CACAO Training part 1

TAMU 2013

BICH485-507

Tues Jan 22, 2013

- What are we doing this semester?
- Big picture
- What is CACAO?
- Housekeeping

Overview of the semester

- Training
  - Today: Training lecture
  - Jan 29: Example papers (we will email you assigned reading)
- Annotation
  - Feb – Apr: 5 rounds of finding papers, reading, doing annotation
    - Class time for meeting with your team and getting in-person help!
- Conclusion
  - April 23: Overview of what we did. Prizes?

Big picture

- This class is about understanding how scientists
  - Infer the function of genes
  - Share knowledge with the larger community
- We will learn this by hands-on experience through CACAO
- **Warnings**:
  - This will be confusing at first. Stick with it!
  - Budget your time. This is not a class where you can cram at the end.

What is CACAO?

- **C**ommunity **A**ssessment of **C**ommunity **A**nnotation with **O**ntologies (CACAO)
  - Annotation of gene function
  - Competition
    - Within this class
    - Between TAMU and other schools (BTHO everyone!)
    - Rules next week

Annotation

- Annotation: a note that is made while reading any form of text

- For genome biology,
  - Nucleotide level: Where the genes are in the genome
  - Protein level: What their functions are

From Wikipedia

Annotation

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- For CACAO,
  - ~~Nucleotide level: Where the genes are in the genome~~
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From Wikipedia

Functional Annotation

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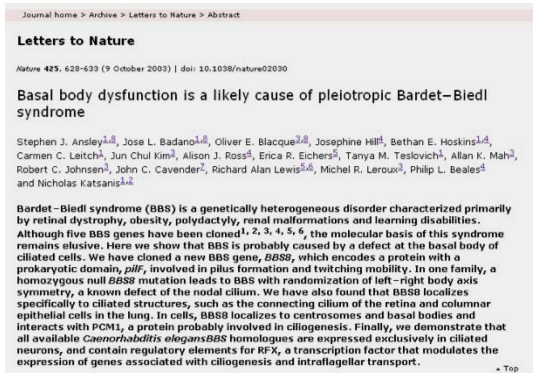
- Functional Annotation: a database entry in a **specific format** that is made based on **evidence** in a peer-reviewed **paper** about the function of a **protein**

Why do functional annotation?

- Allow us to:
  - Infer the function of genes
    - Related by common descent
    - Related by similar expression patterns
    - Related by phylogenetic profiles
    - …
- Allow us to:
  - Understand the capabilities of organisms' genomes
  - Understand patterns of gene expression
    - In different environments
    - In different tissues
    - In disease states
    - …

Where do functional annotations come from?



Journal home > Archive > Letters to Nature > Abstract

Letters to Nature

Nature **425**, 628-633 (9 October 2003) | doi: 10.1038/nature02030

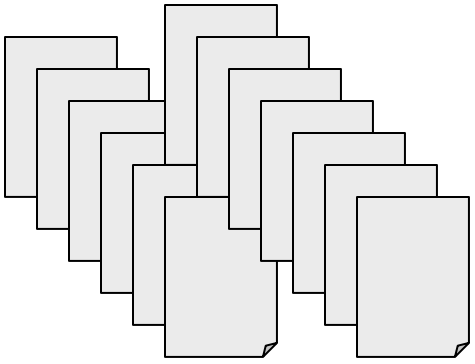
Basal body dysfunction is a likely cause of pleiotropic Bardet–Biedl syndrome

Stephen J. Ansley[1,8], Jose L. Badano[1,8], Oliver E. Blacque[3,8], Josephine Hill[4], Bethan E. Hoskins[1,5], Carmen C. Leitch[1], Jun Chul Kim[3], Alison J. Ross[3], Erica R. Eichers[5], Tanya M. Teslovich[1], Allan K. Mah[3], Robert C. Johnsen[3], John C. Cavender[2], Richard Alan Lewis[5,6], Michel R. Leroux[3], Philip L. Beales[4] and Nicholas Katsanis[1,2]

Bardet–Biedl syndrome (BBS) is a genetically heterogeneous disorder characterized primarily by retinal dystrophy, obesity, polydactyly, renal malformations and learning disabilities. Although five BBS genes have been cloned[1, 2, 3, 4, 5, 6], the molecular basis of this syndrome remains elusive. Here we show that BBS is probably caused by a defect at the basal body of ciliated cells. We have cloned a new BBS gene, *BBS8*, which encodes a protein with a prokaryotic domain, *pilF*, involved in pilus formation and twitching mobility. In one family, a homozygous null *BBS8* mutation leads to BBS with randomization of left–right body axis symmetry, a known defect of the nodal cilium. We have also found that BBS8 localizes specifically to ciliated structures, such as the connecting cilium of the retina and columnar epithelial cells in the lung. In cells, BBS8 localizes to centrosomes and basal bodies and interacts with PCM1, a protein probably involved in ciliogenesis. Finally, we demonstrate that all available *Caenorhabditis elegansBBS* homologues are expressed exclusively in ciliated neurons, and contain regulatory elements for RFX, a transcription factor that modulates the expression of genes associated with ciliogenesis and intraflagellar transport.

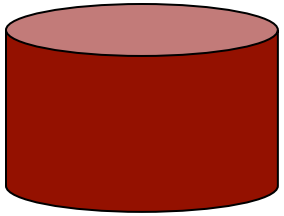
▲ Top

Literature



Datasets

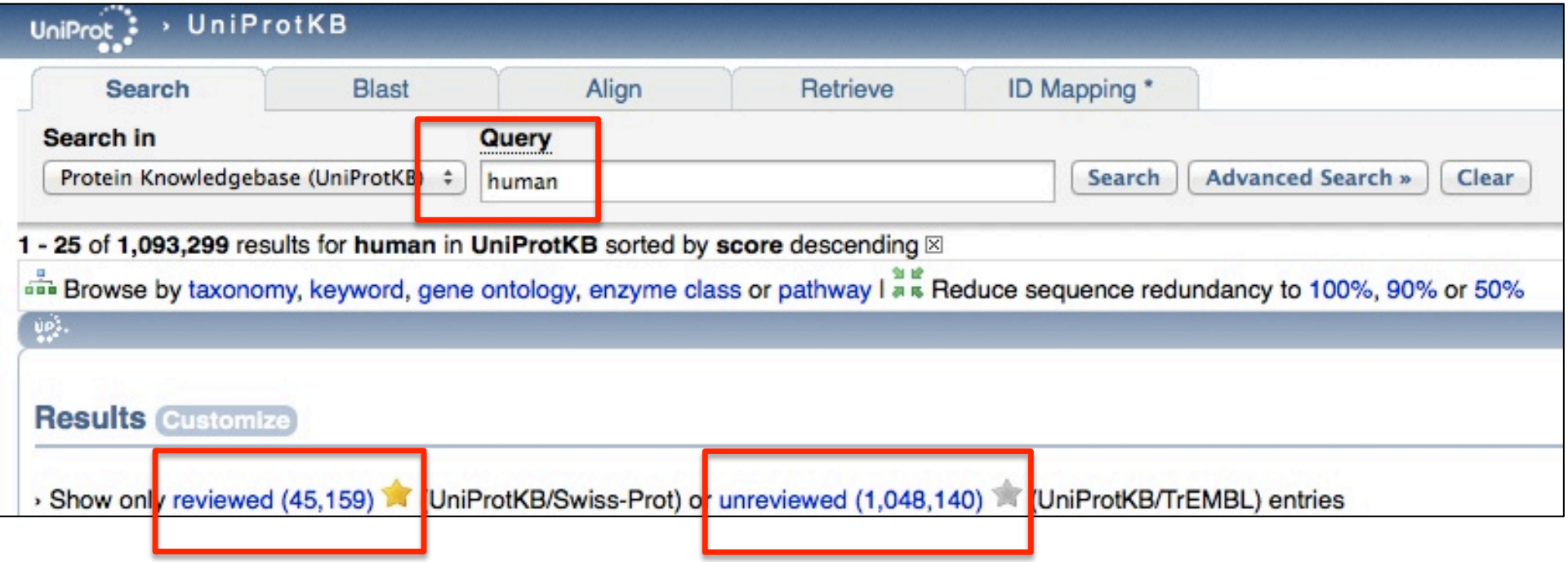
Biocurators
(rate limiting)



Database

Databases need help!

- >21 million peer-reviewed articles in PubMed
- Many millions of proteins recorded in UniProt



http://www.uniprot.org

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What to annotate

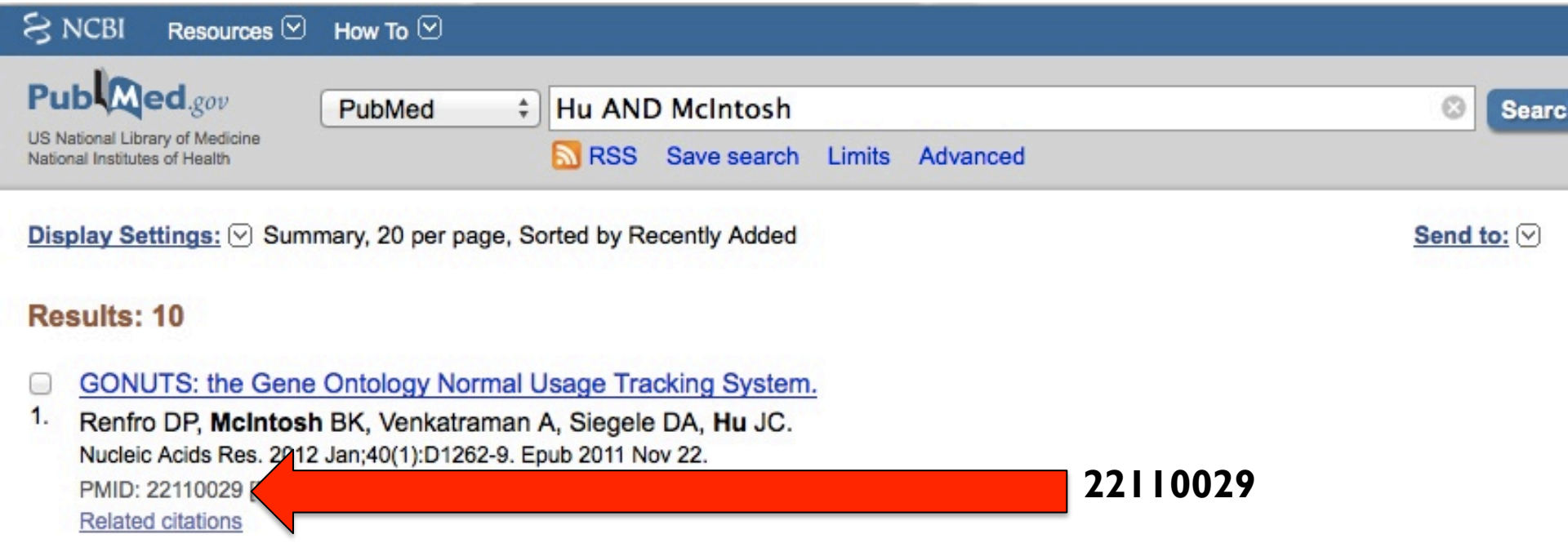
- You can start with a paper
  - Find the proteins discussed
  - Start with a GO term
- You can start with a protein
  - Find papers about the protein
- Either way, don't get stuck on what you started with
  - Your first paper may not have **experiments** about function
  - Reading about your initial protein may lead you to better information about other proteins

Starting with a paper

- Need a scientific paper with experimental data
  - No review articles, no books, no textbooks, no wikipedia articles, no class notes…
  - BUT you should start with those!
  - DON'T start with a random PubMed search

Starting with a paper

- Need a scientific paper with experimental data
  - You will need the PMID number



Getting the full text

- The abstract is not enough
  - But may be enough to reject a paper!!!
- Some papers are open access
  - Pubmed Central
  - Journal sites
    - TAMU pays for lots of subscriptions
    - Access from off campus via http://library.tamu.edu
      - E-journals
      - Citation search takes PMIDs

Beware!

- Good science ≠ good for annotation

Second Extracellular Loop of Human Glucagon-like Peptide-1 Receptor (GLP-1R) Differentially Regulates Orthosteric but Not Allosteric Agonist Binding and Function*[S]

Received for publication, September 30, 2011, and in revised form, November 29, 2011 Published, JBC Papers in Press, December 6, 2011, DOI 10.1074/jbc.M111.309369

Cassandra Koole[‡], Denise Wootten[‡], John Simms[‡], Emilia E. Savage[‡], Laurence J. Miller[§], Arthur Christopoulos[‡1], and Patrick M. Sexton[‡2]

From the [‡]Drug Discovery Biology, Monash Institute of Pharmaceutical Sciences and Department of Pharmacology, Monash University, Parkville, Victoria 3052, Australia and the [§]Department of Molecular Pharmacology and Experimental Therapeutics, Mayo Clinic, Scottsdale, Arizona 85259

Background: The ECL2 of the GLP-1R is critical for GLP-1 peptide-mediated selective signaling.
Results: Mutation of most ECL2 residues to alanine results in changes in binding and/or efficacy of oxyntomodulin and exendin-4 but not allosteric agonists.
Conclusion: ECL2 of the GLP-1R has ligand-specific as well as general effects on peptide agonist-mediated receptor activation.
Significance: This work provides insight into control of family B GPCR activation transition.

Beware!

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Robust design and optimization of retroaldol enzymes

Eric A. Althoff,[1,2] Ling Wang,[1] Lin Jiang,[1,3] Lars Giger,[4] Jonathan K. Lassila,[5] Zhizhi Wang,[1] Matthew Smith,[1] Sanjay Hari,[1] Peter Kast,[4] Daniel Herschlag,[5] Donald Hilvert,[4] and David Baker[1]*

[1]Department of Biochemistry, University of Washington and HHMI, Seattle, Washington 98195
[2]Arzeda Corp., Seattle, Washington 98102
[3]Department of Biological Chemistry, UCLA, Los Angeles, California 90095
[4]Laboratory of Organic Chemistry, ETH Zurich, 8093 Zurich, Switzerland
[5]Department of Biochemistry, Stanford University, Stanford, California 94305

Beware!

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Cell Stem Cell
Short Article

Cell PRESS

Vitamin C Enhances the Generation of Mouse and Human Induced Pluripotent Stem Cells

Miguel Angel Esteban,[1,6] Tao Wang,[1,6] Baoming Qin,[1,6] Jiayin Yang,[1] Dajiang Qin,[1] Jinglei Cai,[1] Wen Li,[1] Zhihui Weng,[1] Jiekai Chen,[1] Su Ni,[1] Keshi Chen,[1] Yuan Li,[1] Xiaopeng Liu,[1] Jianyong Xu,[1] Shiqiang Zhang,[1] Feng Li,[1] Wenzhi He,[1] Krystyna Labuda,[2] Yancheng Song,[3] Anja Peterbauer,[4] Susanne Wolbank,[2] Heinz Redl,[2] Mei Zhong,[5] Daozhang Cai,[3] Lingwen Zeng,[1] and Duanqing Pei[1,*]

[1]Stem Cell and Cancer Biology Group, Key Laboratory of Regenerative Biology, South China Institute for Stem Cell Biology and Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou 510663, China

[2]Ludwig Boltzmann Institute for Clinical and Experimental Traumatology, Austrian Cluster for Tissue Regeneration, Vienna 1200, Austria

Beware!

- Good science ≠ good for annotation

10624 • The Journal of Neuroscience, August 11, 2010 • 30(32):10624–10638

Neurobiology of Disease

Excess Phosphoinositide 3-Kinase Subunit Synthesis and Activity as a Novel Therapeutic Target in Fragile X Syndrome

Christina Gross,[1] Mika Nakamoto,[2]* Xiaodi Yao,[1]* Chi-Bun Chan,[3] So Y. Yim,[1] Keqiang Ye,[3] Stephen T. Warren,[2,4,5] and Gary J. Bassell[1,6]

Departments of [1]Cell Biology, [2]Human Genetics, [3]Pathology and Laboratory Medicine, [4]Biochemistry, [5]Pediatrics, and [6]Neurology, Emory University School of Medicine, Atlanta, Georgia 30322

Finding proteins

- Search UniProt for something interesting
- Look in UniProt for the protein(s) in the paper you are reading.

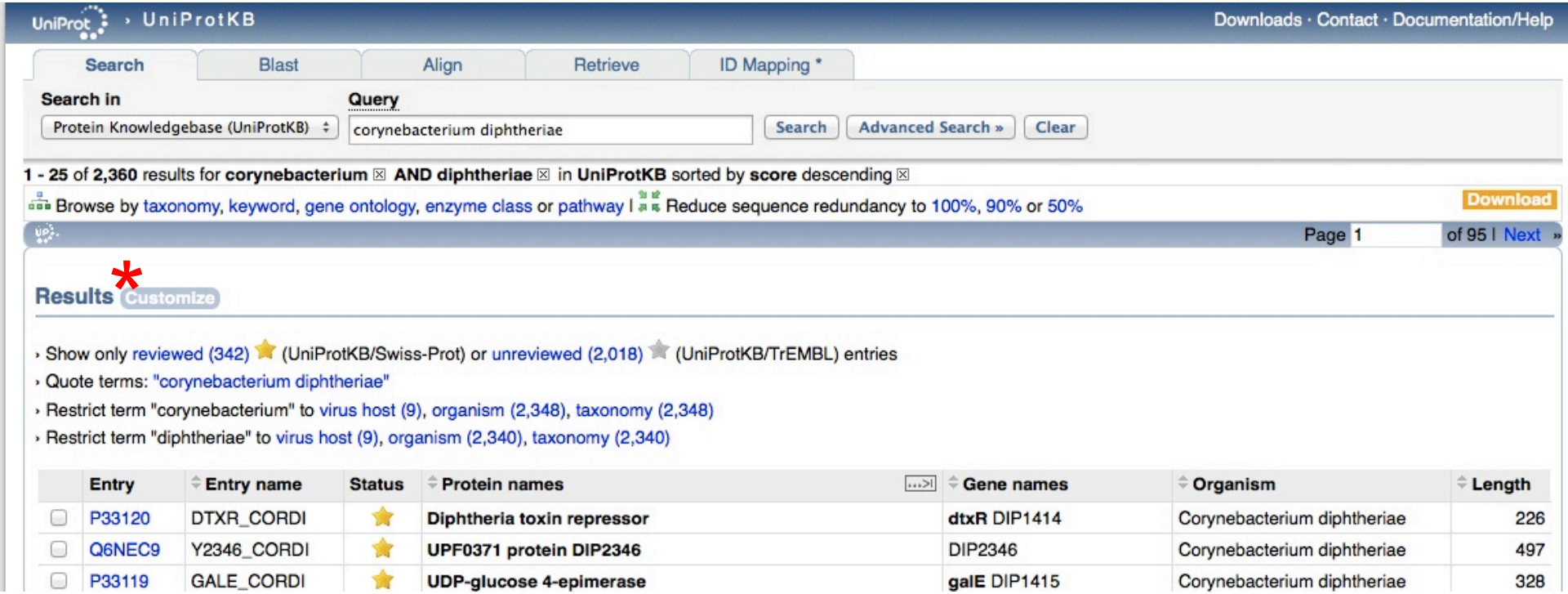
No matter what, you will need to find the protein's accession on UniProt (http://uniprot.org)

Use that accession to make a page for that protein on GONUTS (http://gowiki.tamu.edu)

Add your GO annotations to the protein's page on GONUTS

UniProt (http://www.uniprot.org)

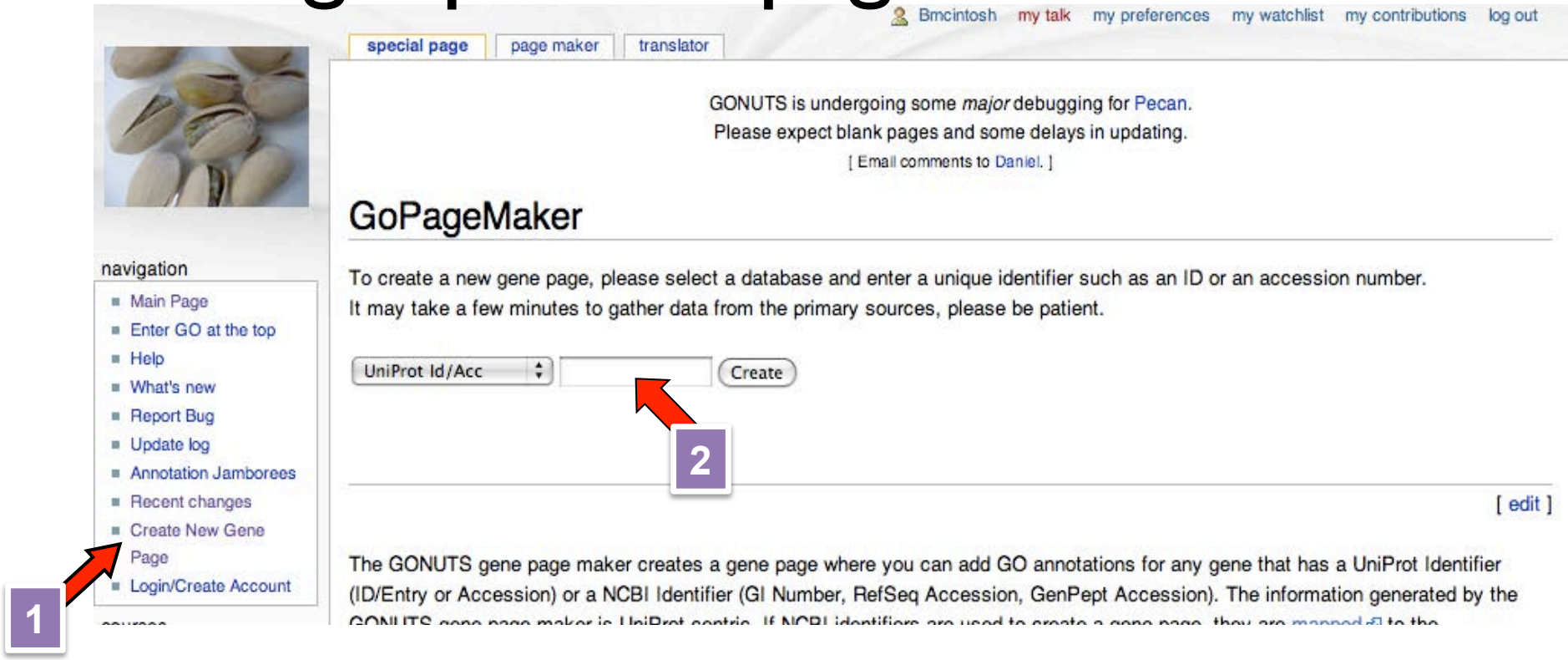
- If you have a paper, look for an accession
- Otherwise, search by name/keyword



Make sure you have the right protein

- Right species/strain
- Not a fragment
- Sometimes UniProt has multiple entries for the same protein
  - Gold star = SwissProt = reviewed
  - Blank star = TrEMBL = computational entry
- Sometimes the protein you want is not in UniProt
  - May want to find another paper/protein
- Ask for help
  - OK to email the UniProt help desk
  - check your reasoning with us!

Making a protein page in GONUTS



- GoPageMaker will:
  - Check if the page exists in GONUTS & take you there if it does.
  - Make a page if it does not exist in GONUTS already & pull all of the annotations from UniProt into a table that you can edit.

- Make as many protein pages as you would like!

navigation
- Main Page
- Enter GO at the top
- Help
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- Annotation Jamborees
- Recent changes
- Create New Gene Page
- Login / Create Account

cacao
- Links about CACAO
- Fall 2011

journal clubs
- Journal Clubs
- Create new literature page

page contributors
- SMoore
- Wikientrybot

search
Go Search

toolbox
- What links here
- Related changes
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- Printable version
- Permanent link

The Spring 2012 season of CACAO has started!

LAMBD:VLYS

Species (Taxon ID)	*Enterobacteria phage lambda (Bacteriophage lambda).* ([1])
Gene Name(s)	S
Protein Name(s)	Holin gpS protein Lysis protein S Lysis inhibitor
External Links	
EMBL	J02459 M14035
PIR	H94164
RefSeq	NP_040644.1 YP_001551775.1
TCDB	1.E.2.1.1
GeneID	2703479 5740919
GenomeReviews	J02459_GR
ProtClustDB	CLSP2343227
GO	GO:0020002 GO:0016021 GO:0016998 GO:0019835
InterPro	IPR006481
Pfam	PF05106
TIGRFAMs	TIGR01634

Contents [hide]
1 Annotations
2 Notes
3 References

Annotations

[edit]

Qualifier	GO ID	GO term name	Reference	Evidence Code	with/from	Aspect	Notes	Status
	GO:0016020	membrane	GO_REF:0000004	IEA: Inferred from Electronic Annotation	SP_KW:KW-0472	C	Seeded From UniProt	
	GO:0033644	host cell membrane	GO_REF:0000004	IEA: Inferred from Electronic Annotation	SP_KW:KW-1043	C	Seeded From UniProt	
edit table								

edit table

Notes

[edit]

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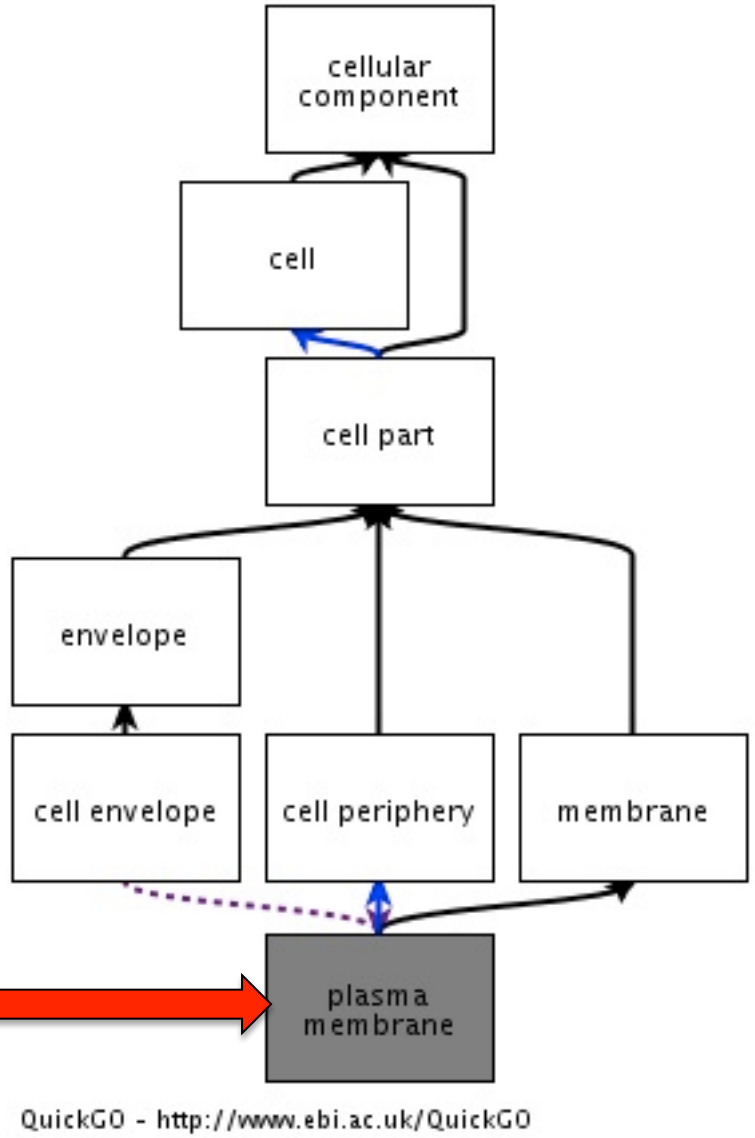
GO (Gene Ontology) Annotations

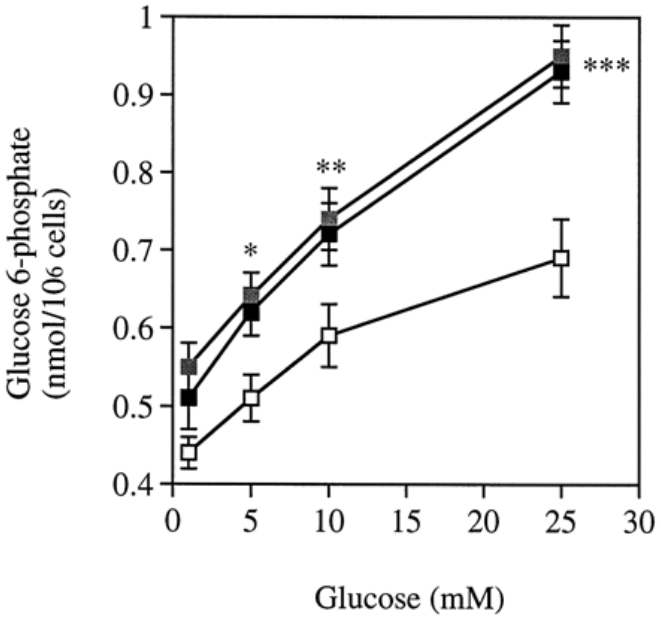
- 3 aspects (ontologies) :
  - Molecular Function
  - Biological Process
  - Cellular Component
- Controlled vocabulary
  - ID number for computers
  - Name and definition for humans
- Relationships



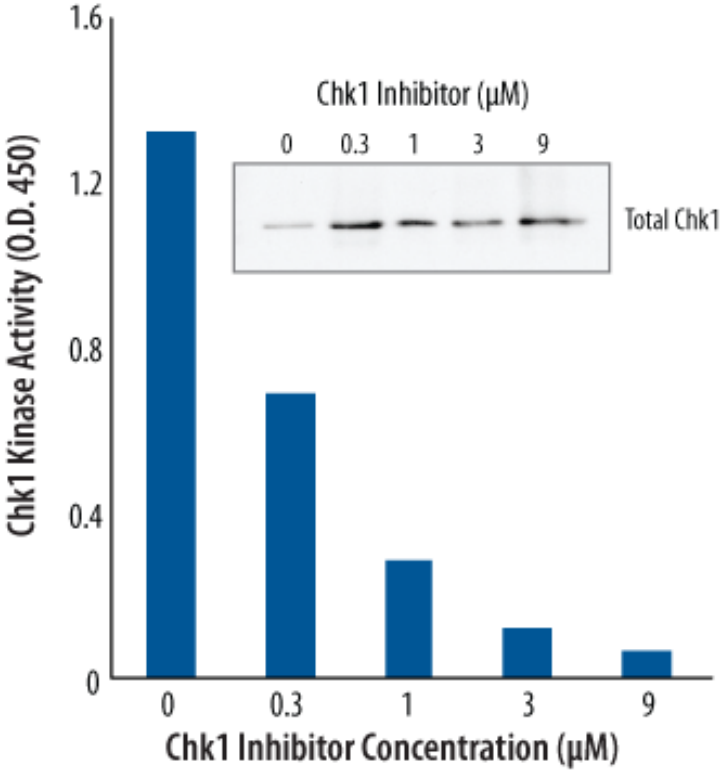
GO:0005886

Molecular Function

- activities or what a protein can do by itself



GO:0004347 hexokinase activity

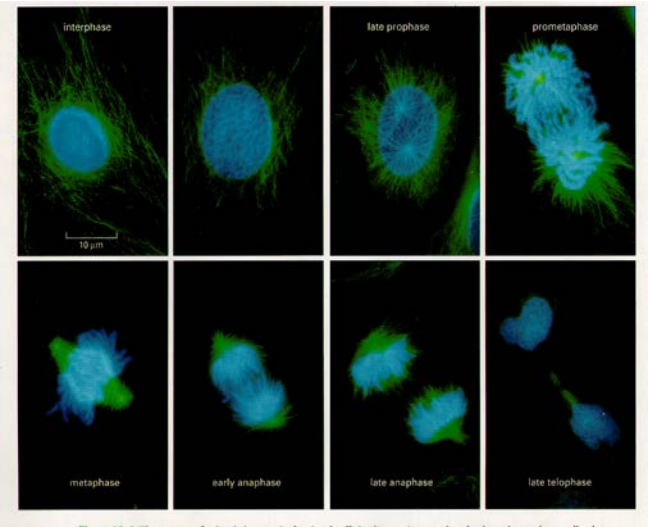


GO:0016301 Kinase activity

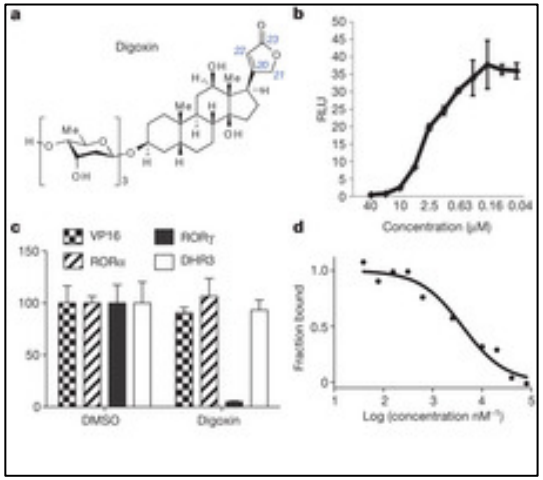
From PMID:9341134, rndsystems.com

Biological Process

- a commonly recognized series of events
  - Including, but not just biochemical pathways



GO:0051301 cell division



GO:0006351 transcription, DNA dependent

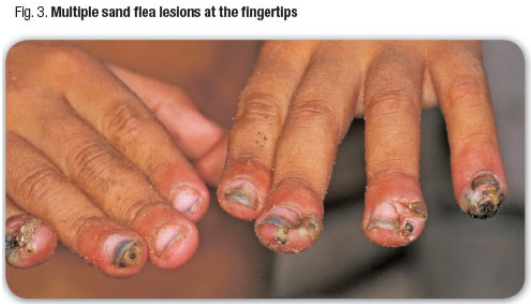


Fig. 3. **Multiple sand flea lesions at the fingertips**

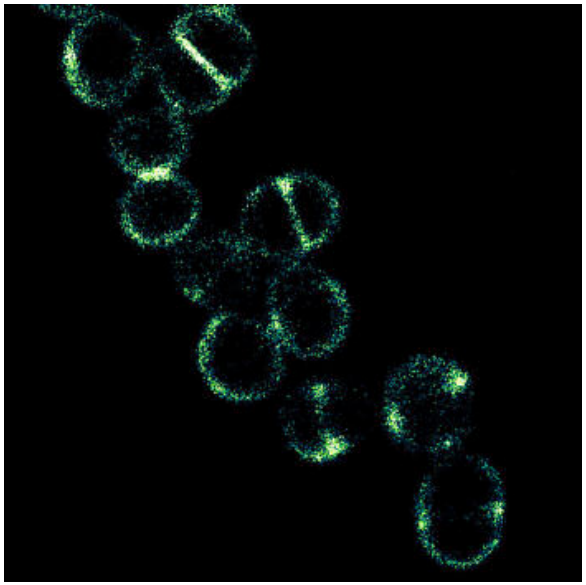
GO:0009405 pathogenesis

From ridge.icu.ac.jp, edtech.clas.pdx.edu, scielosp.org

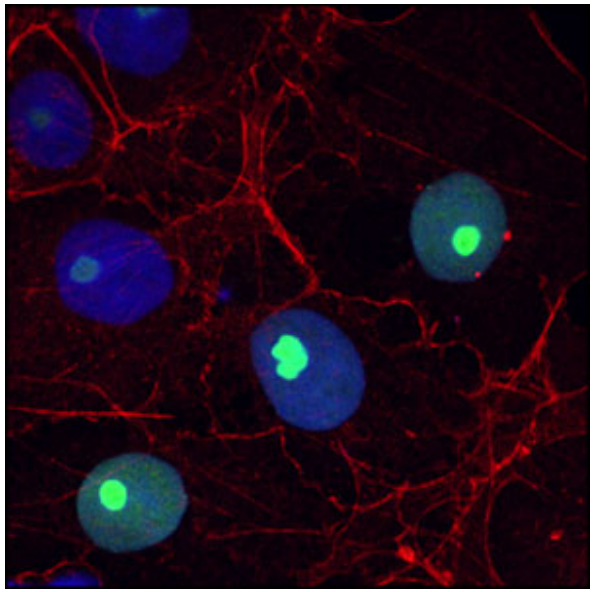
Cellular Component

- where a gene product acts
  - Subcellular location
  - Multicomponent complex

GO:0005739
mitochondrion



GO:0009274
peptidoglycan-based cell wall

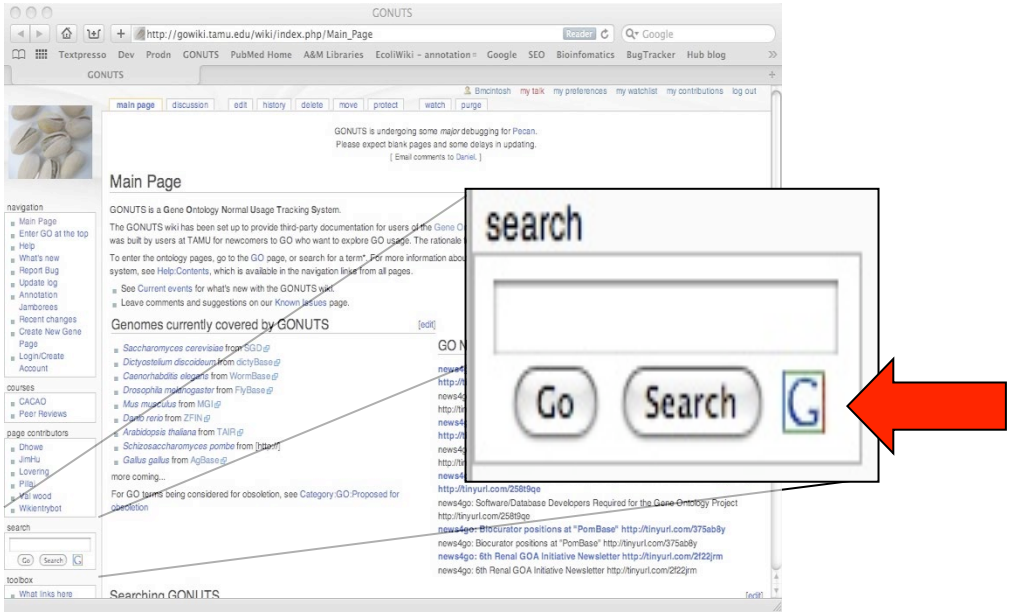


GO:0005840
ribosome

From visualphotos.com, epmm.group.shef.ac.uk, http://www.cellsignal.com/products/2415.html

Finding GO terms

- GONUTS: http://gowiki.tamu.edu
- QuickGO: http://www.ebi.ac.uk/QuickGO
- AmiGO: http://amigo.geneontology.org



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- Peer Reviews

page contributors
- Wikientrybot

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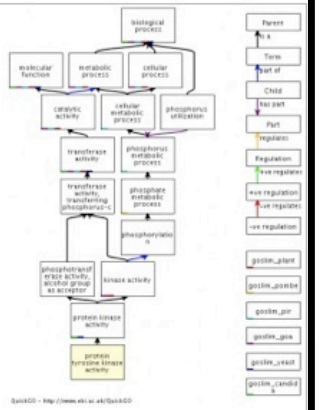
- Special pages
- Printable version
- Permanent link

GONUTS is undergoing some *major* debugging for Pecan.
Please expect blank pages and some delays in updating.
[Email comments to Daniel.]

GO:0004713 ! protein tyrosine kinase activity

id: GO:0004713
name: protein tyrosine kinase activity
namespace: molecular_function
alt_id:GO:0004718
def: "Catalysis of the reaction: ATP + a protein tyrosine = ADP + protein tyrosine phosphate." [EC:2.7.10]
subset: gosubset_prok
synonym: "JAK" NARROW []
synonym: "Janus kinase activity" NARROW []
synonym: "protein-tyrosine kinase activity" EXACT []
xref: EC:2.7.10
xref: MetaCyc:EC-2.7.10
xref: Reactome:11065 "protein tyrosine kinase activity"
is_a: GO:0004672 ! protein kinase activity



AmiGO

Last version checked	Last updated
date: 14:01:2011 17:26	date: 08:10:2010 13:21
saved-by: rfoulger	saved-by: dph
auto-generated-by: OBO-Edit 2.0	auto-generated-by: OBO-Edit 2.0

Gene Ontology Home
The contents of this box are automatically generated. You can help by adding information to the "Notes"

Usage Notes [edit]

References [edit]

See Help:References for how to manage references in GONUTS.

Child Terms

This term has the following 4 child terms.

- [+] GO:0004714 - transmembrane receptor protein tyrosine kinase activity (13)
- [ ] GO:0004715 - non-membrane spanning protein tyrosine kinase activity
- [+] GO:0004716 - receptor signaling protein tyrosine kinase activity (1)
- [+] GO:0035400 - histone tyrosine kinase activity (1)

Pages in category "GO:0004713 ! protein tyrosine kinase activity"

The following 200 pages are in this category, out of 732 total.

Show articles starting with: --All results-- Go

(previous 200) (next 200)

C
- CHICK:A0M8T9
- CHICK:A0SVH2
- CHICK:BTK

C cont.
- CHICK:Q90960
- CHICK:Q90961
- CHICK:Q90962

F cont.
- FB:Tk4
- FB:Tk6
- FB:tor

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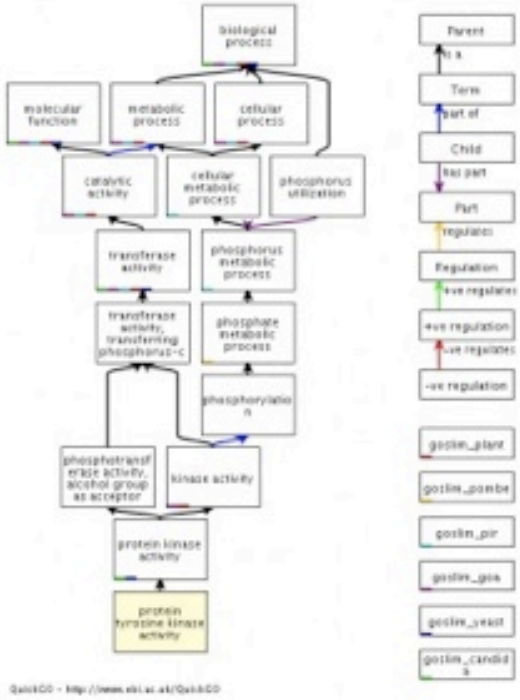

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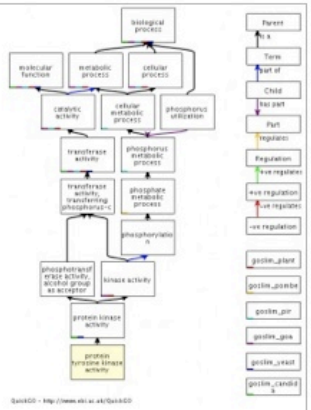

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Pages in category "GO:0004713 ! protein tyrosine kinase activity"

The following 200 pages are in this category, out of 732 total.

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C
- CHICK:A0M8T9
- CHICK:A0SVH2
- CHICK:BTK

C cont.
- CHICK:Q90960
- CHICK:Q90961
- CHICK:Q90962

F cont.
- FB:Tk4
- FB:Tk6
- FB:tor

Strategies

- Search for a keyword and browse the ontology for the right term
- Look at terms suggested by others for your protein
  - Computational with the IEA evidence code
  - Curators with TAS or IC
- Look at terms used for homologous proteins in model organisms

Functional Annotation

- Annotation: a note that is made while reading any form of text

- Functional Annotation: a database entry in a **specific format** that is made based on **evidence** in a peer-reviewed **paper** about the function of a **protein**

Evidence Codes for CACAO

- Evidence codes describe the type of work or analysis done by the authors
  - IDA: Inferred from Direct Assay
  - IMP: Inferred from Mutant Phenotype
  - IGI: Inferred from Genetic Interaction
  - ISO: Inferred from Sequence Orthology
  - ISA: Inferred from Sequence Alignment
  - ISM: Inferred from Sequence Model
  - IGC: Inferred from Genomic Context

- Expert biocurators get to use others, but we restrict them for CACAO. If it's not one of these 7, your annotation is incorrect!!!

- http://gowiki.tamu.edu/wiki/index.php/evidence_codes

Evidence Codes for CACAO

- Picking the right evidence code is important
- Use the evidence code decision tree
- Use the evidence code guidelines at the GO consortium website:
  - http://www.geneontology.org/GO.evidence.shtml
- Discuss!

Functional Annotation

- Annotation: a note that is made while reading any form of text

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4 REQUIRED parts of EVERY GO annotation

Qualifier	GO ID	GO term name	Reference	Evidence Code	with/from	Aspect	Notes	Status
	GO:0000183	chromatin silencing at rDNA	~~SGD_REF:S000182194~~ PMID:19737915[3]	IMP: Inferred from Mutant Phenotype		P	From SGD	

GO

Reference

Evidence code

Notes (about evidence)

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The Spring 2012 season of CACAO has started!

LAMBD:VLYS

Species (Taxon ID)	*Enterobacteria phage lambda (Bacteriophage lambda).* ([1])
Gene Name(s)	S
Protein Name(s)	Holin gpS protein Lysis protein S Lysis inhibitor
External Links	
EMBL	J02459 M14035
PIR	H94164
RefSeq	NP_040644.1 YP_001551775.1
TCDB	1.E.2.1.1
GeneID	2703479 5740919
GenomeReviews	J02459_GR
ProtClustDB	CLSP2343227
GO	GO:0020002 GO:0016021 GO:0016998 GO:0019835
InterPro	IPR006481
Pfam	PF05106
TIGRFAMs	TIGR01634

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Annotations

[edit]

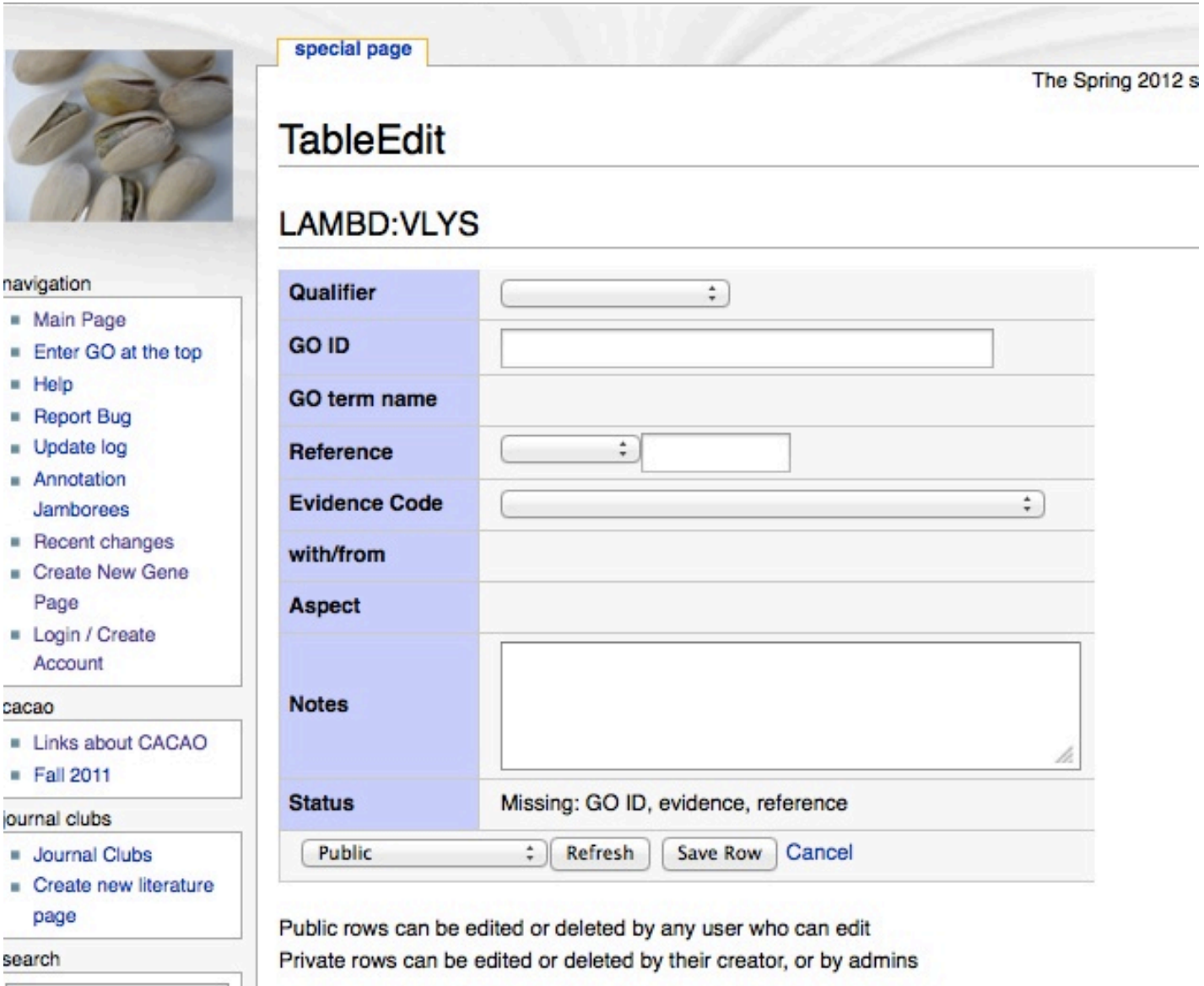
Qualifier	GO ID	GO term name	Reference	Evidence Code	with/from	Aspect	Notes	Status
	GO:0016020	membrane	GO_REF:0000004	IEA: Inferred from Electronic Annotation	SP_KW:KW-0472	C	Seeded From UniProt	
	GO:0033644	host cell membrane	GO_REF:0000004	IEA: Inferred from Electronic Annotation	SP_KW:KW-1043	C	Seeded From UniProt	
edit table								

edit table

Notes

[edit]

Entering/editing annotations



4 REQUIRED parts of EVERY GO annotation

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GO

Reference

Evidence code

Notes (about evidence)

2 other parts that may be required…

Qualifier

Qualifier	GO ID	GO term name	Reference	Evidence Code	with/from	Aspect	Notes	Status
contributes_to	GO:0004402	histone acetyltransferase activity	SGD_REF:S000074492 PMID:11773077[10]	IDA: Inferred from Direct Assay		F	From SGD	
	GO:0004340	glucokinase activity	PMID:1097393[1]	IGI: Inferred from Genetic Interaction	UniProtKB:P69797	F	table two: gpt glk mpt = no glucose activity	

With/From

Example paper

http://www.ncbi.nlm.nih.gov/pubmed/8227000