Recent Developments in the MetaCyc Database

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Introduction

MetaCyc Scope

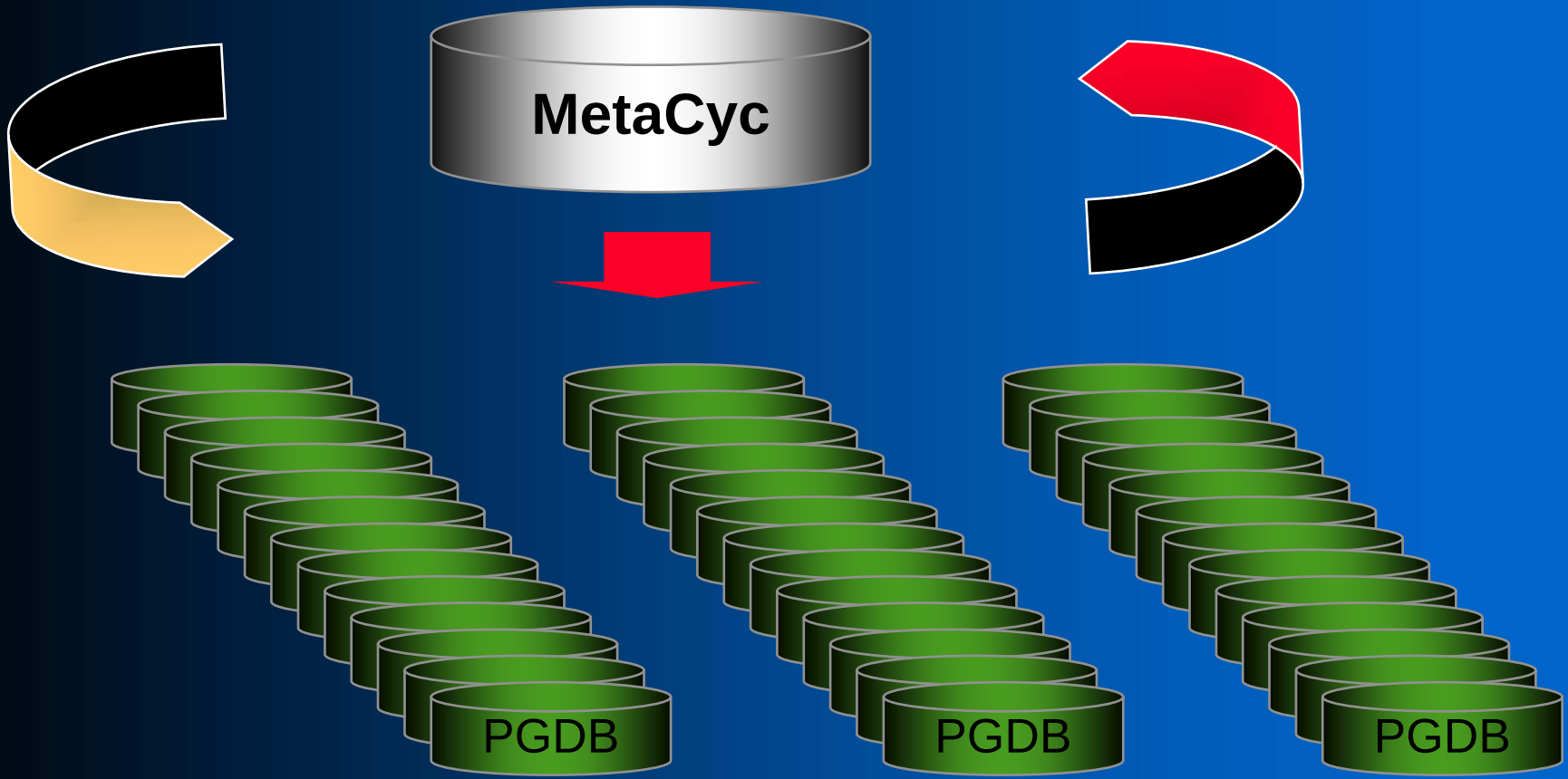
- MetaCyc is a collection of metabolic pathways and enzymes from a wide variety of organisms, primarily microorganisms and plants
- The goal of MetaCyc is to contain a representative sample of every experimentally elucidated pathway, thereby cataloging the universe of known pathways and enzymes.

MetaCyc Curation

- Continuous curation by Ph.D level curators
  - Information gathered from biological and biomedical literature
- An update is released every three months

http://biocyc.org/metacyc/release-notes.shtml

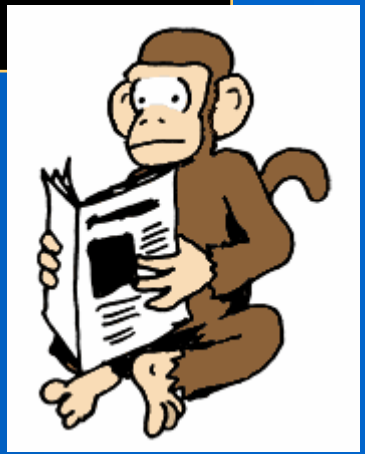
MetaCyc Is Used to Create Computationally-Derived Organism-Specific Databases



Curation Conventions

- Curate pathway enzymes for species with most experimental data
- Add enzymes from additional species if compelling reason exists (e.g., different subunit structure)
- Create pathway variants if reactions of variant differ from existing pathway
- Species list for pathway is often not exhaustive

A detailed description of the curation conventions is found in the Curator's Guide



Criteria for Defining Pathway End Points

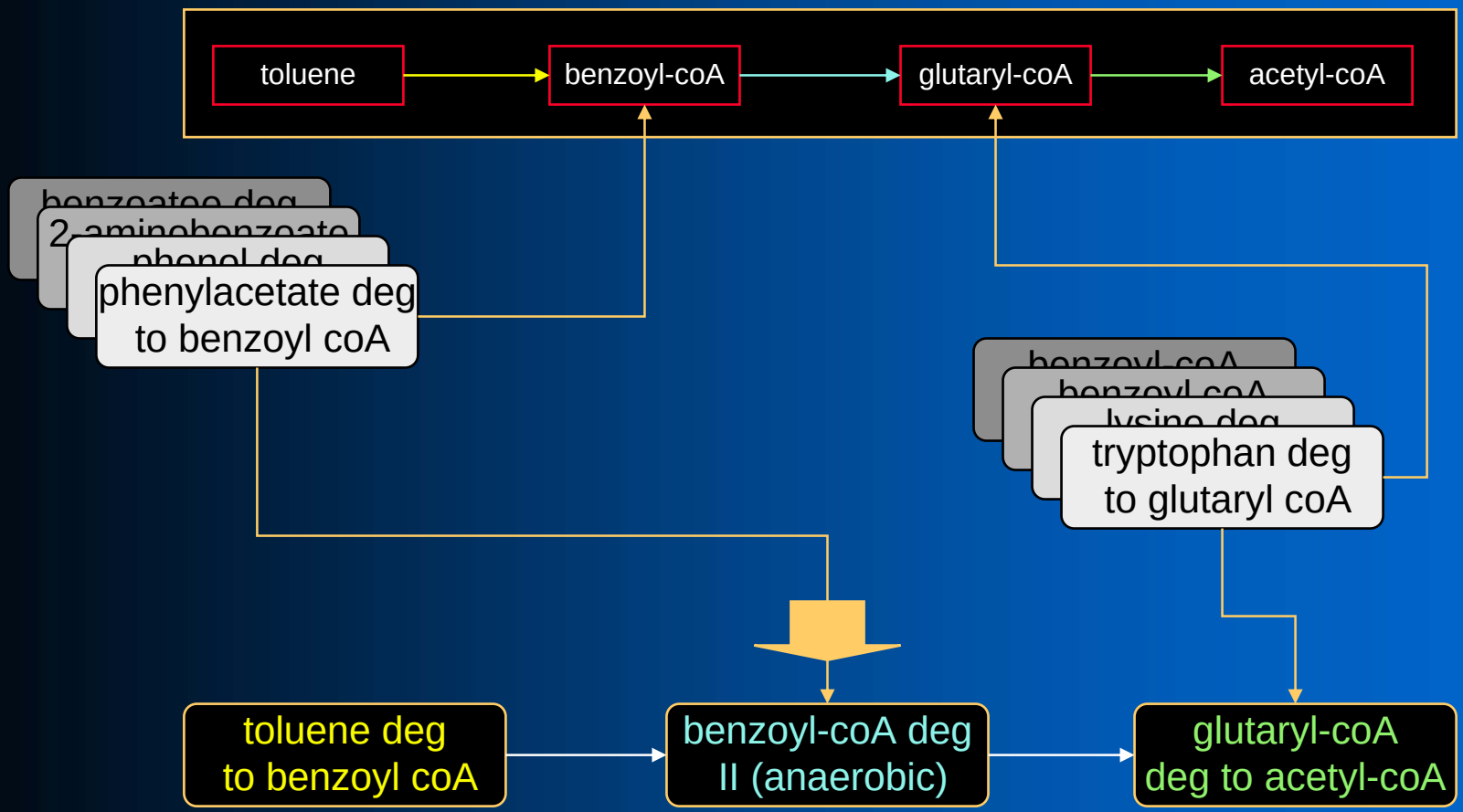
- End points should be stable compounds.
- Biosynthetic pathways should begin with one of the 13 intermediates of central metabolism from which all biosyntheses begin.
- A pathway (or a transport reaction) link should be created to indicate the pathway that produces the precursor metabolite.
- Degradative pathways that produce an intermediate of central metabolism should stop at that point.
- If appropriate, a pathway link should be created to indicate the pathway that processes the resulting metabolite.
- Very large or complex pathways should usually be defined as superpathways that combine several smaller base pathways divided at breakpoints.

The 13 intermediates of central metabolism from which all biosyntheses begin

- pyruvate
- acetyl CoA
- oxaloacetate
- triose phosphate
- 3-phosphoglycerate
- phosphoenolpyruvate
- ribose-5-phosphate
- α-ketoglutarate
- succinyl CoA
- erythrose-phosphate
- fructose-6-phosphate
- glucose-6-phosphate
- sedoeptulose-7-phosphate

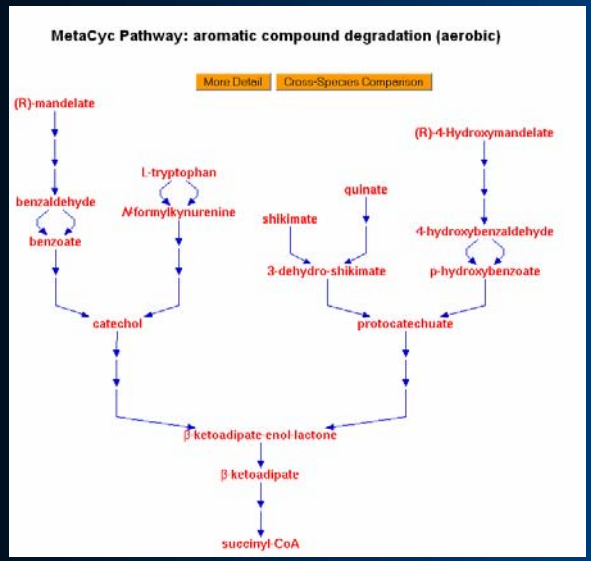
Modular Pathway Design

toluene degradation VI (anaerobic)



Different Kinds of Superpathways

- Groups of pathways linked by their substrates
- Super-pathways are defined by their component pathways
- Multiple levels of super-pathways can be defined
- Pathway prediction algorithms accommodate super-pathways



We currently have over 65 superpathways in MetaCyc

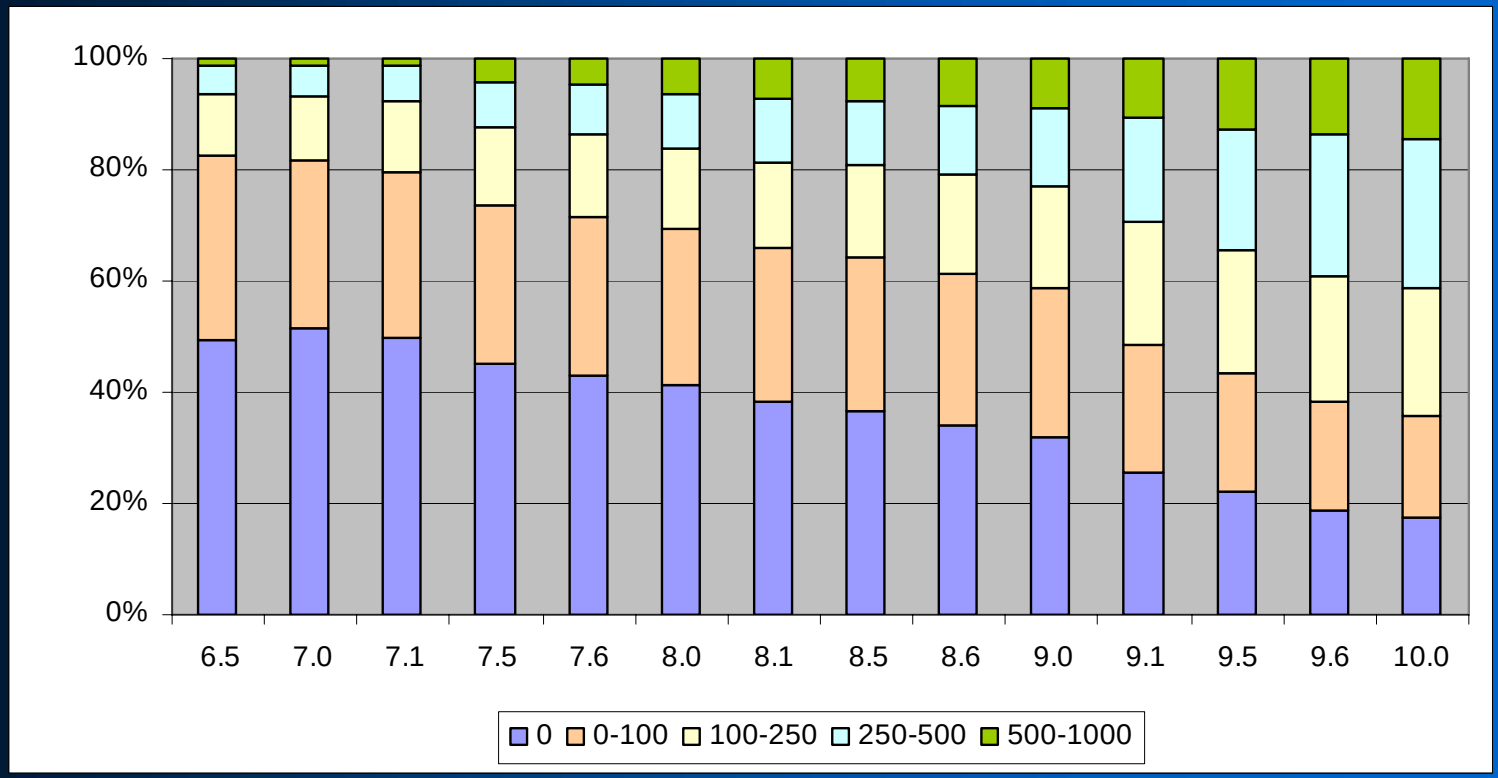
Data

Curation Progress

	Feb 2002	June 2006	Difference
Pathways Pathways with comments	**449** **161**	**785** **618**	+ 336 (75%) + 457 (283%)
Reactions	**4214**	**5869**	+ 1655 (39%)
Enzymes Enzymes with comments	**1147** *****	**3446** **3146**	+ 2299 (200%) + 3146
Chemical compounds Chemical structures	**2339** **1858**	**5177** **4658**	+ 2838 (121%) + 2800 (150%)
Organisms	**158**	**711**	+ 553 (350%)
Citations	**2597**	**10039**	+7442 (286%)

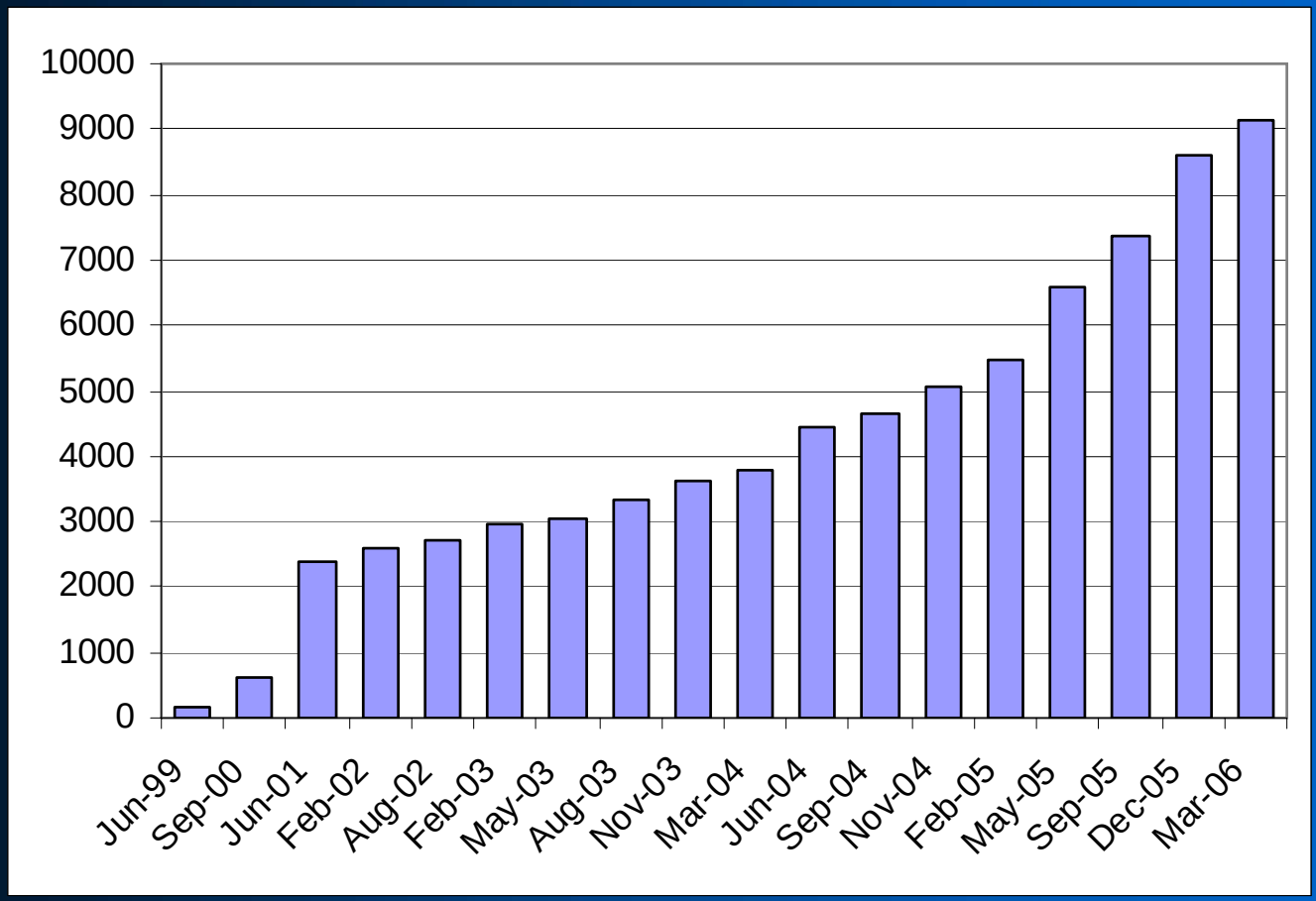
* data not available

Distribution of Comment lengths



Pathways were divided to groups based on comments length, measured by the number of characters.

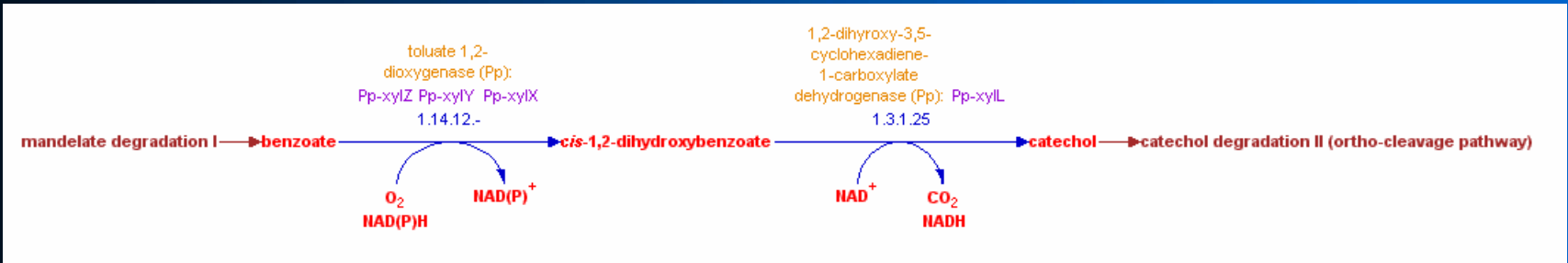
Increase in the Number of Citations



Features

Hyperlinks in Pathways and Comments

Use links to other pathways whenever possible



Use hyperlinks to other database objects within comments

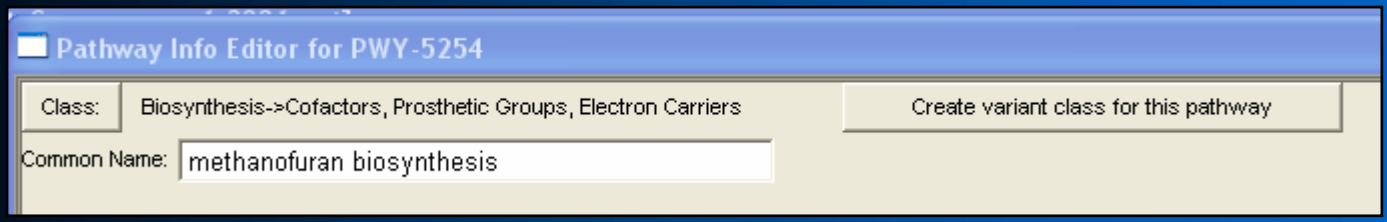
Comment:

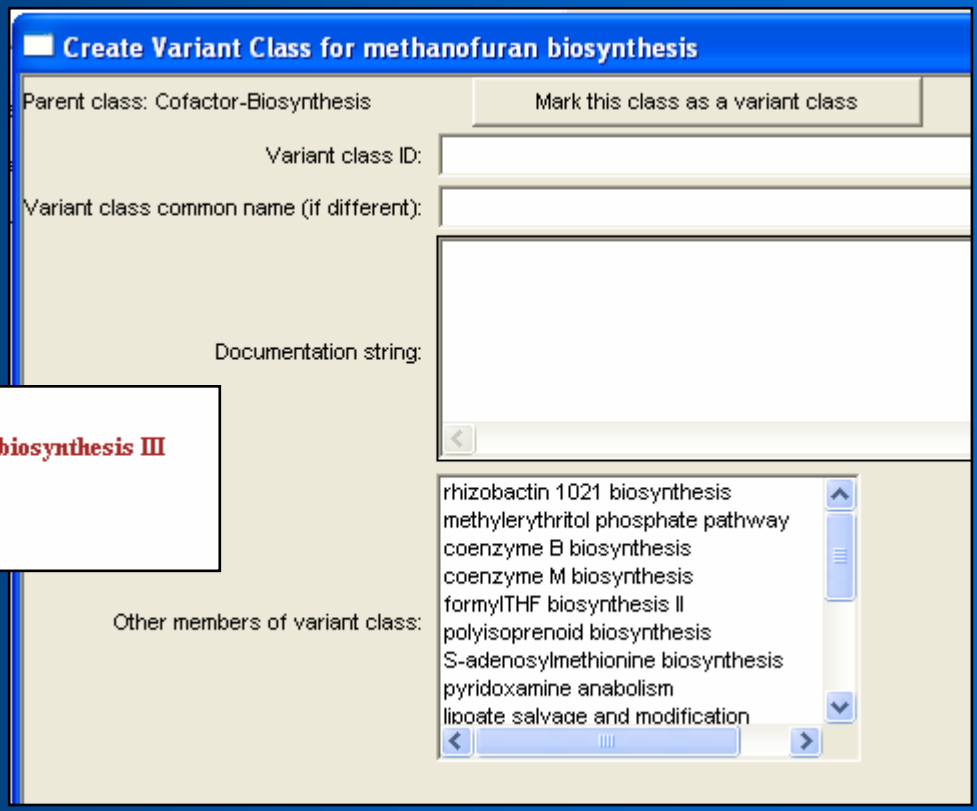
Most organisms degrade **L-leucine** to **acetoacetate** and **acetyl-CoA** (see **leucine degradation I**). The anaerobic bacterium ***Clostridium sporogenes*** degrades **L-leucine** to different products, which include **isobutyrate** and **acetate** [Poston76] . This alternative pathway starts with isomerization of **L-leucine** to **β-leucine** , performed by the enzyme **leucine 2,3-aminomutase** . **β-leucine** is then converted, presumably by a transaminase, to **β-ketoisocaproate** , which is then broken into **isobutyrate** and **acetate** [Poston86] .

The only enzyme that has been characterized from this pathway is **leucine 2,3-aminomutase** [Poston76] . The enzyme was reported to also be present in mammalian tissues [Poston80] and green plants [Freer81] . However, recent work disputes this claim, having found no **β-leucine** in human blood and no **leucine 2,3-aminomutase** activity in rat liver [Stabler88]

Variants: leucine degradation III , leucine degradation I

Pathway Variant Classes





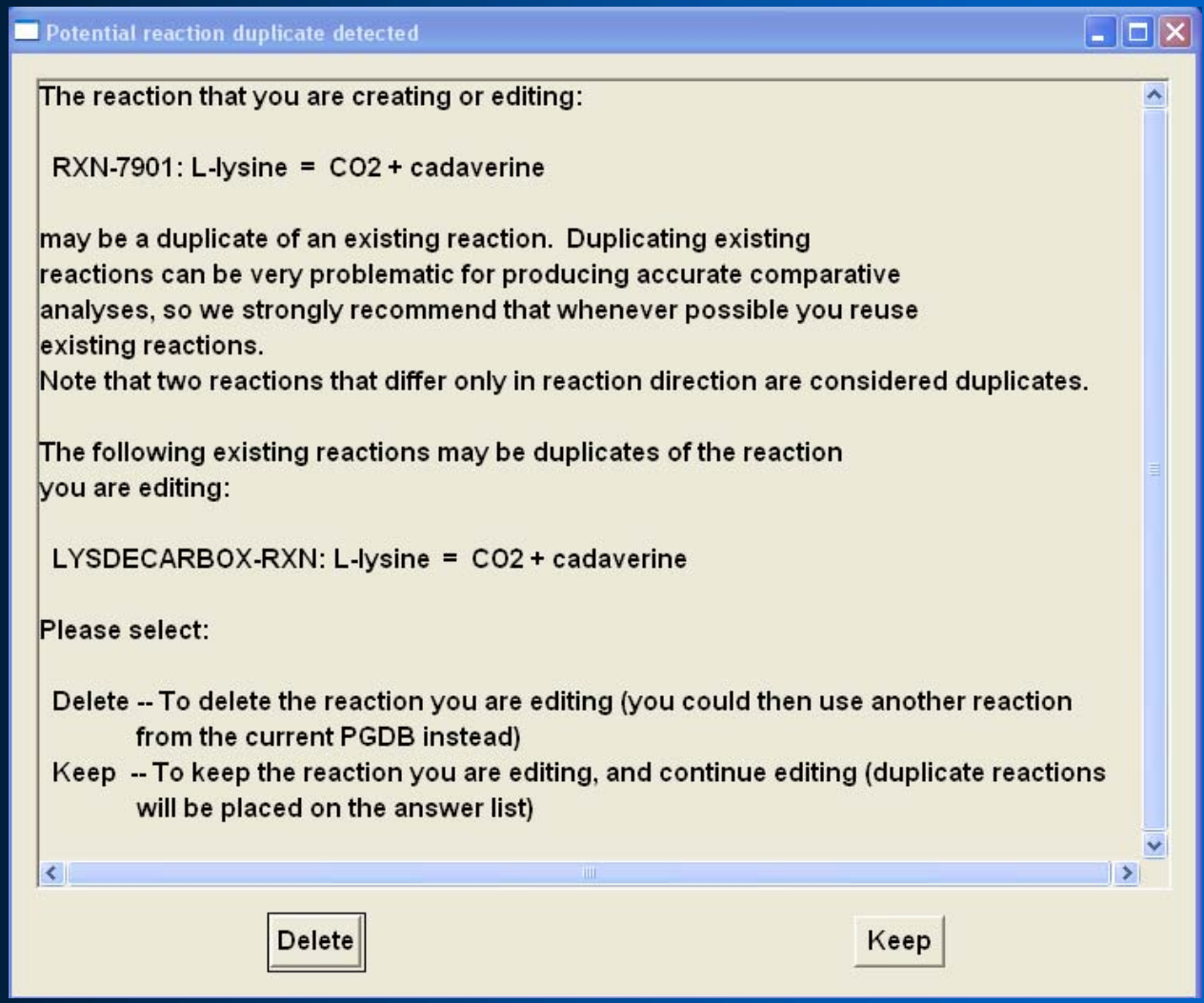
Variants: β-alanine biosynthesis IV, β-alanine biosynthesis II, β-alanine biosynthesis III

Created by: christ on 30-Jun-2005

MetaCyc2GO Mapping

- The MetaCyc2GO mapping file contains the correspondence between MetaCyc pathways and GO process terms, and between MetaCyc reactions and GO function terms.
- It allows to propagate annotations from one database to another.
- The MetaCyc2GO file was originally maintained by GO.
- It is now continuously updated in an ongoing effort by Carnegie and SRI and the GO consortium.
  - The existing GO reactions and function terms have been checked against the latest EC nomenclature.
  - Discrepancies between GO and MetaCyc have been reviewed and corrected manually.

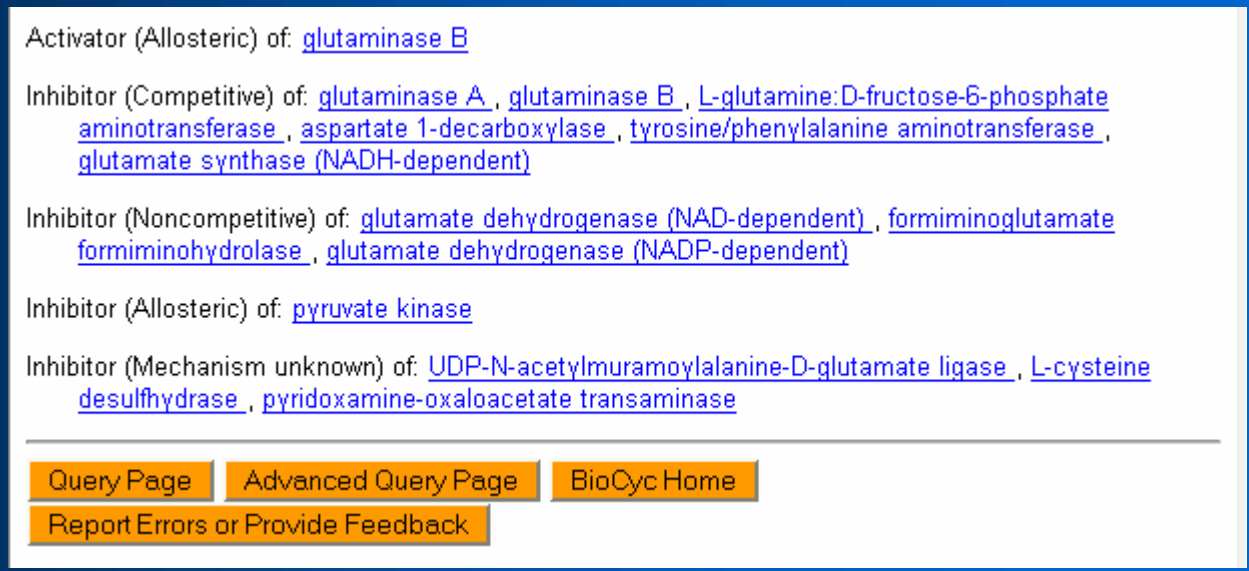
Eliminating Unwanted Duplicate Frames



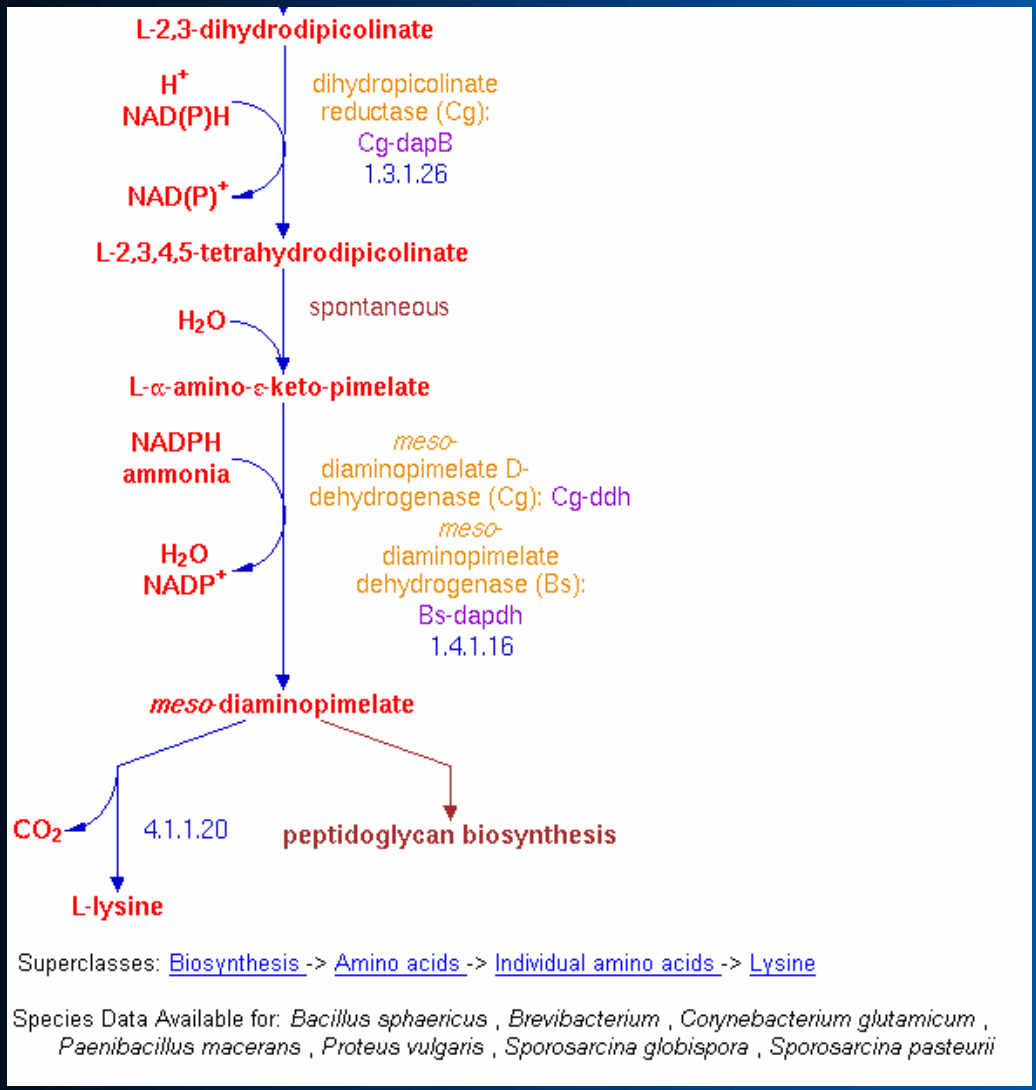
Compound Pages Link to Regulated Enzymes

Compound pages list the enzymes that are regulated by the compounds

example: L-glutamate



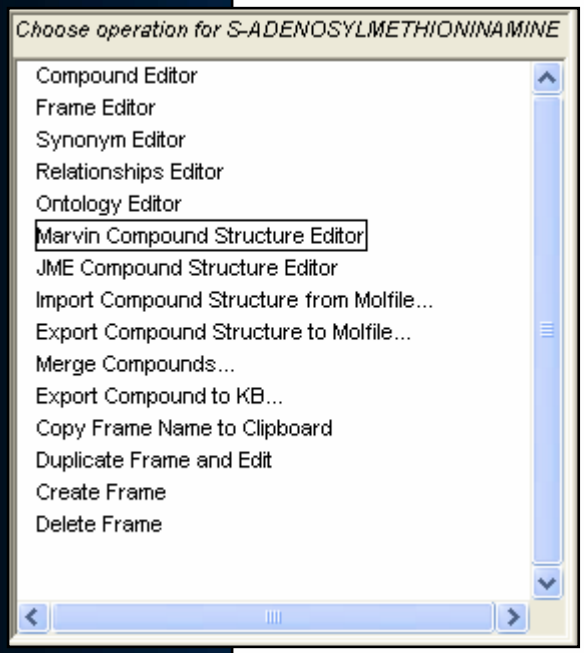
Species Abbreviations in Pathway Display

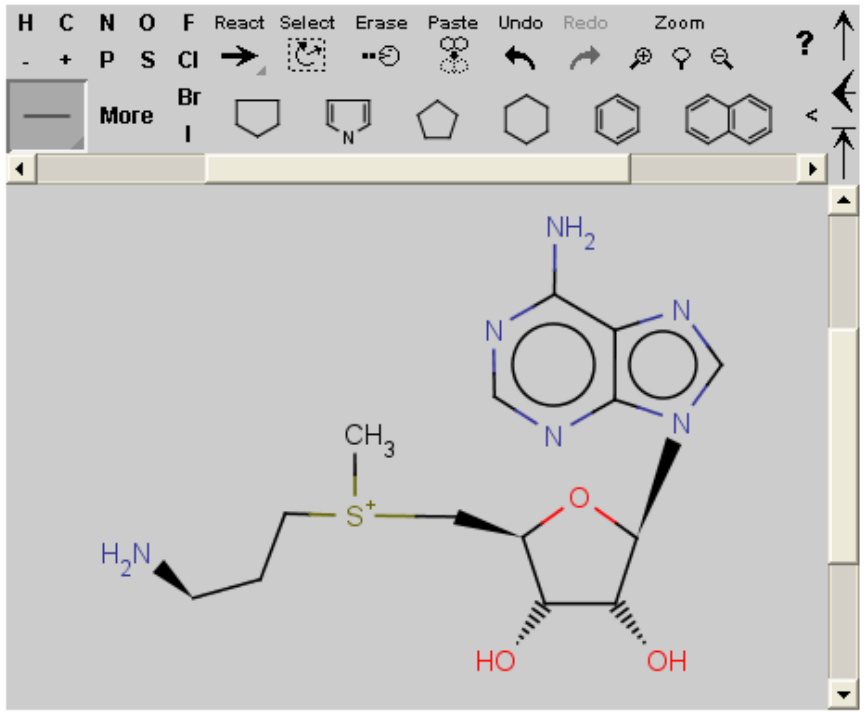


Genes and proteins are labeled in graphical diagrams with the initials of the organism's genus and species names

Support for More Chemical Structure Editors

S-ADENOSYLMETHIONINAMINE : _S_-adenosyl-L-methioninamine





Marvin MSketch Editor

To use the editor, please enable Java and JavaScript in your WWW browser.

Submit Will write back the structure into frame S-ADENOSYLMETHIOI

Expected Taxonomic Range

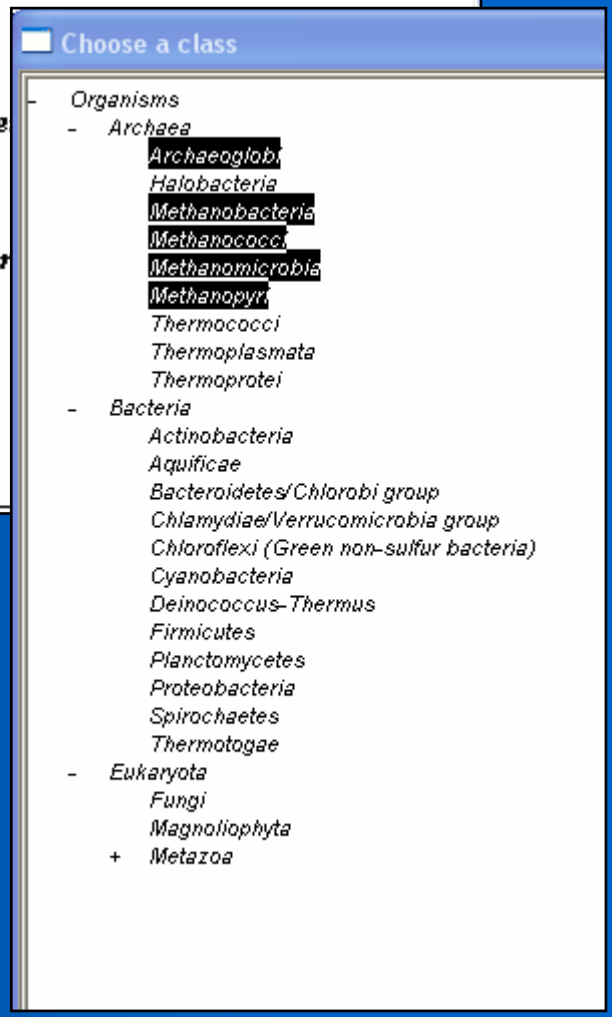
Superclasses: **Biosynthesis -> Cofactors, Prosthetic Groups, Electron Carriers**

Species Data Available for: ***Archaeoglobus fulgidus, Methanobacteria, Methanobrevibacte***
Methanothermobacter thermautotrophicus, Methanothermus

Expected Taxonomic Range: ***Archaeoglobi, Methanobacteria, Methanococci, Methanomicr***

Created by: caspi on 1-Jun-2006

Credits: Created 01-Jun-2006 by **Caspi R, SRI**



Other MetaCyc-related Pathway Tools Improvements

- **Pathways:**
  - Made pathway displays more compact
  - Search for pathways and reactions by substrates
- **Chemical structures:**
  - Import/export of mol files
  - Search for compounds by combining name, MW, formula, and substructure
- **Auto-checkpointing**

Future Directions

Future Curation

- Environmental pathways (degradation of explosives, pesticides etc)
- Medical pathways (antibiotics biosynthesis, microbial secondary metabolites etc)
- Pathways of commercial importance (food industry, vitamins, chemicals etc)
- General metabolism

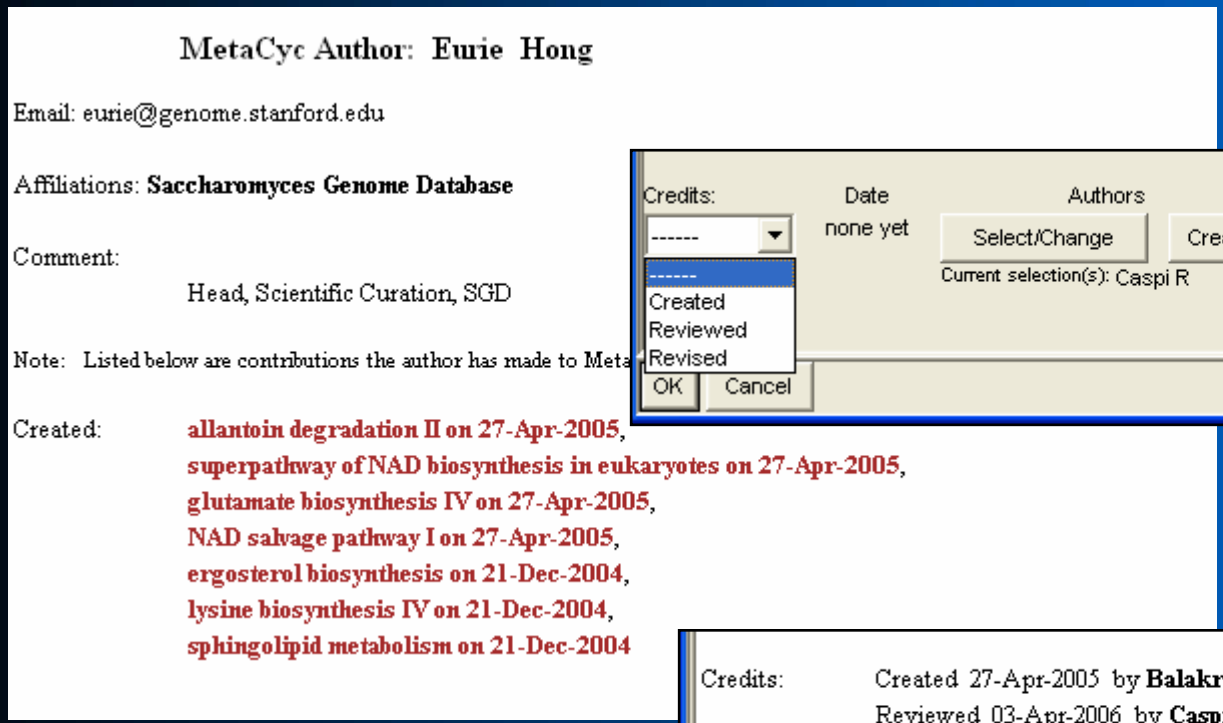
Submitting Pathways to MetaCyc

- The pathway must be experimentally proven and described in one or more published journal articles
- Pathways and enzymes should have comments, literature citations and evidence codes
- Genes and enzymes should have links to sequence databases (e.g. Entrez and UniProt) and citations, if available
- Enzymes should have as much information as possible, such as optimal pH and temperature, Km values, inhibitor, activator and cofactor information, etc.
- Once in MetaCyc, your pathway will be used routinely by PathoLogic during the creation and updating of PGDBs

More about the pathway submission can be found at http://www.metacyc.org/MetaCycPosting.shtml

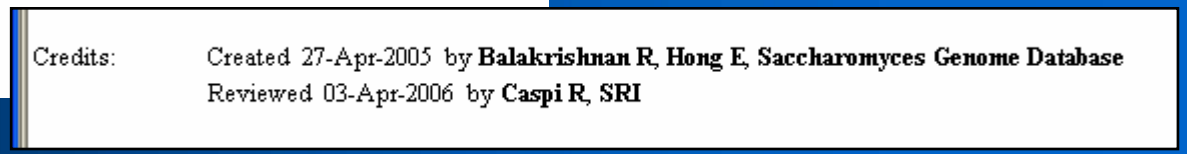
Author Crediting System

Added the ability to credit authors and institutions for creating, reviewing, or revising a pathway



Editor:

Display:



End