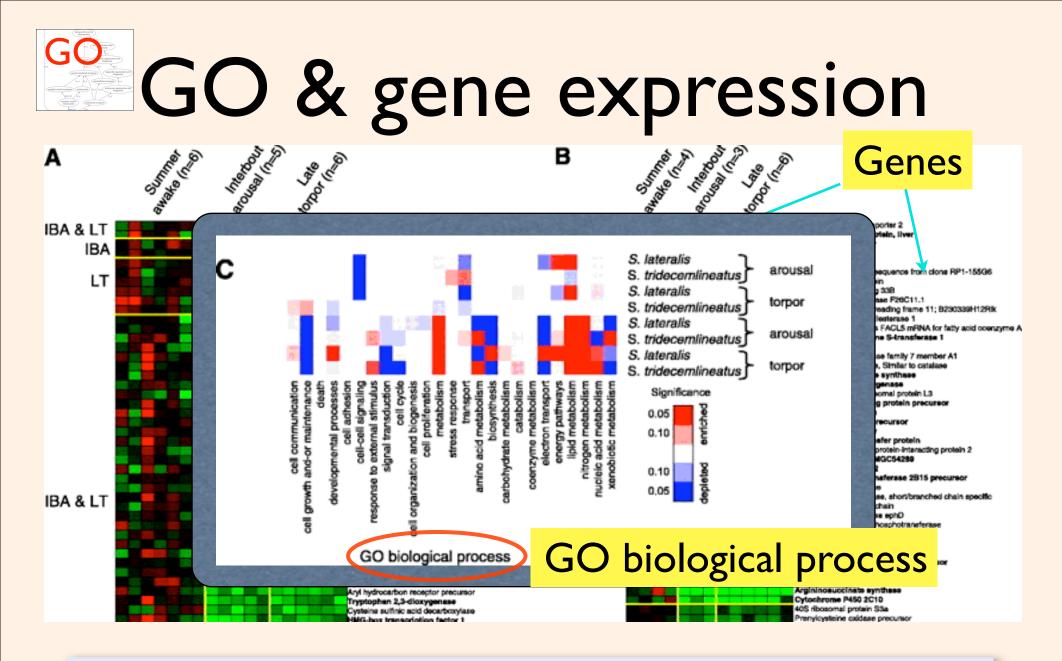
# GO & gene expression

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104 4 1 7	S man	10 <sup>01</sup>	Fatty acid-binding protein, liver		the store of the	Monocarboxy/kile transporter 2
IBA & LT			Peroxisomal carnitine octanoy@raneferase	IBA & LT	Contraction of the local division of the loc	Fetty sold-binding protein, liver
IBA			Adpophilin (Adpose differentiation-related protein) Acyl-coenzyme A cicidase 1, perceisomal	IBA	the second se	Endoplasmin precursor FAD104
			Putative RNA-binding protein 3 Fatty ackt-binding protein, liver			FLN29 gene product 3/UTR in Human DNA sequence from clone RP1-155G6
LT			ELOVL family member 6, elongation of long chain fa	<sup>my ackia</sup> LT		DKFZP564K2062 protein
			Apolipoprotein C-II precursor	LI		Vacuolar protein sorting 33B
			Alpha-2-macroglobulin precursor			Putative acid phosphatase F26C11.1 chromosome 13 open reading frame 11; B290339H12Rik
			Hemopexin precursor (Beta-18-glycoprotein) UDP-glucuronosyttransferase 2815 precursor			Tyrosyl-DNA phosphotlesterane 1
			Hypothetical protein MOC54289			3'UTR in Homo sapiens FACL5 mRNA for fatty acid openzyme A
			Glutathione S-transferase alpha 1			Microsomal glutathione S-transferase 1
			Aldo-keto reductase family 1 member C3			Arginase 1
			Argininosuccinate synthese			Aldehyde dehydrogensse family 7 member A1
			Carbamoyi-phosphate synthese			SUTR in Homo septene, Similar to catalase
			Carbamoyi-phosphate synthese			Carbamoyi-phosphale synthase Tryptophen 2,3-dioxygenase
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			Selenoprotein P precursor			Plasma retinol-binding protein precursor
			Carbamoyi-phosphate synthese			ATP synthese a chain
			Cytochrome P450 2C21			Apolipoprotein C-III precursor
			Plasma retinol-binding protein precursor			Transitiynetin precursor
			3/UTR in Homo sapiens SLC25A15 gene			Nonspecific lipid-transfer protein Polyadenylate-binding protein-interacting protein 2
			Cytochrome P450 2C10			hypothetical protein MGC54289
			Phenylalanina-4-hydroxylase	IBA & LT		Cytochrome P450 1A2
			Gamma-glutamy hydrolase precursor			UDP-glucuronosyltransferase 2815 precursor
			Microsomal glutathione S-transferase 1			Quinone oxidoreductase
IBA & LT			multiple coegulation factor deficiency 2			Acyl-CoA dehydrogenase, short/branched chain specific
			Cytochrome P450 1A2			ATP synthese gamma chain
			ARL-6 interacting protein-1			Probable oxidoreductase ephD Discylg/ycerol cholinephosphotransferase
			UDP-glucose 6-dehydrogenese			3UTR In Homo septens C1ort22 mRNA
			Sodiumbile sold cotransporter Dna.) homolog subtamily B member 9			Phonylalanino-4-hydroxylase
			Glutathione S-transferase Yo-1			C-4 methyl storol oxidase
			ETS-related transcription factor EIf-1			Anglopoletin-related protein 3 precursor
	Contraction of the local division of the loc		Conserved oligomeric Golgi complex component 6			Sodium/bile acid cotransporter
			Cytochrome P450 51A1			Cytochrome c oxidane polypeptide II
		100 Million 100	Aryl hydrocarbon receptor precursor			Argininosuccinate synthese Cytochrome P450 2C10
			Tryptophen 2,3-dioxygenase			40S ribosomal protein S3a
			Cysteine suffric acid decarboxylase			Prenyloyateine oxidaae precumor

# GO & gene expression

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	and the second se			roxisomal carnitine octanoytransferase spophilin (Adipose differentiation-related protein)			Endoplasmin procursor
IBA		State of the local division of the local div	Ac	syl-coenzyme A oxidase 1, percolsomal	IBA		FAD104
				tative RNA-binding protein 3			FLN29 gene product
LT				itty sold-binding protein, liver			SUTR in Human DNA sequence from clone RP1-15536 DKFZP564K2052 protein
L1				OVL family member 6, elongation of long chain fatty a polycorotein C-II precursor	ut LT		Vacuolar protein sorting 33B
				pha-2-macroglobulin precursor			Putative acid phosphatase F29C11.1
				mopexin precursor (Beta-1B-ptycoprotein)			chromosome 13 open reading frame 11; 8230339H12Rik
			U	DP-glucuronosyltransferase 2815 productor			Tyrosyl-DNA phosphodiesterase 1
				pothetical protein MOC54289			3'UTR in Homo sapiens FACL5 mRNA for fatty acid ocenzyme A
				utathione S-transferase alpha 1			Microsomal glutathione S-transferase 1 Arginase 1
				do-keto reductase family 1 member C3 gininosuccinate synthese			Aldehyde dehydrogensae family 7 member A1
				stamoyi-phosphate synthese		E41	S'UTR in Homo sepiene, Similar to catalase
				stamoyi-phosphale synthese			Carbamoyi-phosphate synthese
			C	stalase			Tryptophen 2,3-dioxygenase
				dehyde dehydrogenase 1A1			Mitochondrial 80S ribosomal protein L3
				elenoprotein P precursor			Plasma retinol-binding protein precursor ATP synthese a chain
			2	arbamoyi-phosphate synthese			A P synthese a chain Apolipoprotein C-III precursor
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				UTR in Homo aspiens SLC25A15 pene			Nonapecific lipid-transfer protein
				tochrome P450 2C10			Polyadenylate-binding protein-interacting protein 2
				pothetical protein yobX	IBA & LT		hypothetical protein MGC54289
				enyisisnine 4-hydroxylase			Cytochrome P450 1A2
			3	amma-glutamyl hydrolase precursor			UDP-glucuronosyttransferase 2815 precursor Quinone oxidomductase
				crosomal glutathione S-transferase 1			Acyl-CoA dehydrogenase, short/branched chain specific
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				U-6 interacting protein-1			Probable oxidoreductase ephD
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				had homolog subfamily B member 9			Phenylaianine-4-hydroxylase
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				onserved oligomeric Golgi complex component 6 tochrome P450 51A1			Cytochrome c oxidase polypeptide II
				y hydrocarbon receptor precursor			Argininosuccinate synthese
				yptophen 2,3-dioxygenase			Cytochrome P450 2C10
			0	steine suffnic acid decarboxylase			40S ribosomal protein S3a
				G-box transcription factor 1			Prenylcysteine cxidase precursor







# **GO** Tools

- Database (and schema)
- Perl API
- Browsers, e.g. AmiGO
- Editing tool: OBO-Edit
- Tool collection:
  - Microarray analysis tools
  - Annotation tools
  - others ...

http://www.geneontology.org/GO.tools.shtml

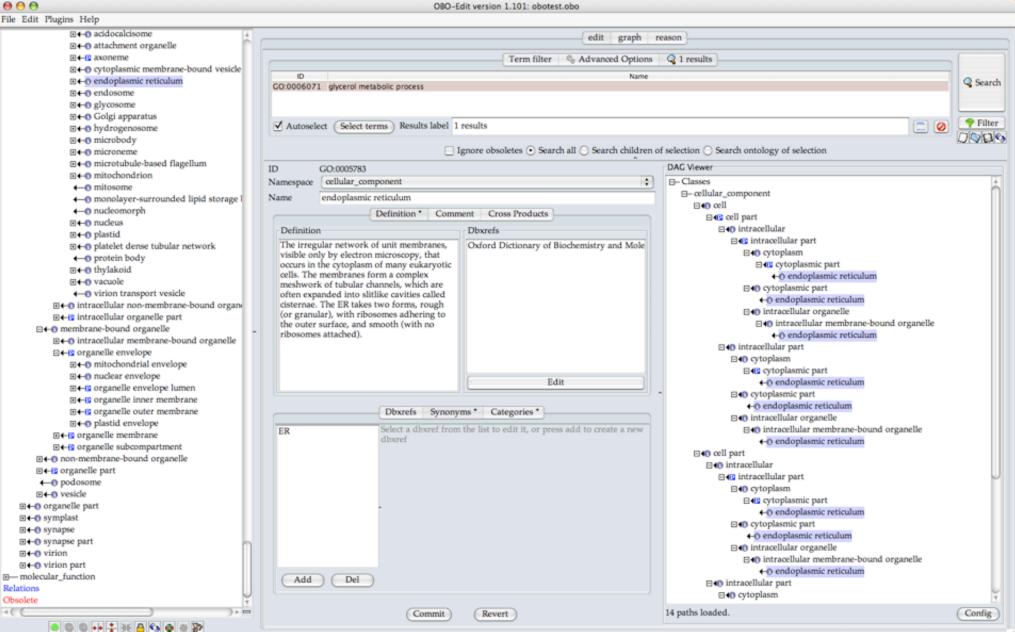
### GO Tools page

GO

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search gol gene or protein name :						
Close menus						
Home	Gene Ontology Tools					
Downloads						
Ontologies						
Annotations	Consortium Tools					
Database	Non-Consortium Tools					
Mappings to GO						
Teaching Resources	Кеу					
Monthly Reports						
GO Tools						
Browsers	web-based tool downloadable tool compatible OSs					
Microarray tools	(for downloadable tools)					
Annotation tools	Conceptions Table					
Other tools	Consortium Tools					
Submit New Tools	mit New Tools The tools below are developed within the Gene Ontology Consortium. They continue to be improve					
Documentation	expanded and you can receive support in using these tools by writing to the GO mailing list.					
FAQ						
Introduction	The tools on this page are free to academics.					
	AmiGO AmiGO					
Evidence Code Guide						
File Format Guide Berkeley Drosophila Genome Project						
Editorial Style Guide						
Component Ontology	AmiGO allows you to search for a GO term and view all gene products annotated to it, or search for a					
	gene product and view all its associations. You can also browse the ontologies to view relationships					
Process Ontology	between terms as well as the number of gene products annotated to a given term. AmiGO accesses the					
GO Slim Guide	GO mySQL database (see below); the browser and documentation are available from					
Meeting minutes About GO	http://www.godatabase.org/dev/.					
GO Consortium						
Publications	AmiGO uses the GO database, which is updated monthly.					
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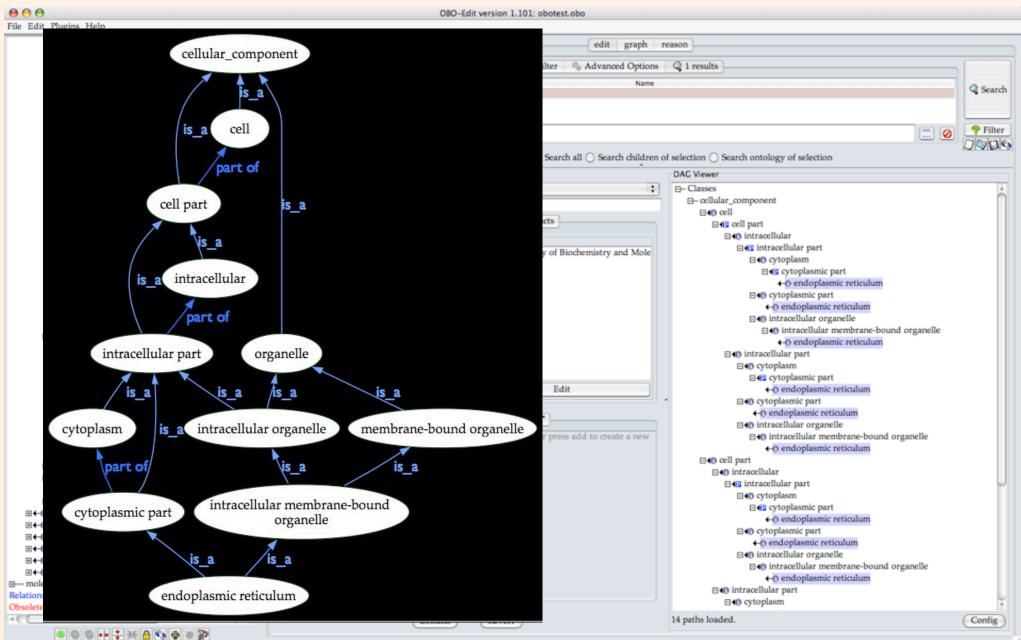


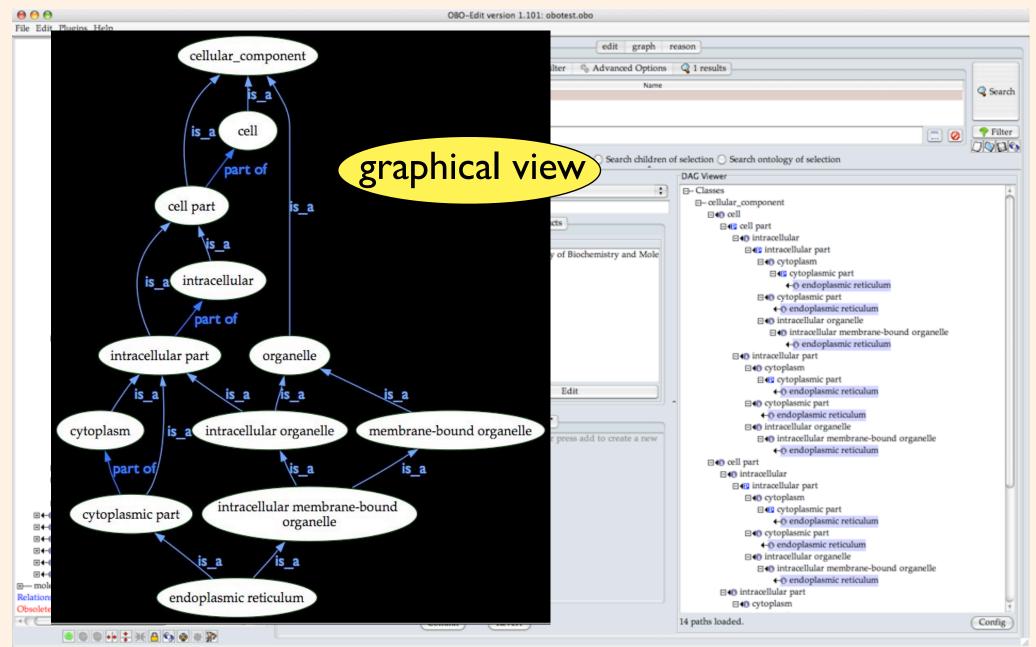
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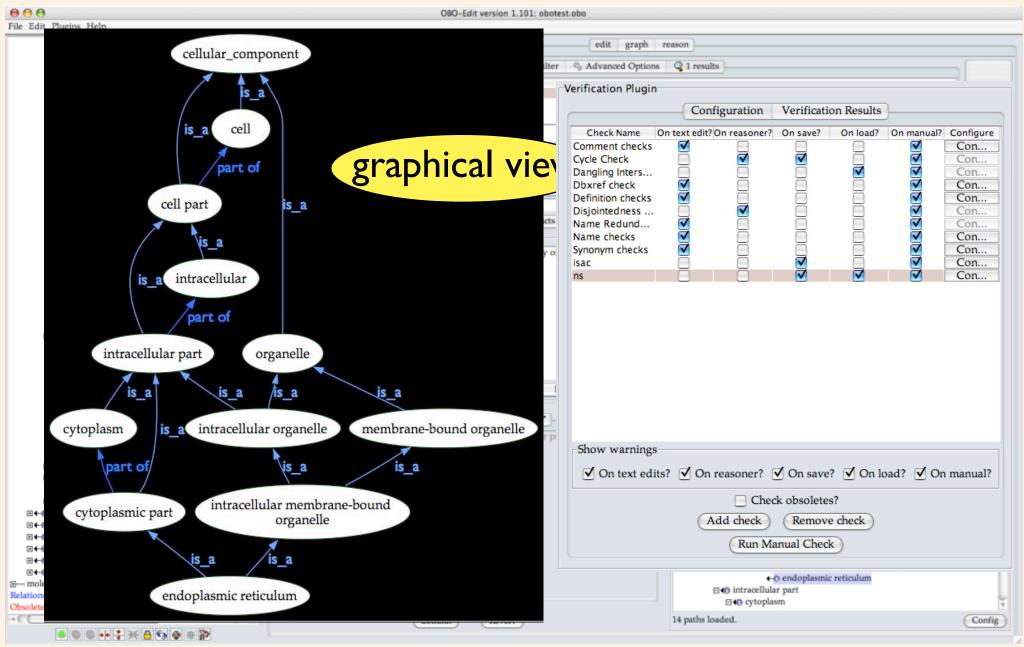
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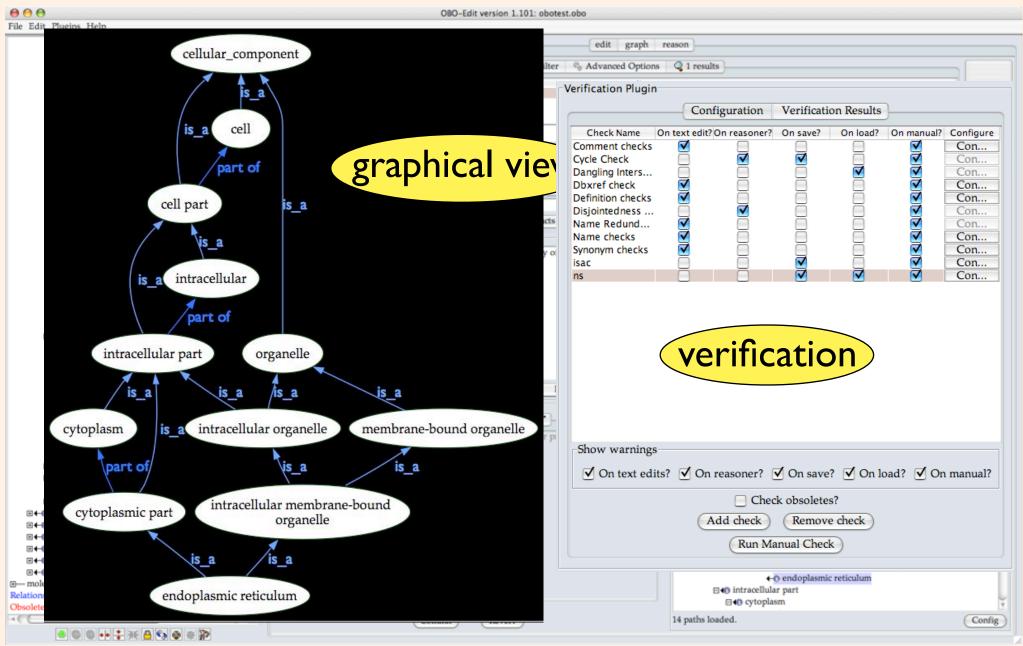










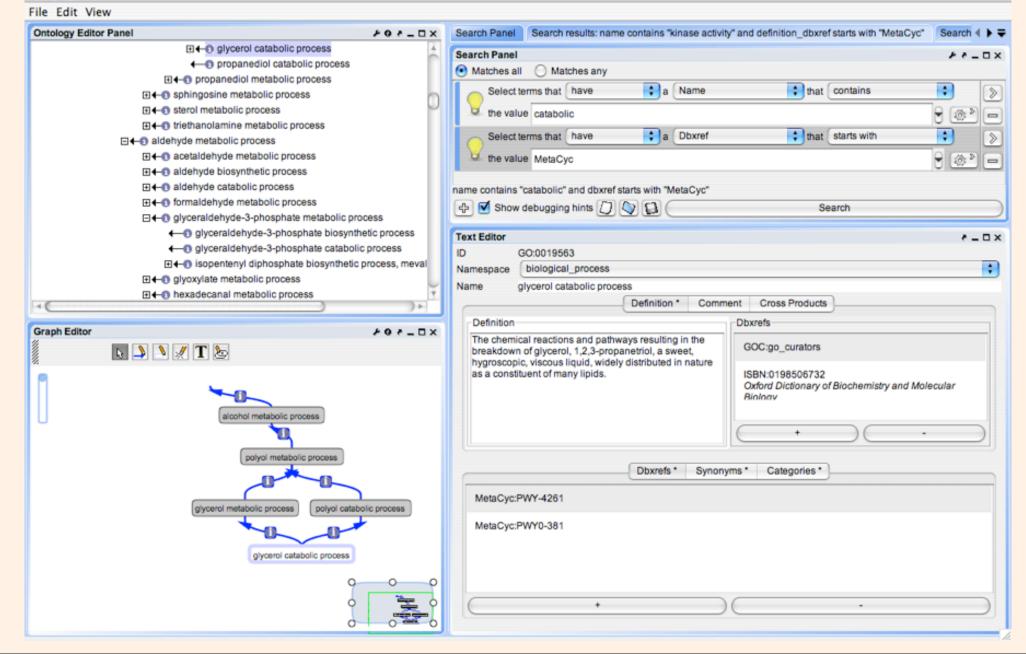




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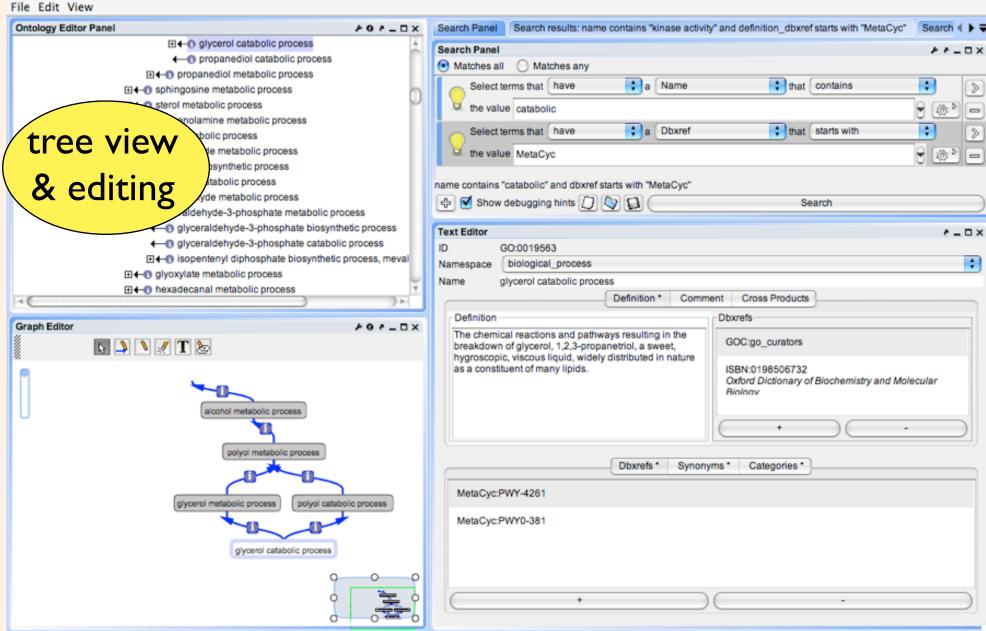
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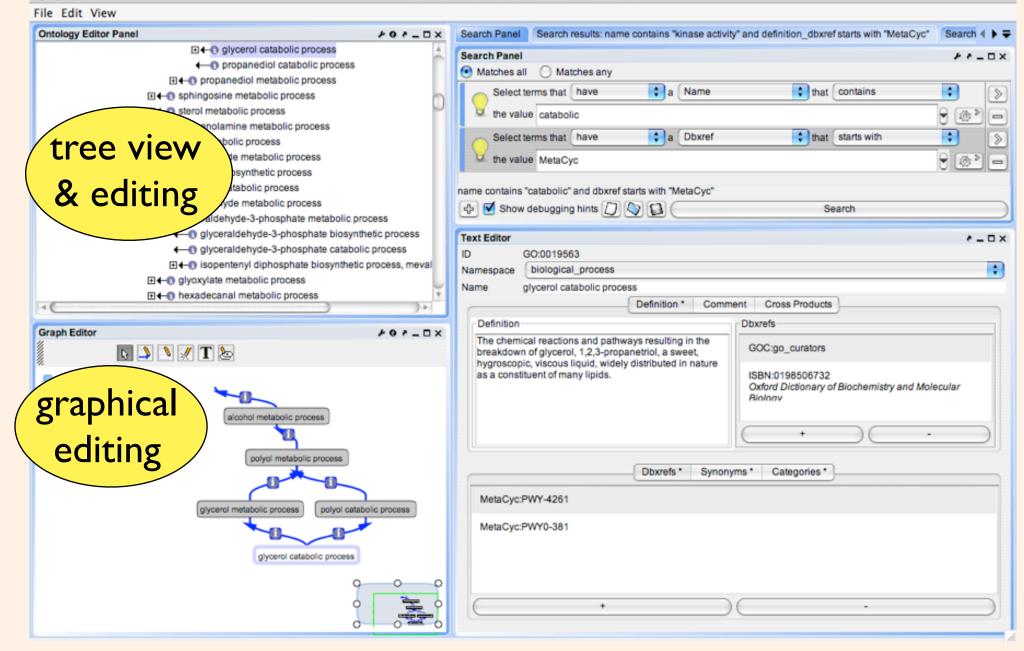
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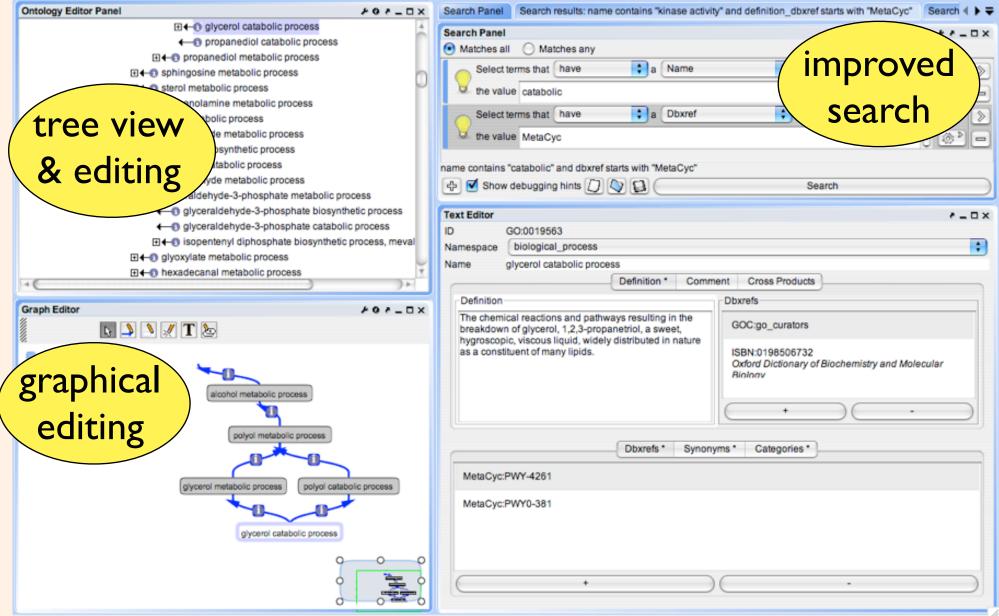


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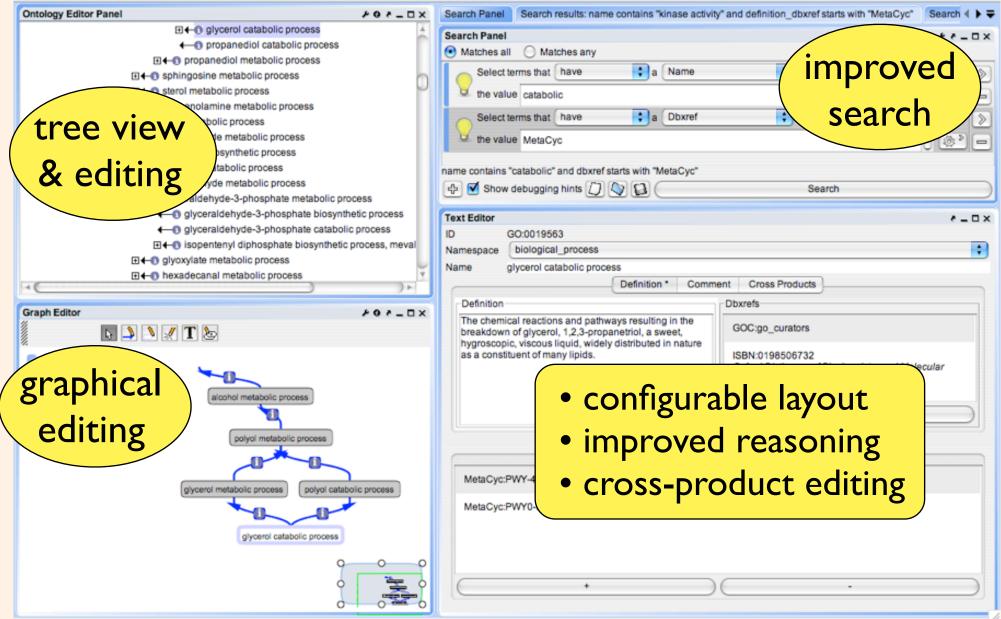
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#### AmiGO

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Accession	GO:0006114				
Ontology	biological process				
Synonyms	exact: glycerol anabolism exact: glycerol biosynthesis exact: glycerol formation exact: glycerol synthesis				
Definition	The chemical reactions and pathways resulting in the formation of glycerol, 1,2,3-propanetriol, a sweet, hygroscopic, viscous liquid, widely distributed in nature as a constituent of many lipids. [source: GOC:ai, ISBN:0198506732]				
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#### AmiGO

GO

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Term Info	ormation	
Accession	GO:0006114	GO:0046173 : polyol biosynthetic process [11]
Ontology	biological process	GO:0006114 : glycerol biosynthetic process [8]
Synonyms	exact: glycerol anabolism exact: glycerol biosynthesis exact: glycerol formation exact: glycerol synthesis	<ul> <li>              GO:0019751 : polyol metabolic process [155]      </li> <li>             GO:0006071 : glycerol metabolic process [122]         </li> <li>             GO:0006114 : glycerol biosynthetic process [8]      </li> </ul>
Definition	The chemical reactions and pathways resulting	
Comment	viscous liquid, widely distributed in nature a None	<ul> <li>         GO:0006114 : glycerol biosynthetic process [8]         GO:0044249 : cellular biosynthetic process [12620]         GO:0046165 : alcohol biosynthetic process [300]         </li> </ul>
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#### AmiGO

GO

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	glycerol b	<ul> <li>GO:0008150 : biological_process [140556]</li> <li>GO:0009987 : cellular process [71496]</li> <li>GO:0044237 : cellular metabolic process [48331]</li> <li>GO:0006066 : alcohol metabolic process [1827]</li> </ul>
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Definition	The chemical reactions and pathways resultinistic viscous liquid, widely distributed in nature a	∃ GO:0046173 : polyol biosynthetic process [11]
Comment	None	<ul> <li>              GO:0006114 : glycerol biosynthetic process [8]      </li> <li>             GO:0044249 : cellular biosynthetic process [12620]         </li> <li>             GO:0046165 : alcohol biosynthetic process [300]      </li> </ul>
Term Lin		<ul> <li>Image: GO:0040103 : alcohol biosynthetic process [500]</li> <li>Image: GO:0046173 : polyol biosynthetic process [11]</li> <li>Image: GO:0006114 : glycerol biosynthetic process [8]</li> </ul>
Filter Gene Data source All	Product Counts Term View Options	<ul> <li>              ● GO:0008152 : metabolic process [55902]      </li> <li>             ● GO:0009058 : biosynthetic process [15503]         </li> </ul>
CGD dictyBase FlyBase	199411	More about AmiGO later!



# GO and Other Ontologies



#### Ontologies and Experiments

human lung fibroblasts treated with cycloheximide



#### Ontologies and Experiments

human lung fibroblasts treated with cycloheximide



human lung fibroblasts treated with cycloheximide



taxonomy human lung fibroblasts treated with cycloheximide

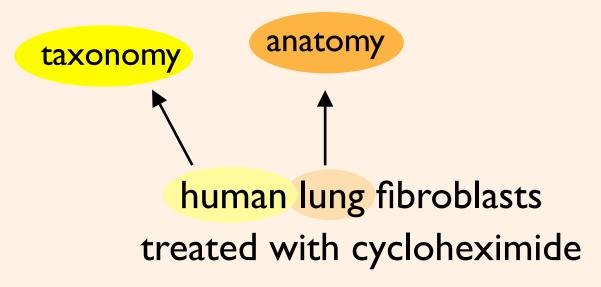


taxonomy human lung fibroblasts treated with cycloheximide

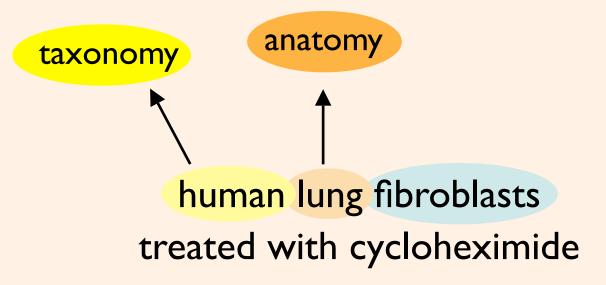


taxonomy human lung fibroblasts treated with cycloheximide

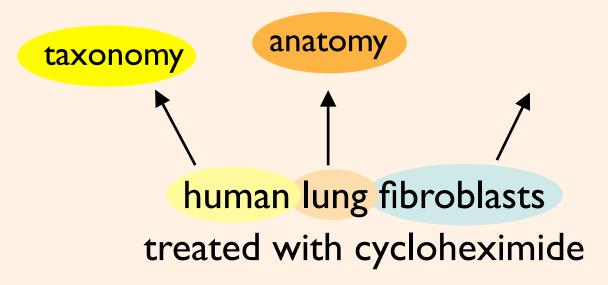




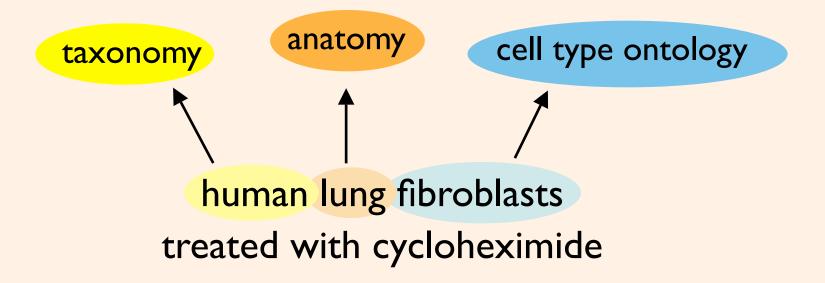




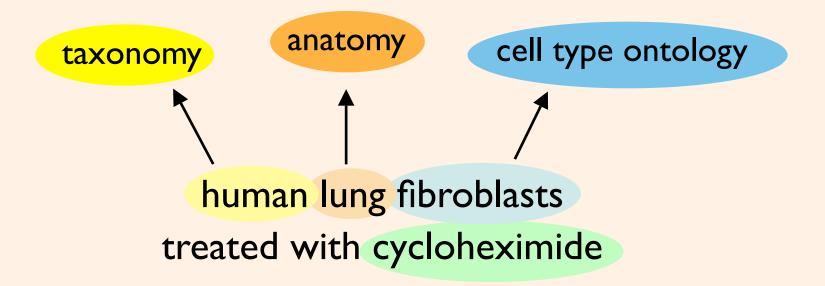




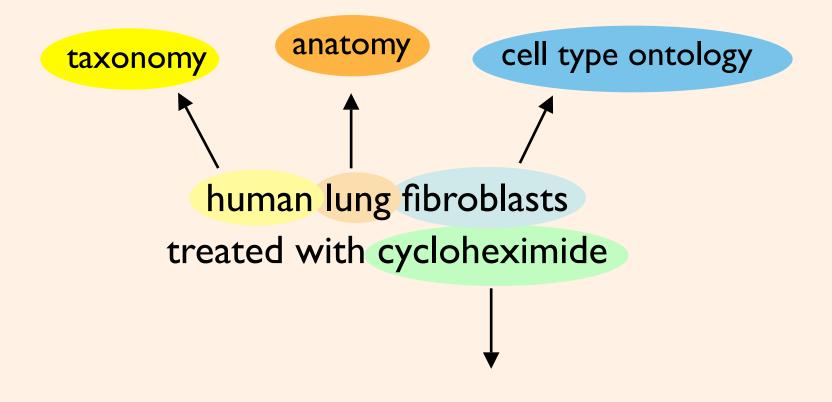




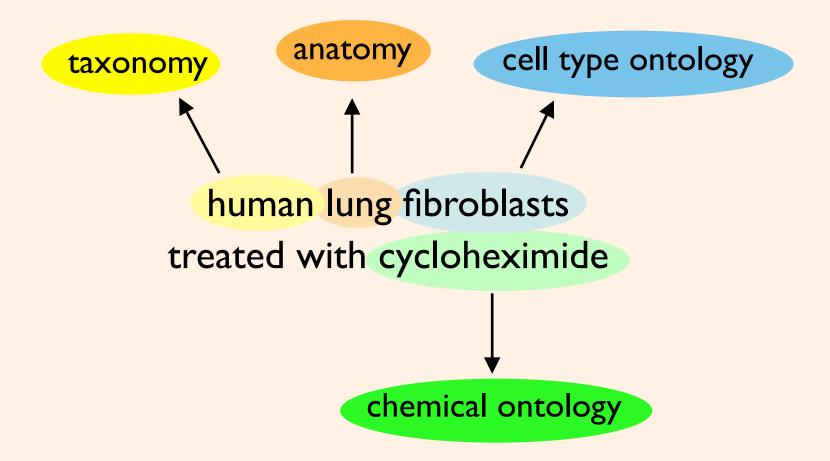














- Open Biomedical Ontologies
  - Collection of shared genomics and proteomics vocabularies
  - Principles:
    - Open source
    - Common syntax (e.g. OWL or OBO)
    - Orthogonal; avoid duplication
    - Share ID space
    - Define terms
    - Involve the community

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Ontologies

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OBO Foundry Ontologies

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## OBO FOUNDRY

Resources

Participate About

#### Welcome to the OBO Foundry Ontologies

Domain	<u>Prefix</u>	Files	<u>Format</u>	Foundry	OBO CVS
Animal natural history and life history	ADW	protege source	Protege	no	no
Biological imaging methods	FBbi	image.obo	<u>OBO</u>	no	yes
Biological process	GO	gene ontology.obo	<u>OBO</u>	yes	yes
BRENDA tissue / enzyme source	вто	BrendaTissue.obo	<u>OBO</u>	no	yes
C. elegans development	WBIs	worm development.obo	<u>OBO</u>	no	yes
C. elegans gross anatomy	WBbt		<u>OBO</u>	no	no
C. elegans phenotype	WBPhenotype	phenotype ontology obo.cgi	<u>OBO</u>	no	no
Cell type	CL	cell.obo	<u>OBO</u>	yes	yes
Cellular component	GO	gene ontology.obo	<u>OBO</u>	no	yes
Cereal plant development	GRO	cereals development.obo	<u>OBO</u>	no	yes
Cereal plant gross anatomy	GRO	po anatomy.obo	<u>OBO</u>	no	yes
Cereal plant trait	то	plant trait.obo	<u>OBO</u>	no	yes
Chemical entities of biological interest	CHEBI	<u>chebi.obo</u>	<u>OBO</u>	yes	yes
Common Anatomy Reference Ontology	CARO	caro.obo	<u>OBO</u>	yes	yes
Dictyostelium discoideum anatomy	DDANAT	dictyostelium anatomy.obo	<u>OBO</u>	no	yes
Drosophila development	FBdv	fly development.obo	<u>OBO</u>	no	yes
Drosophila gross	FRht	fly anatomy oho	080	00	Vec

## Ontology Lookup Service (OLS) (OBO Foundry term lookup)

**Other Ontology Lists** 

Quick Links

Mappings between ontologies
How to join

BioPortal (term lookup from a comprehensive listing)

\* Download alternate formats

### News

#### 2007/06/21: New OBO Foundry Site

This site contains OBO Foundry ontologies and points to some other related efforts. It also provides discussion fora, technical infrastructure, and other services to facilitate ontology development. Please contribute, we welcome feedback and encourage participation.

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6

Ontologies

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#### Resources Participate

OBO FOUNDRY

### Welcome to the OBO Foundry Ontologies

Domain	Prefix	<u>Files</u>	<u>Format</u>	Foundry	OBO CVS	BioPortal (term lo comprehensive lis
Animal natural history and life history	ADW	protege source		no	no	Foundry term loo
Biological imaging methods	FBbi	image.obo	<u>OBO</u>	no	yes	Quick Links
Biological process	GO	gene ontology.obo	<u>OBO</u>	yes	yes	How to join
BRENDA tissue / enzyme source	вто	BrendaTissue.obo	<u>OBO</u>	no	yes	Download alternate
C. elegans development	WBIs	worm development.obo	<u>OBO</u>	no	yes	News
C. elegans gross anatomy	WBbt		<u>OBO</u>	no	no	2007/06/21: New OBO
C. elegans phenotype	WBPhenotype	phenotype ontology obo.cgi	<u>OBO</u>	no	no	This site contains OBO and points to some oth
Cell type	CL	<u>cell.obo</u>	<u>OBO</u>	yes	yes	provides discussion for infrastructure, and othe
Cellular component	GO	gene ontology.obo	<u>OBO</u>	no	yes	ontology development. welcome feedback and
Cereal plant development	GRO	cereals development.obo	<u>OBO</u>	no	yes	participation.
Cereal plant gross anatomy	GRO	po anatomy.obo	<u>OBO</u>	no	yes	
Cereal plant trait	то	plant trait.obo	<u>OBO</u>	no	yes	
Chemical entities of biological interest	CHEBI	<u>chebi.obo</u>	<u>OBO</u>	yes	yes	
Common Anatomy Reference Ontology	CARO	caro.obo		obo	fou	ndry.org
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Drosophila development	FBdv	fly development.obo	<u>OBO</u>	no	yes	
Drosophila gross	FBht	fly anatomy obo	OBO	20	Vec	

## **Other Ontology Lists**

(term lookup from a ensive listing)

Lookup Service (OLS) (OBO erm lookup)

between ontologies alternate formats

#### lew OBO Foundry Site

ains OBO Foundry ontologies some other related efforts. It also ission fora, technical and other services to facilitate lopment. Please contribute, we back and encourage

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Domain	Prefix	File	Th	OBO Download Matrix         This page is for downloading OBO ontologies in a variety of formats, and for downloading reports from each of the ontologies. The data below is derived automatically from the primary sources, available from the main OBO website. The status of this page is EXPERIMENTAL. See below for caveats.         This page will be retired when the current functionality is subsumed by the BioPortal resource developed by the NCBO         Ontologies         Logical Definitions         Mappings         Format Guide         Metadata         Reports         FTP Archive					
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Biological imaging methods	FBbi	image.obo							
Biological process	GO	gene ontology.							
BRENDA tissue / enzyme source	вто	BrendaTissue.c	Fo						
C. elegans development	WBIs	worm developn	FT						
C. elegans gross anatomy	WBbt			atistics					
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Cereal plant trait	то	plant trait.obo				obo_xml[19969 kb] obo[6909 kb] o	bo xml[12263 kb] obo[6909 kb]		
Chemical entities of biological interest	CHEBI	<u>chebi.obo</u>	bio	biological_process:Biological process		<pre>go_ont[2987 kb] owl[25382 kb] cha godb_prestore[26749 kb] rdf[11461 k validation_report[0 kb] stats[2 kb]</pre>	adoxml[31966 kb] kb] tbl[4304 kb] prolog[13859 kb] -		
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caro:Common Anatomy Reference Ontology CARO

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cell:Cell type

Drosophila

development

Drosophila gross

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fly developmen

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FRht

fly anatomy oh

cell:Cell type

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Domain	Prefix	File				reports from each of the ontologies. The data below
Animal natural history and life history	ADW	protege source	is derived automatically from the primary sources for caveats.	, available from	n the main OBO website	. The status of this page is EXPERIMENTAL. See below
Biological imaging methods	FBbi	image.obo	This page will be retired when the current functio Ontologies	natity is subsur	ned by the bioPortal res	ource developed by the NCBO
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BRENDA tissue / enzyme source	вто	BrendaTissue.c	Format Guide Metadata			
C. elegans development	WBIs	worm developn	Reports FTP Archive			
C. elegans gross anatomy	WBbt		Statistics			
C. elegans phenotype	WBPhenotype	phenotype ont	Ontologies			
Cell type	CL	cell.obo	Ontology	ID Prefix		Files
Cellular component	GO	gene ontology.			obo_xml[595 kb] ob	o[285 kb] go_ont[169 kb] owl[1311 kb]
Cereal plant development	GRO	cereals develop	adult_mouse_anatomy:Mouse adult gross anatomy	ма	chadoxml[1614 kb] g prolog[676 kb] valid	odb_prestore[1498 kb] rdf[830 kb] tbl[93 kb] ation_report[2 kb] stats[2 kb] pellet_report[0 kb
Cereal plant gross anatomy	GRO	po anatomy.ob	animalhist:Animal natural history and life history	ADW	obo.html[1737 kb]	
Cereal plant trait	то	plant trait.obo			obo_xml[19969 kb] 0	obo[6909 kb] obo_xml[12263 kb] obo[6909 kb]
Chemical entities of biological interest	CHEBI	chebi.obo	biological_process:Biological process	GO	go_ont[2987 kb] owl godb_prestore[26749 l	[25382 kb] chadoxml[31966 kb] (b] rdf[11461 kb] tbl[4304 kb] prolog[13859 kb] (b] stats[2 kb] pellet_report[0 kb]
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Drosophila development	FBdv	fly developmen	caro:Common Anatomy Reference Ontology	CARO	kb] godb_prestore[3 validation_report[0 kb	7 kb] rdf[20 kb] tbl[6 kb] prolog[18 kb] ] stats[2 kb] pellet_report[14 kb] obo.html[44
Drosophila gross	CRbt	fly anatomy ob			kb]	

obo\_xml[351 kb] -- obo[200 kb] -- go\_ont[66 kb] -- owl[783 kb] -chadoxml[978 kb] -- godb\_prestore[830 kb] -- rdf[409 kb] -- tbl[102 kb] --



 Explicit links between one GO term and another ontology term

# Many GO terms are *implicitly* composite

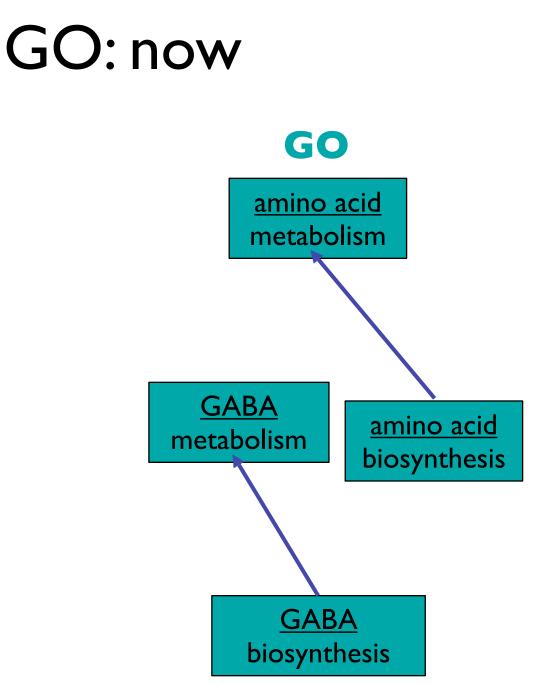
- <u>cysteine</u> biosynthesis
- <u>myoblast</u> fusion
- <u>ATP</u> synthesis coupled <u>proton</u> transport (ChEBI)
- <u>snoRNA</u> catabolism
- <u>wing disc</u> pattern formation
- <u>epidermal cell</u> differentiation
- regulation of <u>flower</u> development
- <u>interleukin-18</u> receptor complex
- <u>B-cell</u> differentiation
- <u>dorsal</u> ectoderm

# Opaque references to other **OBO** ontologies

- <u>cysteine</u> biosynthesis (ChEBI)
- <u>myoblast</u> fusion (Cell Type Ontology)
- <u>ATP</u> synthesis coupled <u>proton</u> transport (ChEBI)
- <u>snoRNA</u> catabolism (Sequence Ontology)
- <u>wing disc</u> pattern formation (*Drosophila* anatomy)
- <u>epidermal cell</u> differentiation (Cell Type Ontology)
- regulation of <u>flower</u> development (*Plant* anatomy)
- <u>interleukin-18</u> receptor complex (not yet in OBO)
- <u>B-cell</u> differentiation (Cell Type Ontology)
- <u>dorsal</u> ectoderm (Spatial Qualifiers)

## Methodology

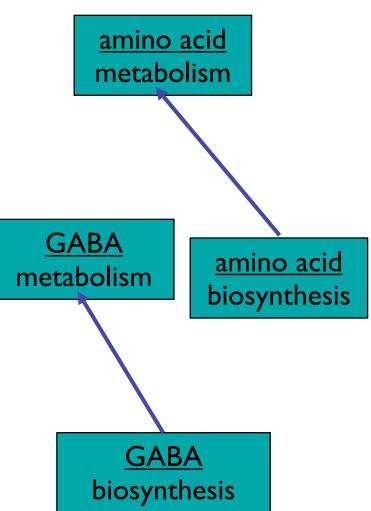
- Make opaque references explicit
- Use OBO ontologies
  - ChEBI
  - Cell
  - PATO (qualities)
  - Anatomy/CARO



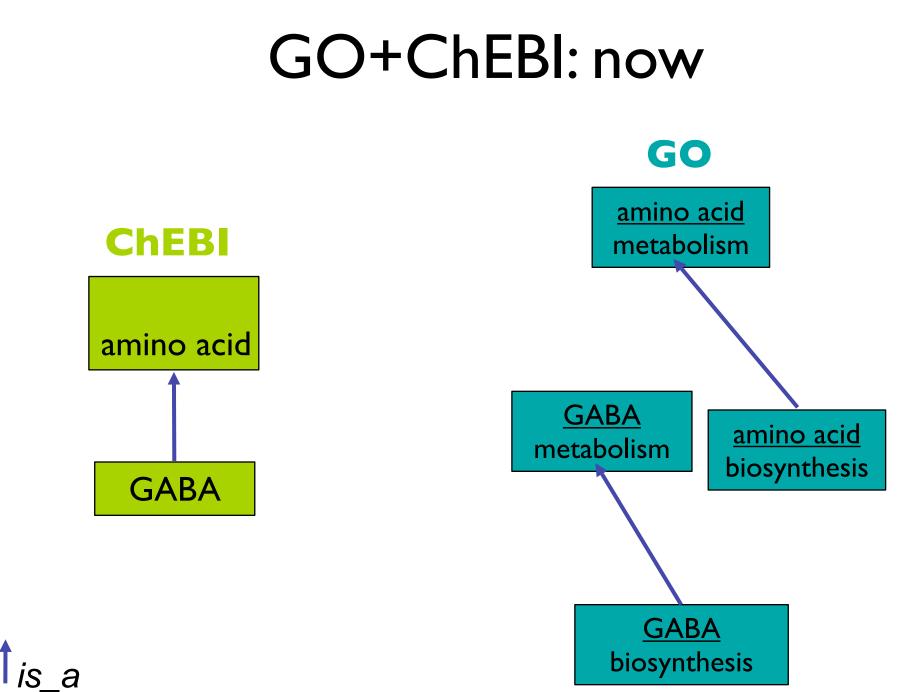
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## GO+ChEBI: now

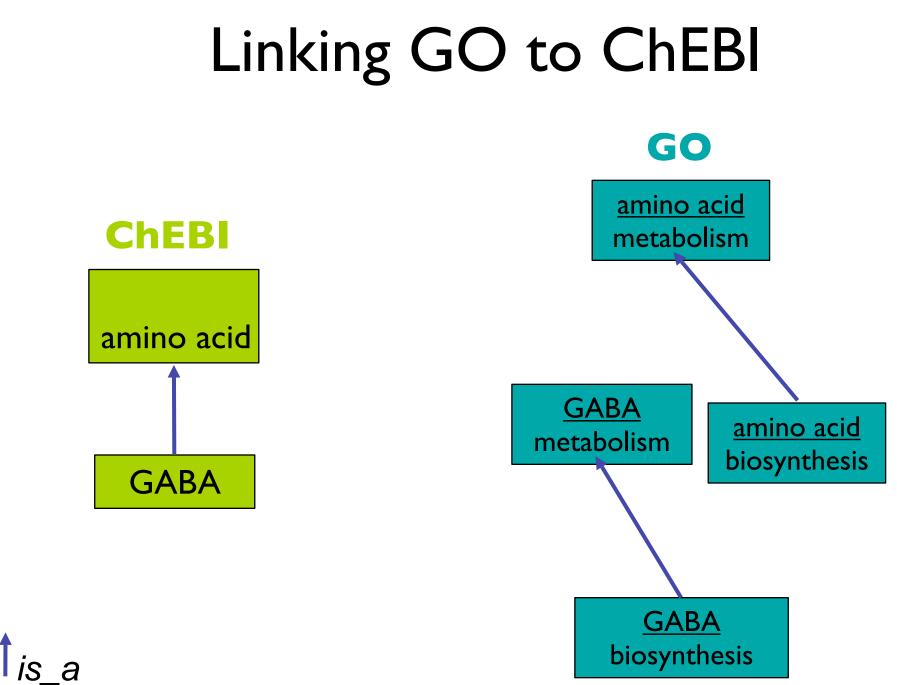
## GO

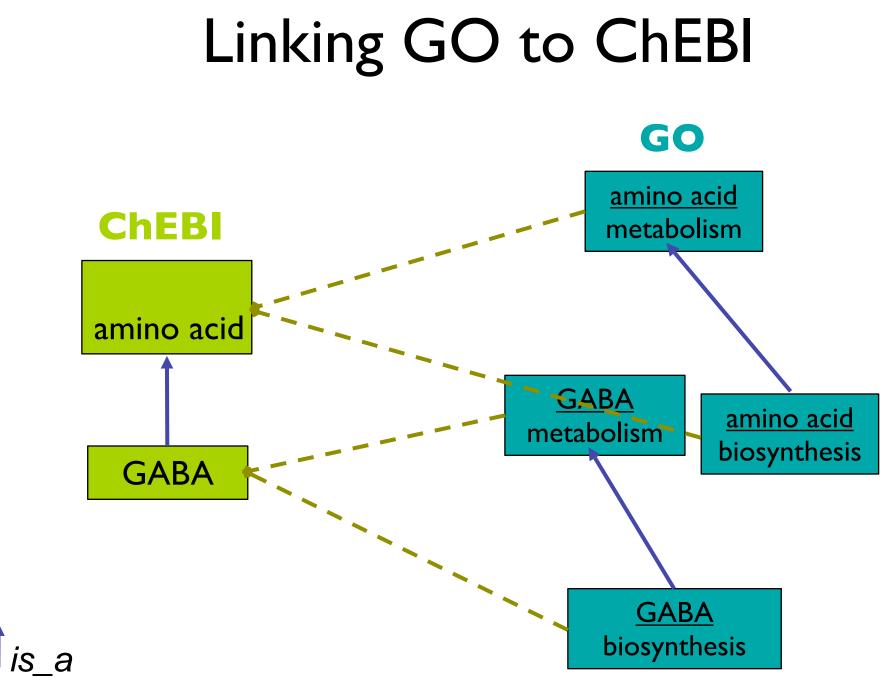


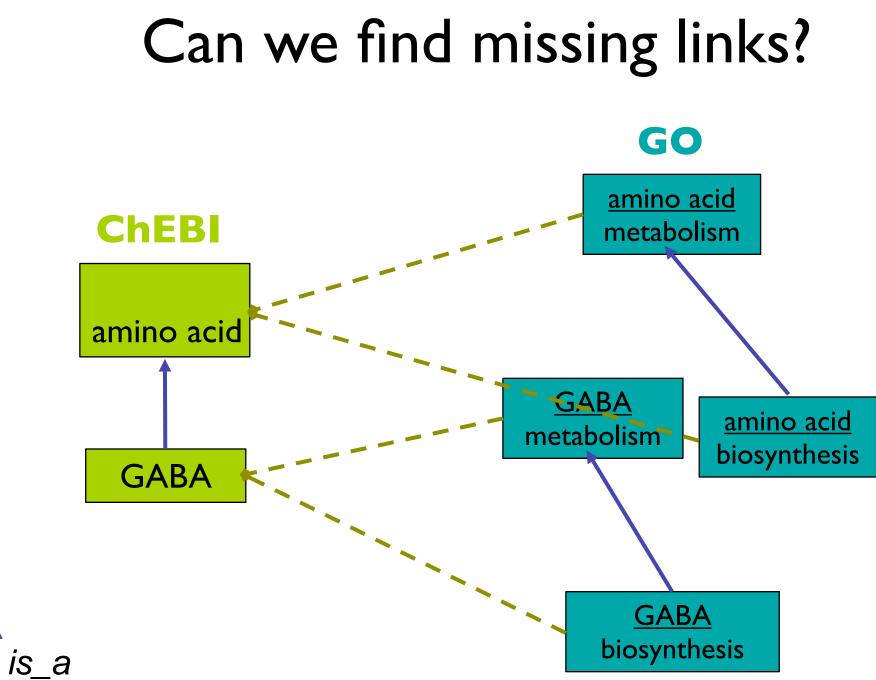


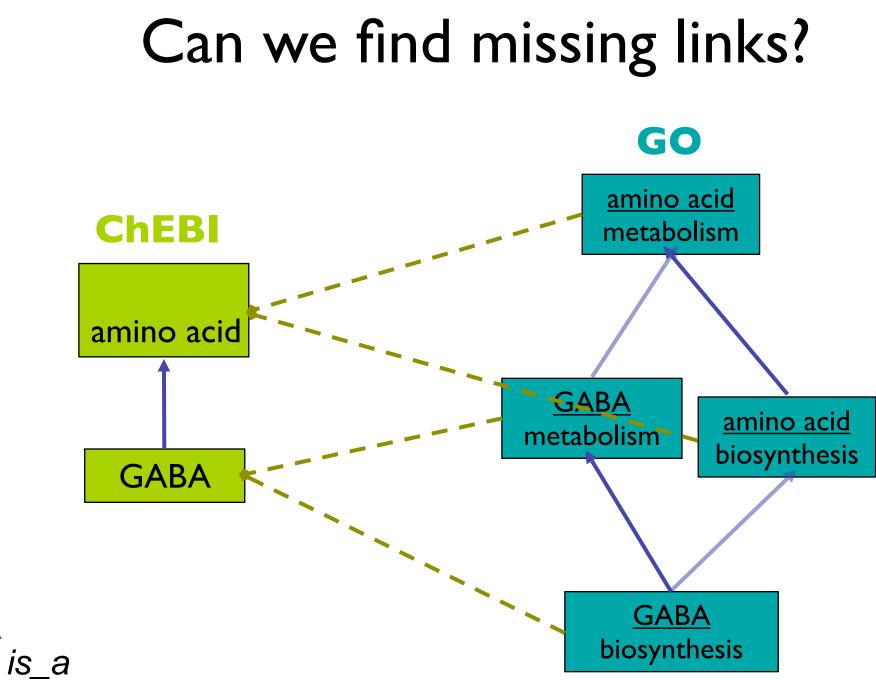


slide credit: Chris Mungall, BBOP









## Simple DAGs are not enough

- We want to define GO terms using ChEBI terms
- DAGs give necessary conditions
- We want to give necessary <u>and sufficient</u> conditions
- Solution:
  - Genus-differentia definitions
  - Aka cross-products, aka intersections

# Example genus-differentia definition

• A GABA metabolic process is:

## – A metabolic process

- That has\_participant **GABA**
- This is saying more than simply adding a DAG link between GABA metabolic process and GABA
  - It allows us to do powerful reasoning
    - Keeps ontologies in sync

```
[Term]
id: GO:0009447
name: putrescine catabolic process
intersection of: GO:0009056 ! catabolism
intersection of: results in division of CHEBI:17148 ! putrescine
[Term]
id: GO:0009448
name: gamma-aminobutyric acid metabolic process
intersection of: GO:0008152 ! metabolism
intersection of: has participant CHEBI:16865 ! gamma-aminobutyric acid
[Term]
id: GO:0009449
name: gamma-aminobutyric acid biosynthetic process
intersection of: GO:0009058 ! biosynthesis
intersection of: results in change to CHEBI:16865 ! gamma-aminobutyric acid
[Term]
id: GO:0009450
name: gamma-aminobutyric acid catabolic process
intersection of: GO:0009056 ! catabolism
intersection of: results in division of CHEBI:16865 ! gamma-aminobutyric acid
```



# GO and Phenotypes

- Phenotype annotation uses GO and other OBO ontologies — in combination with qualities from PATO
- An entity (GO, anatomy, etc. term) has a quality (PATO term)
- Example: decreased rate of sucrose synthesis



# GO and Phenotypes

- Phenotype annotation uses GO and other OBO ontologies — in combination with qualities from PATO
- An entity (GO, anatomy, etc. term) has a quality (PATO term)
- Example: decreased rate of sucrose synthesis

GO:0005986



# GO and Phenotypes

- Phenotype annotation uses GO and other OBO ontologies — in combination with qualities from PATO
- An entity (GO, anatomy, etc. term) has a quality (PATO term)
- Example: decreased rate of sucrose synthesis PATO:000911 GO:0005986





- Java application for annotating phenotypes using biological ontologies
- Uses any ontology in OBO format



# Phenote

$\bigcirc \ominus \ominus \ominus$	Phenote 1.4		
Pub	example		
Genotype			
Gene ALL ext			
Entity GO		Comp	
Quality SO			
Add'l Entity		Comp ^	
Time			
Count			• •
Unit			ing phenotypes
Abnormal			
Description			

## • Uses any ontology in OBO format



# Phenote

€ € €			Phenote 1	.4			
Pu Genotyp	be			-	Term Info sucrose biosynthetic process ONTOLOGY biological_process		
Entity CO Quality ALL Add'l Entity ALL Tim Cour Un Abnorm	ty ALL sucrose 1F-fructosyltransfer sucrose 6F-alpha-galactotra		ity activity _fructofuranos oside 3-dehydr	Comp Comp	ID GO:0005986 Exact sucrose anabolism sucrose biosynthesis sucrose formation sucrose synthesis X-refs MetaCyc:14466 Definition The chemical reactions i resulting in the formation disaccharide fructofuranosyl-glucopy	ion of sucrose, the syranoside.	
Pub (	Genotype	Genetic Context	Entity sucrose biosyn	Quality athetic pr	Add'l Entity	Time	
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# Phenote

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000			Phenote 1.4			
Pub	example				Term Info	
Genotype					decreased rate	
Genetic Context					ONTOLOGY quality ID PATO:0000911	
Entity GO 🛟	sucrose biosynth	etic process	•	Comp	Exact slow rate Synonyms:	
Quality PATO	decreased rate		•		Definition A rate which is relative	ve low.
Add'l Entity ALL	decreased period decreased perme decreased photos	ability	<u></u>	Comp ^	Superclass rate	
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Count	decreased pressu decreased radioa					
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	otype	Genetic Context	Entity	Quality	Add'l Entity	Time
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# Acknowledgements

## The GO Editorial Office

- Jane Lomax
- Amelia Ireland
- Jennifer Deegan
- GO Consortium members

## • Funding:

The Gene Ontology Consortium is supported by a P41 grant from the National Human Genome Research Institute (NHGRI), and has been supported by grants from the European Union RTD Programme "Quality of Life and Management of Living Resources." The Gene Ontology project also thanks AstraZeneca for financial support.





### **Current GO Consortium Members**

**Berkeley Bioinformatics and Ontology Project (BBOP)** : Drosophila informatics; development of GO database and software; Sequence Ontology development; National Center for Biomedical Ontology biomedical informatics research

dictyBase : informatics resource for the slime mold Dictyostelium discoideum

FlyBase @: database for the fruitfly Drosophila melanogaster

**GeneDB** (part of the Pathogen Sequencing Unit at the Wellcome Trust Sanger Institute): includes databases for the fission yeast *Schizosaccharomyces pombe* and several protozoan parasites a, including *Plasmodium falciparum, Leishmania major* and *Trypanosoma brucei*.

Gene Ontology Annotation @ EBI (GOA) @: annotation of UniProt Knowledgebase ⓓ (Swiss-Prot/TrEMBL/PIR-PSD) and InterPro ⓓ databases

Gramene : a comparative mapping resource for grains, including rice (Oryza)

**HUGO Gene Nomenclature Committee (HGNC)** : committee responsible for human gene nomenclature and annotation of human and other species

Mouse Genome Database (MGD) and Gene Expression Database (GXD) : databases for the mouse Mus musculus

Rat Genome Database (RGD) : database for the rat Rattus norvegicus

**Saccharomyces Genome Database (SGD)** : database for the budding yeast Saccharomyces cerevisiae; maintenance and public access of GO database and web interfaces

The Arabidopsis Information Resource (TAIR) : database for the brassica family plant Arabidopsis thaliana

**The J. Craig Venter Institute (JCVI)** [formerly The Institute for Genomic Research (TIGR)]: databases on several bacterial species

WormBase @: database for the nematode Caenorhabditis elegans

Zebrafish Information Network (ZFIN) : reference datasets and information on Danio rerio



### **Current GO Consortium Members**

**Berkeley Bioinformatics and Ontology Project (BBOP)** : Drosophila informatics; development of GO database and software; Sequence Ontology development; National Center for Biomedical Ontology biomedical informatics research

dictyBase @: informatics resource for the slime mold Dictyostelium discoideum

FlyBase @: database for the fruitfly Drosophila melanogaster

**GeneDB** (part of the Pathogen Sequencing Unit at the Wellcome Trust Sanger Institute): includes databases for the fission yeast *Schizosaccharomyces pombe* and several protozoan parasites a, including *Plasmodium falciparum*, *Leishmania major* and *Trypanosoma brucei*.

Gene Ontology Annotation @ EBI (GOA) @: annotation of UniProt Knowledgebase 丞 (Swiss-Prot/TrEMBL/PIR-PSD) and InterPro ♂ databases

Gramene : a comparative mapping resource for grains, including rice (Oryza)

**HUGO Gene Nomenclature Committee (HGNC)** : committee responsible for human gene nomenclature and annotation of human and other species

Mouse Genome Database (MGD) and Gene Expression Database (GXD) : databases for the mouse Mus musculus

Rat Genome Database (RGD) : database for the rat Rattus norvegicus

Reactome 2: a knowledgebase of biological processes (formerly Genome Knowledgebase)

**Saccharomyces Genome Database (SGD)** : database for the budding yeast Saccharomyces cerevisiae; maintenance and public access of GO database and web interfaces

**The Arabidopsis Information Resource (TAIR)** : database for the brassica family plant Arabidopsis thaliana

The J. Cr several ba

www.geneontology.org

databases on

WormBa\_\_\_

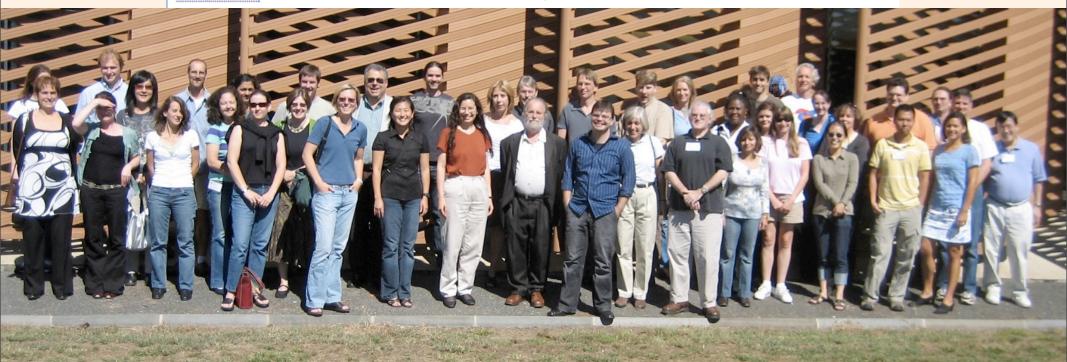
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