### Editing Pathway/Genome Databases

### By Ron Caspi

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This presentation can be found at <u>http://bioinformatics.ai.sri.com/ptools/tutorial/sessions/curation/</u> Curation of genes, enzymes and Pathways/

A lot more information is available in the Curator's Guide, at <u>https://bioinformatics.ai.sri.com/ptools/curatorsguide.pdf</u>

### Pathway Tools in Editing Mode

The database can be accessed by two distinct modes

- The Navigator allows limited interaction with the DB
- The Editors allow complete modification of the DB

Editing is available in **Desktop mode only** 



## Installing H. Pylori PGDB

In order to be able to perform editing, you must have a PGDB other than MetaCyc or EcoCyc installed on your system.



- In the following exercises we will be using the PGDB for *Helicobacter pylori* 26695.
- To install this PGDB: open the PGDB Registry

(Tools  $\rightarrow$  browse PGDB Registry)

- Type pylori and hit Enter
- Double-click on *Helicobacter Pylori* 26695 to move it to the bottom field, then click on "Fetch and install selected PGDBs".
- Click all OK buttons until it is installed, then close the Registry by clicking the Cancel button.

# Saving/Undoing Changes



The user <u>must</u> save changes explicitly

- File => Save Current DB (Control-S works too) or
- Save DB button on upper right

"Undo" is called Revert Current DB in Ptools lingo. It only works with unsaved changes, and it reverts **all** unsaved changes (no step-by step undo).

Storing databases in MySQL or Oracle enables the following commands:

- List Unsaved Changes in Current DB
- Checkpoint Current DB Updates to File
- Restore Updates from Checkpoint File

# Other Editing-related DB commands under the File menu

- Create new version for selected DBs (and modifies the defaultversion file to have the new version opened automatically)
- Save DB as (makes a new copy that can be opened in the same session as the source PGDB)
- Refresh All Open DBs (only MySQL/Oracle DBs)
- Delete a DB



### **Classes and Instances**

- Instance frames describe specific objects (e.g. L-lysine)
- Class frames describe groups of biological objects (e.g. "an amino acid")
- Classes can contain other objects, while instances can't
- Every compound with an "R" in its structure should be a class
- Proteins or modified proteins that are substrates of MetaCyc reactions are always classes

O=As-C

arsenate

[a glutaredoxin



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### **Object Names and Frame Names**



• The frame name (also known as frame ID) is a unique ID of the object within the database. Instance frame IDs are usually assigned automatically and are not intended for human consumption.

Examples: CPD-23 PWYQT-7 RXN0-555 MONOMER-387 CPLXI-345.

The prefix describes the type of object. Frame names generated in a PGDB other than MetaCyc include one or two characters that identify the source database.

Legacy objects in Pathway Tools (created before current naming standards) usually deviate from these guidelines.

- Class frame names are usually created by humans and use language. E.g. Thioglucosides, Amino-Acid-Biosynthesis.
- Object names include common names and synonyms. They are useful for both humans and computer searches. Unlike frame IDs, names may be not unique.

### There are many, many Pathway Tools Editors

- PGDB Info Editor
- Compound Editor and Compound Structure Editors
- Reaction Editor
- Pathway Editor, Pathway Info Editor
- Signaling Pathway Editor
- Protein Editor and Protein Subunit Structure Editor
- Synonym Editor
- Publication Editor
- Curator/Organization Editors
- Gene Editor
- Isoform/Coding-Segment Editor
- RNA Editor
- Transcription Unit Editor
- Regulatory Interaction Editor
- External Database Editor
- Organism Editor
- Frame Editor
- Ontology Editor



## Invoking the Editors

#### Creating a new Object:

Use the New command under certain top menus, or the Create command under the File menu





Right-Click on the any clickable name, select Edit, then the appropriate editor



### Author Credit System



Assigning author credit is the only way to ensure information about the origin of a frame is maintained, even if the frame is exported to other databases.

Author credit is not properly stored unless a curator frame with login information has been created, and the login information was specified as a username under Preferences.



Determined by Windows login, not permanent

Determined by the Author Credit System, permanent



Created by: caspi on 12-Aug-2009

Credits:

Created 12-Jun-2013 by Hoover JE, FBI

### **Organization and Curator Editors**

User ID must be longer than 3 characters

If your User ID should be different from your workstation login, specify it under Preferences -> User ID (see next slide).

Curator Editor			×	
First name: Middle name: Last name: E-mail address: User ID (i.e. login name): Affiliations: Select// Current selection(s): Summary: The first D	Edgar J. Hoover hoover@fbi.gov edgar Change FBI Director of the Federal Bureau of Investigation (FBI). /	An avid user of Pathway Tools.	CITS FRAME Create/Search Citation Hyperlink Spellcheck	
OK Cancel				

### Specifying the User ID

les To	pols Help		
	Answer List	>	1
	Browse PGDB Registry		
°М(	Consistency Checker		
	Dead-end Metabolite Finder		
	Chokepoint Reaction Finder		
	MetaFlux		
vom	History	>	
ton	Instant Patch	>	
top.	MultiOmics Explainer		
	Ontology Editor		
	Pane	>	
	PathoLogic	CTRL+t	
	Preferences	>	Layout of Window Panes >
	Prepare BLAST Reference Data	>	Colors
	Propagate MetaCyc Data Updates		Text Font Size
	Publish DBs	>	Citation Reference Style
	Regulatory Network		Cellular Overview Display
	Search	>	Pathway Display
	Reachability Analysis		Reaction Display
	Upgrade Schema of All DBs		SmartTables
			History and Answer Lists
			Omics Popups
			Database Sharing
			Preferred Database
			UserID

Save

Restore Saved Preferences

Restore Defaults



This needs to be done only if the Pathway Tools User ID has to be different from the workstation login.

#### 

### The Compound Editor

- Create or edit a compound (but not its structure)
- Specify Class
- Common Name and Synonyms
- Comments, citations
- Links to other DBs



	DIPHOSPHATE		
Class: all carbohydr all carbohydr	rates->a carbohydra rates->a carbohydra	⇒a glycan->a carbohydrate derivative->a sugar phosphate->a hexose phosphate->a hexose 6-phosphate, +>a glycan->a carbohydrate derivative->a sugar phosphate->a sugar bisphosphate	
ommon Name: Rhota:	D fructore 1.6 bi	nkeenhate	
onnon name. Jocoeca,	-D-Ildetose 1,0-bi	prospirate	
ynonyms:			
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FBP		Make this the Common Name	
Autoreviated name:			
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inks to other databases:			
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ChemSpider	▼ 4574223	Same Entity	
PubChem-compound	▼ 5460765	Same Entity	
ChEBI	• 32966	Same Entity	
Wikipedia	Fructose_1	Same Entity	
	▼ C00354	Same Entity	
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KEGG LIGAND CAS	▼ 488-69-7	Same Entity	
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KEGG LIGAND CAS  Does this compound Treate:	✓ 488-69-7     ✓	Same Entry Same Entry Currence	
KEGG LIGAND CAS Does this compound Credits:	488-69-7      Aave no plausible str     Date     none yet	Same Entry Same Entry Cure ? Curators Organizations Select/Change Create Select/Change Create Create	

# More Compound Editing

 Pathway Tools supports the Marvin JS structure editor, produced by ChemAxon, which needs to be obtained from them.

https://chemaxon.com/products/marvin-js

http://bioinformatics.ai.sri.com/ptools/installationguide/released/marvin-js.html

#### Other commands:

- Export/Import to Mol files
- Import from ChEBI
- Exporting to other DBs
- Merging
- Duplicate Frame and Edit

Choose operation for O-acylpseudotropines		
Compound Editor	^	
Class Editor		
Frame Editor		
Synonym Editor		
Relationships Editor		
Ontology Editor		
Marvin JS Compound Structure Editor	>	
Deprecated Marvin (Java Applet) Compound Structure Editor	/	
Import Compound Structure from Molfile	1	
Import Compound Structure from ChEBI		
Export Compound Structure to Molfile		
Merge Frames		
Propagate Compound to DB		
Add Object to SmartTable		
Add Object to File Export List		
Duplicate Frame and Edit		
Create Frame		
Delete Frame	~	
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### The PGDB Info Editor

To access: go to the PGDB home page (click on the Home button, then on the organism name) Right-click the organism name, and choose Edit  $\rightarrow$  PGDB Info Editor

This is the place to:

- Specify PGDB authors
- Modify NCBI taxonomy
- Specify a footer
- Set the tier level
- Create a comment for the PGDB home page
- Enter MIGS Data
- Enter Annotation Data

PGDB In	fo Editor			
GDB Info	MIGS Data	Annotation Data		
Synonyms:	Regillus ent	aragia AmagCanbank anta NC	00200	
	Bacillus anti	tracis AmesGenbank entry NC	00399	
	Bacillus anti	hracis strain Amos	_00333	
	Bacillus anti	hracis Ames		
	Bacillus anti	hracis str Ames		
	,			
faxon: Baci	llus anthracis	Ames	NCBI Taxonomy Browser	Current taxonomic lineage: cellular organisms -> Bacteria Firmicutes -> Bacilli -> Bacillales -> Bacillaceae -> Bacillus
				Bacillus anthracis -> Bacillus anthracis Ames
Citations: 12	2721629			
GDB Tier: 2	•			
Genome Source	ce:	Genbank entry NC 003997		
GDB Authors	c	L Bashkin		
		Jonathan Wagg		
		Nan Guo		
		Peter Karp		_
		Ron Caspi		
Project Home F	Page URL:			
Project Primary	Contact Email:			
Copyright strin in HTML form	g: at)	Copyright 2004-2016 SRI Inte	rnational.	
Footer citation	for web pages:	-		
	<u> </u>			

### The Synonym Editor



# Lets you easily edit the synonyms and set the common name

Edit Synonyms for GOOD	
Common Name: good	
Suponume:	
excellent	Make this the Common Name
superb	Make this the Common Name
outstanding	Make this the Common Name
magnificent	Make this the Common Name
excentional	Make this the Common Name
maxellaus	Make this the Common Name
una destru	Make this the Common Name
tirst-rate	Make this the Common Name
first-class	Make this the Common Name
sterling	Make this the Common Name
fabulous	Make this the Common Name
fantastic	Make this the Common Name
terrific	Make this the Common Name
awesome	Make this the Common Name
wicked	Make this the Common Name
OK Cancel	

### The Reaction Editor



With the Reaction Editor you can:

- Enter or edit a reaction equation
- Specify EC numbers (official?)
- Enter a common name (if no full EC number exists)
- Set Conversion Type
- Specify location information (transport, cellular location)
- Specify reaction direction



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# The Pathway Info Editor

- Class (variant class)
- Common Name
- Synonyms
- Evidence Codes
- Citations
- Summary
- External Links
- Hypothetical reactions
- Key reaction
- Rate-limiting steps
- Enzymes not in use
- Author credit

Construct of Procursor Influences and Energy-Okycophia       This class is a variant pathway class.         Construct of Procursor Influence       Image: Classification         Enclose-Neergenet/Parmas pathway       Make this the Common Name         Enclose-Neergenet/Parmas pathway       Make this the Common Name         EMP pathway       Make this the Common Name         EMP pathway       Make this the Common Name         EMP pathway       Make this the Common Name         Summor Termine Termine Name       Make this the Common Name         Summor Termine Name       Evidence Code Datases         Code       Termine Name         Summor Termine Name       Evidence Code Datases         Code       Termine Name         Summor Termine Name       Evidence Code Datases         Code       Termine Name         Summor Termine Name       Evidence Code Datases         Code       Termine Name       Make this the Common Name         Summor Termine Name       Summo	Pathway Info Editor for GLYCOLYSIS				
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۲	Update Last-Curated Date ?				
	< [	m	•		

### **Evidence Codes for Pathways**

http://bioinformatics.ai.sri.com/evidence-ontology/

Experimental evidence codes:

IDA: inferred from direct assay IEP: inferred from expression pattern IPI: inferred from physical interaction TAS: traceable author statement IGI: inferred from genetic interaction IMP: inferred from mutant phenotype



![](_page_18_Picture_5.jpeg)

Full documentation for an evidence code is displayed in the Navigator (click the code icon)

### The Pathway Editor

Graphically create and modify pathways

Reaction Menu: add reactions one by one Pathway Menu: add sub-pathways to create a superpathway

![](_page_19_Figure_3.jpeg)

### Printing Frame IDs in the Lisp Console

A convenient way to work with Pathway Tools frame IDs is to print them to the Lisp console using the right click  $\rightarrow$  Edit  $\rightarrow$  Show frame name command, then copy them from the console and paste them into the respective editors.

![](_page_20_Figure_2.jpeg)

### **Connecting Reactions**

![](_page_21_Figure_1.jpeg)

![](_page_22_Picture_0.jpeg)

# Pathway Editor Limitations

### Complex situations can cause ambiguity:

- reaction directionality not specified
- reaction directionality opposite to direction in pathway
- dialog box for disambiguating
- pathway drawn in bizarre arrangement
- Fix:
  - try disconnecting reactions and adding them in different order

![](_page_22_Picture_10.jpeg)

Limitation: a reaction can appear only once in a pathway.

![](_page_22_Picture_12.jpeg)

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## Overview of Creating a Pathway

![](_page_23_Picture_1.jpeg)

- Identify all the metabolites. Define any missing ones.
- Find the individual reactions in the PGDB/MetaCyc and create new reactions if necessary.
- Compose the pathway from the individual reactions using the pathway editor.
- Assign a class to the pathway.
- Add a summary, citations, and an evidence code.
- Assign the appropriate enzymes, create complexes when appropriate.
- Curate information about enzymes and genes, including evidence codes for the enzymatic reactions.

### **Lisp Breaks**

- When Lisp encounters an unrecognized command it breaks
- A break is NOT a crash
- When a break occurs, the control moves from the GUI to the Lisp console

![](_page_24_Picture_4.jpeg)

To generate a break: type (break) at the listener pane, hit enter

Lisp presents several recovery options

Type :cont x where x is the number of the best option

Allegro Common Lisp Console - [ptools_win32.dxl]	
EC(1): (eco)	^
upening Navigator Window.	
; HUTOIOADING FOR CLASS ECHU-SIREHM:	
; Fast loading from Dundle Code\SIKEHMH.fast	
warning: Enablewindow: (error 127) The speci	fied procedure cou
*debugger-book* colled	
Prock: coll to the 'brock' function	
break. Call to the break function.	
Restart actions (select using :continue):	
0: return from break.	
1: Return to Pathwau Tools version beta com	mand level
2: Pathwau Tools version beta top level	
3: Exit Pathwau Tools version beta	
4: Return to Top Level (an "abort" restart)	
5: Abort entirely from this (lisp) process.	
[1c] EC(2):	
L - J - (-) -	~
2	S

### **Bug Reports**

If you get a break as a result of a bug, get the evaluation stack by typing

:zo :count :all at the lisp prompt

Copy the output, and send it by email to ptools-support@ai.sri.com

![](_page_25_Picture_4.jpeg)

Allegro Common Lisp Console - [ptools_win32.dxl]	
*debugger-hook* called. Break: call to the `break' function.	
Restart actions (select using :continue): 8: return from hreak. 1: Return to Pathway Tools version beta command level 2: Pathway Tools version beta top level 3: Exit Pathway Tools version beta 4: Return to Top Level (an "abort" restart). 5: Abort entirely from this (lisp) process. [Ic] EG(2): zeo :count :all Evaluation stack: (BREAK) [ EXXL::%EVAL ] ->(EVAL (BREAK)) ((METAN))	
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# <ecocyc #x2391bf6a="" @="">. #<non-lisp #x1="" @="" object="">) ((METHOD CLIM:RUN-FRAME-TOP-LEVEL :AROUMD (CLIM:STAMDARD-APELICATION-FRAME)) #<ecocyc #x2391bf6a="" @="">) //LINETMOD / CFCFECTURE METHOD 1 1 MLL 1 1 0</ecocyc></non-lisp></ecocyc>	11
((,:h)(Ennme, (,:FFEC)(VE=METHOU     MIL   1) V) #(ECOOVC @ #x2391bF6a> . #) (ECO) [ EXCL::%EVAL ] (EVAL (ECO))	
(TPL:TOP-LEVEL-READ-EVAL-PRINT-LOOP) (TPL:START-INTERAGTIVE-TOP-LEVEL #CEXCL:TERNINAL-SIMPLE-STREAM [initial terminal io] fd 0/1 @ #X2008e2X2> #CFunction TOP-LEVEL-READ-EVAL-PRINT-LOOP> NIL)	
[1c] EC(3):	~

![](_page_26_Figure_0.jpeg)

### Reuse existing reactions instead of creating duplicates!

If the reaction is already present in your PGDB, you will see a window like this one

- You should choose the option "Delete".
- Before you delete and close this window, write down the frame ID of the identical reaction, so you could use it later when specifying the pathway.

![](_page_27_Picture_4.jpeg)

Potential reaction duplicate detected	~
The reaction that you are creating or editing:	
SUCCDIAMINOPIMDESUCC-RXN: N-succinyl-L,L-2,6-diaminopimelate + L-glutamine + 2 H2O = L,L-diaminopimelate + succinate + L-glutamate + ammonia	
may be a duplicate of an existing reaction. Duplicating existing reactions	
can be very problematic for producing accurate comparative analyses,	
so we strongly recommend that whenever possible, you reuse existing reactions, either in the current PGDB or by importing reactions from MetaCyc.	
Note that two reactions that differ merely by reaction direction are considered duplicates.	
The following existing reactions may be duplicates of the reaction you are editing:	
In the current KB:	
Show RXNI-1578 N-succinyI-L,L-2,6-diaminopimelate + L-glutamine + 2 H2O = L,L-diaminopimelate + succinate + L-glutamate + ammonia	
In MetaCvc:	=
[none]	
Please select:	
Show To view the reaction in the Dethway Tools Nevigetor	
Show - 10 yiew the reaction in the reading you are adding at the second	
Relet = To delet the reaction you are editing (you could then use another reaction	
from the current PGDB instead)	
	Ţ
۰ ( m ) ه	
Keep Delete	_

### Import MetaCyc reactions instead of creating duplicates!

- If the reaction is already present in MetaCyc (but not the current PGDB), you will see a window like this one
- You should choose the option "Import".
- Before you import and close this window, write down the frame ID of the identical reaction, so you could use it later when specifying the pathway.

Potential reaction duplicate detected	×
The reaction that you are creating or editing:	
L-xylulose-5-phosphate = L-ribulose-5-phosphate	
may be a duplicate of an existing reaction. Duplicating existing reactions can be very problematic for producing accurate comparative analyses, so we strongly recommend that whenever possible, you reuse existing reactions, either	in the curr
Note that two reactions that differ merely by reaction direction are considered duplicates	
The following existing reactions may be duplicates of the reaction you are editing:	
In the current KB: [none]	
In MetaCyc: Show LXULRU5P-RXN: D-ribulose-5-phosphate <- L-xylulose-5-phosphate	E
Please select:	
Show To view the reaction in the Pathway Tools Navigator	
Keep To keep the reaction you are editing Delete To delete the reaction you are editing (you could then use another reaction	
from the current PGDB instead)	
Import To delete the reaction you are editing and import one of the preceding	
MetaCyc reactions into this PGDB, from a dialog pop-up	
Keep Delete Import	

### How to get a frame ID?

Navigate to the page of the frame (from the duplicate checker you can click on the Show button)

Right-click on the object name and select Shows  $\rightarrow$  Frame name

Move to the Lisp console and copy the name to the clipboard.

If collecting multiple names, paste it into a text editor

Choose operation for PWY-7912		
Show frame		~
Show frame name		
Pop-up pathway with SmartTable data		
Show entity in other DB		
Show frame in all DBs		
Show frame in pop-up window (Clone)		
Print frame to file		
Show changes in pop-up window		
Show changes to terminal		
Show pathway's reaction validity check for usage in a model in termina	L	
Describe CLIM presentation-type of this link		
List referencing objects in terminal		
Refresh object display		
		~
<	>	

## Fill Reaction frame ID's in your handout

Reaction	Frame ID
alpha-L-gulose + 2 NAD+ = 2 pyruvate + 2 NADH + 4 H+	
alpha-L-gulose + NAD = L-gulono-1,4-lactone + NADH + H+	
L-gulono-1,4-lactone + O2 = L-ascorbate + hydrogen peroxide + H+	

Don't forget to include spaces between chemical names and terms such as "+" and "="

To show a frame ID of an object, you can right-click on it and select Show  $\rightarrow$ Show frame name. The frame ID will be printed in the Lisp console, from which you can copy it.

### Editing Pathway/Genome Databases – Lab Section

Exercise 1: Creating reactions and pathways

- Create organization and curator frames, specify your Pathway Tools username
- Enter new reactions
- Import reactions from MetaCyc
- Construct a new pathway with these reactions

### **Curating Genes and Enzymes**

![](_page_32_Picture_1.jpeg)

### The Gene and Isoform/Coding-Segment Editors

- Enter synonyms/accession numbers
- Enter Links to other databases
- Define transcription direction
- Modify start/end positions
- Define introns
- Create new isoforms
- Define frame shifts

Isoform/Coding-Segment Editor
Isoform Gene Product:
Base numbers are: Re arsenate reductase
If specifying multiple coding segments, please provide the appropriate interpret RNA splicing: The RNA transcript is spliced to remove introns. Protein splicing: The immature pro-peptide is spliced to remove inteins. Ribosomal slippage: The ribosome slips during translation to generate a pro
You do not need to supply an interpretation here if you are merely using this fo Interpretation: Not specified

Class: Gener						
ommon Name: a	sd-2					
asd2			Make this the Com	non Name	1	
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coession-1. GE	ww_3331					
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CD DUELOPI		-1 [Autre1363	former contact	-		
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Isoform Gene Proc	duct: cytochrome P450 2E1	•	
Base numbers are	Relative to start of gene		
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Interpretation Not	t specified 💽		
Coding segments:	Start base	End base	
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3	4223	4372	Gap size: 2944 bp. Please specify interpre
4	4762	4922	Gap size: 369 bp. Please specify interpret
5	5330	5506	Gap size: 407 bp. Please specify interprets
6.	6394	6535	Gap size 1165 hn Disase specify interpret
7.	9701	9888	Gan size: 500 hn. Please specify interpret
0.	10389	10630	Gao size: 887 bo. Please specify interprets
9.	11418	11754	
10.	-	1	_
11.			
12			
13.			
14.	1	1	
15.	[		
16.	1		
17.			
18.			
19.		1	

![](_page_33_Figure_11.jpeg)

### Adding an Enzyme to a Reaction

To add an enzyme to a reaction: First copy the frame ID of the enzyme, then

 Right click the reaction, choose Edit → Create/Add enzyme and paste the ID.

Choose protein	×
Find protein by name or ID:	
OR	
Search by Genes or Create New Protein	
OK Cancel	

Or

- Copy the frame ID of the reaction, then
- Right click the enzyme, choose Edit → Add Reaction(s) and paste the ID.

Add Reactions to Enzyme	$\times$
Enter reaction(s) by ID or EC number:	
[	_
·	_
	—
	_
	-
1. 	
OK Cancel	

### **Creating Protein Complexes**

Right-click on a protein and select
Edit → Protein Subunit Structure Editor
Change "Macromolecule Type" from
polypeptide to protein complex

Example: a simple homohexamer

Specify Protein Subunit Structure				×
Protein: serine acetyltransferase				^
Macromolecule Type: protein complex   Number of distinct subunits:				
Specific Class(es), if any:				
3.9. A homotetramer counts as 1 gene product, not 4 the number supplied here about moteh the number of subusite supplied heleuu.				
For a complex of complexes, check the "Complex?" box below for each subunit				
that is a complex, and enter the number of distinct subunits and the components				
for each. The coefficient can be omitted if it is not known. The Status				
column below tells if a protein already exists or will be created.				
Genes or Subunits:				
Subunit	Complex? Gene or #Subunits	Coefficient	Status	
serine acetyltransferase	Gene: CysE	6 Alrea	dy exists (edit name	
		to cre	ate a new object)	
				~

Choose operation for EG10823-MONOMER		
Protein Editor		^
Protein Subunit Structure Editor		
Add Reaction(s)		
Add Feature		
Frame Editor		
Synonym Editor		
Relationships Editor		
Ontology Editor		
Marvin JS Compound Structure Editor		
Deprecated Marvin (Java Applet) Compound Structure Editor	r	
Import Compound Structure from Molfile		
Import Compound Structure from ChEBI		
Export Compound Structure to Molfile		
Merge Frames		
Merge Proteins		
Propagate Enzyme to DB		
Add Object to SmartTable		
Add Object to File Export List		
Duplicate Frame and Edit		
Create Frame		
Delete Frame		
		~
	× .	

Specifyin	g Multiple Subu	nits
	Gene-Reaction Schematic ₽	3 Mm-msmA 3 Mm-msmB
	1.14.13.111 : methanesulfonate + NADH + oxygen -> form	
Specify Protein Subunit Structure	×	Mm-msmD
Species:       Methylosulfonomonas methylovora       Select         Macromolecule Type:       protein complex <ul> <li>Number of distinct subunits:</li> <li>Specific Class(es), if any:</li> <li>e.g. A homotetramer counts as 1 gene product, not 4 the number supplied here should match the number of subunits supplied below.</li> </ul> For a complex of complexes, check the "Complex?" box below for each subunit that is a complex, and enter the number of distinct subunits and the components for each. The coefficient can be omitted if it is not known. The Status column below tells if a protein already exists or will be created.         Genes or Subunits:       Subunit         methanesulfonate monooxygenase hydroxylase component       methanesulfonate monooxygenase hydroxylase component         methanesulfonate monooxygenase ferredoxin component s       methanesulfonate monooxygenase ferredoxin component s         methanesulfonate monooxygenase ferredoxin component s       methanesulfonate monooxygenase ferredoxin component s	Complex?       Gene or #Subunits       Coefficient       Status         Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:         Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:         Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:         Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:         Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:         Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:         Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:       Image: Subunits:	
OK Cancel		

### The Protein Editor

### (monomer edition)

💷 Edit Pr	rotein HS05414-MONO	MER			
Protein	Enzymatic Activity (4)	Gene	Modified Form	s (0)	
Enzyme: c	ytochrome P450 2E1	Edit Enz	yme Name		
Class:	a polypeptide				

### (protein complex edition)

Edit Protein CPLX-7666	83
Complex Subunits (3) Enzymatic Activity (1) Genes (4) Modified Forms (0)	
Enzyme: methanesulfonate monooxygenase Edit Enzyme Name	
Class:       a protein complex         Evidence for non-enzymatic function of this protein, if any:       Evidence Code	
Mol. Fn and Biol. Proc. GO Terms Cellular Component GO Terms	
Citations:	
Summary: The  FRAME: CPLX-7666  of  FRAME: TAX-50057  was resolved into three distinct fractions, none with individual methanesulfonate oxidizing activity, but which together were reconstituted into an active form  CITS: [8932698]]. The hydroxylase and ferredoxin components have been purified to homogeneity, while the reductase has been partially purified  CITS: [10591843][10094704]]. The genes encoding the complex were cloned, and their sequence was analyzed. The  FRAME: G-10855  and  FRAME: G-10856  genes, encoding the large and small subunits of the hydroxylase component, are similar to several dioxygenases.  FRAME: G-10858  is similar to ferredoxins from toluene and methane monooxygenases, and  FRAME: G-10858  is similar to a number of mono- and dioxygenase reductase components.	]

#### SRI International Bioinformatics

### Protein Editor – First Tab

#### For an example of a complex, open CPLXI-62 in the H. pylori PGDB

Edit Protein CPLXI-62
Complex Subunits (4) Enzymatic Activity (1) Genes (4) Modified Forms (0)
Enzyme: 2-oxoglutarate:acceptor oxidoreductase Class: a protein complex Evidence for non-enzymatic function of this protein, if any: Mol. Fn and Biol. Proc. GO Terms
Cellular Component GO Terms
Synonyms:
Summary: 2-Oxoglutarate:acceptor oxidoreductase (OOR) of <i>H. pylori</i> is a heterotetramer consisting of the following four subunits, OorA, OorB, OorC and OorD. 2-Oxoglutarate:acceptor oxidoreductase (OOR) catalyzes the reversible oxidative decarboxylation of 2-oxoglutarate to form succinyl-CoA [CITS: [9495749]]. OOR is one of three atypical enzymes in the proposed complete citric acid cycle of <i>H. pylori</i> replacing the typical citric acid cycle enzyme α-ketoglutarate dehydrogenase, which is not found in the annotated genome of <i>H. pylori</i> [00R from <i>H. pylori</i> has been partially purified and characterized [CITS: [9495749]]. OOR from <i>H. pylori</i> and other bacteria are extremely oxygen labile, unlike their 2-oxoacid dehydrogenase multienzyme complex counterparts
Molecular Weight (kD, experimental): Citation: pl: Citation:
Links to other databases: Database D Relationship ? Credits: Date Curators Organizations Create Cre
Create     Select/Change     Create       Current selection(s): Krieger CJ     Current selection(s): SRI International       Image: Select/Change     Create       Select/Change     Create       Current selection(s):     Create       Current selection(s):     Create       Current selection(s):     Current selection(s):
OK Cancel

### **Protein Editor - Subunits Tab**

- Edit the copy number of each subunit
- Specify UniProt ID or links to other databases
- Specify experimental MW and any useful info that may apply

💷 Edit Prote	in CPLXI-62														8	3
Complex	Subunits (4)	Enzymatic	Activity (1)	Genes	(4) Modified	d Forms (0)										
Sections below are for the following subunits: HP0585 gene product: dela subunit of 2-oxoglutarate: acceptor oxidoreductase HP0599 gene product: bela subunit of 2-oxoglutarate: acceptor oxidoreductase HP0599 gene product: bela subunit of 2-oxoglutarate: acceptor oxidoreductase HP0591 gene product: gamma subunit of 2-oxoglutarate: acceptor oxidoreductase																
Subunit: HP0588 gene product     Edit Subunit in New Dialog       Name:     delta subunit of 2-oxoglutarate:acceptor oxidoredu     Coefficient:       Gene Classes:     metabolism->energy metabolism, carbon->TCA cycle       Mol. Fn and Biol. Proc. GO Terms     Cellular Component GO Terms																
Synonyms: UDDE9																
	OorD					δ: su	ounit (	of 2-oxor	glutaratera	ccepto	r oxidore					
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Citations:	,									-						
Molecular Wei Is initial me Links to other	ght (kD, experim ethionine cleaver databases:	ental):		Citation:	[								FRAME Create Hyperlink Spellche	/Search Cita	ation	
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InterPro				-	IPR017896	In Family		-								
InterPro				-	IPR017900	In Family		-								
Pfam				•	PF13237	In Family		•								
Prosite				•	PS00198	In Family		•								
Prosite				-	PS51379	In Family		•								
Protein Model	I Portal			•	O25310	Same Entit	Y	•								
Mint				•	MINT-17035	Same Entit	Y	•								
String				•	85962.HP05	5 Same Entit	y	-								
Database of I	Interacting Prote	ins		-	DIP-3580N	Same Entit	y	-								
UniProt				-	O25310	Same Entit	y	-								
				-		Same Entit	, ,	-								
Features:	Edit Protein F	eature(s)	There are n	o feature	es currently ass	sociated with	this pro	otein								Ŧ
OK Cance	el															

### Protein Editor - Enzymatic Activity Tab

![](_page_40_Figure_1.jpeg)

Activators/Inhibitors/Cofactors/Alternative substrates:

Activator (allosteric)	•
Activator (allosteric)	
Activator (nonallosteric)	
Activator (mechanism unknown or not curated)	
Inhibitor (competitive)	
Inhibitor (noncompetitive)	
Inhibitor (uncompetitive)	
Inhibitor (mixed)	
Inhibitor (irreversible)	
Inhibitor (allosteric)	
Inhibitor (mechanism unknown or not curated)	
Inhibitor (other)	
Cofactor or prosthetic-group	
Alt. substrate for L-ornithine	
Alt. substrate for urea	
Alt. substrate for H2O	
Alt. substrate for L-arginine	

	0 0 0				
Add New Activity					
Enzyme activity name: arginase					
Reaction (shown in EC left-to-right direction): L-argi	nine + $H_2O \iff$ urea + L-ornithine				
Evidence for this activity: EV-EXP-IDA-PURIFIED-	PROTEIN Citation: 2241902	EV-EXP-IDA-PURIFIED-PROTEIN	Citation: 2515788		
Evidence Code Citation	n:		J '		
Synonyms:					
Citations:					
Summary:				^	слтя
					FRAME
					Create/Search Citation
					Usedeb
					пурегіінк
					Spellcheck
				~	
Reaction Direction: No Direction Stored 💌 Cit	ation: 🔽 Activity i	is physiologically relevant?			
·					
Reaction Location: cytosol (default)	A del apothes legation	for this activity			
Reaction Location: cytosol (default)	Add another location	for this activity			
Reaction Location: cytosol (default) Activators/Inhibitors/Cofactors/Alternative substrate	Add another location	for this activity Physiologically relevant? K <sub>i</sub> (µM)	Citation(s):		
Reaction Location: cytosol (default) Activators/Inhibitors/Cofactors/Alternative substrate Activator (allosteric)	Add another location Add another location	for this activity Physiologically relevant? K <sub>i</sub> (µM)	Citation(s): 11370664	_	
Reaction Location: orytosol (default) Activators/Inhibitors/Cofactors/Atternative substrate Activator (allosteric) Activator (allosteric)	Add another location	for this activity Physiologically relevant? Κ <sub>i</sub> (μM)	Citation(s): 11370664 2515788		_
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Reaction Location: ovtosol (default) Activators/Inhibitors/Cofactors/Atternative substrate Activator (aliosteric) Activator (aliosteric) Inhibitor (noncompetitive) Inhibitor (noncompetitive) Inhibitor (noncompetitive) Inhibitor (noncompetitive)	Add another location  S:  C-omithine  Mn2+  L-arginino-succinate  L-canavanine  D-octopine	for this activity Physiologically relevant? K; (µM)	Citation(s): 11370664 2515788 2241902 2241902 2241902		
Reaction Location: ovtosol (default) Activators/Inhibitors/Cofactors/Atternative substrate Activator (aliosteric) Activator (aliosteric) Inhibitor (noncompetitive) Inhibitor (noncompetitive) Inhibitor (noncompetitive) Inhibitor (competitive) Inhibitor (competitive)	Add another location  S:	for this activity Physiologically relevant? K; (µM)	Citation(s): 11370664 2515788 2241902 2241902 2241902 2241902		
Reaction Location: ovtosol (default) Activators/Inhibitors/Cofactors/Atternative substrate Activator (allosteric) Activator (allosteric) Inhibitor (noncompetitive) Inhibitor (noncompetitive) Inhibitor (competitive) Inhibit	Add another location  S:   L-omithine  Mn2+  L-arginino-succinate  L-canavanine  D-octopine  L-chysine  L-bysine  L-bysine L-b	for this activity Physiologically relevant? K; (µM)	Citation(s): 11370664 2515788 2241902 2241902 2241902 2241902 2241902 2241902		
Reaction Location: ovtosol (default) Activators/Inhibitors/Cofactors/Atternative substrate Activator (allosteric) Activator (allosteric) Inhibitor (noncompetitive) Inhibitor (noncompetitive) Inhibitor (competitive) Inhibit	Add another location	for this activity Physiologically relevant? K, (µM)  Freevant? Fre	Castion(s): 11370664 2515788 2241902 2241902 2241902 2241902 2241902 2241902 2241902		
Reaction Location: ovtosol (default) Activators/Inhibitors/Cofactors/Atternative substrate Activator (allosteric) Activator (allosteric) Inhibitor (noncompetitive) Inhibitor (noncompetitive) Inhibitor (competitive) Inhibitor (competitive) Activator (mechanism unknown or not curated)	Add another location is:	for this activity Physiologically relevant? K, (µM)  F	Ctation(s): 11370664 2515788 2241902 2241902 2241902 2241902 2241902 2241902		
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Reaction Location: ovtosol (default) Activators/Inhibitors/Cofactors/Atternative substrate Activator (allosteric) Activator (allosteric) Inhibitor (noncompetitive) Inhibitor (noncompetitive) Inhibitor (competitive) Inhibitor (competitive) Inhibitor (competitive) Activator (mechanism unknown or not curated) Activator (mechanism unknown or not curated)	Add another location	for this activity Physiologically relevant? K. (µM)	Ctation(s): 11370664 2515788 2241902 2241902 2241902 2241902 2241902		
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### Citations

- Citation boxes
- The CITS field

#### PubMed citations:

- Use PubMed IDs
- Automatically imported when exiting editor
- You can invoke the Publication
   Editor by right clicking on a citation

#### Non PubMed citations:

- Enter an ID in the form Smith06 in a citation box, invoke editor by clicking out of the box. Click on "Search or Create Publication Frame".
- If you have a DOI number, enter it and click outside the DOI ID box, and it will be retrieved automatically.
- If there is no DOI, type in the details.

![](_page_41_Picture_11.jpeg)

Edit Publication Da	ata for PUB-5033403		
PubMed ID: 5033403	AGRICOLA ID:	DOI ID:	
Title: Catabolism of	f pipecolate to glutamate in Pse	eudomonas putida.	
Authors (surname first):	1. Perfetti R 3. Titus J 5.	2. Campbell RJ 4. Hartline RA 6.	
Source: J Biol Chen	n 247(12);4089-95		Year: 1972
OK Cancel			

![](_page_41_Picture_13.jpeg)

### Editing Pathway/Genome Databases – Lab Section

Exercise 2 : Curating enzymes, entering citations, and exporting pathways

- Assign enzymatic activities to proteins
- Define protein complexes
- Create a publication frame
- Export a pathway to a file

#### Exercise 3 : Constructing Superpathways

• Construct a superpathway

Exercise 4 : Creating a complicated protein complex

• Create a protein complex that involves modified proteins.