




# Using a data triangle to understand molecular nutrition


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Department of  
Bioinformatics - BiGCaT  
Maastricht University


Presented at INCON,  
Guarujá, Sep 28 2010





Nature Precedings : doi:10.1038/npre.2011.5689.1 : Posted 16 Feb 2011

 **edyong209** Ed Yong  
 Ah Valentine's day - when intelligent people the world over forget that emotions come from the brain not the heart.  
 6 hours ago

 **Chris\_Evelo** Chris Evelo  
 S Prasaka K. doc2b differences in methylation in cervical and oral cancers promising biomarkers, but what is the cause? #SHG  
 7 hours ago

 **Chris\_Evelo** Chris Evelo  
 #SHG a meeting about genetic and phenotypic diversity and yet they add sugar and milk to all coffee.  
 7 hours ago

 **Chris\_Evelo** Chris Evelo  
 Interesting presentations by youngsters at #SHG, but why do they all think a 15 min limit means you should speak faster, not say less?  
 7 hours ago ☆ Favorite ↶ Reply 🗑 Delete

 **utopiadocs** Utopia Documents  
 Researchers: what area would you like to use #utopiadocs for? #drill  
 7 hours ago

 **abhishektiware** Abhishek Tiwari  
 Yes, The Khan Academy IS the Future of Education (video) -


close x

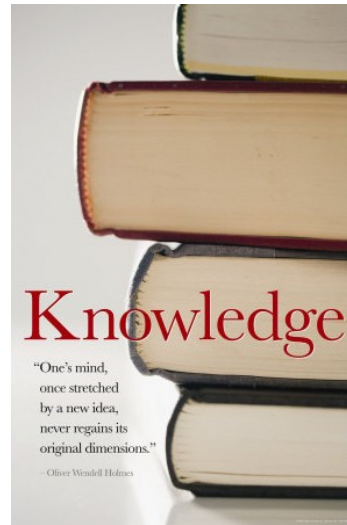
 **@Chris\_Evelo**  
 Chris Evelo

Interesting presentations by youngsters at #ISHG, but why do they all think a 15 min limit means you should speak faster, not say less?

7 hours ago via [Twitter for BlackBerry®](#) ☆ Favorite ↶ Reply 🗑 Delete

Tweets tagged with #SHG

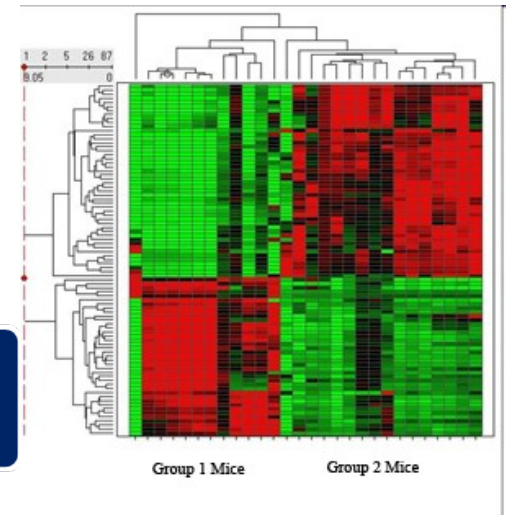
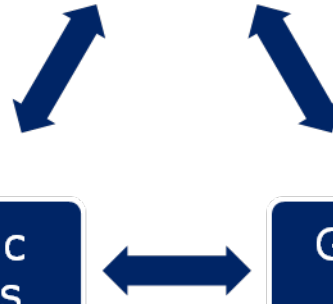
 **proflucia** Lucia Regina Ribeiro  
 Chris Evelo talk at #ISHG 36th Ann Conf of the Indian Soc Hum Genet: Integrative systems biology: how to deal with large scale genetics data  
 1 hour ago



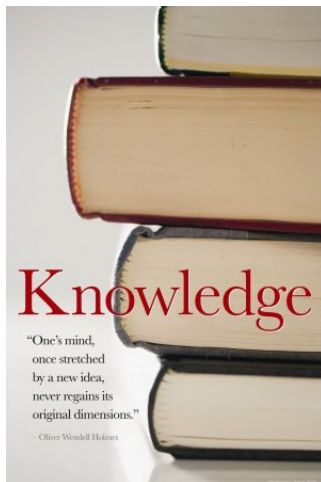
Existing knowledge

Genetic Results

Genomic Results

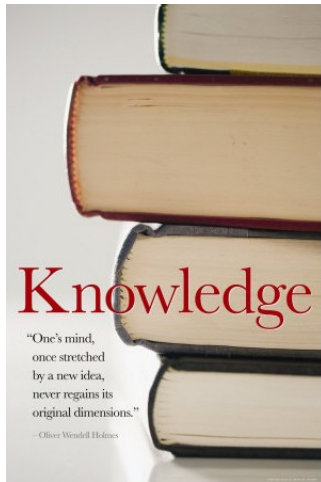


# Existing Knowledge Carefully Hidden in:



# Computers aren't good at:

## Reading



## Listening



# There is a lot of knowledge to structure

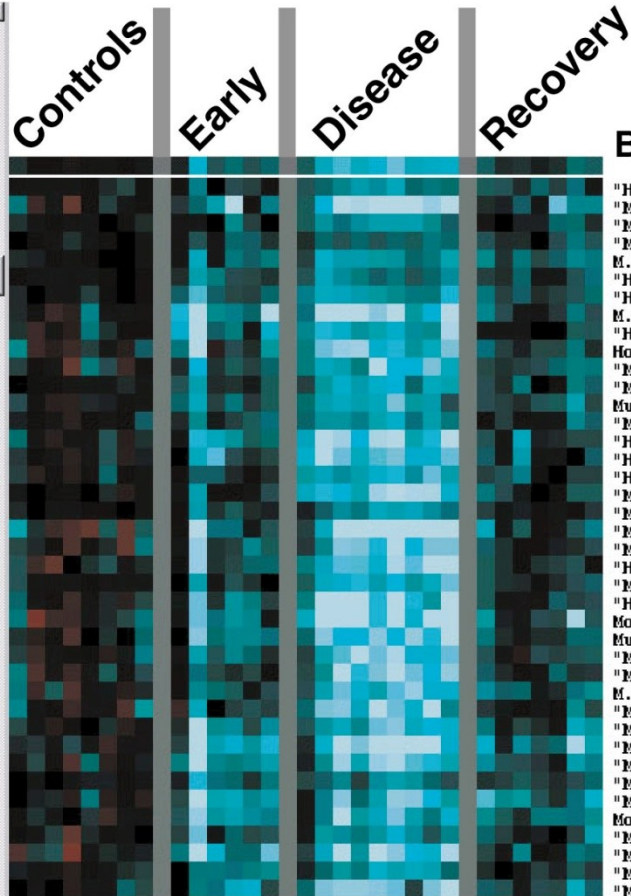


# What do we really need? Well...



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# Cardiomyopathy: Downregulated genes

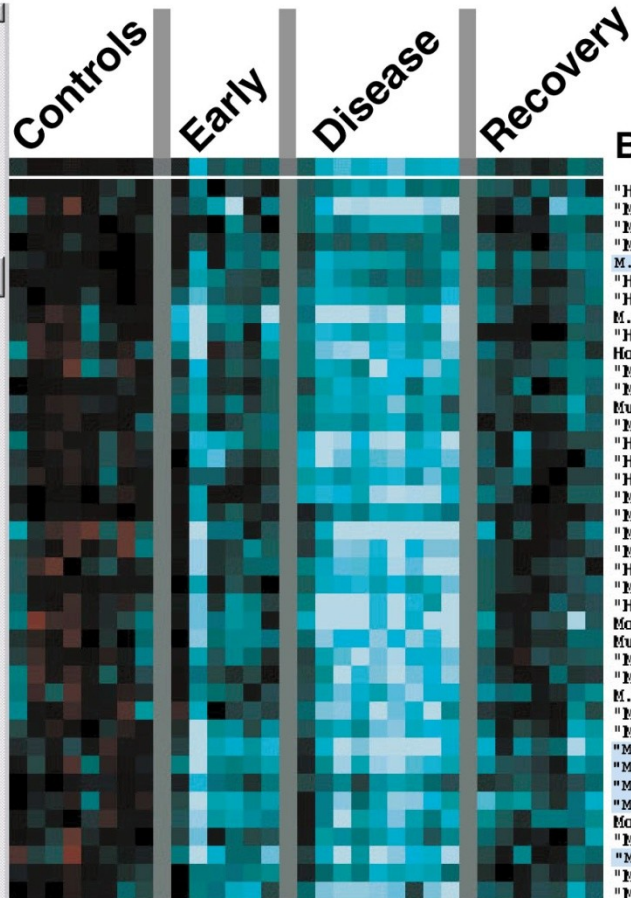


## BLAST Definitions

"Homologous to sn 007021: PRE-mRNA SPLICING FACTOR SF2, P32 SUBUNIT PRECURSOR (GCIQ-R PROTEIN)"  
 "Mus musculus proteasome activator PA28 alpha subunit mRNA, complete cds"  
 "Mus musculus cdc37 homolog mRNA, complete cds"  
 "Mus musculus ornithine decarboxylase antisense gene, complete cds"  
 M.musculus mRNA for carnitine acetyltransferase  
 "Homologous to sn 000779: CALCIUM-TRANSPORTING ATPASE SARCOPLASMIC RETICULUM TYPE (EC 3.6.1.34)"  
 "Homologous to sn P11507: CALCIUM-TRANSPORTING ATPASE ENDOPLASMIC RETICULUM TYPE (EC 3.6.1.38)"  
 M.musculus ENO3 mRNA for enolase beta subunit  
 "Homologous to sn P47858: 6-PHOSPHOFRUCTOKINASE, MUSCLE TYPE (EC 2.7.1.11) (PHOSPHOFRUCTOKINASE)"  
 Homologous to sn P23327: SARCOPLASMIC RETICULUM HISTIDINE-RICH CALCIUM-BINDING PROTEIN PRECURSOR  
 "Mouse AE3 mRNA, complete cds"  
 "M.musculus glucose transporter 2 mRNA, complete cds"  
 Mus musculus aspartate aminotransferase gene 5'-flank and exon 1  
 "Mus musculus thioredoxin-dependent peroxide reductase (tox) mRNA, complete cds"  
 "Homologous to sn P47858: 6-PHOSPHOFRUCTOKINASE, MUSCLE TYPE (EC 2.7.1.11) (PHOSPHOFRUCTOKINASE)"  
 "Homologous to sn P11508: CALCIUM-TRANSPORTING ATPASE SARCOPLASMIC RETICULUM TYPE (EC 3.6.1.34)"  
 "Homologous to sn P35434: ATP SYNTHASE DELTA CHAIN, MITOCHONDRIAL PRECURSOR (EC 3.6.1.34)."  
 "Mus musculus F1FOATP synthase complex E subunit (Atp5k) gene, complete cds"  
 "Mus musculus NAD(H)-specific isocitrate dehydrogenase gamma subunit precursor, mRNA, complete cds"  
 "M.musculus gene for dodecenoyl-CoA delta-isomerase, exons 1 and 2"  
 "Mus musculus cytochrome c oxidase subunit VIII-H precursor (COX8H) mRNA, complete cds"  
 "Homologous to sn P35745: ACYLPHOSPHATASE, MUSCLE TYPE ISOZYME (EC 3.6.1.7) (ACYLPHOSPHATE PHOSPHATASE)"  
 "Mus musculus CD-1 cardiac troponin I mRNA, complete cds"  
 "Homologous to sn P00566: CREATINE KINASE, M CHAIN (EC 2.7.3.2) (MU-2 PROTEIN)."  
 Mouse mRNA for protein with homology to transition protein 2 (TP2)  
 Mus musculus Selenium-binding liver protein mRNA  
 "Mus musculus (clone MAR1) aldose reductase mRNA, complete cds"  
 "Mus musculus vascular endothelial growth factor B 186 (VEGF-B) precursor, mRNA, complete cds"  
 M.musculus mRNA for NADP transhydrogenase  
 "Mus musculus aldehyde dehydrogenase (ALDH2) mRNA, nuclear gene encoding mitochondrial protein"  
 "Mouse cytosolic epoxide hydrolase mRNA, complete cds"  
 "Mus musculus 129SV carnitine palmitoyltransferase II mRNA, complete cds"  
 "Mus musculus medium-chain acyl-CoA dehydrogenase mRNA, complete cds"  
 "Mus musculus long-chain acyl-CoA dehydrogenase mRNA, complete cds"  
 "Mus musculus very-long chain acyl-CoA dehydrogenase mRNA, partial cds"  
 Mouse muscle creatine kinase mRNA (EC 2.7.3.2)  
 "Mus musculus isocitrate dehydrogenase mRNA, complete cds"  
 "Mus musculus long chain fatty acyl CoA synthetase mRNA, complete cds"  
 "Mus musculus sterol carrier protein-2 (SCP-2) gene, complete cds"  
 "Mouse alpha-tubulin isotype M-alpha-4 mRNA, complete cds"



# Cardiomyopathy: Downregulated genes



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 "Mus musculus aldehyde dehydrogenase (ALDH2) mRNA, nuclear gene encoding mitochondrial protein"  
 "Mouse cytosolic epoxide hydrolase mRNA, complete cds"  
 "Mus musculus 129SV carnitine palmitoyltransferase II mRNA, complete cds"  
 "Mus musculus medium-chain acyl-CoA dehydrogenase mRNA, complete cds"  
 "Mus musculus long-chain acyl-CoA dehydrogenase mRNA, complete cds"  
 "Mus musculus very-long chain acyl-CoA dehydrogenase, partial cds"  
 Mouse muscle creatine kinase mRNA (EC 2.7.3.2)  
 "Mus musculus isocitrate dehydrogenase mRNA, complete cds"  
 "Mus musculus long chain fatty acyl CoA synthetase mRNA, complete cds"  
 "Mus musculus sterol carrier protein-2 (SCP-2) gene, complete cds"  
 "Mouse alpha-tubulin isotype M-alpha-4 mRNA, complete cds"

Fatty Acid Degradation?  
 Other pathways / processes?

## Find the pathways:

Biological processes in duodenal mucosa affected by glutamine administration

Pathway	number of genes			Measured	Total	Z Score
	Changed	Up	Down			
<a href="#">Hs_Mitochondrial_fatty_acid_betaoxidation</a>	6	6	0	16	16	4.456
<a href="#">Hs_Electron_Transport_Chain</a>	17	17	0	85	105	4.278
<a href="#">Hs_Fatty_Acid_Synthesis</a>	5	5	0	21	22	2.757
<a href="#">Hs_Fatty_Acid_Beta-Oxidation</a>	6	6	0	31	32	2.424
<a href="#">Hs_mRNA_processing_Reactome</a>	16	6	10	118	127	2.402
<a href="#">Hs_Unsaturated_Fatty_Acid_Beta_Oxidation</a>	2	2	0	6	6	2.342
<a href="#">Hs_HSP70_and_Apoptosis</a>	4	4	0	18	18	2.299
<a href="#">Hs_Oxidative_Stress</a>	5	5	0	27	28	2.097
<a href="#">Hs_Fatty_Acid_Omega_Oxidation</a>	3	3	0	14	15	1.915
<a href="#">Hs_Proteasome_Degradation</a>	8	8	0	60	61	1.629
<a href="#">Hs_RNA_transcription_Reactome</a>	5	5	0	38	40	1.25
<a href="#">Hs_Irinotecan_pathway_PharmGKB</a>	2	1	1	12	12	1.154
<a href="#">Hs_Synthesis_and_Degradation_of_Ketone_Bodies_KEGG</a>	1	1	0	5	5	1.023

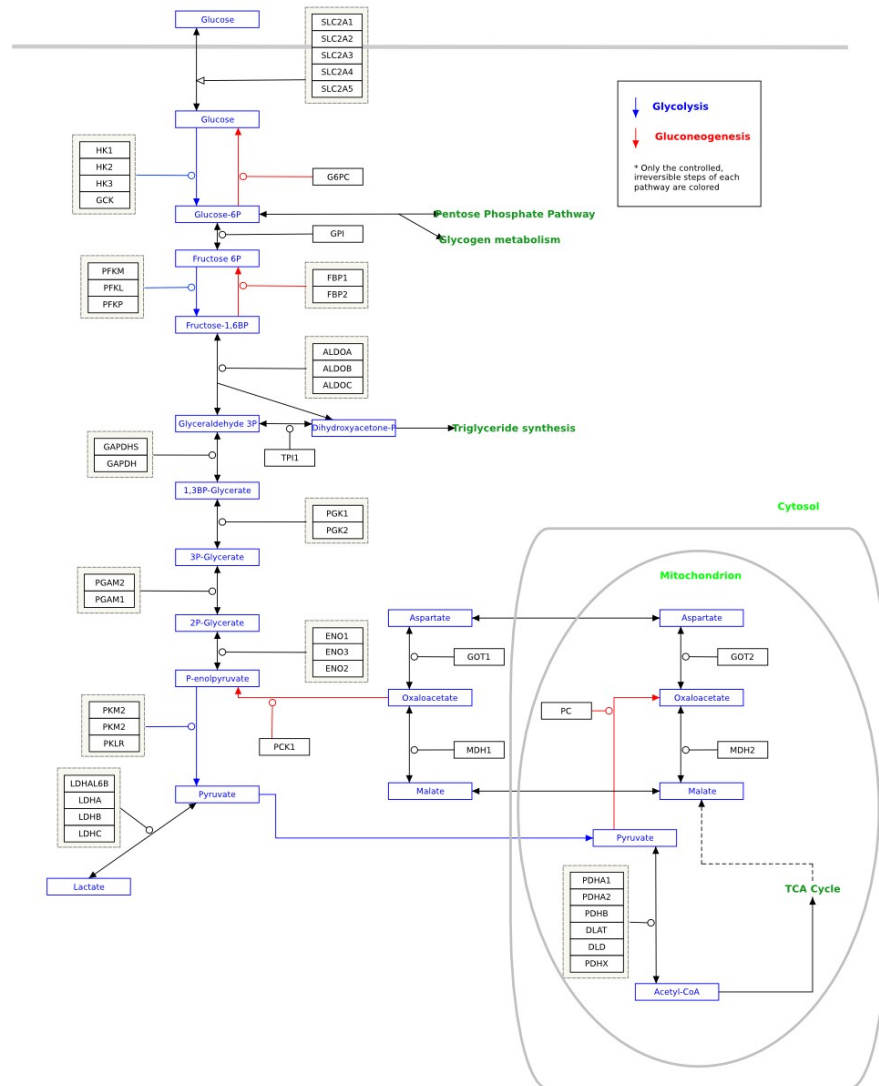
Title: Glycolysis and Gluconeogenesis  
Organism: Homo sapiens

# Understand genomics

## Example WikiPathway Pathway

Pathway on glycolysis. Using modern systems biology annotation.

And genes and metabolites connected to major databases.



Nature Precedings : doi:10.1038/npre.2011.5689.1 : Posted 16 Feb 2011

PathVisio / WikiPathways - Mozilla Firefox

http://www.pathvisio.org/

PathVisio and WikiPathways Development

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Start Page Index History Last Change

Version 2.0 available!

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- Plugin Developers Guide
- API Docs
- Developer Meetings
- Continuous build system reports
- Scripts and Tools
- More...

For WikiPathways Developers

- report a bug
- Test protocol for WikiPathways
- Setup a local copy of WikiPathways
- Community Curation Events
- More...

Download Now Visual Tour

News

Aug 27, 2010 PathVisio 2.0.8 Has been released! See [ReleaseNotes](#)

PathVisio / WikiPathways Development

is the wiki + bug tracker for [PathVisio](#) and [WikiPathways](#).

License

PathVisio is licensed to you under the [Apache License, version 2.0](#)

Attachments

[PathVisioSite-1.png](#) (135.8 KB) - added by [martijn](#) 11 months ago.

# PathVisio

[www.pathvisio.org](http://www.pathvisio.org)

- Visualize data on biological pathways
- It can use gene expression, proteomics and metabolomics data

- Identify significantly changed processes

Martijn P van Iersel, Thomas Kelder, Alexander R Pico, Kristina Hanspers, Susan Coort, Bruce R Conklin, Chris Evelo (2008) Presenting and exploring biological pathways with PathVisio. BMC Bioinformatics 9: 399

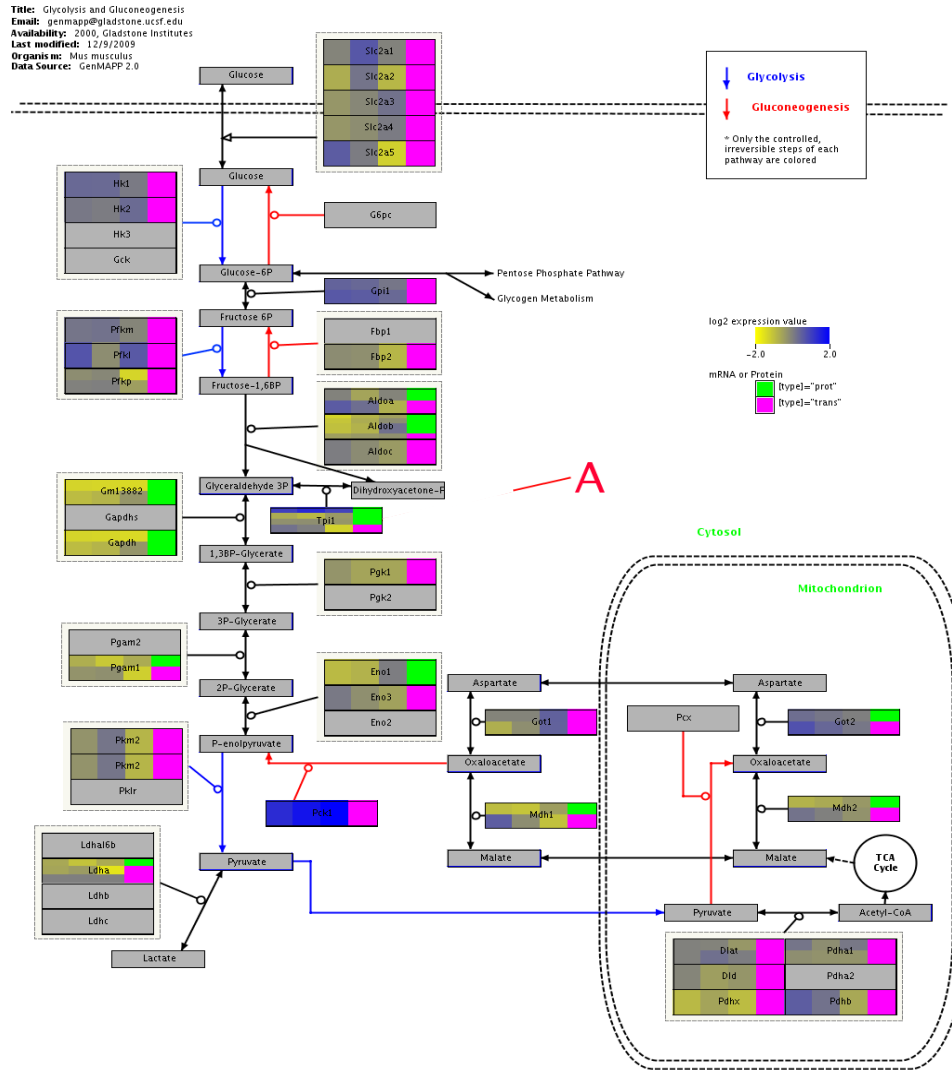
Nature Precedings doi:10.1038/npre.2011.5689.1 Posted 16 Feb 2011

# adding data = adding colour

## Example PathVisio result

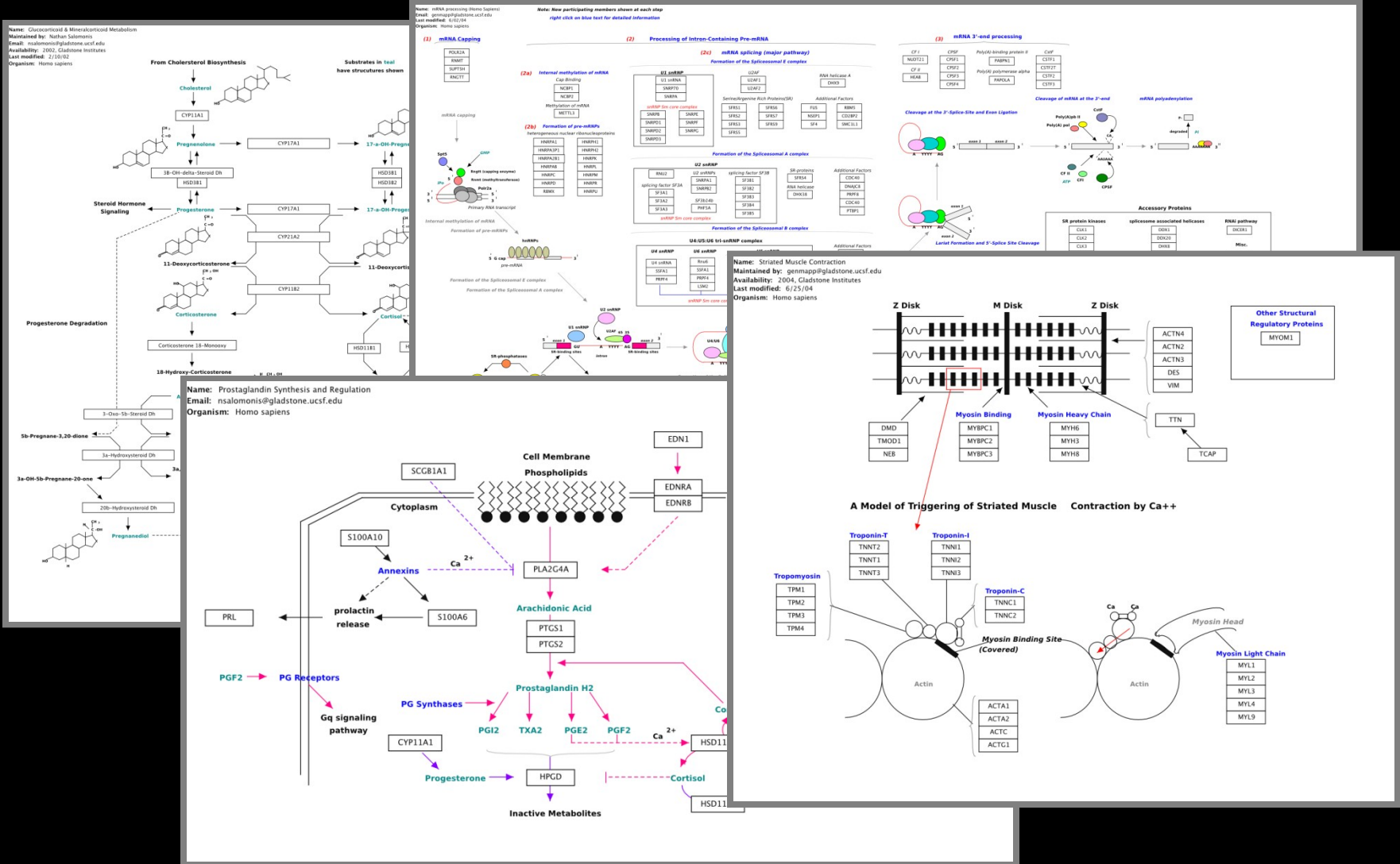
Showing proteomics and transcriptomics results on the glycolysis pathway in mice liver after starvation.

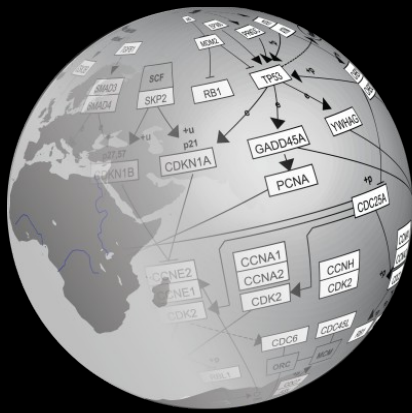
[Data from Kaatje Lenaerts and Milka Sokolovic, analysis by Martijn van Iersel]



Nature Precedings : doi:10.1038/npre.2011.5689.1 : Posted 16 Feb 2011

# Now we just need the Pathways





# WikiPathways

- Public resource for biological pathways
- **Anyone** can contribute and curate
- More up-to-date representation of biological knowledge

**WikiPathways: Pathway Editing for the People.** Alexander R. Pico, Thomas Kelder, Martijn P. van Iersel, Kristina Hanspers, Bruce R. Conklin, Chris Evelo. **PLoS Biology** 2008: 6: 7. e184

*Commentaries:*

**Big data: Wikiomics.** Mitch Waldrop. **Nature** 2008: 455, 22-25

**We the curators.** Allison Doerr. **Nature Methods** 2008: 5, 754–755

**No rest for the bio-wikis.** Ewen Callaway. **Nature** 2010: 468, 359-360

article discussion view source history watch

**Welcome to WikiPathways** <sup>BETA</sup>  
 In the new tradition of **Wikipedia**, WikiPathways is an open, public platform dedicated to the curation of biological pathways by and for the scientific community. [More about WikiPathways...](#)

## Finding Pathways

### Search

Google Custom Search

Search

You can search by:

- Pathway name (*Apoptosis*)
- Gene or protein name (*p53*)
- Any page content (*cancer*)

### Browse

Browse Pathways

Display pathways from species:  in category:

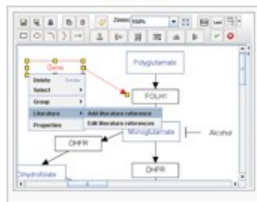
- Antidiuretic hormone
- Antoine Lavoisier metabolism K000
- Fatty Acid Oxidation: Mitochondria
- Fatty Acid Synthesis: Mitochondria
- Fatty Acid Beta Oxidation: Mitochondria
- Glutathione Metabolism
- One-carbon metabolism

Browse by species and category

**Search: "One carbon"**

## Contributing New Pathways

### Create



Create a new pathway page

### Suggest

Pathway wishlist

Add new wanted item here

Pathway name	Assigned by	Date	Comments	Vote	Watch	Resolve
Estrogen receptor-mediated regulation	John	07/27/09	We want to use this to evaluate CRP data from Andros	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Protein Translation Regulation	John	08/26/10	Should be centered around ART, mTOR	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
DNA damage response	John	02/28/10	According to Wilson-Watson this should be linked with cancer	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Substantive use of the pathway	John	11/02/09	Gene set during discussion with professor Mary Stouffer-Stouffer about path. use	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Add a pathway to the wish list

## Sample Pathway Pages

### Sandbox

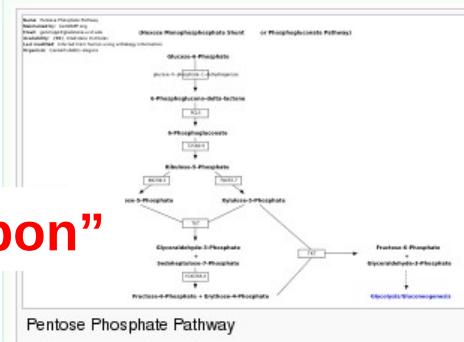


Check out the following pages:

- Show recent changes
- Show new pathways
- Show most edited pathways
- Show most viewed pathways

## Today's featured pathway

Pentose Phosphate Pathway (Caenorhabditis elegans)



Pentose Phosphate Pathway

## New!

- WikiPathways won the application showcase at the [NBIC BioRange Consortium Meeting](#)!
- Pathway Wish List
- New embedded pathway editor
- [Batch download page](#)
- Visual diff tool for comparing pathway versions

## Coming Soon...

- Converted content from KEGG and Reactome
- Tagging pathways with terms from Gene Ontology and other biological ontologies

## Statistics

- There are **497** pathways
- Number of **pathways** (and unique genes) per species:
 

Homo sapiens:	<b>103</b> (3436)
Rattus norvegicus:	<b>105</b> (3049)
Mus musculus:	<b>109</b> (3725)



Navigation menu: Home, Help

pathway: Create, Browse, Wish List, Download, About Us

overview: Recent Changes, Most Viewed, Most Edited, New Pathways

link: GenMAPP, PathVisio

search: Google Custom Search, Titles only

toolbox: What links here, Related changes, Special pages, Printable version, Permanent link

Footer: Nature Precedings, doi:10.1038/npre2011.5689



special

# Find pathways

Search for:  ALL SPECIES Search

Tip: use AND, OR, \*, ?, parentheses or quotes

## 23 pathways found



One Carbon Metabolism (Mus musculus)



One Carbon Metabolism (Canis familiaris)



One Carbon Metabolism (Drosophila melanogaster)



One Carbon Metabolism (Anopheles gambiae)



One Carbon Metabolism (Bos taurus)



One Carbon Metabolism (Danio rerio)



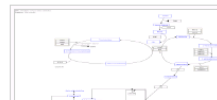
One Carbon Metabolism (Homo sapiens)



One Carbon Metabolism (Pan troglodytes)



One Carbon Metabolism (Rattus norvegicus)



Glutathione and one carbon metabolism (Mus musculus)



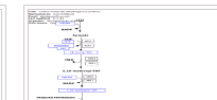
One Carbon Metabolism (Gallus gallus)



One carbon pool by folate (Mycobacterium tuberculosis)



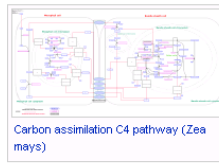
One carbon metabolism and related pathways (Mus musculus)



Carbon monoxide dehydrogenase pathway (Saccharomyces cerevisiae)



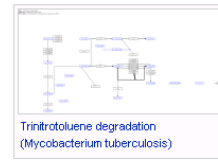
Principle Pathways of Carbon Metabolism (Saccharomyces cerevisiae)



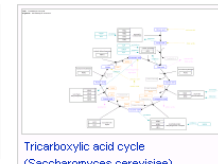
Carbon assimilation C4 pathway (Zea mays)



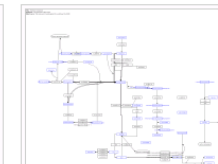
Photosynthetic Carbon Reduction (Arabidopsis thaliana)



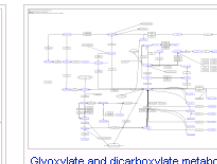
Trinitrotoluene degradation (Mycobacterium tuberculosis)



Tricarboxylic acid cycle (Saccharomyces cerevisiae)



Methane metabolism (Mycobacterium tuberculosis)



Glyoxylate and dicarboxylate metabolism (Mycobacterium tuberculosis)

Click

Nature Precedings  
DOI: 10.1038/npre.2011.15689.1  
Posted 16 Feb 2011



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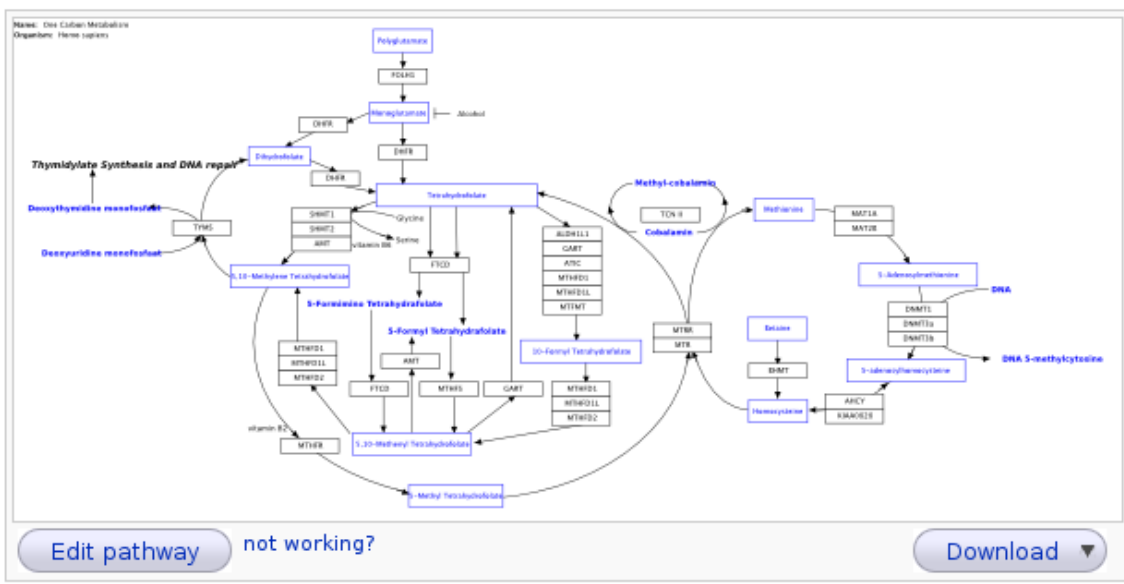
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# Pathway:Homo sapiens:One-carbon metabolism



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  - 4.2 Data formats
  - 4.3 Actions
  - 4.4 Batch
- 5 History
- 6 Pathway Info
  - 6.1 DataNodes

## Description

This one-carbon metabolism pathway is centered around folate. Folate is the primary methyl-group donor for processes such as DNA methylation reactions, nucleotide synthesis and DNA repair mechanisms. An important pathway for any study related to folate or DNA methylation.

[edit](#)

Differential methylation (e.g. hypermethylation of tumor suppressors) as well as disturbances in nucleotide synthesis and repair, are associated with several forms of cancer. There are also indications that hypermethylation is involved in the progression of adenomas to cancer.

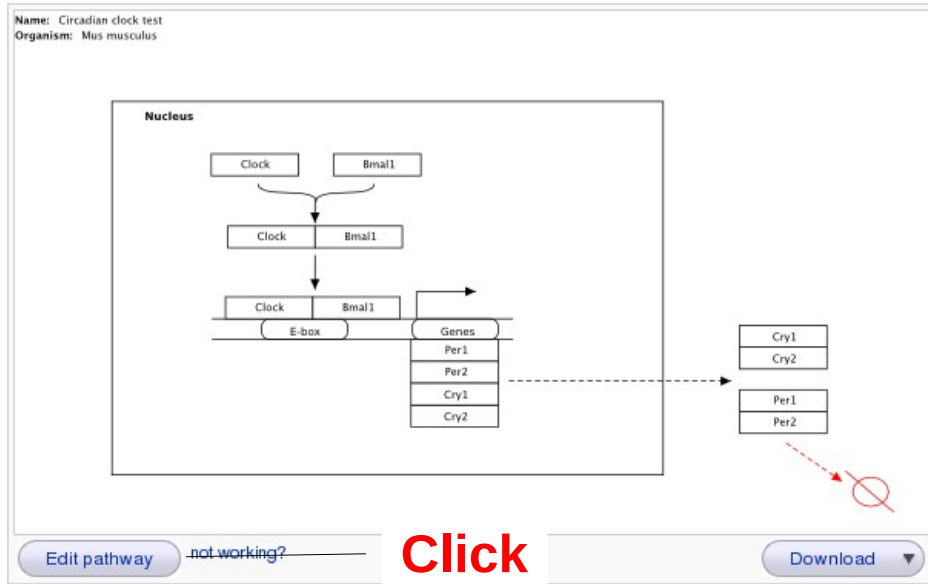
## Bibliography

- Hazra A, Wu K, Kraft P, Fuchs CS, Giovannucci EL, and Hunter DJ. *Twenty-four non-synonymous polymorphisms in the one-carbon metabolic pathway and risk of colorectal adenoma in the Nurses' Health Study*. Carcinogenesis 2007 Jul; 28(7) 1510-9. doi:10.1093/carcin/bgn062

# Editing

16 Feb 2011  
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## Pathway:Mus musculus:Circadian clock pathway



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### Description

The circadian clock is a molecular mechanism that maintains the cell's metabolism, physiology and behaviour. This is a simplified version of t

nes, involved in

edit

Login needed

Registration by e-mail address

All edits logged



# Draw the proteins and interactions

16 Feb 2011  
15:09  
10:03  
doi:10.038 more 2011

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pathway discussion edit history delete move protect unwatch

## Pathway: Mus musculus: Circadian clock pathway

Zoom: 100%

Name: Circadian clock test  
Organism: Mus musculus

Properties Backpage

Property	Value
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not working?

# How to ever do data visualization?

	A	B	D	E	
1	ID	System	t0	t1	t2
2	177140_s_X		0.693	-2.856	
3	186328_atX		1.327	3.497	
4	192151_atX		3.863	-3.457	
5	187703_s_X		1.16	-3.352	
6	193913_s_X		-0.435	3.356	
7	173437_atX		-2.36	-1.633	
8	173452_s_X		-2.43	0.035	
9	no affy	X	-1.878	2.211	
10	178221_atX		-1.758	-3.223	
11	173832_atX		-3.386	1.695	
12	184510_atX		0.109	-1.045	
13	192371_s_X		-3.075	-0.404	
14	172670_x_X		3.642	3.428	
15	176778_s_X		-0.112	1.072	-1.695

**RNA interference and miRNA**

Some famous miRNA's

- let-7
- lin-4
- lin-14
- lin-28

Other genes involved in RNAi

- RDE-2/MUT-8
- MUT-7
- RDE-3/MUT-2
- RDE-4

Legend: t0

- up (red)
- down (green)
- No criteria met (grey)
- Not found (white)

# Connect to Genome Databases

**Ce\_RNA\_interference\_and\_miRNA - GenMAPP 2.0**

File Tools Format View Data Help

Author: Martijn van Iersel  
 Maintained by: Martijn van Iersel  
 E-mail: martijn.vaniersel@bigcat.unimaas.nl

## RNA interference and miRNA

Some famous miRNA's

The diagram illustrates the RNA interference pathway. It starts with dsRNA (double-stranded RNA) being processed by Dicer (DCR-1) into 22nt siRNA (small interfering RNA). These siRNAs then form the RNA-dependent RNA polymerase family, which includes RRF-1, RRF-2, EGO-1, and RRF-3. These proteins act as inhibitors or competitors. The pathway also involves Feedback / Spreading.

No Gene Database

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http://www.wormbase.org/db/gene/gene?name=WBGene0006924

Home Genome Blast / Blat WormMart Batch Sequences Markers Genetic Maps Submit Searches Site Map

Find: WBGene0006924  
 Anything

WormBase The Biology and Genome of *C. elegans*.

Gene Summary	Locus Summary	Sequence Summary	Protein Summary	EST Alignments	Genome Browser	Genetic Map	Nearby Genes	Bibliography	Tree Display	XML Schema	Acedb Image
--------------	---------------	------------------	-----------------	----------------	----------------	-------------	--------------	--------------	--------------	------------	-------------

## Gene Summary for vig-1

Specify a gene using a gene name ([unc-26](#)), a predicted gene id ([R13A5.9](#)), or a protein ID ([CE02711](#))

[\[identification\]](#) [\[location\]](#) [\[function\]](#) [\[expression\]](#) [\[gene ontology\]](#) [\[alleles\]](#) [\[similarities\]](#) [\[reagents\]](#) [\[bibliography\]](#)

IDs:	Main name	Sequence name	Other name(s)	WB Gene ID
	vig-1 - ( <i>VIG (Drosophila Vasa Intronic Gene) ortholog</i> ) via person evidence: <a href="#">Ronald Plasterk</a>	F56D12.5	2B613 (inferred automatically)	WBGene00006924

**Concise Description:** vig-1 encodes a predicted RNA-binding protein orthologous to Drosophila VIG (Vasa Intronic Gene); vig-1 activity is required for proper function of the let-7 miRNA in vivo and thus, for regulating the transition from late larval to adult cell fates; VIG-1 is a component of the 250 kDa RNA-induced silencing complex (RISC) complex and co-immunoprecipitates with both TSN-1, the *C. elegans* Tudor-SN ortholog, and the let-7 miRNA. [\[details\]](#)

**NCBI KOGs\*:** Predicted RNA-binding protein [[KOG2945](#)]; [[OMpre\\_WH000977](#)]

**Species:** *Caenorhabditis elegans*  
 Other sequences

**NCBI:** [[AceView: 2B613](#)]

Done 4472 1087 thomaskelder@gmail.com

# Double click to annotate the proteins

Posted 16 Feb 2011

BETA  
WIKIPATHWAYS  
Pathways for the People

Navigation

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## Pathway: Mus musculus: Circadian clock pathway

Zoom: 100%

Name: Circadian clock test  
Organism: Mus musculus

**DataNode properties**

Comments Literature **Annotation**

Search

Manual entry

Text label: Per1  
Identifier: ENSMUSG00000020893  
Database: Ensembl

Cancel Ok

**Properties Backpage**

**Gene information**

Gene ID:	ENSMUSG00000020
Gene Symbol:	Per1
Description:	period homolog (Drosophila) [Source:MGI;Acc:MGI:10
Chr:	11

not working?



# Add reference to literature

Feb 2011  
BETA  
WIKIPATHWAYS  
Pathways for the People

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## Pathway: Mus musculus: Circadian clock pathway

Name: Circadian clock test  
Organism: Mus musculus

Zoom: 100%

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Overview: receive most viewed new

link: detail path

search: Google

titles: Nature Precedings: doi:10.1038/npre.2011.5689.1

What? Relat? Spec? Print? Perr?

**Literature reference properties**

Pubmed ID	17430084	Query PubMed
Title	The clockwork of metabolism.	
Year	2007	
Source	Annu Rev Nutr	
Authors (separate with ;)	Ramsey KM; Marcheva B; Kohsaka A; Bass J	

Cancel Ok

**Click**

# Download

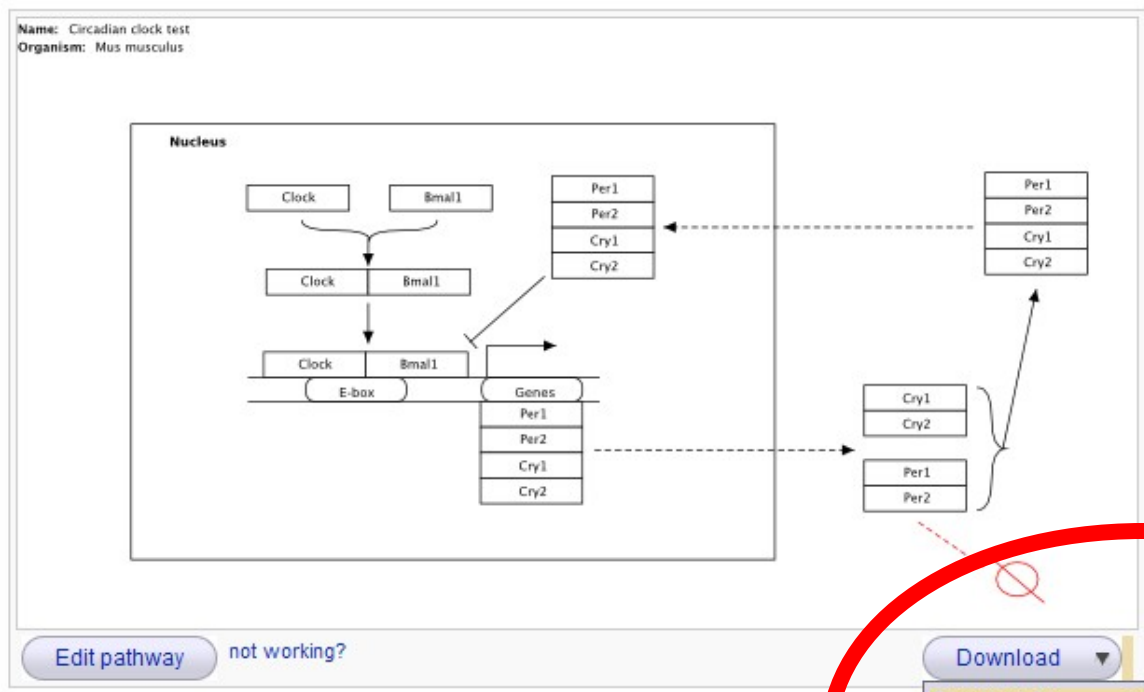


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## Pathway:Mus musculus:Circadian clock pathway



- Contents [hide]
- 1 Description
  - 2 Bibliography
  - 3 Categories
  - 4 Download files
    - 4.1 Image formats
    - 4.2 Data formats
    - 4.3 Actions
    - 4.4 Batch
  - 5 History
  - 6 Pathway Info
    - 6.1 DataNodes

Download

- Download for
  - PathVisio (.gpm)
  - GenMAPP (.mapp)
  - Gene list (.txt)
  - Eu.Gene (.pwf)
  - Png image (.png)
  - Acrobat (.pdf)
- Open in Cytoscape

### Description

The circadian clock is a molecular mechanism that maintains the cell's 24-hour molecular rhythm by driving the rhythmic expression of a wide range of genes, involved in metabolism, physiology and behaviour. This is a simplified version of the pathway, restricting to the mPer/mCry feedback loop

### Bibliography

1. Ramsey KM, Marcheva B, Kohsaka A, and Bass J. *The clockwork of metabolism*. Annu Rev Nutr 2007; 27 219-40. doi:10.1146/annurev.nutr.27.061406.093546 pmid:17430084 PubMed HubMed [doi]

# Cytoscape visualization used to group

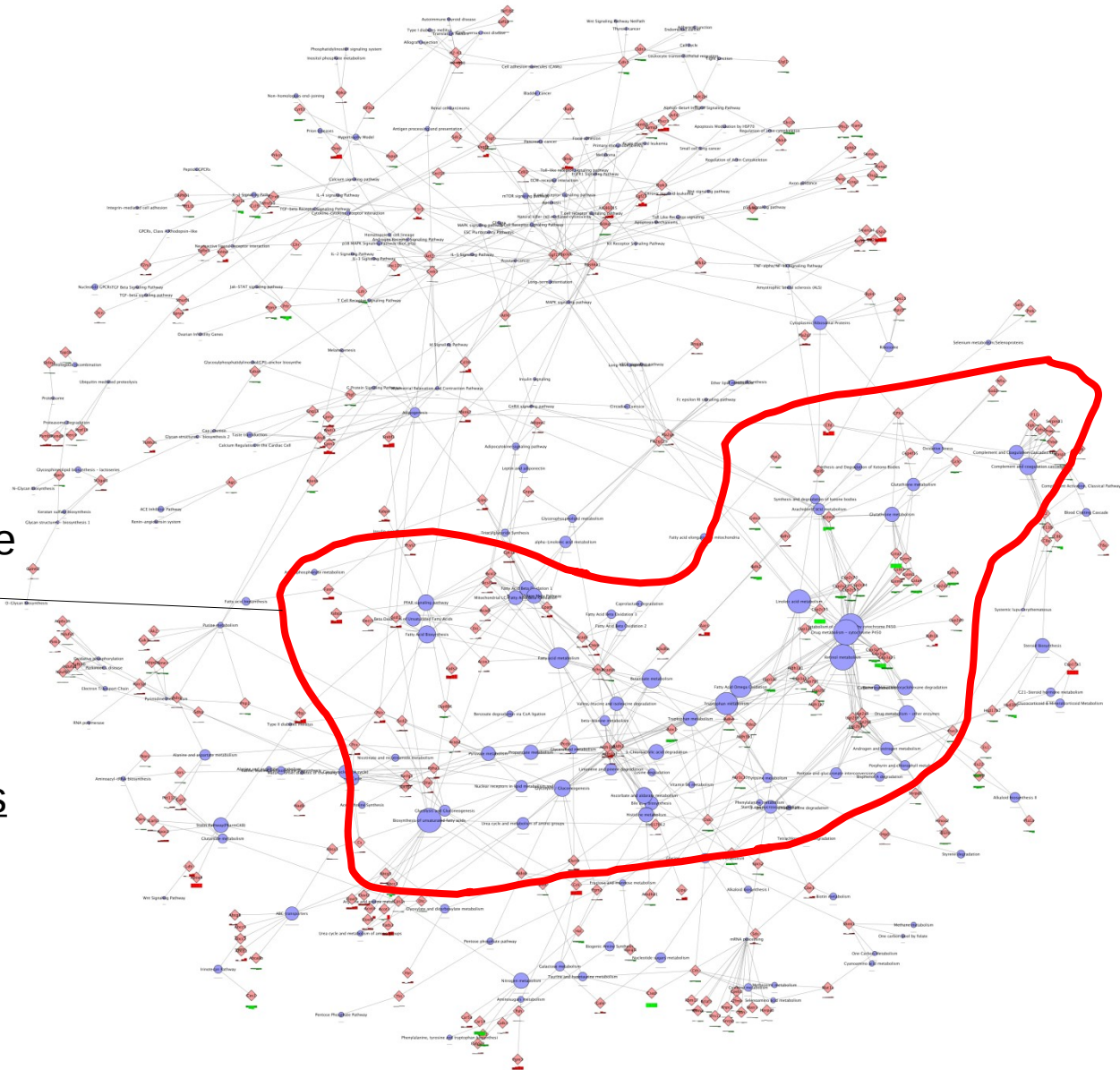
PPS1

Liver

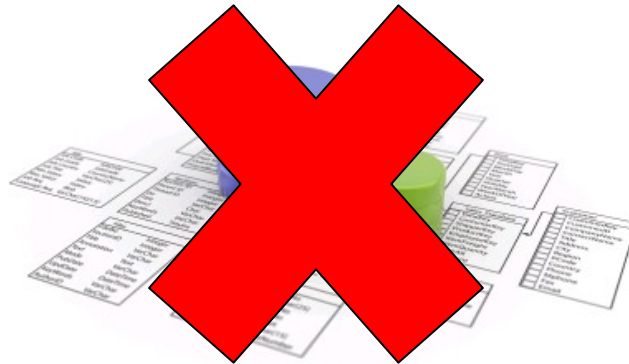
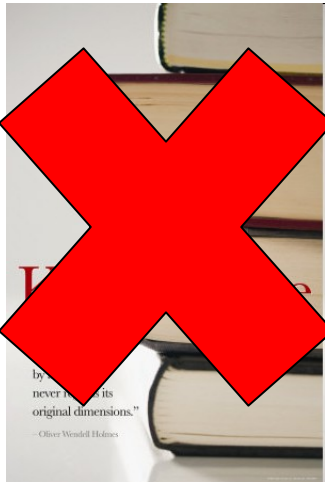
All pathways

Pathways with high z-score grouped together.

Explains why there are relatively few significant genes, but many pathways with high z-score.



# Existing Knowledge Carefully Hidden in:



Nature Precedings : doi:10.1038/npre.2011.5689.1 : Posted 16 Feb 2011

# Assisted content generation

Suggestions from:

- Compound sources (HMDB)
- Gene resources (UniProt, IntAct)
- Pathways & processes (KEGG, GO, local)
- Text mining
- Semantic web data stores

Title: New Pathway

Nature Precedings : doi:10.1038/npre.2011.5689.1 : Posted 16 Feb 2011



Oxaloacetate

GOT1

Properties Backpage Search PPP

Property	Value
Backpage head	
Center X	5400.0
Center Y	1980.0
Color	
Comments	
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Database Name	
Height	300.0
Text Label	LAT
Type	GeneProduct
Width	1200.0

Title: New Pathway

Nature Precedings : doi:10.1038/npre.2011.5689.1 : Posted 16 Feb 2011



- Delete
- Select
- Order
- Literature
- Properties
- PPP
  - HMDB Suggestions
  - PHASAR Suggestions
  - KEGG
  - WikiPathways (local) Suggestions
  - Bind Suggestions

Oxaloacetate

GOT1

Properties Backpage Search PPP

Property	Value
Backpage head	
Center X	5400.0
Center Y	1965.0
Color	
Comments	[]
Database Identifier	2828026
Database Name	
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Type	GeneProduct
Width	1200.0

Title: New Pathway

Nature Precedings : doi:10.1038/npre.2011.5689.1 : Posted 16 Feb 2011

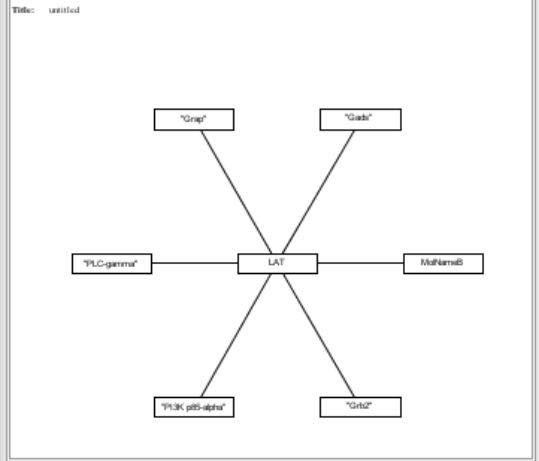


Oxaloacetate

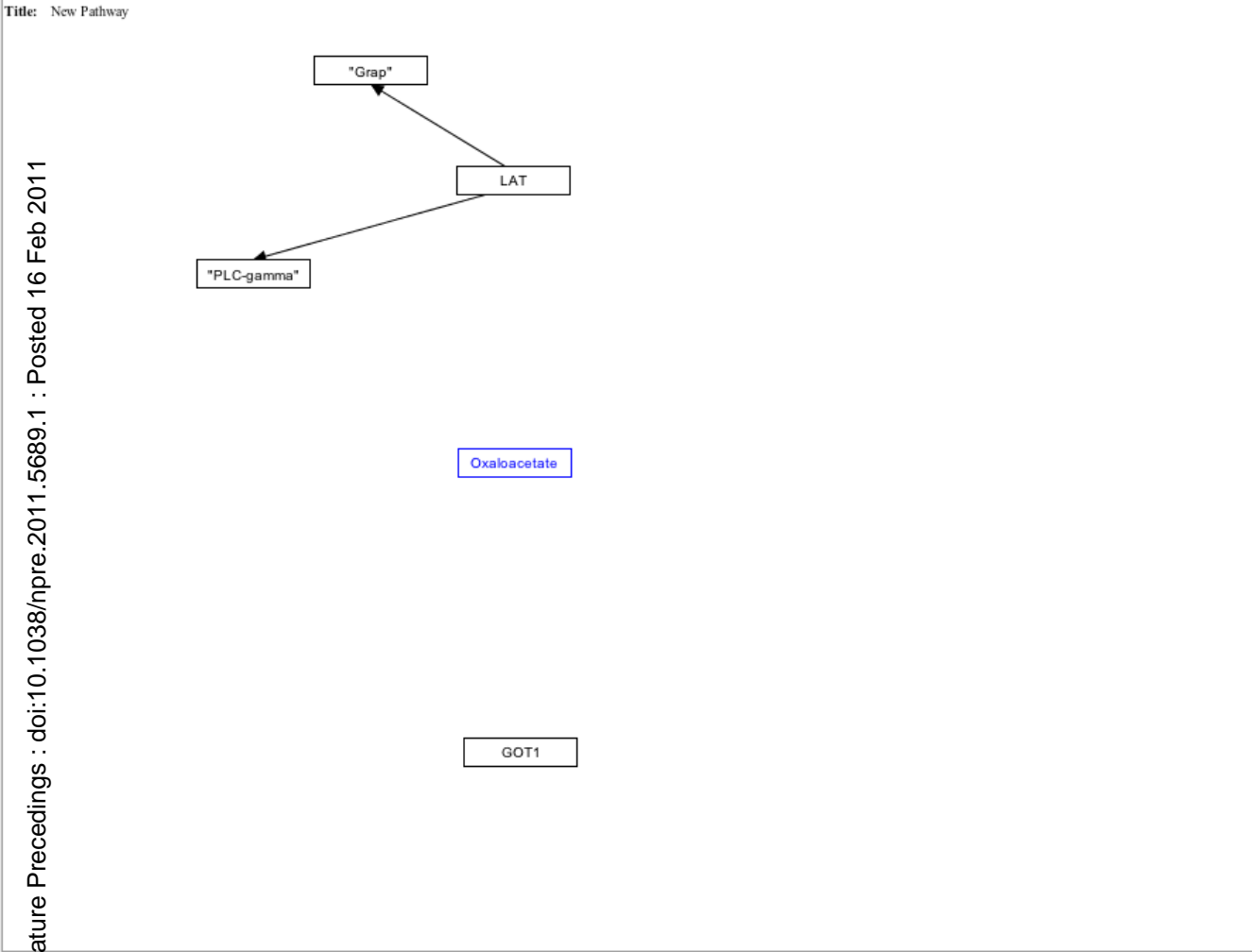
GOT1

Help

Putative pathway part: Bind

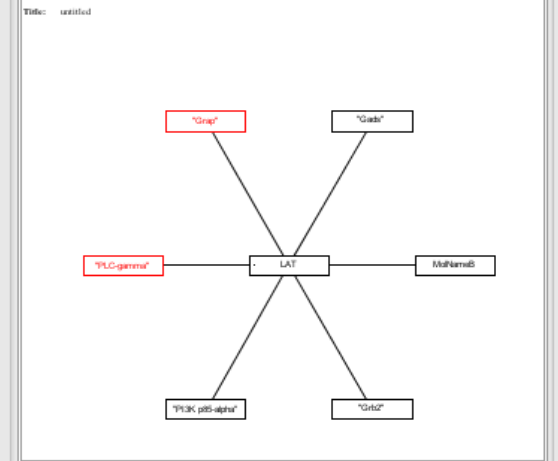




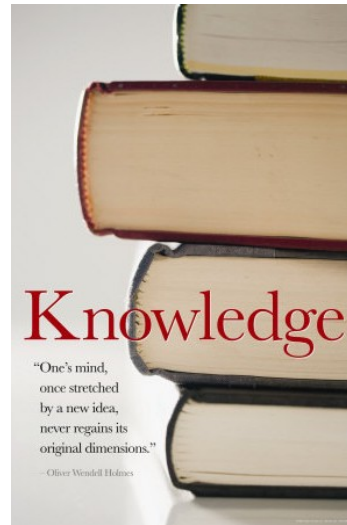


Help

Putative pathway part: Bind



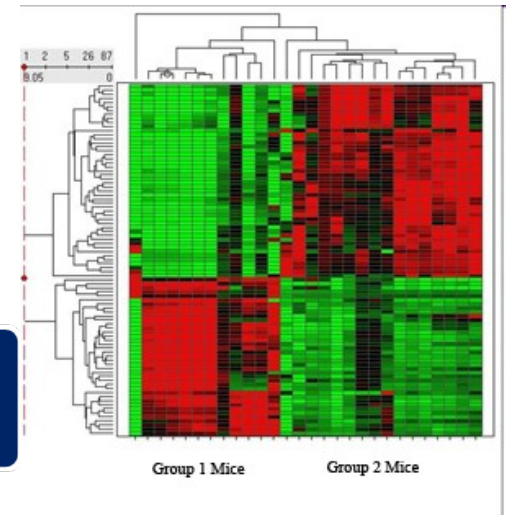
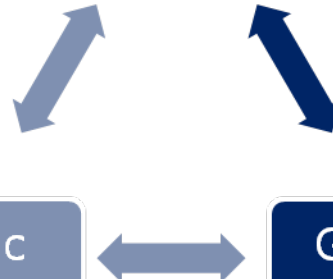
Nature Precedings : doi:10.1038/npre.2011.5689.1 : Posted 16 Feb 2011

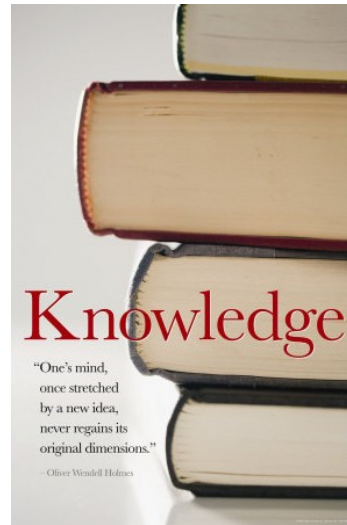


Existing knowledge

Genetic Results

Genomic Results

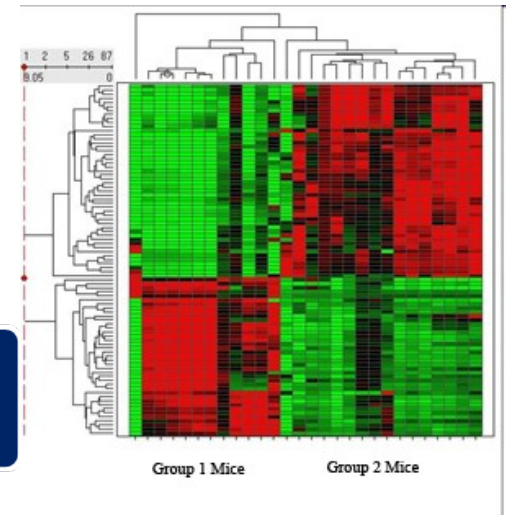
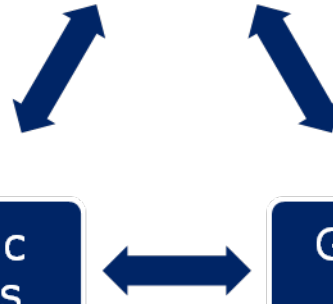


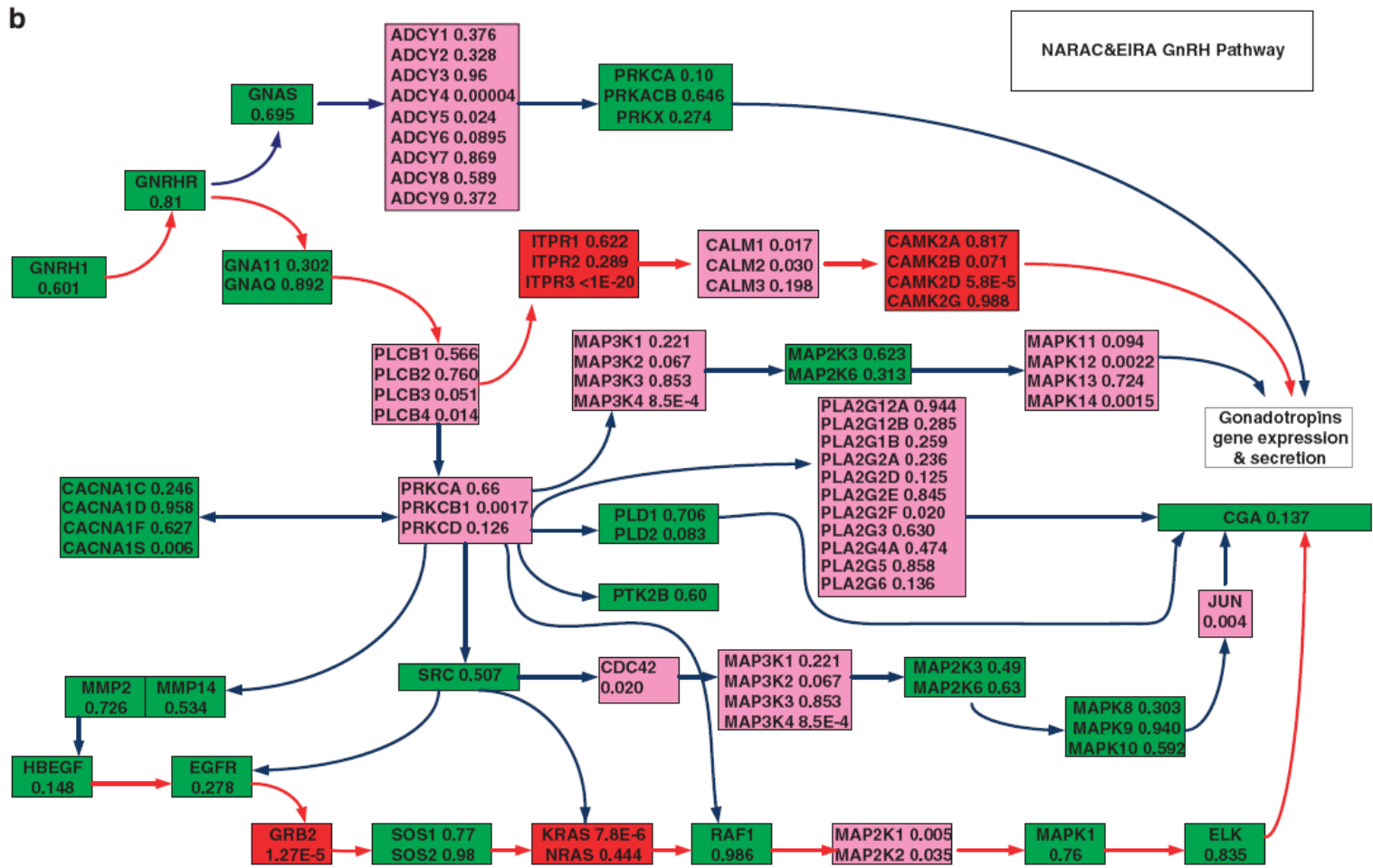


Existing knowledge

Genetic Results

Genomic Results





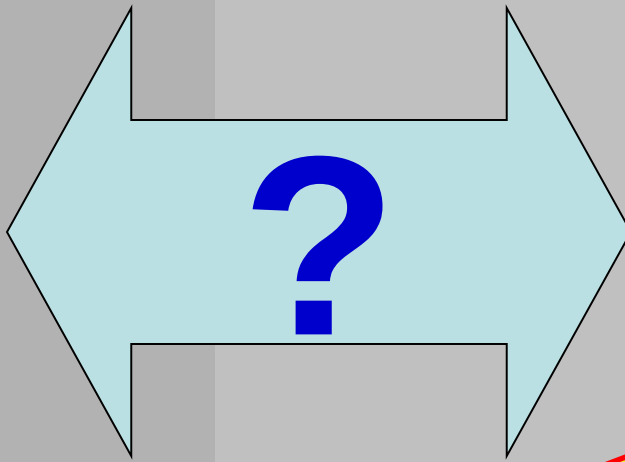
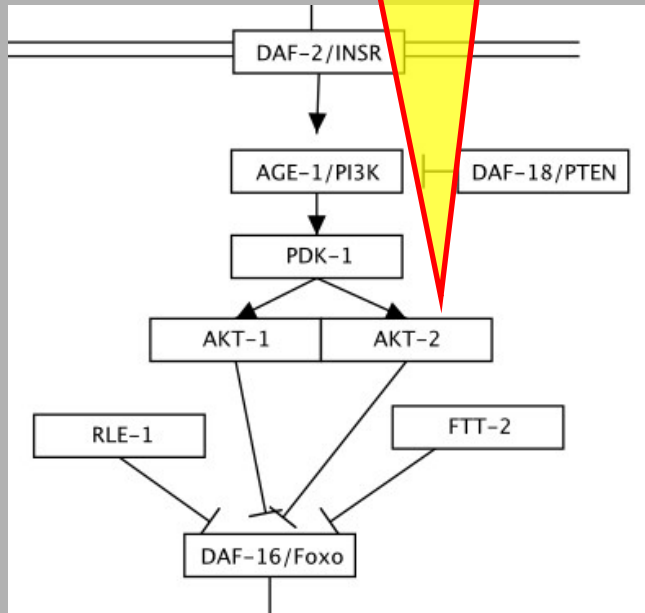
**Figure 1** *P*-values of genes in GnRH pathway for RA. (a) *P*-values of genes in GnRH pathway for RA in WTCCC studies. Blocks containing significant genes are in red color, blocks containing mild significant genes are in light red color and blocks containing no significant genes are in green color. (b) *P*-values of genes in GnRH pathway for RA in NARAC and EIRA studies. Blocks containing significant genes are in red color, blocks containing mild significant genes are in light red color and blocks containing no significant genes are in green color.

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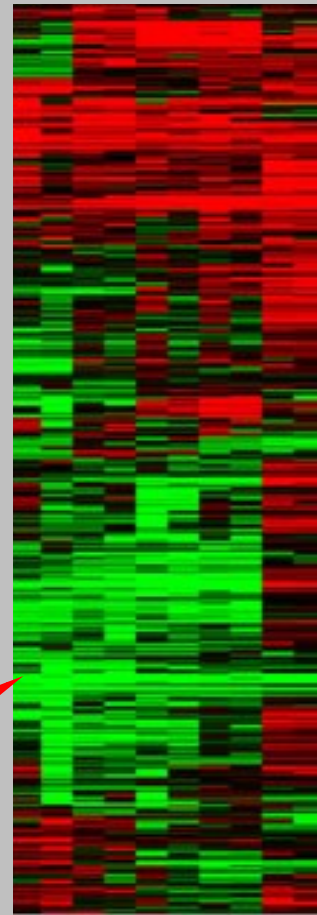
# Problem: Identifier Mapping

Nature Precedings : doi:10.1038/npre.2011.5689.1 : Posted 16 Feb 2011

Entrez Gene  
3643

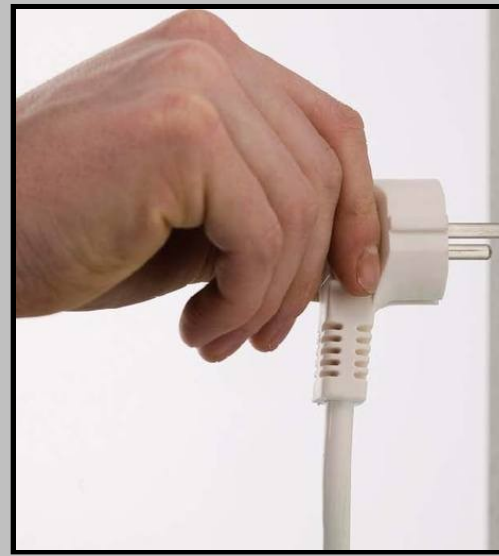
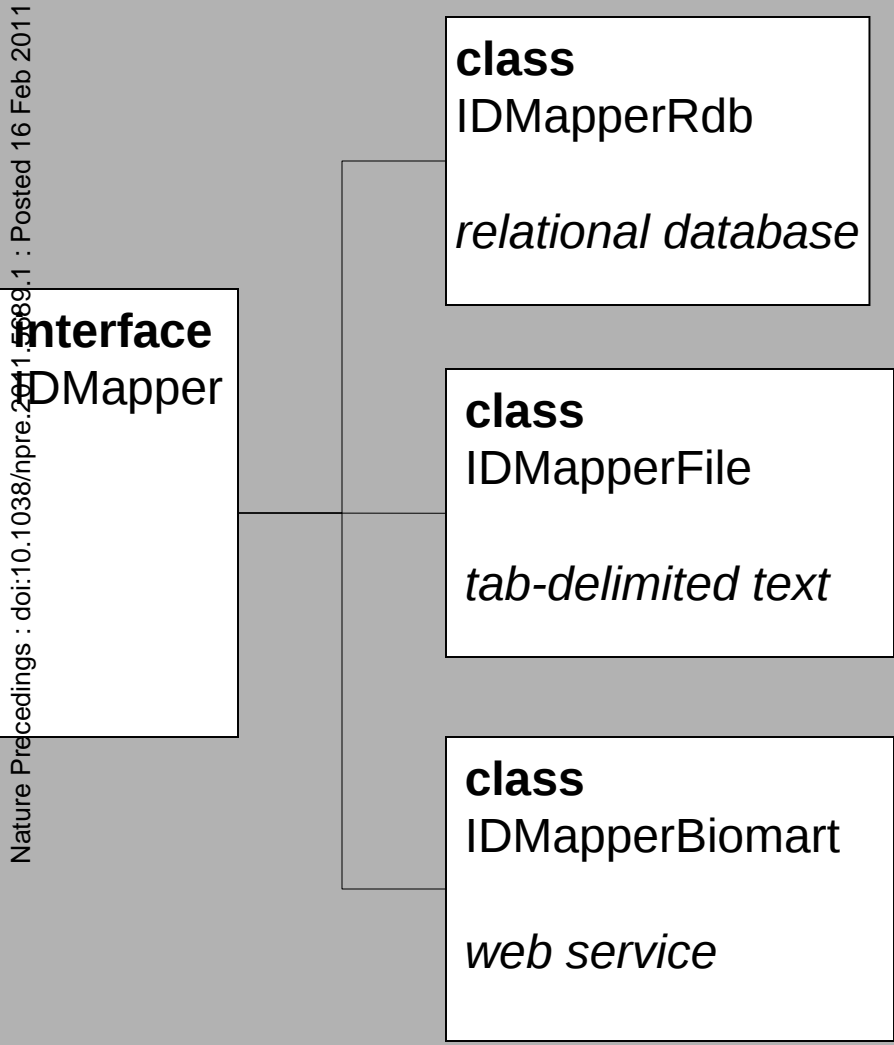


Affymetrix probeset  
100234\_at



# BridgeDB: Abstraction Layer

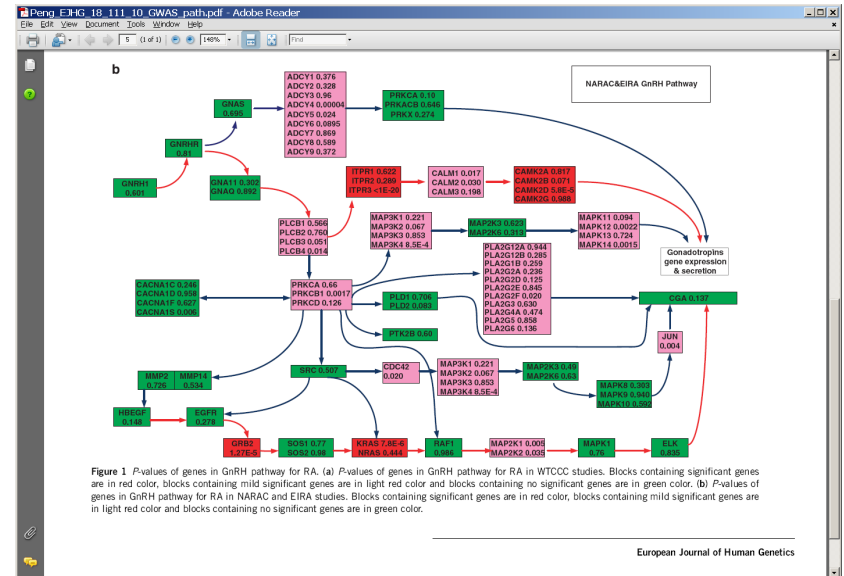
Nature Precedings : doi:10.1038/npre.2011.5689.1 : Posted 16 Feb 2011



# Can we show SNPs?

YES WE CAN

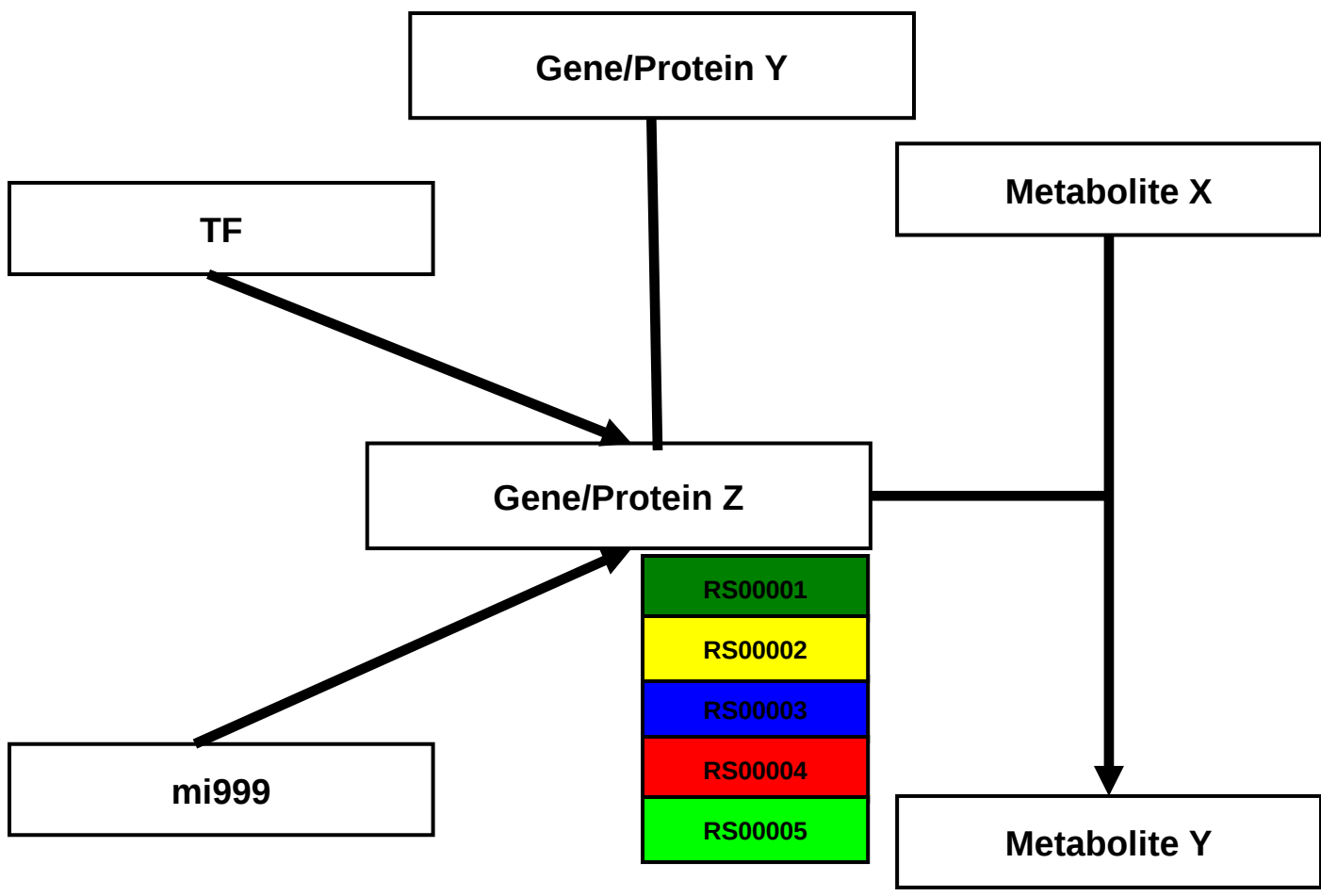
Using dbSNP links in ENSEMBL as part of BridgeDB libs

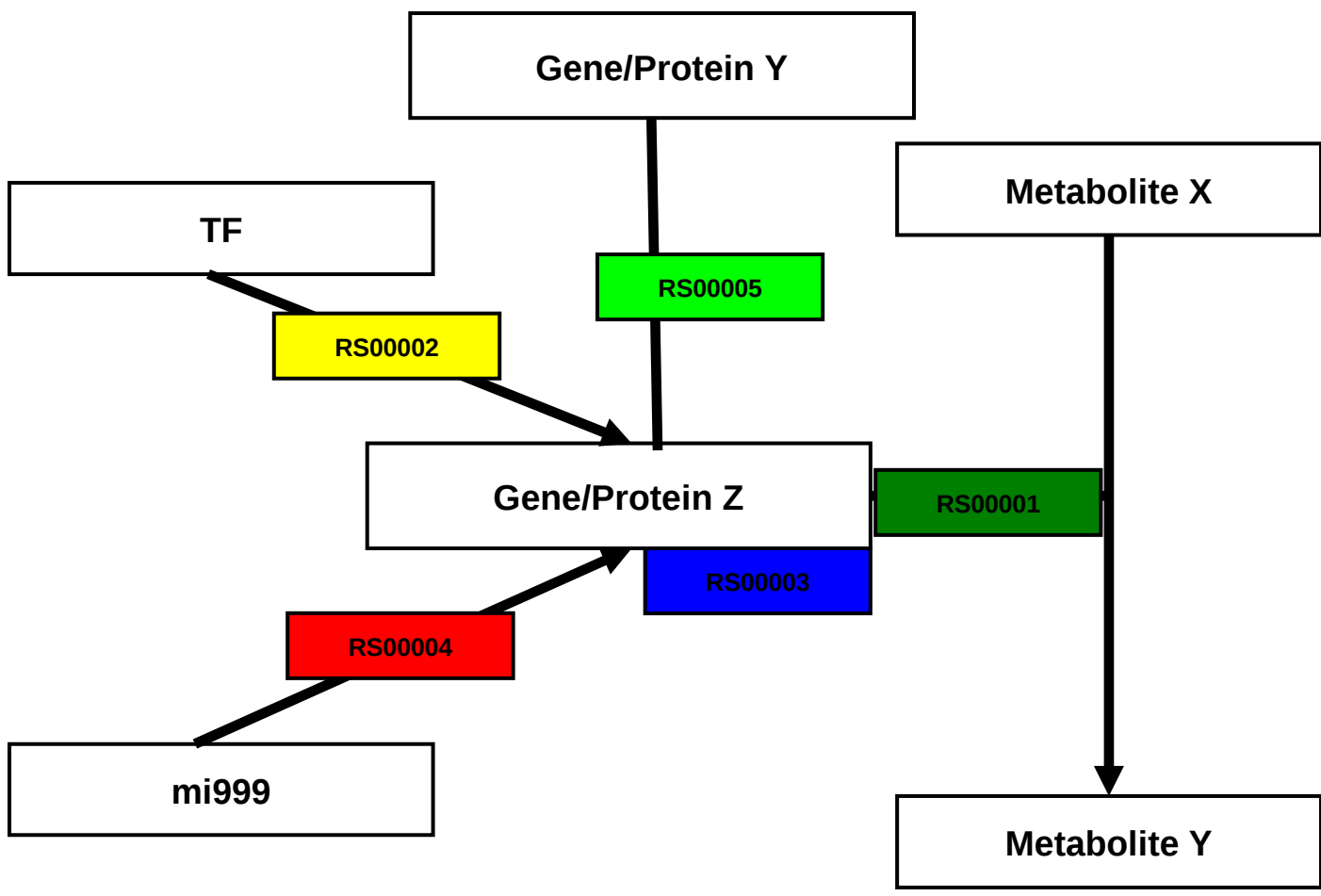


# But it will look like this....









### Functionalize SNPs

Unkown function (attribute to gene)

In miRNA binding site

In TF binding site

Changing protein functionality (coding)

Changing protein interactions (coding)



So we just have to color the jellies, ehmm SNPs





Thanks!



Nature Precedings : doi:10.1038/npre.2011.5689.1 : Posted 16 Feb 2011

