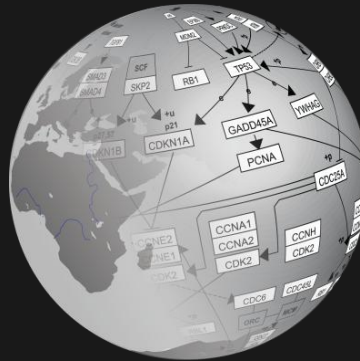


WikiPathways Tutorial



Mining biological pathways and
more...

Thomas Kelder

www.wikipathways.org

- Wiki for biological pathways
- Free and open pathway resource
- Share, curate and discuss!

Latest edits

Today
 [Cardiovascular Signaling \(Rattus norvegicus\)](#) by [Thomas Kelder](#)
12 March 2009
 [TNF-alpha/NF-kB Signaling Pathway \(Homo sapiens\)](#) by [Alexander Pico](#)
11 March 2009
 [Endochondral Ossification \(Homo sapiens\)](#) by [Alla](#)

Latest discussions

Today
 [Reverted to previous version \(1\)](#) by [Thomas Kelder](#)
12 March 2009
 [Connecting Edges \(1\)](#) by [Alexander Pico](#)

Statistics

- There are **1351** pathways
- Number of **pathways** (and unique genes) per species:

Anopheles gambiae:	24	(391)
Arabidopsis thaliana:	8	(82)
Bos taurus:	119	(3202)
Bacillus subtilis:	2	(14)
Caenorhabditis elegans:	39	(838)
Canis familiaris:	117	(3064)
Danio rerio:	105	(2726)
Drosophila melanogaster:	34	(587)
Equus caballus:	12	(214)
Gallus gallus:	102	(2410)
Homo sapiens:	198	(4339)
Mus musculus:	165	(4581)
Mycobacterium tuberculosis:	10	(104)
Oryza sativa:	4	(15)
Pan troglodytes:	120	(3060)
Rattus norvegicus:	152	(3836)
Saccharomyces cerevisiae:	129	(991)
Sus scrofa:	10	(106)
Zea mays:	1	(19)

- There are **1,250** registered users

Topics

- How to...
 - Find and filter pathway information
 - Download pathway information
 - Use it in your research
 - Integrate it with other resources

Topics

- Pathway information and curation
- WikiPathways design & tools
- Web service
- Real life examples

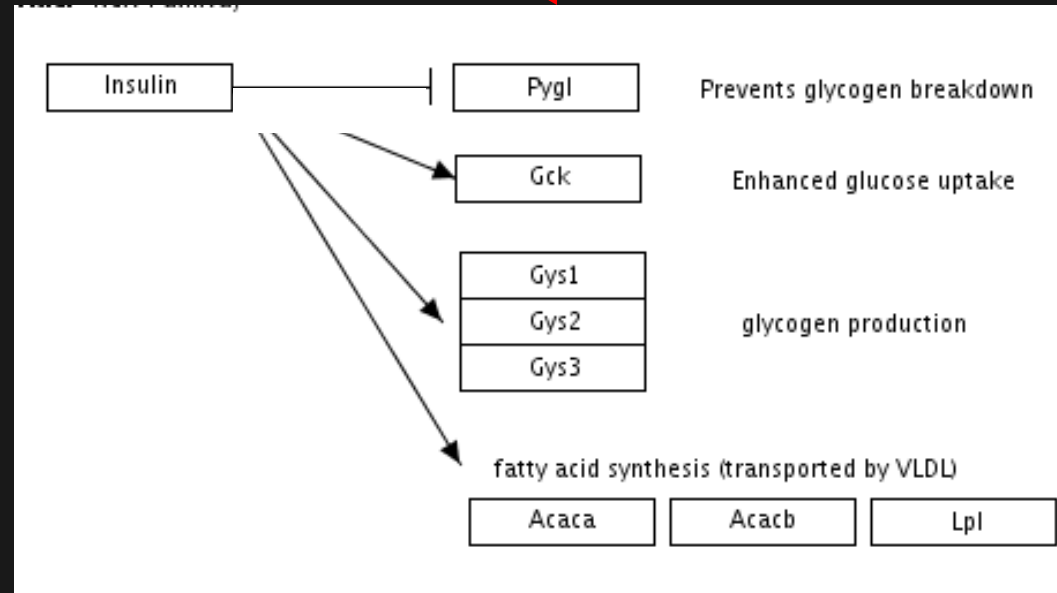
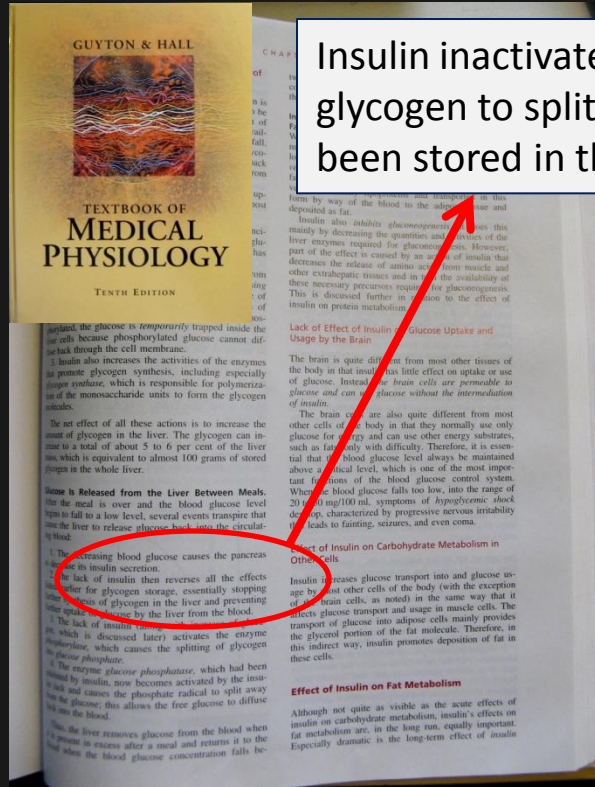
Pathway information and curation

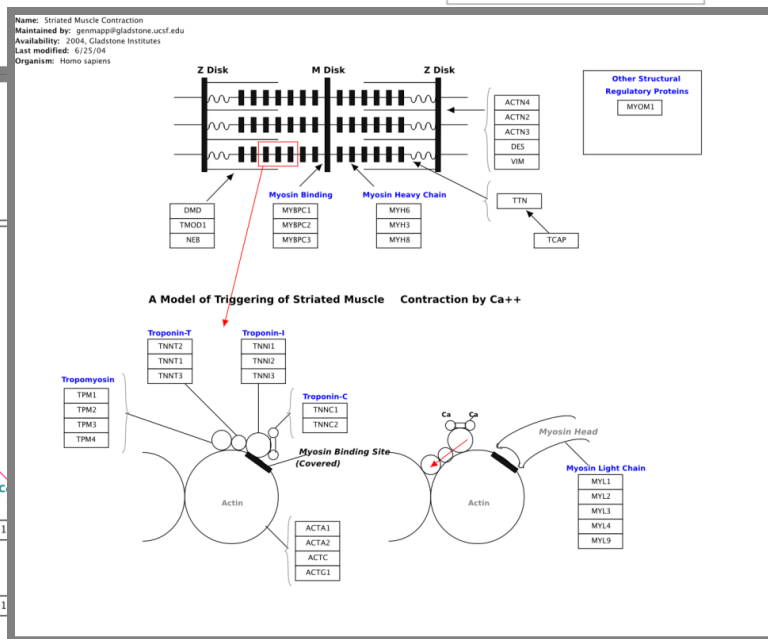
Biological pathways

- Organize our knowledge about biology
- Using graphics:
 - Intuitive representation of complex systems
 - Facilitates communication and discussion
 - Visualization of experimental data

Organize knowledge

Insulin inactivates liver phosphorylase, the principal enzyme that causes liver glycogen to split into glucose. This prevents breakdown of the glycogen that has been stored in the liver.





How pathway information is used

WIKIPEDIA
The Free Encyclopedia

Main page
Contents
Featured content
Current events

Article Discussion

Dihydrolipoyl transacetylase

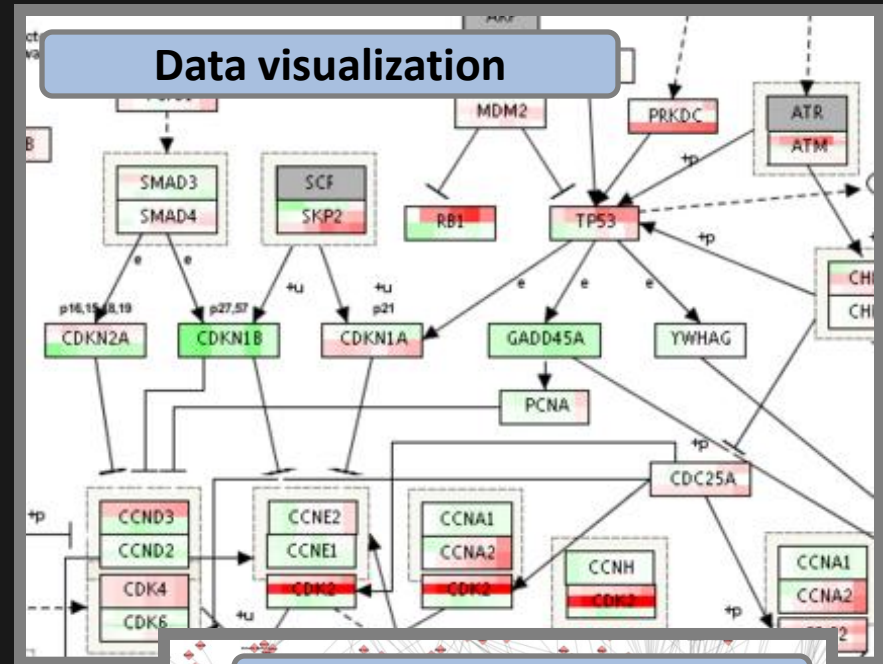
From Wikipedia, the free encyclopedia

Dihydrolipoyl transacetylase (or dihydrolipoamide acetyltransferase) is a component of the pyruvate dehydrogenase complex. The pyruvate dehydrogenase complex is a multi-enzyme complex that links glycolysis to the citric acid cycle. This complex actually consists of several enzymes, including pyruvate dehydrogenase, which is the main enzyme in the citric acid cycle. The complex is involved in the conversion of pyruvate to acetyl-CoA, which is then used in the citric acid cycle. The complex is also involved in the regulation of the citric acid cycle. The complex is a prominent disease marker in several diseases, including episodic hypoketotic hypoglycemia and lactic acidosis.

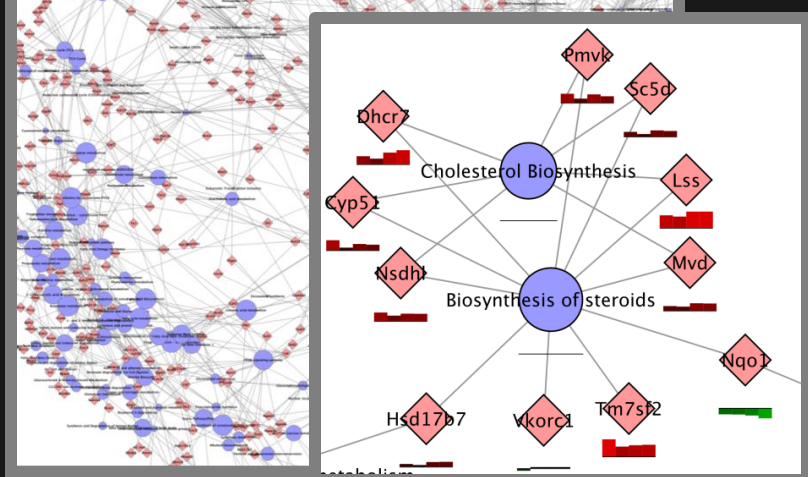
Interactive pathway map

Click on genes, proteins and metabolites below to link to respective article

Knowledgebase



Network analysis



Pathway	positive...	measur...	total	%
TCA Cycle	14	28	29	50.00%
TGF Beta Signaling Pathway	19	43	52	44.19%
Cholesterol Biosynthesis	7	12	15	58.33%
Prostaglandin Synthesis and Regulation	12	28	31	42.86%
TGF-beta Receptor Signaling Pathway	41	135	149	30.37%
Adipogenesis	35	113	132	30.97%
Androgen Receptor Signaling Pathway	28	90	108	31.11%
Fatty Acid Biosynthesis	8	19	22	42.11%
Fatty Acid Beta Oxidation				
mRNA processing				

Enrichment analysis

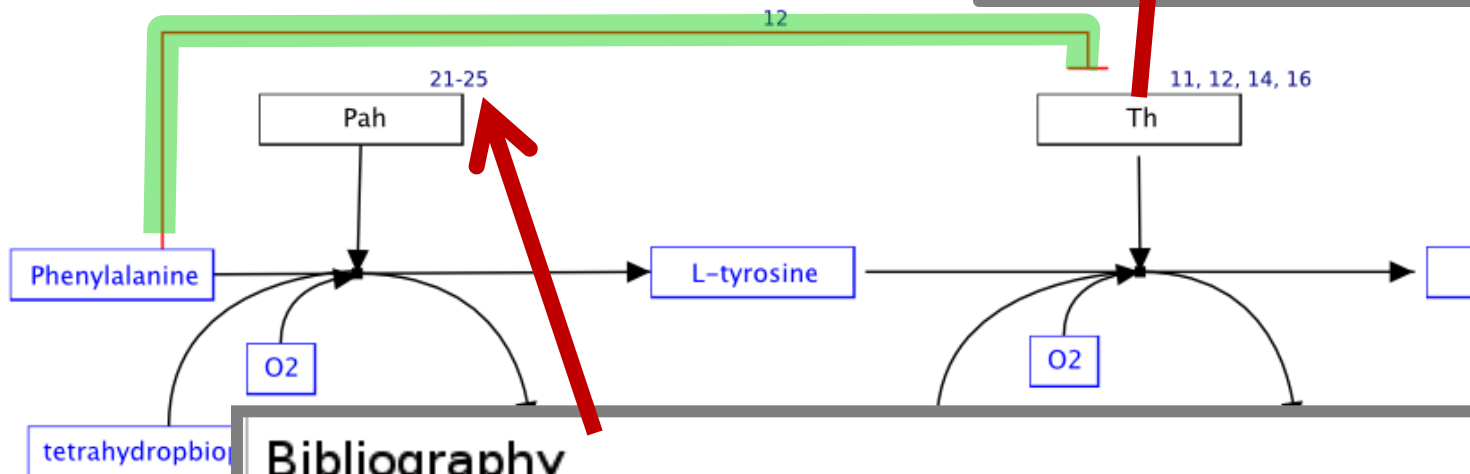
Challenges of curating pathways

- Not just an image
 - Relations
 - Annotations
 - Literature references

DataNodes

[View all 21 DataNodes](#)

Name	Type	Database reference
Dehydroascorbate	Metabolite	10280 (PubChem)
L-DOPA	Metabolite	6047 (PubChem)
Adrenaline	Metabolite	5816 (PubChem)
Th	GeneProduct	25085 (Entrez Gene)
Pah	GeneProduct	24616 (Entrez Gene)



Bibliography

1. Hazra A, Wu K, Kraft P, Fuchs CS, Giovannucci EL, and Hunter DJ. *Twenty-four non-metabolic pathway and risk of colorectal adenoma in the Nurses' Health Study*. *Cancer Epidemiology and Prevention*. doi:10.1093/carcin/bgm062 pmid:17389618. [PubMed](#) [HubMed](#) [dd0]

Challenges of wikifying pathways

- Most wiki engines are designed for textual information
- Our pathways are stored as XML and rendered using Java libraries

WikiPathways design & pathway tools



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- Micronutrient Portal

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☐ titles only

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Michiel Adriaens, Frank, Thomas Kelder, Txr24, et al.

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- 5 History
- 6 Pathway Info
 - 6.1 DataNodes

This one-carbon metabolism pathway is centered around folate. Folate has two key carbon-carbon double bonds. Saturating one of them yields dihydrofolate (DHF) and adding an additional molecule of hydrogen across the second yields tetrahydrofolate (THF). The folate pathway is central to any study related to DNA methylation, dTMP synthesis or purine synthesis. 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.

1. Hazra A, Wu K, Kraft P, Fuchs CS, Giovannucci EL, 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 - PubMed

One Carbon Metabolism (Homo sapiens)

WARNING: This page is 42 kilobytes long; some browsers may have problems editing pages approaching or longer than 32kb. Please consider breaking the page into smaller sections.



```

<Xref Database="Entrez Gene" ID="10840" />
</DataNode>
<DataNode TextLabel="TCN II" GraphId="fc6">
  <BiopaxRef>cf5</BiopaxRef>
  <Graphics CenterX="804.0" CenterY="660.0" Width="80.0" Height="20.0" ZOrder="32768" FontSize="10" Valign="Middle" />
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</DataNode>
<DataNode TextLabel="MTHFR" GraphId="c0a" GroupRef="cffba">
  <BiopaxRef>cf5</BiopaxRef>
  <Graphics CenterX="265.0" CenterY="531.0" Width="80.0" Height="20.0" ZOrder="32768" FontSize="10" Valign="Middle" />
  <Xref Database="Entrez Gene" ID="4524" />
</DataNode>
<DataNode TextLabel="BHMT" GraphId="a0c">
  <BiopaxRef>cf5</BiopaxRef>
  <Graphics CenterX="997.4916666666668" CenterY="473.0" Width="80.0" Height="20.0" ZOrder="32768" FontSize="10"
Valign="Middle" />
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  </DataNode>
<DataNode TextLabel
  <BiopaxRef>cf5</B
  <Graphics CenterX
  <Xref Database="E
  </DataNode>
<DataNode TextLabel
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  <BiopaxRef>fd6</B
  </DataNode>
  <Xref Database="E
  </DataNode>
  <BiopaxRef>cf5</BiopaxRef>
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Valign="Middle" />
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  <BiopaxRef>cf5</BiopaxRef>
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```

```

</DataNode>
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</DataNode>
<DataNode TextLabel="BHMT" GraphId="a0c">
  <BiopaxRef>cf5</BiopaxRef>
  <Graphics CenterX="997.4916666666668" CenterY="473.0" Width="80.0" Height="20.0" ZOrder="32768" FontSize="10" Valign="Middle" />
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  <Graphics CenterX="1173.0" CenterY="304.0" Width="80.0" Height="20.0" ZOrder="32768" FontSize="10" Valign="Middle" />
  <Xref Database="Entrez Gene" ID="1173" />
</DataNode>
  
```

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PERMISSION!

Summary:

☐ This is a minor edit
 ☐ Watch this page

Templates used on this page:

- Template:CheckAvailable
- Template:Help:LiteratureReference
- Template:PathwayPage:Bottom (protected)



BETA

WIKIPATHWAYS
Pathways for the People

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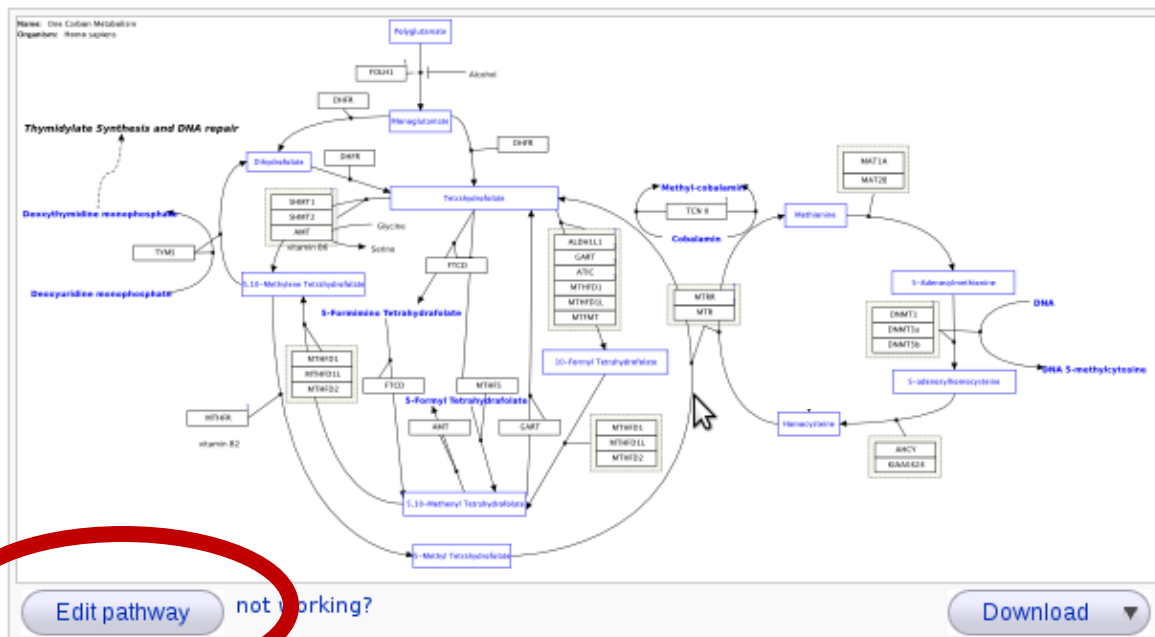
delete

protect

unwatch

One Carbon Metabolism (Homo sapiens)

Michiel Adriaens, Frank, Thomas Kelder, Txr24, et al.



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- 6 Pathway Info
- 6.1 DataNodes

Description

This one-carbon metabolism pathway is centered around folate. Folate has two key carbon-carbon double bonds. Saturating one of them yields dihydrofolate (DHF) and adding an additional molecule of hydrogen across the second yields tetrahydrofolate (THF). The folate pathway is central to any study related to DNA methylation, dTMP synthesis or purine synthesis. 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

1. Hazra A, Wu K, Kraft P, Fuchs CS, Giovannucci EL, 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 - PubMed [PubMed](#)

edit

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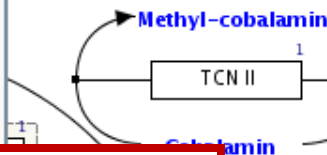
pathway discussion edit

One Carbon Metabolism

Michiel Adriaens, Frank, Thor

Zoom: 100

Save the pathway to WikiPathways



Betaine

Homocysteine

Betaine

Homocysteine

BHMT

MTHFD1

MTHFD1L

MTHFD2

DataNode properties

Comments Literature Annotation

Search

betaine

Search

Results

Please select one of the references and press Ok

Name	Identifier	Datasource
Betaine	HMDB00043	HMDB
Betaine aldehyde	HMDB01252	HMDB
Proline betaine	HMDB04827	HMDB

Cancel Ok

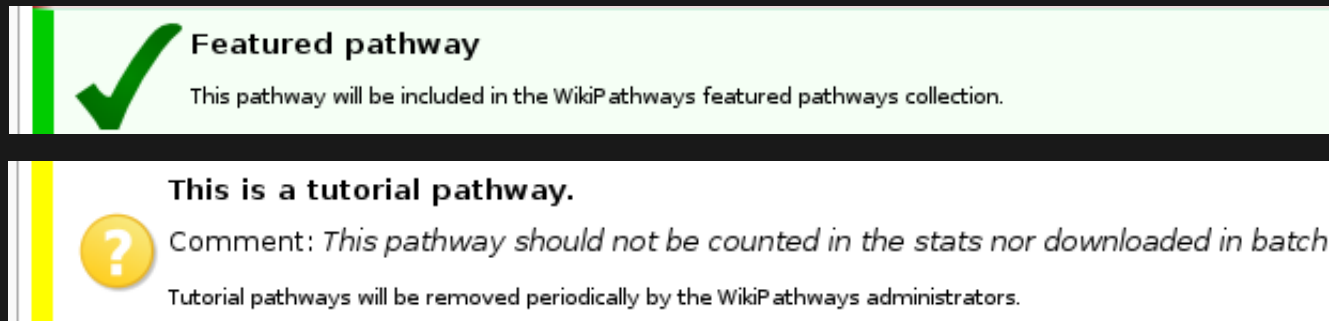
Element properties

Comments Literature

2: Twenty-four non-synonymous polymorphisms in the one-carbon metabolic pathway and risk of colorectal adenoma in the Nurses' Health Study.; **Hazra A; Wu K; Kraft P; Fuchs CS; Giovannucci EL; Hunter DJ;** *Carcinogenesis*, 2007; [PubMed](#)

WikiPathways data model

- Pathway identifiers
 - Unique & stable
 - WP1, WP43, WP1373
- Curation tags provide quality annotations



- All other information is stored in GPML

Working with the GPML format

```
<?xml version="1.0" encoding="UTF-8"?>
<Pathway xmlns="http://genmapp.org/GPML/2010a" Name="Demo" Version="20101122"
Organism="Homo sapiens">
  <Graphics BoardWidth="113.3" BoardHeight="116.6" />
  <DataNode TextLabel="P53" GraphId="aa8f6" Type="Protein">
    <Graphics CenterX="63.0" CenterY="49.0" Width="80.0" Height="20.0"
ZOrder="32768" FontSize="10" Valign="Middle" />
    <Xref Database="Uniprot/TrEMBL" ID="P04637" />
  </DataNode>
  <DataNode TextLabel="MDM2" GraphId="dc426" Type="Protein">
    <Graphics CenterX="63.0" CenterY="96.0" Width="80.0" Height="20.0"
ZOrder="32769" FontSize="10" Valign="Middle" />
    <Xref Database="Uniprot/TrEMBL" ID="Q00987" />
  </DataNode>
  <Line>
    <Graphics ZOrder="12288" LineThickness="1.0">
      <Point X="63.0" Y="59.0" GraphRef="aa8f6" RelX="0.0" RelY="1.0" />
      <Point X="63.0" Y="86.0" GraphRef="dc426" RelX="0.0" RelY="-1.0"
ArrowHead="TBar" />
    </Graphics>
  </Line>
  <InfoBox CenterX="0.0" CenterY="0.0" />
</Pathway>
```

Title: Demo

Organism: Homo sapiens

P53

MDM2

Working with the GPML format

- XML format, platform independent
- PathVisio Java library

org.pathvisio.model

Pathway

- readFrom/writeToXml
- writeToSvg
- getDataObjects
- add/remove

A GPML pathway

Read/write GPML

Convert to image

Get the pathway elements

Add/remove elements

PathwayElement

- getObjectType
- get/setTextLabel

An element on the pathway

DataNode, Line, Shape

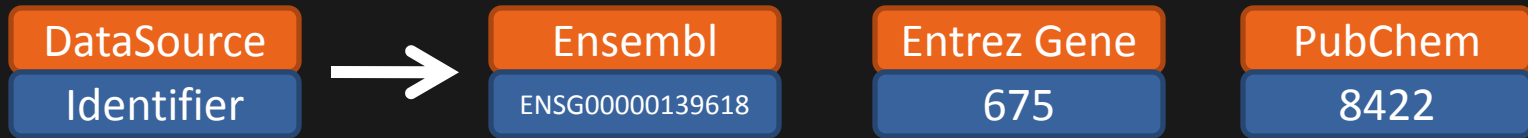
Get or set GPML properties

org.pathvisio.view

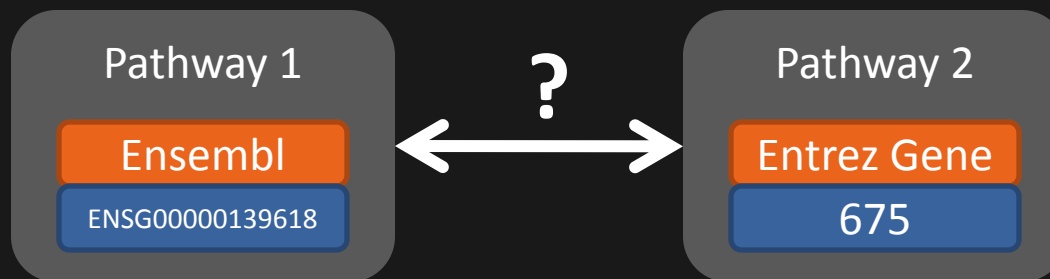
Render the pathway in your own application!

Working with annotations

- DataNodes are annotated with an Xref



- Which DataSource to use is up to the user

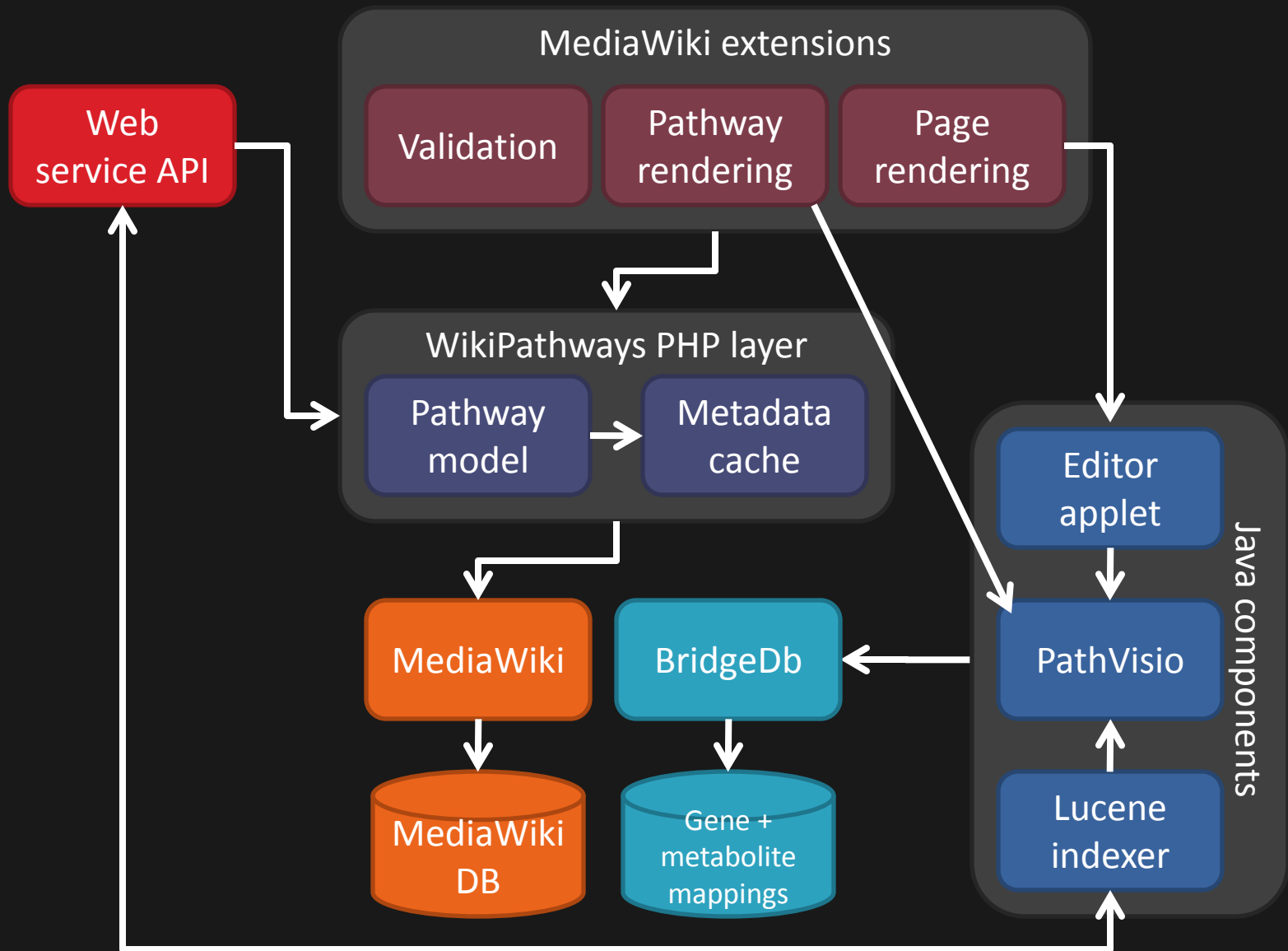


Working with annotations

- WikiPathways provides functions where the identifiers have been mapped for you
- Use BridgeDB library for solving your own mapping problems

<http://www.bridgedb.org>

Putting it all together...



WikiPathways Web service

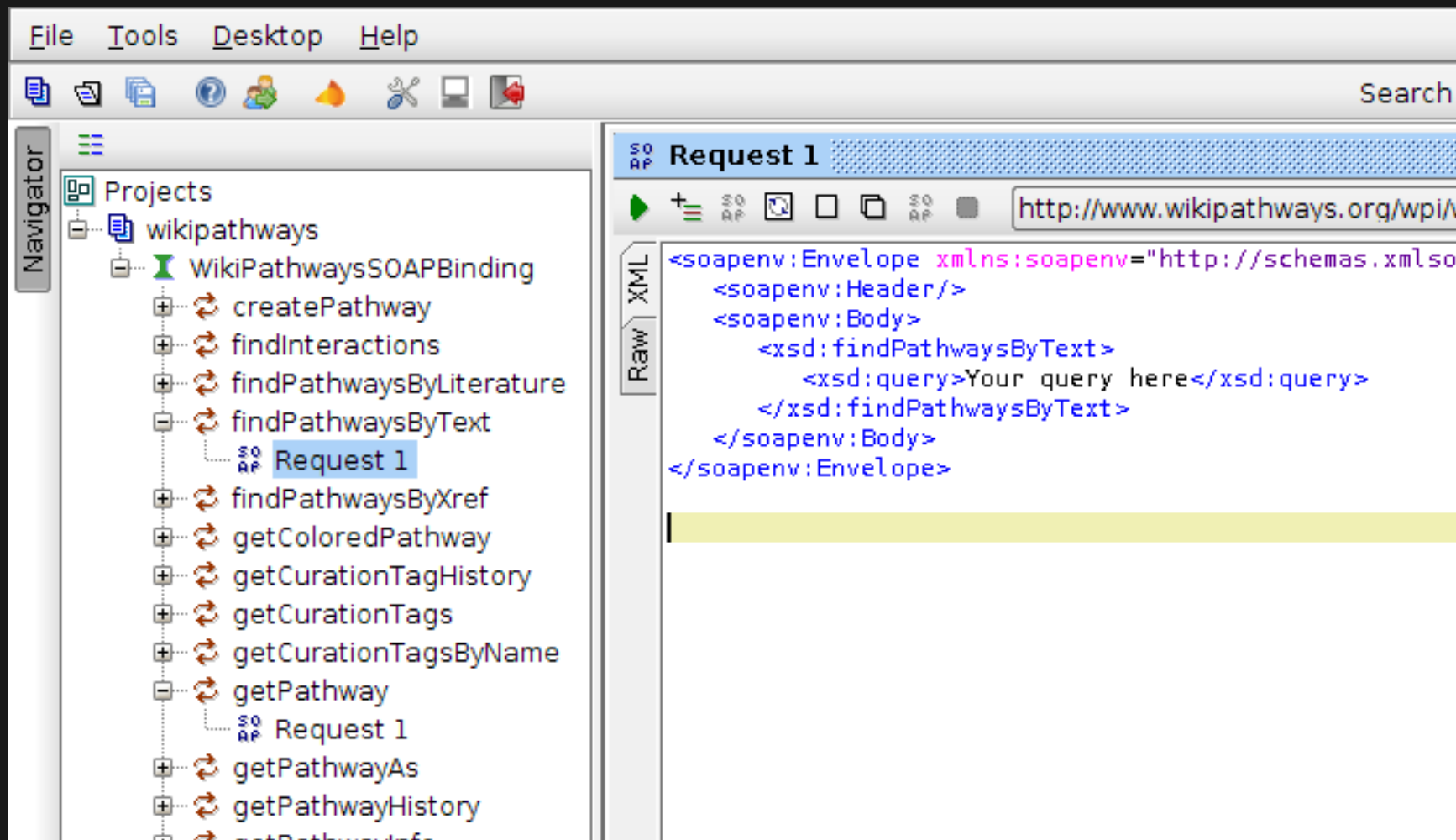


SOAP

- Simple Object Access Protocol
- How your code 'talks' to WikiPathways
- XML-based
- Platform independent
- Language independent

WSDL

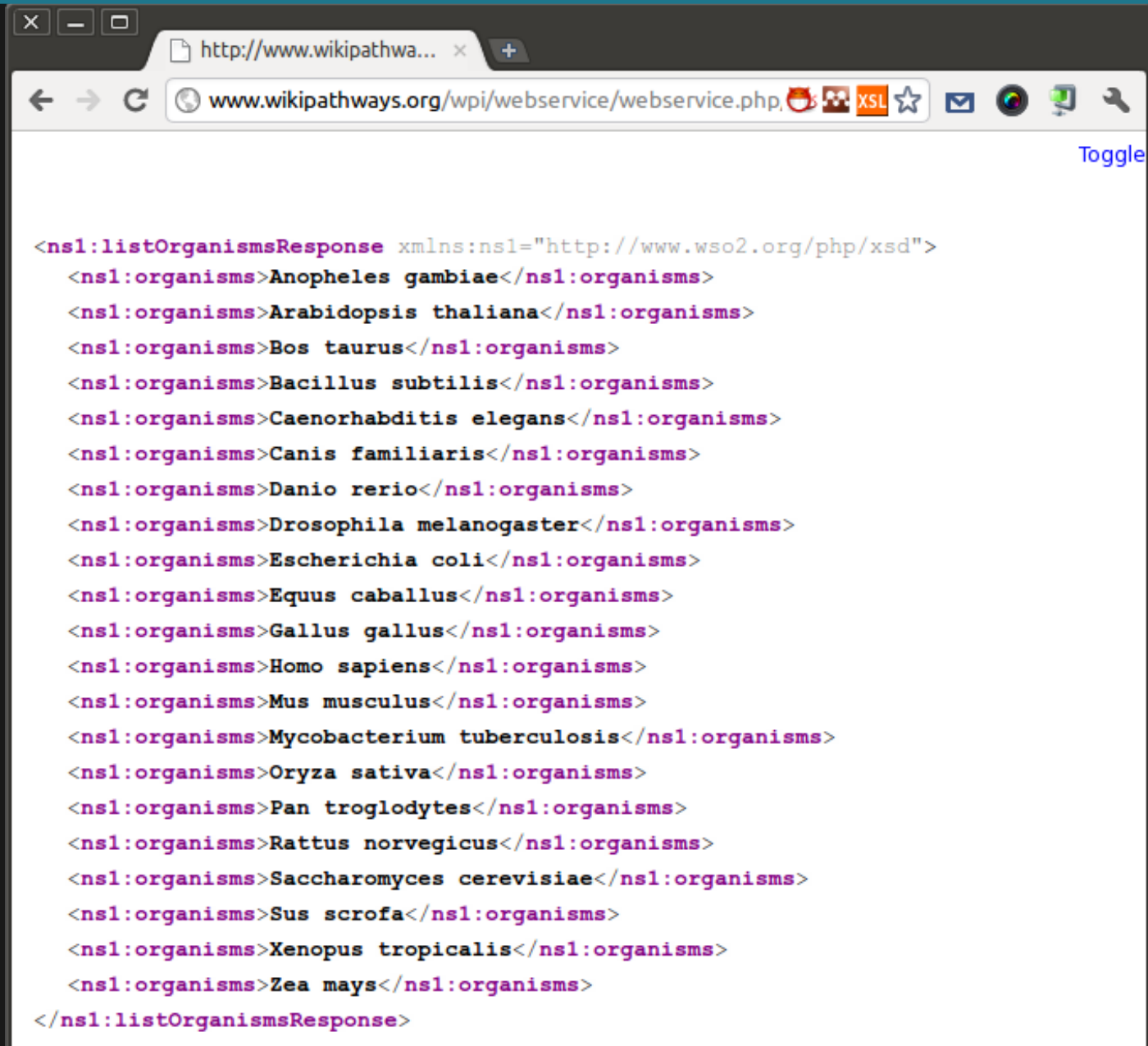
- Web Services Description Language
- Defines:
 - Function signatures
 - Data structures
- Automatic client method/class generation



REST

- Representational State Transfer
- URL based, HTTP requests
- Not bound to XML
- Platform independent
- Language independent

<http://www.wikipathways.org/wpi/webservice/webservice.php/listOrganisms>



The screenshot shows a web browser window with the address bar displaying `http://www.wikipathways.org/wpi/webservice/webservice.php`. The page content is an XML response from the `listOrganisms` endpoint. The XML is wrapped in a `<ns1:listOrganismsResponse>` tag and contains a list of organism names, each enclosed in a `<ns1:organisms>` tag. The organisms listed are: *Anopheles gambiae*, *Arabidopsis thaliana*, *Bos taurus*, *Bacillus subtilis*, *Caenorhabditis elegans*, *Canis familiaris*, *Danio rerio*, *Drosophila melanogaster*, *Escherichia coli*, *Equus caballus*, *Gallus gallus*, *Homo sapiens*, *Mus musculus*, *Mycobacterium tuberculosis*, *Oryza sativa*, *Pan troglodytes*, *Rattus norvegicus*, *Saccharomyces cerevisiae*, *Sus scrofa*, *Xenopus tropicalis*, and *Zea mays*. A "Toggle" link is visible in the top right corner of the page content.

```
<ns1:listOrganismsResponse xmlns:ns1="http://www.wso2.org/php/xsd">
  <ns1:organisms>Anopheles gambiae</ns1:organisms>
  <ns1:organisms>Arabidopsis thaliana</ns1:organisms>
  <ns1:organisms>Bos taurus</ns1:organisms>
  <ns1:organisms>Bacillus subtilis</ns1:organisms>
  <ns1:organisms>Caenorhabditis elegans</ns1:organisms>
  <ns1:organisms>Canis familiaris</ns1:organisms>
  <ns1:organisms>Danio rerio</ns1:organisms>
  <ns1:organisms>Drosophila melanogaster</ns1:organisms>
  <ns1:organisms>Escherichia coli</ns1:organisms>
  <ns1:organisms>Equus caballus</ns1:organisms>
  <ns1:organisms>Gallus gallus</ns1:organisms>
  <ns1:organisms>Homo sapiens</ns1:organisms>
  <ns1:organisms>Mus musculus</ns1:organisms>
  <ns1:organisms>Mycobacterium tuberculosis</ns1:organisms>
  <ns1:organisms>Oryza sativa</ns1:organisms>
  <ns1:organisms>Pan troglodytes</ns1:organisms>
  <ns1:organisms>Rattus norvegicus</ns1:organisms>
  <ns1:organisms>Saccharomyces cerevisiae</ns1:organisms>
  <ns1:organisms>Sus scrofa</ns1:organisms>
  <ns1:organisms>Xenopus tropicalis</ns1:organisms>
  <ns1:organisms>Zea mays</ns1:organisms>
</ns1:listOrganismsResponse>
```

Finding pathways

- Get all pathways / organisms

listPathways

listOrganisms

- Pathways with text “apoptosis”

findPathwaysByText

- Pathways containing Glucose (CHEBI:17634)

findPathwaysByXref

- Pathways citing *Lakin et al., Oncogene 1999*

findPathwaysByLiterature

Downloading pathways

- Get the pathway title, species, last revision
getPathwayInfo
- Get the GPML
getPathway
- Other formats (SVG, PDF, PNG)
getPathwayAs
- Mapped identifier list
getXrefList
- Color gene boxes
getColoredPathway

Wiki information

- Get the revision history

getPathwayHistory

- Recently changed pathways

getRecentChanges

- Curation tags (e.g. quality annotations)

getCurationTags

Alternatives to the web service

- Download all pathways as GPML or image
- Text file with info on all pathways

	A	B	D	E	F	G	H	I	J
1	Pathway Name	Organism	Url to WikiPathway	Last Changed	Last Rev	Author	Count	Ensembl	Uniprot/
2	Notch Signaling Pathway	Anopheles	http://www.wiki	20100212161051	35627	Thomas	20	AGAP0085	Q7PWJ9
3	Eukaryotic Transcription	Anopheles	http://www.wiki	20100212135512	35523	Thomas	38	AGAP0021	Q5TSX9
4	Non-homologous end joining	Anopheles	http://www.wiki	20100212095429	35402	MartijnVar	6		
5	Heme Biosynthesis	Anopheles	http://www.wiki	20100211225536	35294	Mills42	17	AGAP0031	Q5TVW6
6	mRNA processing	Anopheles	http://www.wiki	20100211192204	35234	Khanspers	93	AGAP0001	A0NE83
7	DNA Replication	Anopheles	http://www.wiki	20100211155536	35223	Thomas	37	AGAP0005	Q17033
8	Fatty Acid Biosynthesis	Anopheles	http://www.wiki	20091208234509	33735	MaintBot	15	AGAP0026	Q7PVV2
9	Fatty Acid Beta Oxidation	Anopheles	http://www.wiki	20091208234448	33734	MaintBot	22	AGAP0016	A0NDN8
10	Mitochondrial LC-Fatty Acid Oxidation	Anopheles	http://www.wiki	20091208234359	33732	MaintBot	13	AGAP0036	Q5TJN3



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Pathways for the People

search

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pathway

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Basic examples



Java example



- Use the wikipathways-client library

org.pathvisio.wikipathways.WikiPathwaysClient

```
//Create a client to the WikiPathways web service
WikiPathwaysClient client = new WikiPathwaysClient(
    new URL("http://www.wikipathways.org/wpi/webservice/webservice.php")
);
```

Find pathways



```
//Find a pathway by affymetrix probeset
Xref affy = new Xref("201746_at", DataSource.AFFY);
System.out.println("Searching for pathways with Affymetrix probeset " + affy);

WSSearchResult[] result = client.findPathwaysByXref(affy);
for(WSSearchResult r : result) {
    System.out.println("Found pathway: " + r.getName() + " (" + r.getSpecies())
}
```

```
Searching for pathways with Affymetrix probeset X:201746_at
Found pathway: MAPK signaling pathway (Homo sapiens)
Found pathway: G1 to S cell cycle control (Homo sapiens)
Found pathway: G1 to S cell cycle control (Homo sapiens)
Found pathway: Androgen Receptor Signaling Pathway (Homo sapiens)
Found pathway: Delta-Notch Signaling Pathway (Homo sapiens)
Found pathway: Apoptosis (Homo sapiens)
Found pathway: TGF-beta Receptor Signaling Pathway (Homo sapiens)
Found pathway: Cell cycle (Homo sapiens)
```

Extract pathway information



- org.pathvisio.model.Pathway
- Automatic GPML parsing

```
//Download a pathway from WikiPathways
WSPathway wsPathway = client.getPathway("WP274");
System.out.println("Downloaded pathway " + wsPathway.getName() +
    ", revision " + wsPathway.getRevision());
//Create a pathway object
Pathway pathway = WikiPathwaysClient.toPathway(wsPathway);
```

```
Downloaded pathway B Cell Receptor Signaling Pathway, revision 21255
```

List genes, proteins and metabolites



```
//Get all genes, proteins and metabolites for a pathway
for(PathwayElement pwElm : pathway.getDataObjects()) {
    //Only take elements with type DATANODE (genes, proteins, metabolites)
    if(pwElm.getObjectType() == ObjectType.DATANODE) {
        Xref xref = pwElm.getXref();
        //Print information to the screen
        System.out.println(pwElm.getTextLabel());
        System.out.println("\t" + xref.getId() + " (" + xref.getDatabaseName() + ")");
        System.out.println("\t" + pwElm.getDataNodeType());
    }
}

//Save the pathway locally
pathway.writeToXml(new File(wsPathway.getName() + ".gpml"), true);
```

Lyn	GeneProduct 17096 (Entrez Gene) GeneProduct
Syk	20963 (Entrez Gene) GeneProduct
Cd79a	12518 (Entrez Gene) GeneProduct

Advantages of using Java



- We provide a high-level API
 - No need to deal with SOAP/WSDL
- Compatible with PathVisio
 - Easier GPML handling
- Compatible with BridgeDb
 - Faster and customizable identifier mapping

R Example



- SSOAP

<http://www.omegahat.org/SSOAP/>

```
## Install SSOAP from Bioconductor ##  
source("http://bioconductor.org/biocLite.R")  
biocLite("SSOAP")
```

```
## Load the SSOAP library ##  
library(SSOAP)
```

List available organisms



```
## Create a SOAPServer instance for the web service ##
srv = SOAPServer("http://www.wikipathways.org/wpi/webservice/webservice.php");

## List all organisms on WikiPathways ##
reply = .SOAP(srv, "listOrganisms",
  action=I("listOrganisms"), handlers=NULL)

# Create an object model of the XML reply
doc = xmlParse(reply$content, asText=TRUE)
```

```
<?xml version="1.0"?>
<soapenv:Envelope xmlns:soapenv="http://schemas.xmlsoap.org/soap/envelope/">
  <soapenv:Header/>
  <soapenv:Body>
    <ns1:listOrganismsResponse xmlns:ns1="http://www.wso2.org/php/xsd">
      <ns1:organisms>Homo sapiens</ns1:organisms>
      <ns1:organisms>Rattus norvegicus</ns1:organisms>
      <ns1:organisms>Mus musculus</ns1:organisms>
      <ns1:organisms>Drosophila melanogaster</ns1:organisms>
      <ns1:organisms>Caenorhabditis elegans</ns1:organisms>
      <ns1:organisms>Saccharomyces cerevisiae</ns1:organisms>
      <ns1:organisms>Danio rerio</ns1:organisms>
    </ns1:listOrganismsResponse>
  </soapenv:Body>
</soapenv:Envelope>
```

Real life examples

Demo: Cytoscape

Import Network from Database



Import Network From Database

Data Source:

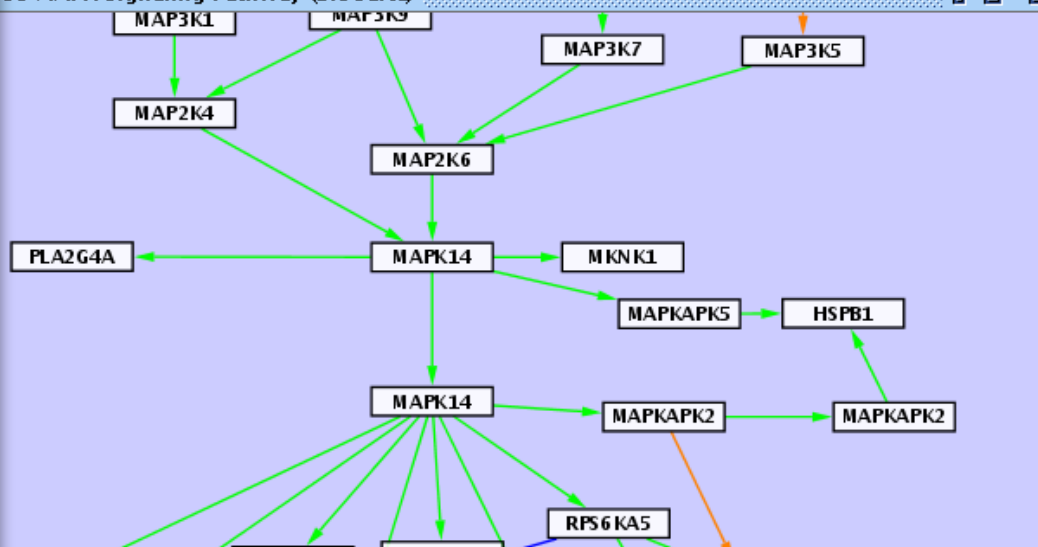
Search:

Name	Organism
MAPK Cascade	Homo sapiens
MAPK signaling pathway	Homo sapiens
p38 MAPK Signaling Pathway (BioCarta)	Homo sapiens
P2X4	Homo sapiens
NLR proteins	Homo sapiens
Notch Signaling Pathway	Homo sapiens
Hypothetical Network for Drug Addiction	Homo sapiens
Id Signaling Pathway	Homo sapiens
ErbB signaling pathway	Homo sapiens
Sandbox Pathway	Homo sapiens
Cell cycle	Homo sapiens
Insulin Signaling	Homo sapiens
Toll-like receptor signaling pathway (for ...	Homo sapiens
Toll-like receptor signaling pathway	Homo sapiens
Regulation of Actin Cytoskeleton	Homo sapiens
Myometrial Relaxation and Contraction P...	Homo sapiens

Cytoscape Desktop (New Session)

Search:

p38 MAPK Signaling Pathway (BioCarta)



Panel

Attribute Browser | Edge

Click to ZOOM | Middle-click + drag to PAN

listOrganisms
findPathwaysByText
getPathway

Automate curation tasks

- Propose to clean up test/tutorial pathways

The screenshot shows a WikiPathways page for a pathway titled "test (Mycobacterium tuberculosis)". The page has a navigation bar with tabs: pathway, discussion, edit, history, delete, protect, unwatch, and permissions. The main content area contains a placeholder diagram with the text "Just testing..." and a single node labeled "A". The sidebar on the right lists the contents: [hide], 1 Curation Tags, 2 Description, 3 Ontology Tags, 4 Bibliography, and 5 Categories. The left sidebar includes a search box, navigation links (Home, Help), and a community section.

This is a tutorial, demo or test pathway.



? Tutorial pathways will be removed periodically by the WikiPathways administrators. If this is not a tutorial, demo or test pathway, please edit the pathway. You may remove this message if you improve the pathway or otherwise object to its deletion for any reason.



- Most Edited
- New Pathways

community

- About us
- Contact us
- How to cite
- GenMAPP Portal
- BiGCaT Portal
- Micronutrient Portal
- Development

toolbox

- What links here
- Related changes
- Upload file

Curation Tags

hide

This is a tutorial, demo or test pathway.



? Tutorial pathways will be removed periodically by the WikiPathways administrators. If this is not a tutorial, demo or test pathway, please edit the pathway. You may remove this message if you improve the pathway or otherwise object to its deletion for any reason.



Description

Automate curation tasks

- List all tutorial pathways

`getCurationTagsByName`

- Check if they have recently been edited

`getPathwayHistory`

- If not, add proposed deletion tag

`saveCurationTag`

It is proposed that this article be deleted because of the following concern:

This tutorial pathways hasn't been edited for a week and can be removed.

If you can address this concern by modifying the pathway, please edit this pathway and do so. You may remove this message if you improve the pathway or otherwise object to its deletion for any reason. To avoid confusion, it helps to explain why you object to the deletion on the [discussion page](#) for this pathway. See the [deletion policy](#) for more information. The article may be deleted if this message remains in place for five days. This template was added **2010-11-24 13:18**; five days from then is **2010-11-29 13:18**.

Enrichment analysis in R



- Get all human pathways as mapped gene lists
getXrefList
- Download a GEO dataset
- Perform Parametric Gene Set Enrichment
- ~75 LOC (including comments)

```
# Load the required libraries
library(SSOAP)           #To use WikiPathways web service
library(GEOquery)        #To download GEO experiments
library(GSEABase)        #Gene Set data structures
library(PGSEA)           #Parametric Gene Set Enrichment
```

Step 1a: List all human pathways



```
# Create a SOAPServer instance for the web service
srv = SOAPServer("http://www.wikipathways.org/wpi/webservice/webservice.php");

# Get a list of all pathways from WikiPathways
reply = .SOAP(
  srv, "listPathways",
  action=I("listPathways"), handlers=NULL
)
# Parse the xml document
doc = xmlParse(reply$content, asText=TRUE)
```

```
<ns1:pathways>
  <ns2:id>WP584</ns2:id>
  <ns2:url>http://www.wikipathways.org/index.php/Pathway:WP584</ns2:url>
  <ns2:name>test-cell-graphics</ns2:name>
  <ns2:species>Homo sapiens</ns2:species>
  <ns2:revision>26291</ns2:revision>
</ns1:pathways>
<ns1:pathways>
  <ns2:id>WP585</ns2:id>
  <ns2:url>http://www.wikipathways.org/index.php/Pathway:WP585</ns2:url>
  <ns2:name>Interferon type I</ns2:name>
  <ns2:species>Homo sapiens</ns2:species>
  <ns2:revision>26377</ns2:revision>
</ns1:pathways>
<ns1:pathways>
```

Step 1b: List all human pathways



```
# Extract the pathway info
pathwayNodes = xmlElementsByTagName(xmlRoot(doc), "pathways", TRUE)
pathways = lapply(pathwayNodes, function(n) {
  children = xmlChildren(n, addNames= TRUE)
  if(xmlValue(children$species) == "Homo sapiens") {
    p = list()
    p[["id"]] = xmlValue(children$id)
    p[["name"]] = xmlValue(children$name)
    p[["species"]] = xmlValue(children$species)
    p[["url"]] = xmlValue(children$url)
    return(p)
  }
  else {
    return() # Skip non-human pathways
  }
})

# Remove NULL entries (non-human pathways)
pathways = pathways[!sapply(pathways, is.null)]
```

Step 2: Create gene sets



```
# A function that downloads a GeneSet for a pathway
createGS = function(p) {
  print(p[["id"]])
  # Download the gene list (translated to Entrez ids)
  reply = .SOAP(srv, "getXrefList", pwId = p[["id"]], code="L",
               action=I("getXrefList"), handlers=NULL)
  doc = xmlParse(reply$content, asText=TRUE)
  # Find the xref nodes with an xpath query
  resultNodes = xmlElementsByTagName(xmlRoot(doc), "xrefs", TRUE)
  # Extract the gene ids
  geneIds = sapply(resultNodes, xmlValue)
  if(length(geneIds) > 0) { # Skip empty lists
    # Create a GeneSet object
    geneSet = GeneSet(geneIds, geneIdType=EntrezIdentifier(),
                     setName=paste(p[["id"]], " (", p[["name"]], ")", sep="")
    )
    return(geneSet)
  }
}

geneSets = lapply(pathways, createGS) #Apply the createGS function on all pathways
geneSets = geneSets[!sapply(geneSets, is.null)] #Remove empty sets
geneSetCollection = GeneSetCollection(geneSets)
```

Step 3: Enrichment analysis

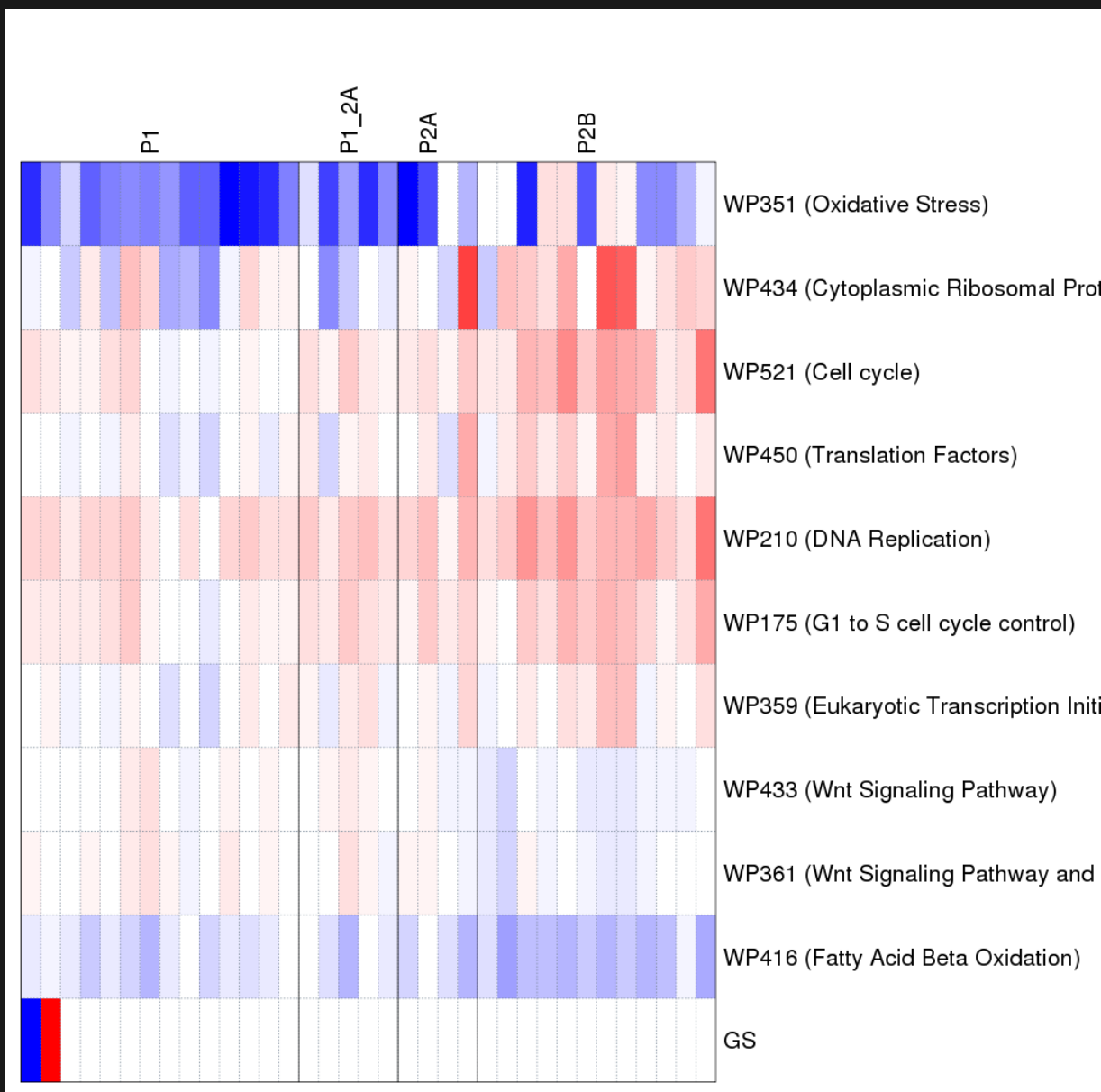


```
# Get an expression set from GEO
gse = getGEO("GSE7023", GSEMatrix = TRUE)
eset = gse[[1]]

# Reformat the phenotype labels
subtype = gsub("subtype: ", "", phenoData(eset)$characteristics_ch1)
subtype = gsub("\\\\.", "_", subtype)

# Run the PGSEA calculation (reference sample is 'NO')
pg = PGSEA(eset, geneSetCollection, ref = which(subtype == "NO"), p.value=0.005)

# Plot the result matrix
smcPlot(
  pg, factor(subtype), scale=c(-15,15), show.grid = TRUE, margins = c(1, 1, 4, 10),
  col = .rwb, r.cex = 0.35
)
```



SNPLogic

- Provide biological context for SNPs
- SNPs -> Genes -> Pathways
- Uses functions:
 - findPathwayByXref
 - getColoredPathway

[+ List Info](#)

 Total 34,158 SNPs in Score using [Calculate](#)

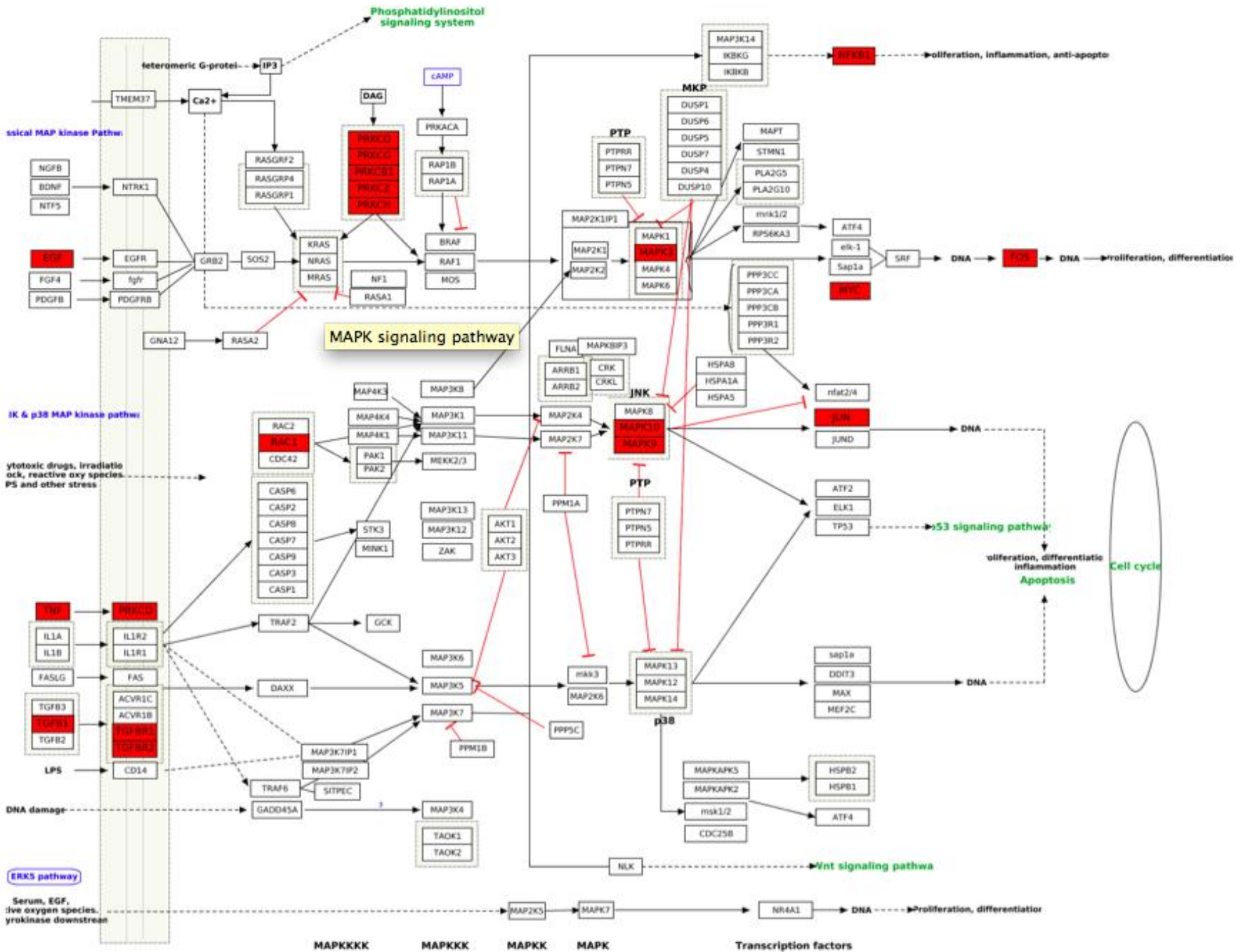
 Filtered SNPs: 34,129 Filter by Sorted by id ASC

Pages	<	1	>	342	Page Size	100	+Fields	Go	Export
-------	---	---	---	-----	-----------	----------------------------------	-------------------------	--------------------	------------------------

#	Del	id	score	cnt	logic	gene_id	symbol	function	protein
1		673	0	1	pw	7124	TNF	nearGene-5	
2		688	0	1	pw	3949	LDLR	cds-refere...	NP_000518
3		868	0	1	pw	7046	TGFBR1	UTR-3	
4		902	0	1	pw	7049	TGFBR3	UTR-3	
5		958	0	1	pw	5602	MAPK10	UTR-3	
6		990	0	1	pw	7049	TGFBR3	UTR-3	
7		994	0	1	pw	7046	TGFBR1	UTR-3	
8		1153	0	1	pw	25805,7295...	BAMBI,LOC7...	nearGene-3...	
9		1190	0	1	pw	4090	SMAD5	UTR-3	
10		1201	0	1	pw				
11		1202	0	1	pw				
12		1287	0	1	pw	4790	NFKB1	intron	
13		1352	0	1	pw	8325	FZD8	UTR-3	
14		1353	0	1	pw	8325	FZD8	UTR-3	
15		1355	0	1	pw	8325	FZD8	UTR-3	
16		1590	0	1	pw	7046	TGFBR1	UTR-3	
17		1801	0	1	pw	4790	NFKB1	intron	
18		1914	0	1	pw	324	APC	intron	
19		1949	0	1	pw	4052	LTBP1	intron	

Total 34,158 SNPs in

#	Pathway Name	WikiPW	SNPs in Genes	Affected Genes
1	Wnt Signaling Pathway	wiki	19191 SNPs map to 60 genes	View
2	Wnt Signaling Pathway and Pluripotency	wiki	19775 SNPs map to 59 genes	View
3	TGF Beta Signaling Pathway	wiki	14940 SNPs map to 51 genes	View
4	DNA damage response (only ATM dependent)	wiki	7527 SNPs map to 38 genes	View
5	Wnt Signaling Pathway NetPath	wiki	9635 SNPs map to 37 genes	View
6	TGF-beta Receptor Signaling Pathway	wiki	9990 SNPs map to 31 genes	View
7	EGFR1 Signaling Pathway	wiki	9907 SNPs map to 19 genes	View
8	MAPK signaling pathway	wiki	8239 SNPs map to 18 genes	View
9	MicroRNAs in cardiomyocyte hypertrophy	wiki	5086 SNPs map to 17 genes	View
10	Insulin Signaling	wiki	9531 SNPs map to 15 genes	View
11	IL-6 Signaling Pathway	wiki	4459 SNPs map to 15 genes	View
12	Adipogenesis	wiki	2168 SNPs map to 15 genes	View



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en.wikipedia.org/wiki/Template:Interactive_pathway_maps

Template

Discussion

Read Edit View history

Search 

From Wikipedia, the free encyclopedia

 Template documentation

[\[edit\]](#) [\[purge\]](#)

This template is the product of a custom export process of [WikiPathways](#) content as interactive pathway maps for Wikipedia articles. Please do not edit these templates directly as they include calculated hyperlinks and annotations based on original content curated at [WikiPathways](#). Please feel free to edit and update the pathway content at [WikiPathways](#). Your changes will be reflected here when the template is regenerated.

Features

[edit]

- **Gene Wiki links** - click on blue-underlined gene boxes in pathway to go to the corresponding Gene Wiki article
- **Metabolite links** - click on blue-underlined metabolite boxes in pathway to go to the corresponding metabolite article
- **Start new pages** - click on red-underlined boxes to start a *new* Wikipedia article where one currently does not exist
- **Bold self links** - the gene or metabolite focused on in the current article is displayed as a bold-bordered self link
- **Pathway links** - click anywhere in the background on the pathway to go to the corresponding pathway article with an expanded view of the interactive pathway map
- **Variable-controlled cropped view** - pathway maps can be cropped by referencing a gene or metabolite (*see Usages #2 and #3 below*).
- **Variable-controlled scroll view** - pathway maps can be viewed in a scrollable window at a particular width and height (*see Usage #4 below*).

Usage

[\[edit\]](#)

This template is commonly transcluded into the following types of articles in the following ways:

1. Pathway articles

Where you want to see the full pathway

```
{{TCACycle WP78}}
```

2. Gene Wiki articles

Where you want to crop the pathway view to center on a particular gene

```
{{TCACycle WP78|highlight=Dihydrolipoyl transacetylase}}
```

3. Metabolite articles



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Citric acid cycle

From Wikipedia, the free encyclopedia
(Redirected from Tca cycle)

The **citric acid cycle** — also known as the **tricarboxylic acid cycle** (TCA cycle), the **Krebs cycle**, or the **Szent-Györgyi-Krebs cycle**, ^{[1][2]} — is a series of **enzyme-catalysed chemical reactions**, which is of central importance in all living **cells** that use **oxygen** as part of **cellular respiration**. In **eukaryotic cells**, the citric acid cycle occurs in the matrix of the **mitochondrion**. The components and reactions of the citric acid cycle were established by seminal work from **Albert Szent-Györgyi** and **Hans Krebs**.

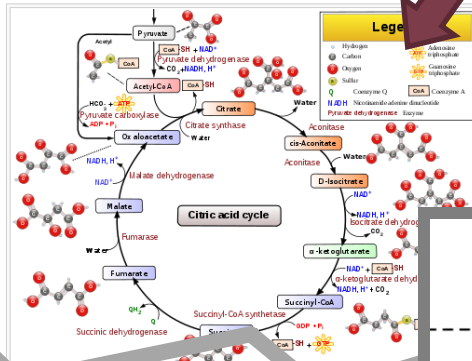
In **aerobic organisms**, the citric acid cycle is part of a **metabolic pathway** involved in the chemical conversion of **carbohydrates**, **fats** and **proteins** into **carbon dioxide** and **water** to generate a form of usable energy. Other relevant reactions in the pathway include those in **glycolysis** and **pyruvate oxidation** before the citric acid cycle, and **oxidative phosphorylation** after it. In addition, it provides **precursors** for many compounds including some **amino acids** and is therefore functional even in cells performing **fermentation**.

Contents [\[hide\]](#)

- 1 A simplified view of the process
- 2 Steps
- 3 Products
- 4 References

Interactive pathway map

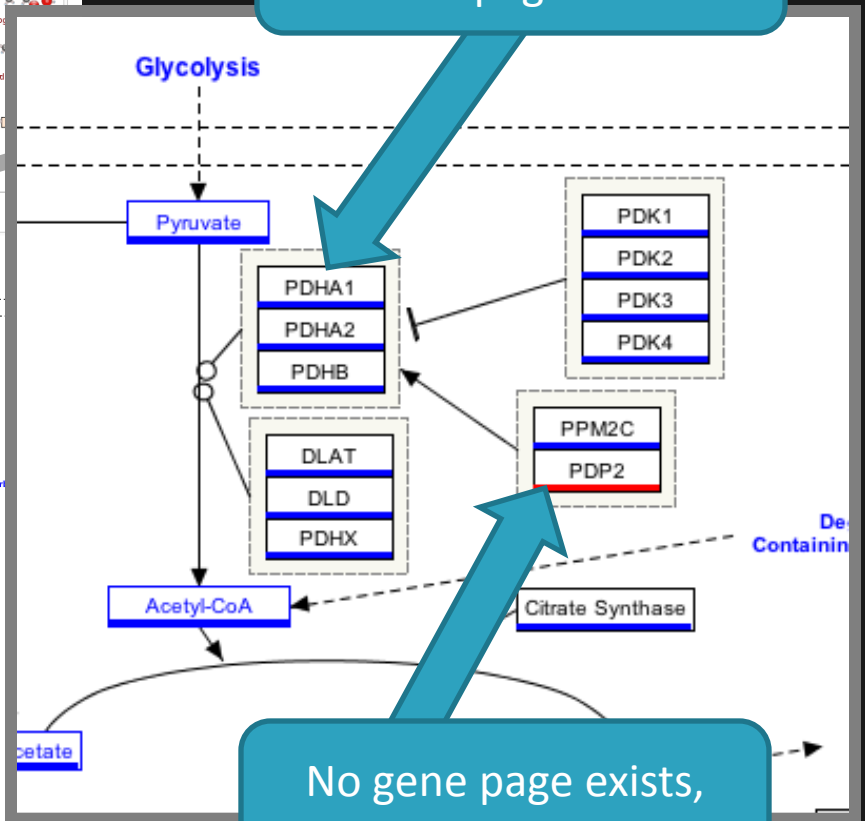
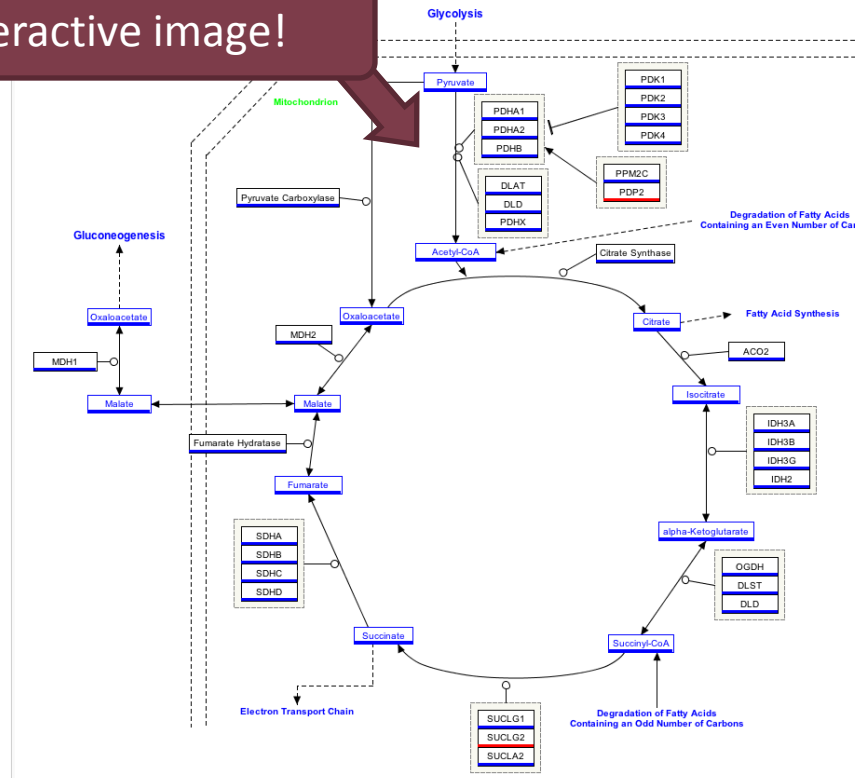
Click on genes, proteins and metabolites below to link to respective articles. ^[13]



Static image

Link to Wikipedia gene page

Interactive image!



No gene page exists,
link to create new page



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The Free Encyclopedia

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Malate dehydrogenase 2

From Wikipedia, the free encyclopedia

Malate dehydrogenase 2, NAD (mitochondrial), also known as **MDH2**, is a [protein](#) which in humans is encoded by the *MDH2* [gene](#).^[1]

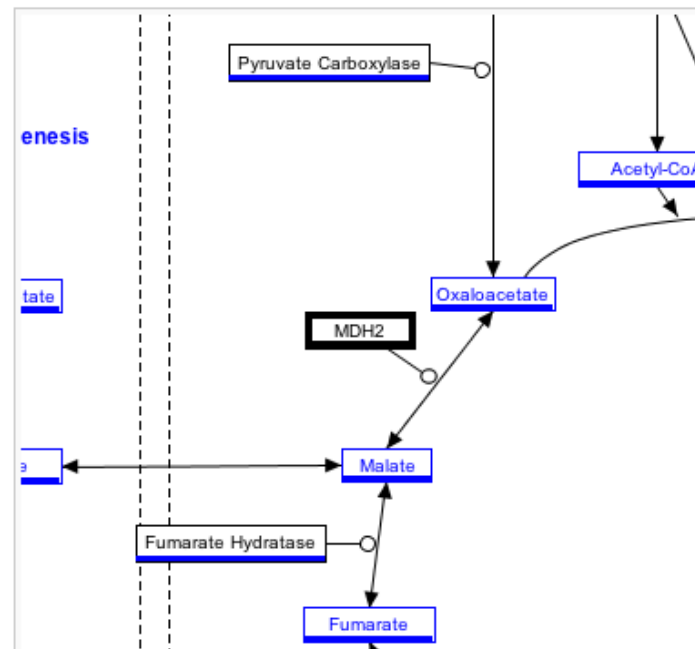
[edit](#)

Malate dehydrogenase catalyzes the reversible oxidation of [malate](#) to [oxaloacetate](#), utilizing the [NAD/NADH](#) cofactor system in the citric acid cycle. The protein encoded by this gene is localized to the [mitochondria](#) and may play pivotal roles in the [malate-aspartate shuttle](#) that operates in the metabolic coordination between [cytosol](#) and mitochondria.^[2]

Interactive pathway map

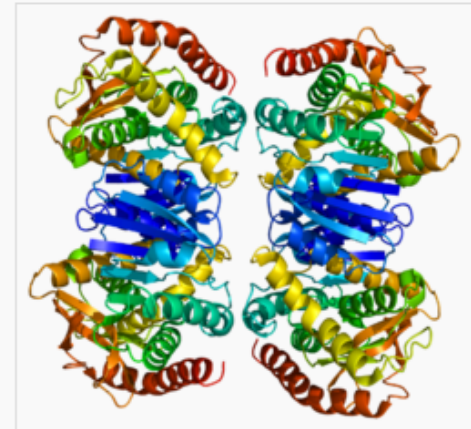
[\[edit\]](#)

Click on genes, proteins and metabolites below to link to respective articles. ^[3]



Citric acid cycle [edit](#)

Malate dehydrogenase 2, NAD (mitochondrial)



PDB rendering based on 1mld.

[Available structures](#)

[\[show\]](#)

Identifiers

Symbols	MDH2; M-MDH; MDH; MGC:3559; MOR1
External IDs	OMIM: 154100 MGI: 97050 HomoloGene: 55938 GeneCards: MDH2 Gene
EC number	1.1.1.37

[Gene Ontology](#)

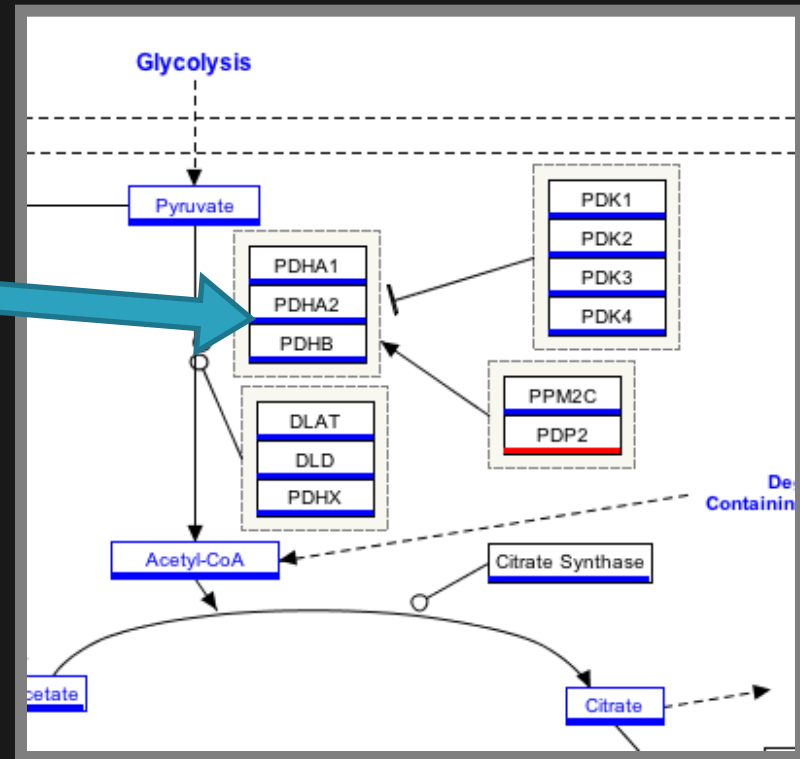
[\[show\]](#)

RNA expression pattern

209036_s_at

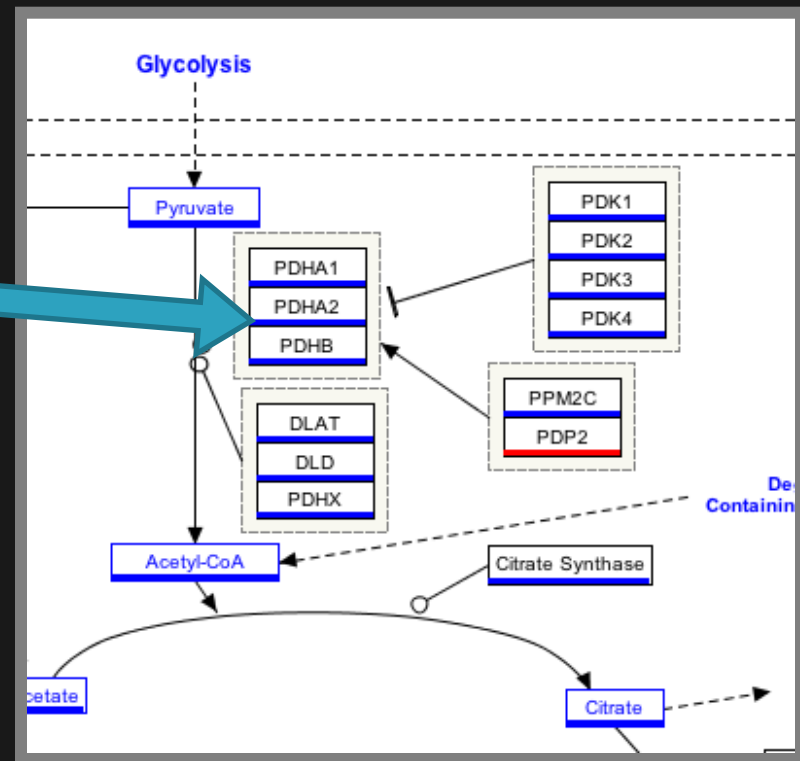


Each blue line is a
<div> display:block



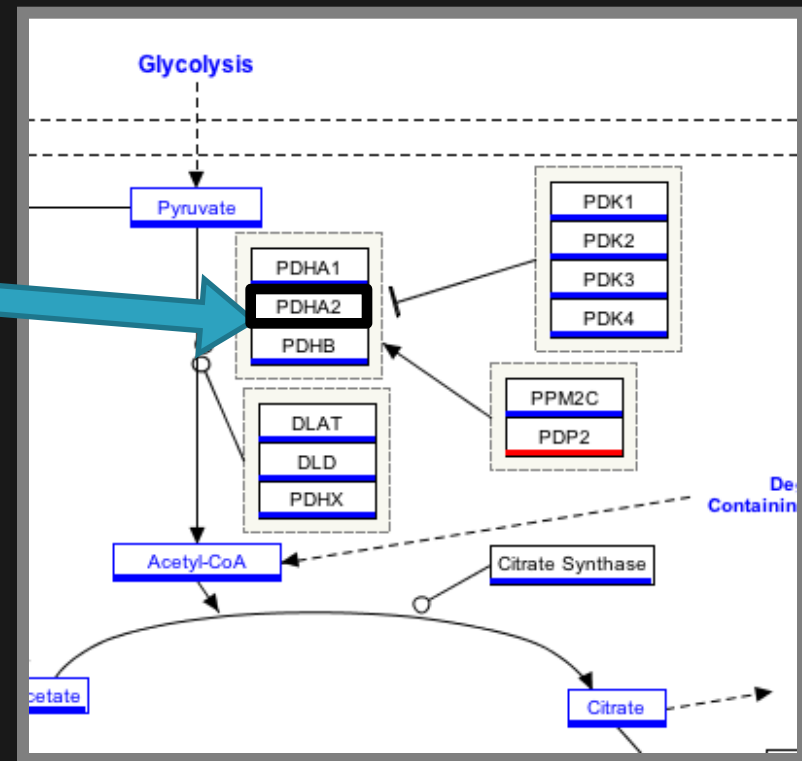
```
<div style="display:block; width:60px; height:0px;
overflow:hidden; position:relative; left:502.0px; top:181.3px;
background:transparent; border-top:3px blue solid"></div>
```

which fits into an
Annotation template



{{Annotation|0|0|[[<div>]]}}

There is one for each line, plus a special switch statement to highlight one gene per article.



```
{{Annotation|0|0|[[<div>]]}}
{{Annotation|0|0|[[<div>]]}}
{{Annotation|0|0|[[<div>]]}}
```

...

```
{{#switch:{{{highlight}}}}
```

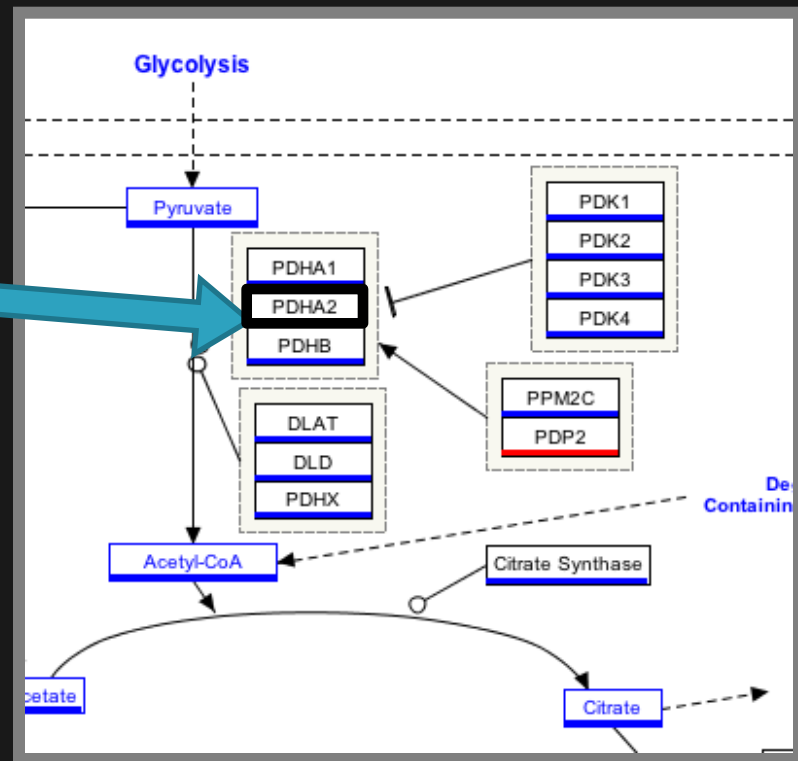
```
|PDHA1={{Annotation|0|0|[[<div>]]}}
```

```
|PDHA2={{Annotation|0|0|[[<div>]]}}
```

```
|PDHB={{Annotation|0|0|[[<div>]]}}
```

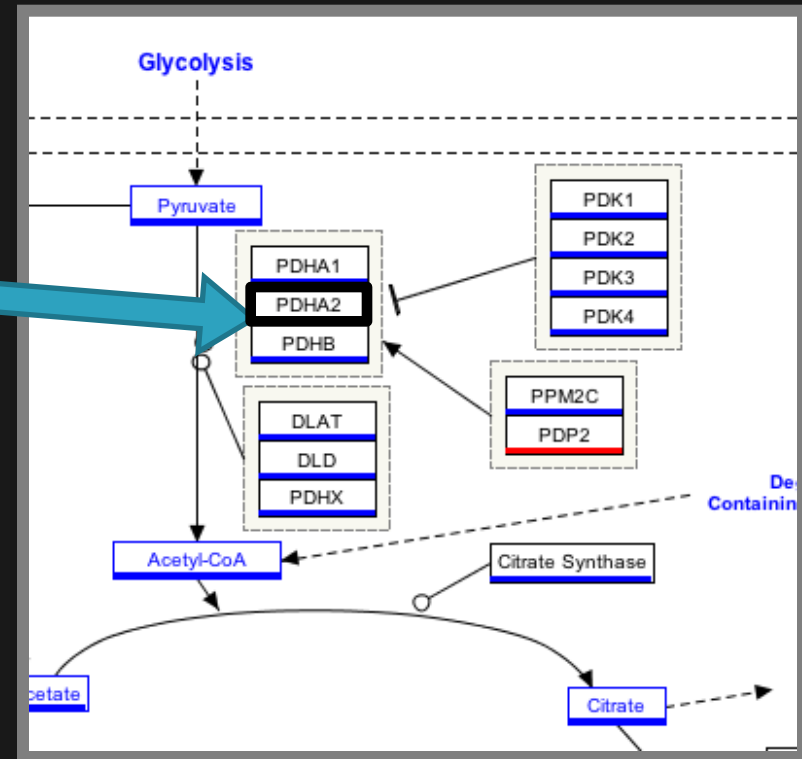
```
... }}
```

All of this is added to an Annotated Image template along with the image map itself.



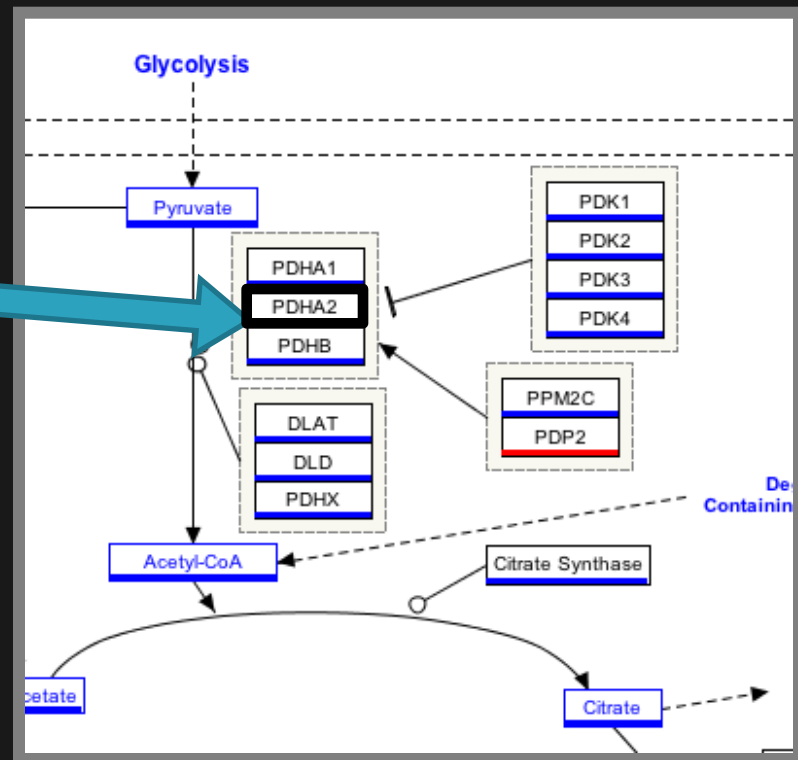
{{Annotated image |||<image map>|{{{[[<div>]]}}}}}}

The Annotated Image is added to a Preview Crop template with its own switch cases.



```
{{Preview crop |Image={{Annotated image |<>|{{{[[<>]]}}}}}
|cWidth={{#switch:{{{highlight}}}|...}}
|cHeight={{#switch:{{{highlight}}}|...}}
|oTop={{#switch:{{{highlight}}}|...}}
|oLeft={{#switch:{{{highlight}}}|...}}
|Description}}
```

Finally, all of this is put into a <div> tag to control full-size width and height.



<div style="">{{Preview crop |{{<>|{{{{[[<>]]}}}}}}}</div>

Template usage

Usage

[4]

This template is commonly transcluded into the following types of articles in the following ways:

1. Pathway articles

Where you want to see the full pathway

```
{{TCACycle_WP78}}
```

2. Gene Wiki articles

Where you want to crop the pathway view to center on a particular gene

```
{{TCACycle_WP78|highlight=Dihydrolipoyl_transacetylase}}
```

3. Metabolite articles

Where you want to crop the pathway view to center on a particular metabolite

```
{{TCACycle_WP78|highlight=Fumaric_acid}}
```

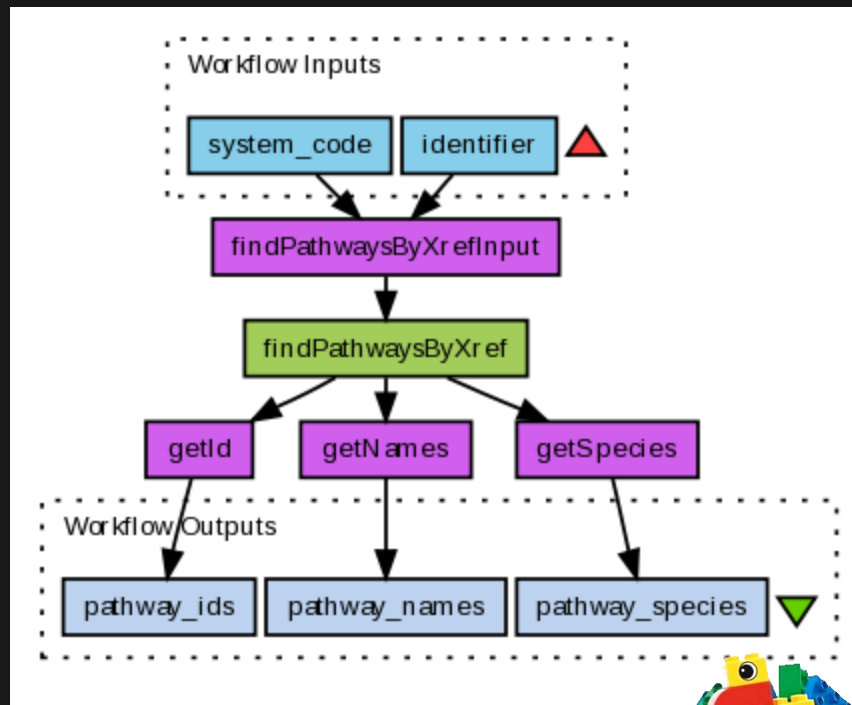
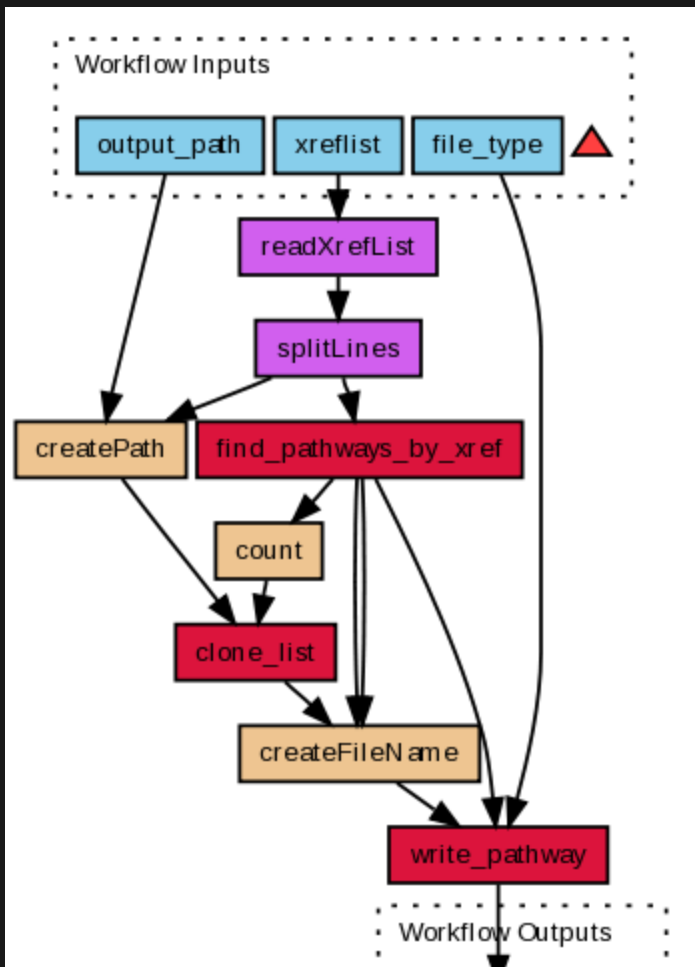
4. Miscellaneous

Where you override default views and specify the width and height of a scrollable window in which to view the entire pathway

```
{{TCACycle_WP78|width=600|height=300}}
```

- **width**: the width of the scrollable window
- **height**: the height of the scrollable window

Demo: Taverna workflows



- Include pathway information in Taverna workflows.
- Get basic workflows you can use as building blocks at:
<http://www.myexperiment.org/packs/40>

<http://www.wikipathways.org/>

Help -> Web service

- Example applications and source code
- API Documentation
- Links to useful libraries

Also see:

<http://www.pathvisio.org>

PathVisio library for handling GPML

<http://www.bridgedb.org>

BridgeDb library for identifier mapping