AraCyc: Birth and Growth

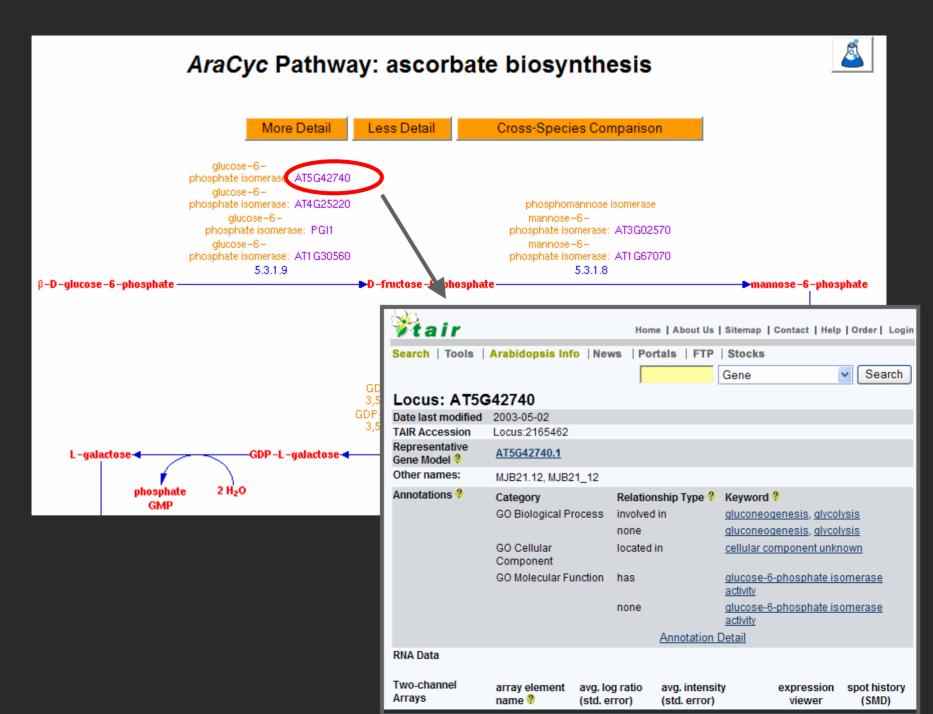
Peifen Zhang The Arabidopsis Information Resource

Outline

- The PathoLogic build of AraCyc
- The manual curation and results
- Systematically updating AraCyc

What is AraCyc

- The Biochemical pathway and enzyme database for Arabidopsis
- Open Database
- Created and supported by Pathway Tools
- Manually curated



from that found in mammals. It proceeds via GDP-D-mannose, L-galactose, and L-galactono-1,4lactone. The intermediate GDP-mannose is also used for cell wall carbohydrate biosynthesis and protein glycosylation, in addition to ascorbic acid biosynthesis.

Citations: [Wheeler98, Smirnoff01]

Unification Links: MetaCyc:PWY-882

References

Smirnoff01: Smirnoff N, Conklin PL, Loewus FA (2001). "BIOSYNTHESIS OF ASCORBIC ACID IN PLANTS: A Renaissance." Annu Rev Plant Physiol Plant Mol Biol 52;437-467. PMID: 11337405

Wheeler98: Wheeler GL, Jones MA, Smirnoff N (1998). "The biosynthetic pathway of vitamin C in higher plants." Nature 393(6683);365-9. PMID: 9620799

Download Genes

Query Pa ascorbate biosynthesis

Gene name	Reaction id	Reaction EC	Enzymatic activity	Evidence
AT5G28840	RXN-1882	5.1.3.18	GDP-mannose 3,5-epimera	se NIL
AT5G28840	RXN-1882	5.1.3.18	GDP-mannose 3,5-epimera	se EV-EXP
AT5G28840	RXN-1882	5.1.3.18	GDP-D-mannose-3,5-epime	rase EV-EXP
AT2G39770	RXN-1881	2.7.7.13	GDP-D-mannose pyrophosp	horylase EV-EXP
AT3G47930	GALACTONOLACTONE	-DEHYDROGENASE-H	XXN 1.3.2.3 galacto	nolactone dehydr
AT2G45790	PHOSMANMUT-RXN	5.4.2.8 phosphor	nannomutase EV-COMP	
AT3G02570	MANNPISOM-RXN	5.3.1.8 mannose-	-6-phosphate isomerase	EV-COMP
AT1G67070	MANNPISOM-RXN	5.3.1.8 mannose-	-6-phosphate isomerase	EV-COMP
AT5G42740	PGLUCISOM-RXN	5.3.1.9 glucose-	-6-phosphate isomerase	EV-COMP
AT4G25220	PGLUCISOM-RXN	5.3.1.9 glucose-	-6-phosphate isomerase	EV-COMP
AT4G24620	PGLUCISOM-RXN	5.3.1.9 glucose-	-6-phosphate isomerase	EV-COMP
AT1G30560	PGLUCISOM-RXN	5.3.1.9 glucose-	-6-phosphate isomerase	EV-COMP

The Computational Build

- As of 2004, the Arabidopsis genome contained 7900 genes annotated to the GO term 'catalytic activity'
- 4900 enzymes in small molecule metabolism (19% of the total genome)
- PathoLogic inferred 219 pathways and mapped 940 (19% enzyme-coding) genes to the pathways

Pathway Hole-filler Results

- Before: 528 holes (62% of total reactions)
- Additional holes filled: 58 (11% of total holes)

Category of holes	Holes	Portion to all holes	Holes with seque nce retriev ed	Holes-filled	Hole-filling rate	Maximum percent ile of hole- filling
EC1 (oxidoreductase)	114	21.6%	74	12	16.2%	3.5%
EC2 (transferase)	128	24.2%	98	15	15.3%	3.7%
EC3 (hydrolase)	41	7.8%	32	2	6.3%	0.5%
EC4 (lyase)	40	7.6%	29	2	6.9%	0.5%
EC5 (isomerase)	22	4.2%	15	2	13.3%	0.6%
EC6 (ligase)	17	3.2%	14	9	64.3%	2.1%
No EC assignment	166	31.4%	50	16	32.0%	10.1%
Sum	528	100.0%	312	58	-	20.9%

Manual Curation Procedure

- Validating predicted pathways from the literature
 - A pathway that is described in the Arabidopsis literature (EV-EXP)
 - A pathway whose critical metabolites are described in the Arabidopsis literature (EV-COMP)
 - A pathway that has reactions unique to it and having genes assigned to the unique reactions (EV-COMP)
- Curating plant pathway variants
- Curating missing pathways

Manual Curation Results

- Deleted 118 non-plant pathways:
 - Pathways not operate in plants at all
 - Fermentation (*purine fermentation*)
 - Non-plant metabolites (glycogen biosynthesis)
 - Other (glucose and glucose-1P degradation)
 - Pathway variants of bacteria-origin
 - Amino acid metabolism (e.g. *cysteine biosynthesis II*)
 - Sugar metabolism (trehalose biosynthesis II, III)
 - Fatty acid/lipid metabolism (glycerol degradation II)
 - Nutrient assimilation (sulfate assimilation I, II)
 - Energy metabolism (TCA cycle variants)

Manual Curation Results (cont.)

- Added 127 new pathways:
 - Pathway variants of plant-origin
 - Plant pathways that were not in MetaCyc
 - Plant metabolites (hormone, chlorophyll, cell wall, secondary metabolites)
 - Plant-specific metabolism (photorespiration, xanthophyll cycle)

- Universal pathways that were not in MetaCyc

• fatty acid alpha-oxidation, fatty acid omegaoxidation, glycolipid biosynthesis, etc

Current Status of AraCyc

	AraCyc (2.6)		
Total pathways	228		
Pathways with literature supports	201 (88%)		
Total enzymes	4909		
Enzymes of pathways	1808		
Enzymes with comments	150 (8%)		
Pathway holes	38%		
Total compounds	1133		
Compounds with structures	1114 (98%)		
Total citations	1572		

Expert Curation Jamborees

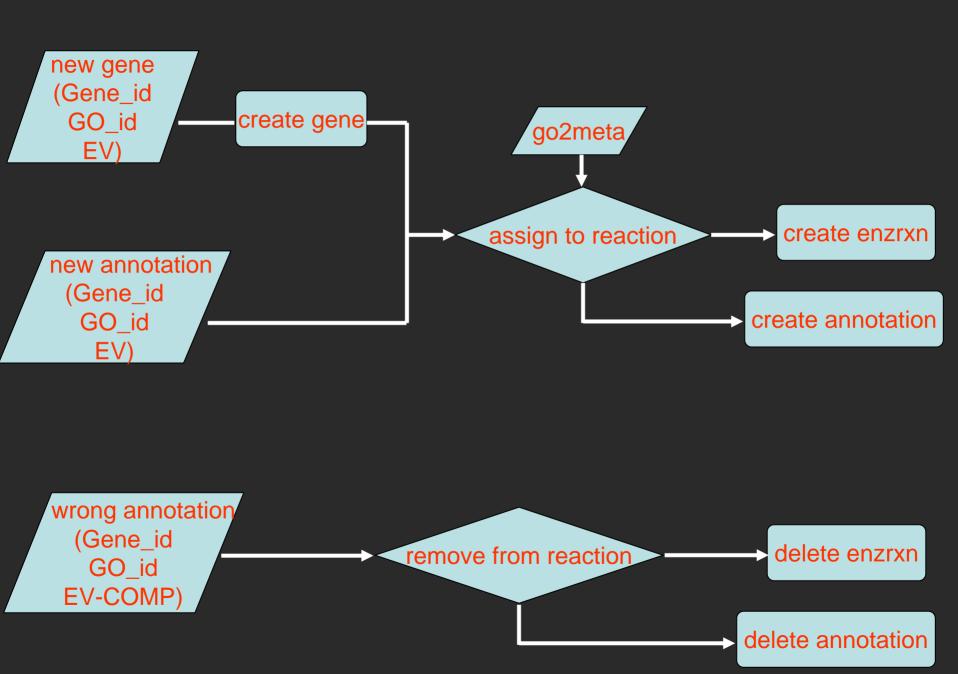
- 2X 1.5 days
- Session 1:
 - Clint Chapple from Purdue (phenylpropanoids)
 - Ed Cahoon from Danforth (lipids)
 - Maor Bar-Peled from CCRC (carbohydrates)
- Session 2:
 - Peter Facchini from U. Calgary (alkaloids)
 - Jon Page from NRC Saskatoon (terpenoids)
 - David Seigler from U. Illinois (flavonoids and polyketides)
- pathways to be updated as a result: 25
- pathways to be added as a result: 40 (previously unknown to curators)

The MetSearch Tool

Biosynthesis, [5400 Hits.]					
Uitamin-Biosynthesis , [No Hits.]					
vitamin E biosynthesis , [3 Hits.]					
p-hydroxyphenylpyruvate dioxygenase , [11 Hits.]					
gamma-tocopherol methyltransferase , [8 Hits.]					
tocopherol cyclase , [9 Hits.]					
MPBQ/MSBQ methyltransferase , [1 Hits.]					
homogentisate phytyltransferase , [6 Hits.]					
Iactoylglutathione lyase , [No Hits.]					
Iactoylglutathione lyase , [No Hits.]					
delta-tocopherol, [22 Hits.]					
gamma-tocopherol, [78 Hits.]					
2,3-dimethyl-6-phytyl-1.4-benzoquinone , [1 Hits.					
2-methyl-6-phytyl-1.4-benzoquinone , [1 Hits.]					
homogentisate , [28 Hits.]					
02 , [704 Hits.]					
p-hydroxyphenylpyruvate , [13 Hits.]					
phytyl pyrophosphate , [3 Hits.]					
S-adenosyl-L-methionine , [174 Hits.]					

AraCyc Maintenance and Updates

- Updating genes and annotations from the TAIR database
 - New enzyme-coding genes
 - Updated gene function annotations
 - Updated evidence of annotation



AraCyc Maintenance and Updates (cont.)

Propagating Updates from MetaCyc

 Compounds (updates name, structure)
 Reactions (updates EC number)
 Pathways (identify differences)

Future Plans

- Enhance pathway comments (ca. 60 pathways)
- Enhance superpathway curation
- Extensive curation of enzyme functional properties
- Curate transporters and transport reactions (ca. 210 transporters described in the literature)

Acknowledgments

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