Building and Refining AraCyc: Data Content, Sources, and Methodologies

Kate Dreher

TAIR, AraCyc, PMN Carnegie Institution for Science

AraCyc

AraCyc – <u>Ara</u>bidopsis Metabolic En<u>Cyc</u>lopedia

Database of metabolic pathways found in Arabidopsis



Accessible from:



TAIR – The Arabidopsis Information Resource
 www.arabidopsis.org

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AraCyc

AraCyc – <u>Ara</u>bidopsis Metabolic En<u>Cyc</u>lopedia

Database of metabolic pathways found in Arabidopsis

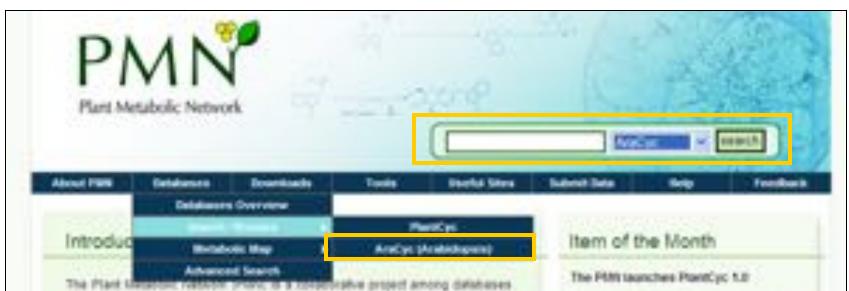


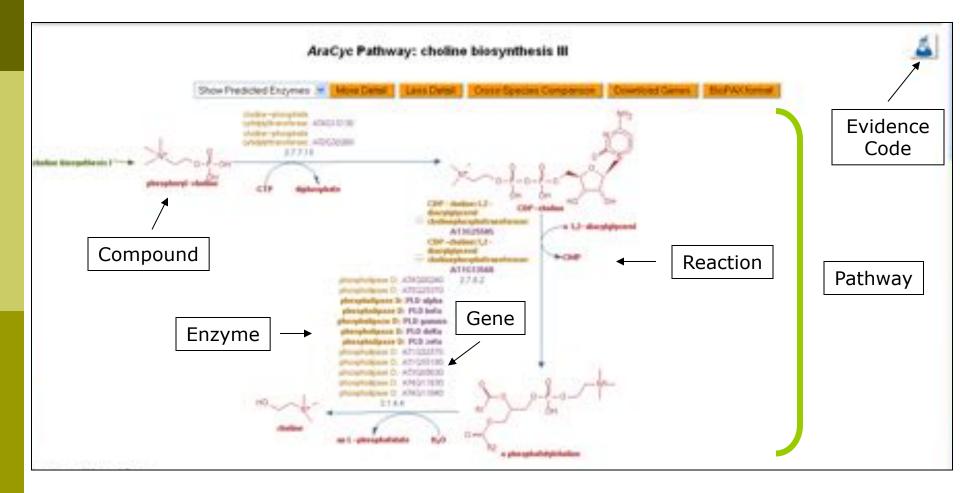
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PMN – Plant Metabolic Network

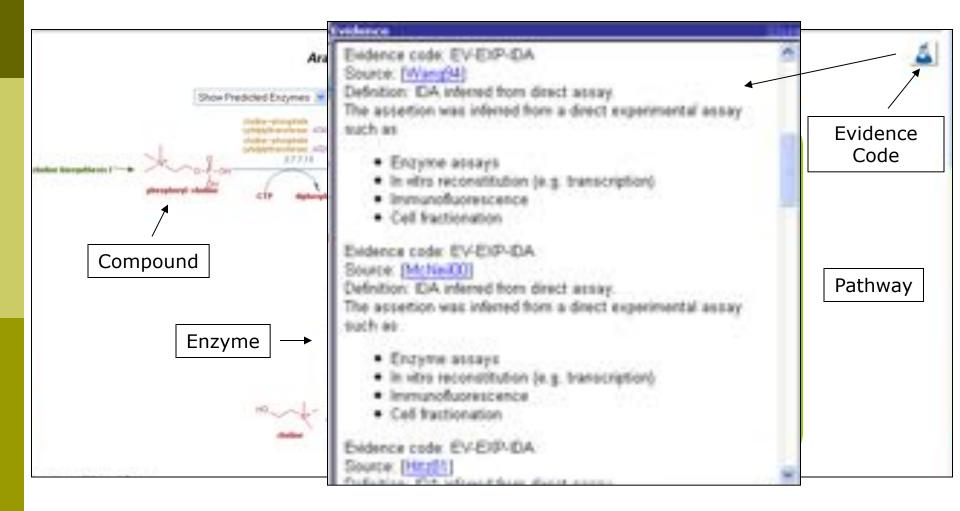
www.plantcyc.org

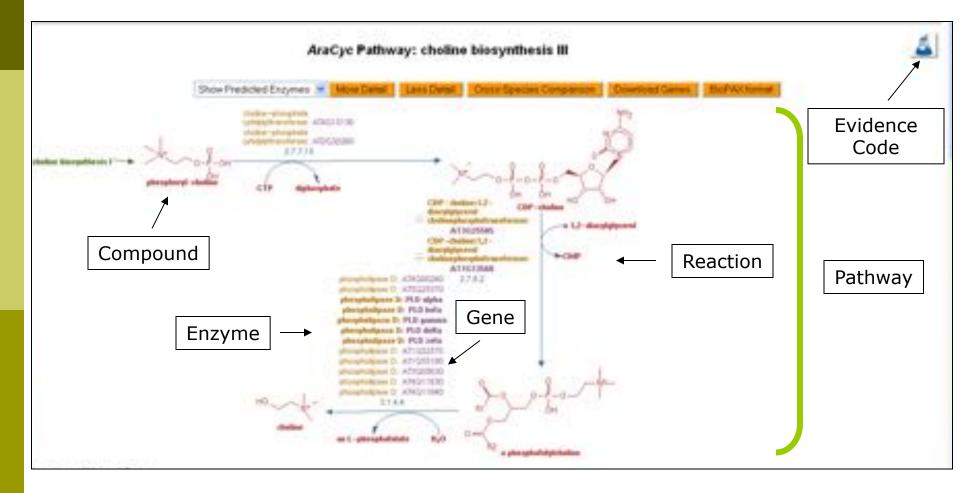




+ Additional curated information

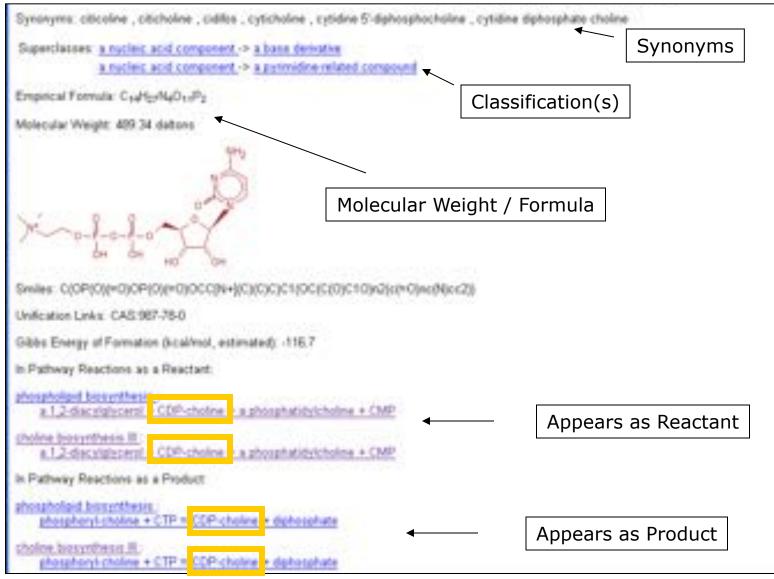
Superclasses Basesthesis, a Eats Acds and Lands, a Chill	te Bezahlern	Classification		
Summary: General Information: Choirs is a fundamental matebolic non-plactic plant membranes [Min(02)] Chailes is also a to accumulated and confers also tolerance to salisity, drou	precursor for the formation of phyci	ne betaine (glycine ketaine)	investigation in the second of the second	tail plants such as spinach, where this correspondentiand
The choice biosynthetic pathway enables plants to decou to environmental conditions where large and variable amou			datafightered Mergenheim.) a	and provides them with the metabolic flexibility to adapt
Pathway information: The first step in choice biosynthe Ethenolamine is widely recognized as the entrance compo		f serine to athendiamine (<u>Bors</u>	mit I, which is catalyzed by a	sente decarborylase unique to plants [<u>RomanD.</u>]
The pathway variant displayed (hocleotide pathway) repres where three consecutive N-methylation steps are carried to [] Hotelt_]				
The synthesis of internediates on both the phospho-base out that the synthesis of phosphatidylethanolamine and ph assumed that the reactions embedded in the nucleotide at <u>kinewy00.1</u>	tosphatidylcholine is characterized	t by a high dispres of interaction	and furcation an the various lieve	ets of arising intermediates. Consequently, it has been
The release of choline from the different pathway levels is in into phosphatidylcholine with the subsequent release of ch bean [Wanght] Although a well-defined physiological rol distinct cellular functions [<u>Mid-90</u>]. The remaining enzyme substrates. This may be beneficial to process the federoge	toline, as in tobacco (<u>McNailO)</u>) Is of phospholipase D (PLD) still a es involved in this pathway, phospi	The latter reaction has been al wad further research, progress hoaminoaicohol cytidylyttavelk	own to be specifically catalyzed has been made to assign some r race and COP-aminoalcohol pho	(by physpholipase D (<u>physpholipases</u>) in cardor members of the haterogeneous family of PLD's to sighotraneferace, cover a broader spectrum of
Dispersion of the second secon	Superpathwa	ays		Summary
Unification Links: MataCast PWV7.0001	Pathway varia	ints		<u>cannary</u>
If an anzyme name is shown in bold, there is experimental evid	lance for this enzymatic activity.			
References				
Darkelli, Darko Alt, Mold SH, (1998); "Estamen of about the	felologia autoria in Letro, au	sheet, and carse " Plant Phys	ef. (1980), 00, 1330-1340.	References
Datistic Curve AH, Mode SH, (1989) "Phosphotolytcholme is	unthesis. Offerns sidteres in ser	tean and carst." Plant Physic	079981.00.054-061	
Hitski Hitz WD, Rhodya D, Hansen AD, 119815 'Redotnicer's 60, 814-822	widence implicating phosphory) en	of phosphatidal basis as inter-	edates in between synthesis by	water-streamed batter leaves." Flant Physiol. (1981),

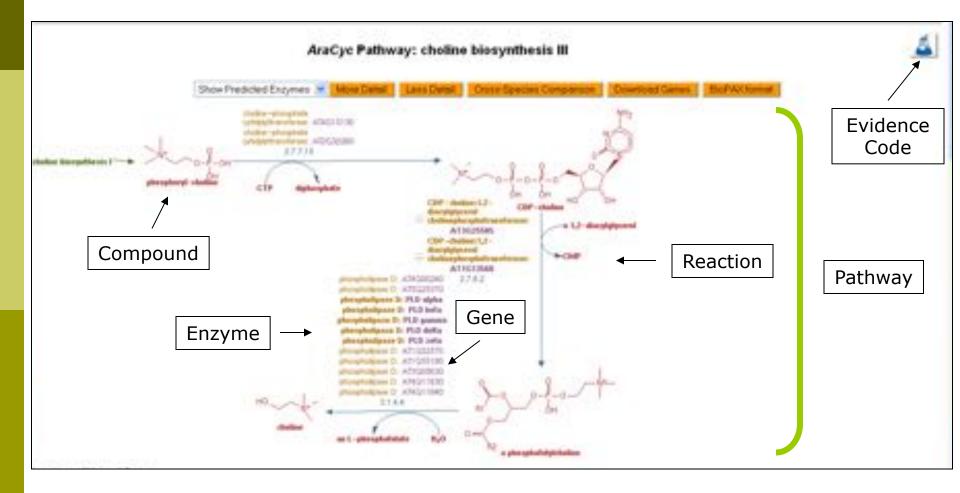




AraCyc Compound pages

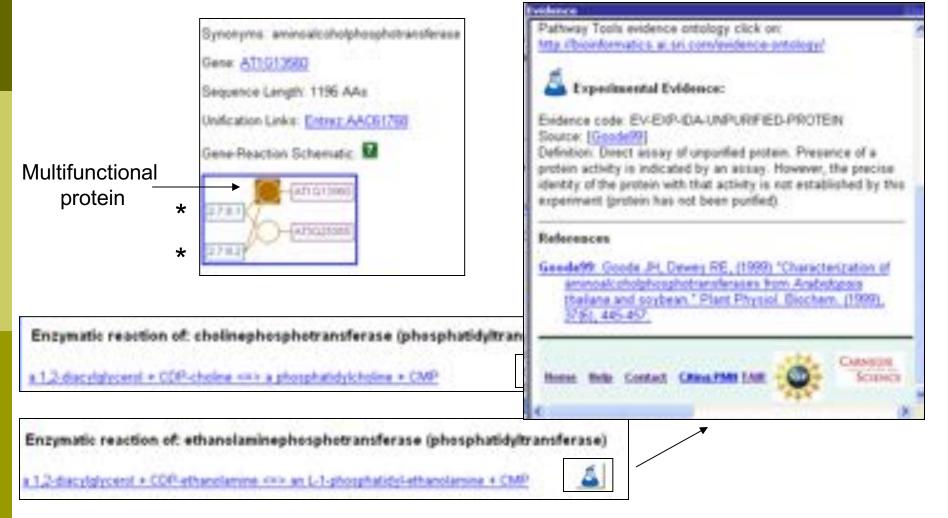
AraCyc Compound: CDP-choline





AraCyc Enzyme detail pages

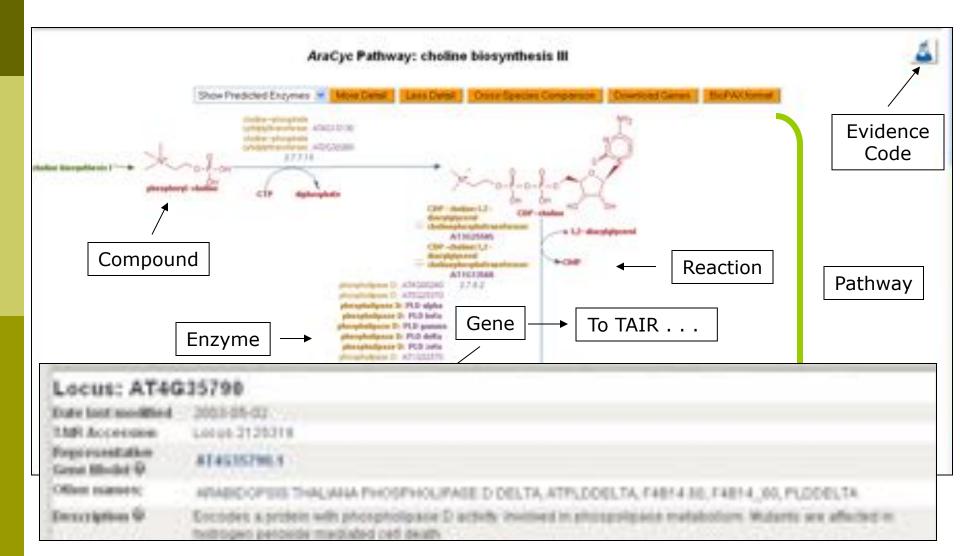
AraCyc Enzyme: phosphatidyltransferase



AraCyc Enzyme detail pages

AraCyc Enzyme: phosphatidyltransferase

Enzymatic reaction of: cholinephosphotran	nsferase (phosphatidy	itransferase)		4
a 1,2-dacylghoand + COP-choine with a photohati	dylcholme + CMP	- Reaction		
The reaction direction shown, that is, A + B errors C	+ D versus C + D crime A	+ B, is in accordance with the Enzyme Commissio	in system.	
Reversibility of this reaction is unspecified.				
In Pathways: choire biosysthesis III., phospholaid	bioxynthesis	– Pathway(s)		
cDNA's encode aminoalcoholphosphotramsferat expression in yeast mutants lacking those enzy phopsphatidylalcohols although with slight differ and was also inhibited to a lesser degree by Ca supporting the proposal that diacyligipcersi, invo equilibrium via the reversibility of the cholinepho	ses involved in the nucleotid yme activities. It has been rences regarding the substr P ²⁴ and Cytidine monophos oved as substrate in both P riphotransferace reaction [Both polypetides contain to	elated from an Arabidopsis cDNA library using the A te pathway of the biosynthesis of phosphatidylethan demonstrated that both A6AAPT1 and A6AAPT2 con- rate preference. A6AAPT2 showed a higher preferen- phate (CMP) than A6AAPT1 [<u>Goode(P</u>]] Both enzy C and triacylghycerol biosynthesis (<u>biacylghycerol</u> <u>Stackin</u>]. A6AAPT1 and A6AAPT2 seem to repress year membrane spanning regions as shown by their	olamine (PE) and phosphatidylc vert CDP-ethanolamine and CDI (a for CDP-choline over CDP-eth mes (AdAAPT1, AdAAPT2) were I biorgethesis), is in equilibrium rtl the only aminoalcoholphosph	holine (PC) as demonstrated by gene P-choline into the corresponding vanolamine in comparison to ADAAPT1 able to catalyze the reverse reaction in with PC and maintains this intransferases in Arabidopsis as
Inhibitors (Allosteric): <u>CMP Goode(P) </u> Inhibitors (Unkmech): <u>Cal²² Goode(P) </u>		Kinetic Parameters, etc.		Summary
Primary Physiological Regulators of Enzyme Activity	Y CMP			
References Geodel99, Goode JH, Devery FE, (1999) "Character Stack#5, Stack CR, Roughan PG, Browse JA, Gard	and and the second second			The second states and the second states and the
		Ť		
		References		



AraCyc 4.5 (released June 2008)

Pathways	288
Compounds	1956
Reactions	1723
Citations	2279

More detailed information available in the Release Notes

PlantCyc 1.0 (released June 2008)

Pathways	508
Compounds	2314
Reactions	2277
Citations	4208
Species	292



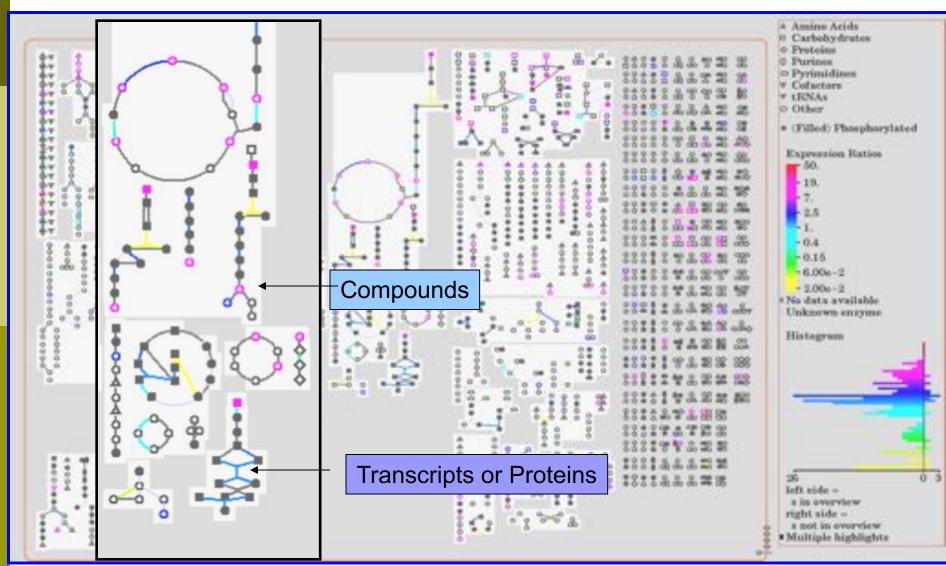
Plant Metabolic Network

Putting AraCyc (and PlantCyc) to use

- Reference information
 - Pathways, Genes, Enzymes, Reactions, and Metabolites
- Data Analysis (AraCyc)
 - Use the OMICS viewer
 - Display the results of experiments on an Arabidopsis metabolic map
 - Study **your data** or **public data sets**

Putting AraCyc to use

Display the results of experiments on an Arabidopsis metabolic map



Putting AraCyc (and PlantCyc) to use

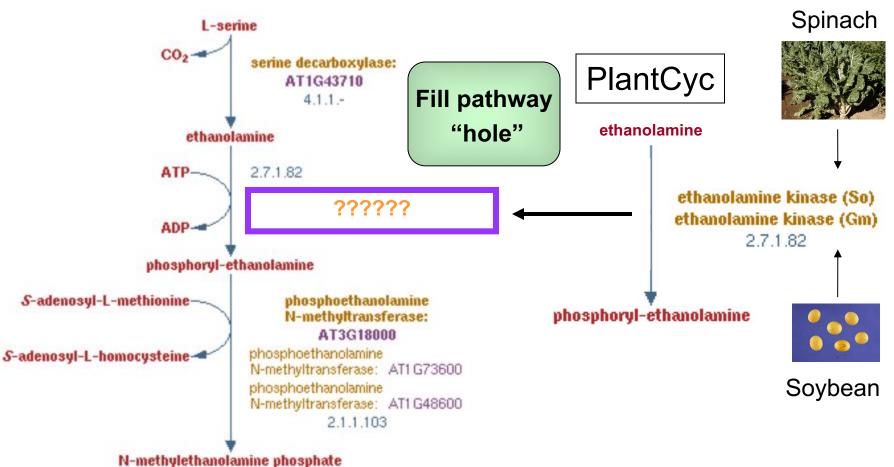
- Reference information
 - Pathways, Genes, Enzymes, Reactions, and Metabolites
- Data Analysis (AraCyc)
 - Use the OMICS viewer
 - Display the results of experiments on an Arabidopsis metabolic map
 - Study your data or public data sets
 - Generate new hypotheses
 - Find metabolic differences in your mutant with "no phenotype"
 - Identify pathways that are related to your favorite biological process
 - See more at "Advanced Bioinformatic Resources for Arabidopsis"
 - Thursday, July 24, 7 PM in the Grand Salon
- Enzyme discovery
 - Fill "pathway holes" through comparative analyses

Putting AraCyc (and PlantCyc) to use

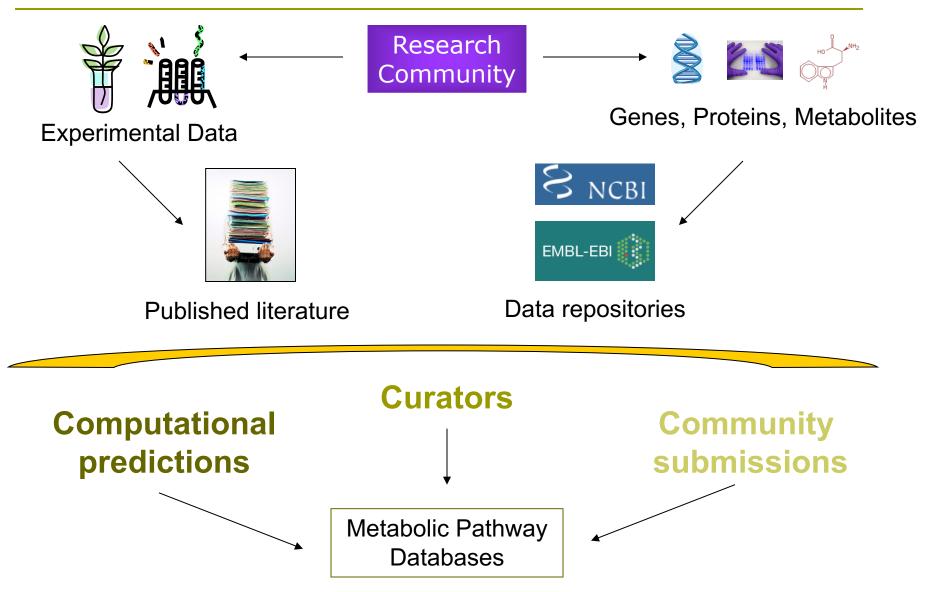
Pathway "Hole Filling"

Choline Biosynthesis I

AraCyc



Data sources and data flow



Data sources and data flow

- Information enters metabolic pathway database in two stages
 - **Stage 1**: Initial build
 - **Stage 2**: Updates and improvements
- AraCyc 1.0 Initial Build 2002

Initial AraCyc Build (2002)

7900 Arabidopsis genes annotated to the GO term `catalytic activity'

4900 loci in small molecule metabolism

19% of the total genome

Goal: Map these loci to metabolic PATHWAYS

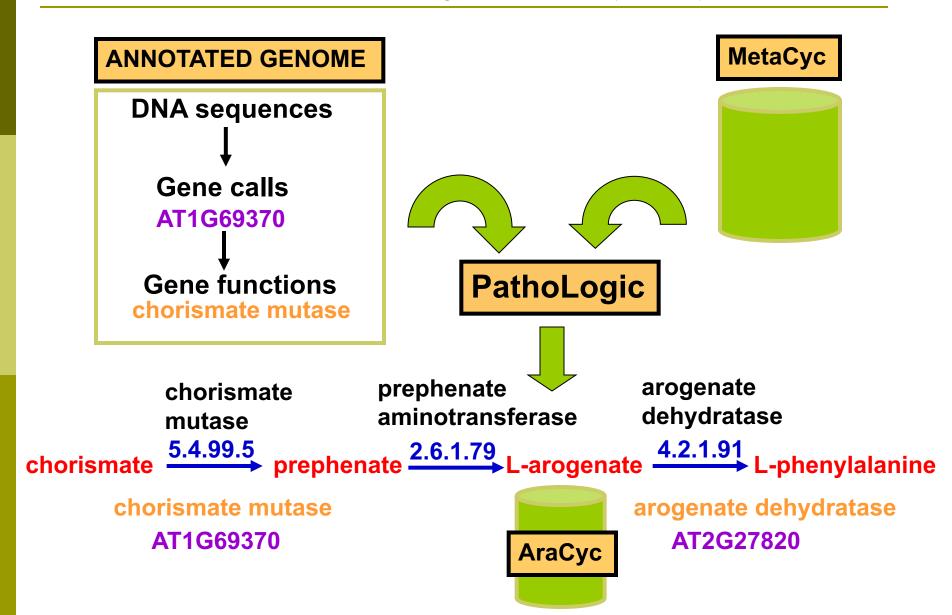
Solution:

- Use reference database: MetaCyc (460 metabolic pathways)
- Run PathoLogic program (SRI International)
- Predict metabolic pathways present in Arabidopsis

MetaCyc

- Multi-kingdom metabolic pathway database
 - METAbolic EnCYClopedia
 - SRI International (www.metacyc.org)
- □ First released in 1999
- All pathways generated by <u>curators</u> extracting information from the <u>scientific literature</u>
- Only contains pathways with <u>experimental support</u>
- Reference database
 - Used to create SINGLE SPECIES databases
 - ... including AraCyc in 2002!

Initial AraCyc Build (2002)



PathoLogic Program

Matches input enzymes to reference enzymes

- Name
- Enzyme Commission (EC) number
- Identifies probable pathways
 - Enzyme coverage
 - Predicted species distribution
- Initial AraCyc 1.0 build (2002)
 - PathoLogic inferred over 200 pathways
 - PathoLogic mapped 940 genes to the pathways

PathoLogic errs on the side of over-prediction

Curators <u>validate</u> pathways . . .

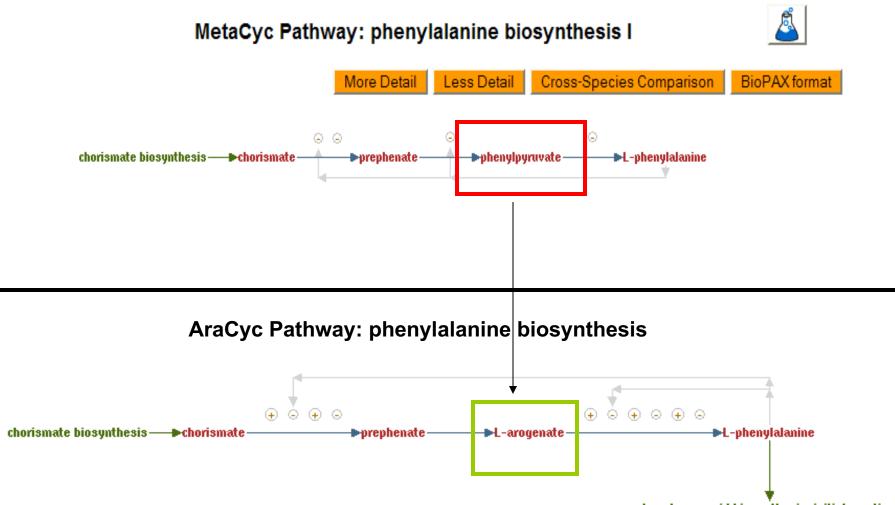
Curators

- Find support for predicted pathways
 - Is the <u>pathway</u> described in *Arabidopsis* literature?
 - Are the <u>crucial metabolites</u> described in *Arabidopsis* literature?
 - Does the pathway include a <u>unique reaction</u> catalyzed by an Arabidopsis protein?

Curators:

- Remove pathways not found in Arabidopsis
 - glycogen biosynthesis
 - C4 photosynthesis
 - caffeine biosynthesis
- Edit pathways operating via a different route
 Phenylalanine biosynthesis in bacteria vs. Arabidopsis

Edit pathways operating via a different route



phenylpropanoid biosynthesis, initial reactions

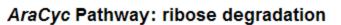
Completion of a New Database

Curators

- Add *Arabidopsis* pathways not present in reference database
- Add Arabidopsis compounds, reactions, and enzymes not mapped to a pathway
- Assign evidence codes to pathways and enzymes

Assignment of Evidence Codes

AraCyc Pathway: phenylalanine biosynthesis





Å



AraCyc Pathway: arginine biosynthesis III



AraCyc 1.0 . . . and beyond

Information enters metabolic pathway database in two stages

- **Stage 1**: Initial build
- **Stage 2**: Updates and improvement

Release	AraCyc 1.0	AraCyc 4.5	AraCyc 5.0
Pathways	219	288	even more!

New rounds of computational pathway prediction

- New TAIR genome releases
- New MetaCyc releases
 - New round of PathoLogic prediction

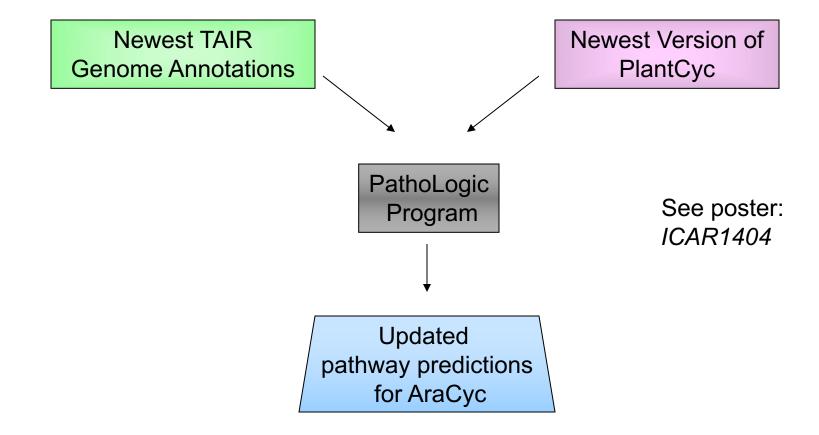
New rounds of computational pathway prediction

- New TAIR genome releases
- New reference database PlantCyc
 - Part of the Plant Metabolic Network
 - Released in June 2008
 - Contains plant pathways supported by:
 - experimental evidence
 - expert hypothesis ***
 - Reviewed by an editorial board of biochemists
 - Will include enzymes from newly sequenced plant genomes and EST collections



www.plantcyc.org

New rounds of computational pathway prediction



Newly predicted pathways undergo pathway validation

New curator entries

Curators search for new information in scientific literature

TAIR curators

Assign new functional annotations to metabolic genes

AraCyc curators

- Manually attach enzymes to pathways
- Identify new and updated pathways
- Write or revise summaries

Database updates and improvements

New community submissions

- Jamborees
 - Experts meet individually with curators
 - Review pathways in specific metabolic domains
 - Provide useful references and suggest important pathways
- Curation Booth *****
 - Open during all poster sessions Booth #1
 - Please come (*free candy*!)
- TAIR or PMN website

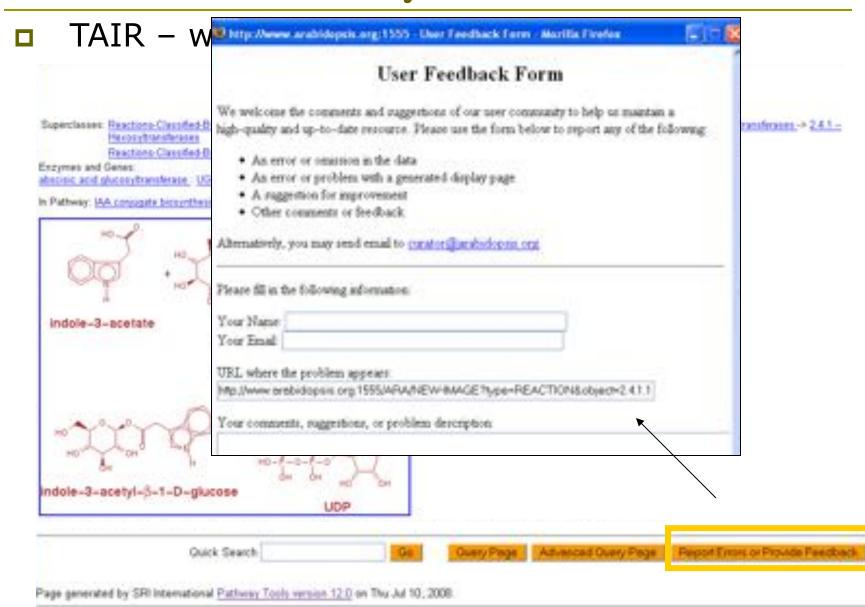
TAIR – www.arabidopsis.org

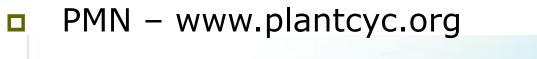
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2	Pathway name (required)	Submission or Correction? (required)	Pathway synonym(s)	Organism(s) where the pathway exists (required)	Reaction (required)	¢	nzyme(s) 'Please add more	Reference(s) / Link(s) to supporting evidence (required)	Gene litract Locus Ideat	skul Armotations are Anantations Des Eurgarst	
3 4	Example isoliquirtige	submission (new enzyme)	424 - trihydroxychalcon e biosynthesis		("Please add more detail information using an enz reaction submission form coenzyme A + 4-couman ATP = 4-coumanyl-CoA + + AMP	rate + 4 + PP) th	Interface information, using an enzyme/ section submission ICL1, 4CL2, 4CL3, ICL5 - Arabidopsis haliana Phytochemistry	PMID 14769935	Data Metabolic Po	Polynoistyllation Mowey Data	
4 54	Example isoliquintige nin biosynthesis	submission			4-coumaroyl-CoA + 3 mi CoA +NADPH = isoliquitingenin + 4 coA - 3CO2 + NADP(+) + H2O	aloyni- n + S	CHR7 (chalcone	Medicage sativa (Ballance, 1995, Plant, Physiol 107(3), 1027-8); srCHR1 (PMID: 10467030)	Protocolls 30.90 Franctional Communics Generalized Phillip francisco, president Phillip francisco, president web site and retrained the difficult version of Phillips, 4		
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to TAIR or Aracyc!

Please join us at our TAIR booth

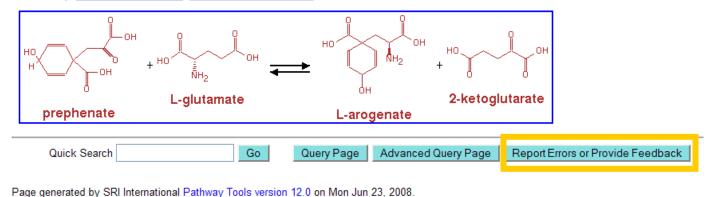
tolles of all 2008 PSP's new in TAB







In Pathway: tyrosine biosynthesis I, phenylalanine biosynthesis



PMN – www.plan	tcyc.org		curator@plantcyc.or	or@plantcyc.org	
PIANT Metabolic Network		2	PlentCys + search		
About PMI Detelances Deverticates PMIN Feedback For		ul Silen Subruit I	Sea lege feedback		
To send a message to a height a category and add a subjects	ul Pathi curator, pleasa fili in yo b your metocage before you out				
E-mail: Category: Sobject:	Ask a question	,			
	http://www.plantcyc.org/ age twee:				

Community submissions = fame!

PMN Contributor page

PMN Contributors

PMIX contributors from around the world have added to or helped to improve the content of AcaCor, PlantCor, and the other PlantCor-dented databases that are part of the PMN

In addition/to the active contributions if on the PBNI editorial board and PBNI coduloration, the following individuals have contributed significantly in improving the content of FlanCor, AraCyc and the other PlantCyc-derived databases that are part of the PBNI.

- Bome contributors have contacted us with supportions and revisions.
- Some have generously responded to appeals for help from the curators.
- · Some have attended curatorial protorees.

Contributors to Pathecays of Princary and Secondary Metabolicas

Printy Metabolism

Analoss and Polyamines

John Jatesso - Viopinia 7ach, UDA

Fatty Acids and Lipids

Daniel Lyhchy - Williams College, USA

General Primary Metabolites:

- · Oliver Frenh Chinenelly of California, Davis, USA
- Hermones and Engelations
 - · Borovie Bartel Rice Chinerally, USA
 - Inivaniti Meapawa Kyolo University, Janan

Your name here!

Acknowledgements

TAIR, AraCyc, and the PMN

Eva Huala (Director and Co-PI) Sue Rhee (PI and Co-PI)

Current Curators:

- Peifen Zhang (Director and lead curator- metabolism)
- Tanya Berardini (lead curator functional annotation)
- David Swarbreck (lead curator structural annotation)
- A. S. Karthikeyan (curator)
- Donghui Li (curator)

Recent Past Curators:

- Christophe Tissier (curator)
- Hartmut Foerster (curator)

CARNEGIE

SCIENCE

Tech Team Members:

- Bob Muller (Manager)
- Larry Ploetz (Sys. Administrator)
- Raymond Chetty
- Anjo Chi
- Vanessa Kirkup
- Cynthia Lee
- Tom Meyer
- Shanker Singh
- Chris Wilks

<u>Metabolic Pathway Software:</u> - Peter Karp and SRI group (**NIH**)

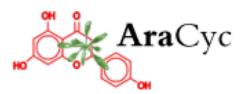


Thank you . . .



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curator@arabidopsis.org



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curator@arabidopsis.org



www.plantcyc.org

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Please visit us at the Curation Booth!

Curation workflow

