

Pathways

Metabolic Pathways

Overview

A pathway is a linked set of biochemical reactions, linked in the sense that the product of one reaction is a reactant of, or an enzyme that catalyzes a subsequent reaction.

Few pathway tools:

- SRI's Pathway Tools (used primarily at JCVI)
- KEGG (KEGG display tool used at JCVI)

Pathways database

A pathway database (DB) is a bioinformatics database that describes biochemical pathways and their component reactions, enzymes, and substrates. Most pathway DBs that are currently available describe metabolic pathways, but pathway DBs containing signaling and genetic-regulatory pathways are now beginning to appear.

Sample Pathways Database : ecoCYC (e.coli), metaCYC (multiorganism), yourgenomeCYC (your genome)

A **Pathway Genome DB (PGDB)** integrates pathway information with information about the complete genome of an organism.

Pathway Tools

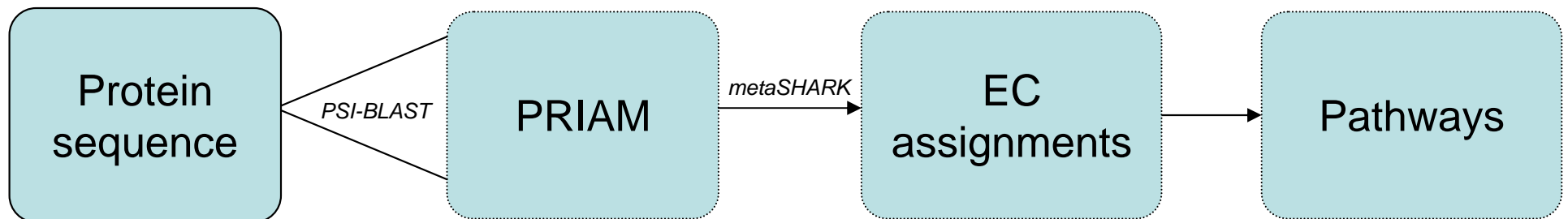
The metabolic pathways pipeline at JCVI is comprised of the generation of a **PGDB** (for each genome) and is based of a customized version of Pathway Tools, developed by Peter Karp's group at SRI International.

<http://bioinformatics.ai.sri.com/ptools/>

This is very much a manual process.

Pathway Tools

- ❑ Take protein PSI-BLAST hits against **PRIAM** profiles.
 - PRIAM profiles are built using protein sequences from the **ENZYME** database.
- ❑ The EC assignments are then done by a modified algorithm used in **metaSHARK**.
 - It looks for the best profile matches and does some heuristics to ensure high quality matching.
- ❑ Based on those EC numbers, pathways, reactions and compounds are assigned to each gene.



Pathway Tools Capabilities

- PathoLogic
 - Creates a new PGDB (Pathway Genome DataBase) containing the predicted metabolic pathways of an organism, given a tab delimited file with identifiers and its EC numbers as input.
- Pathway/Genome Navigator
 - Supports query, visualization, and analysis of PGDBs. The Navigator powers the BioCyc web site at BioCyc.org.
- Pathway/Genome Editors
 - Provide interactive editing capabilities for PGDBs.

Example

Summary of *Entamoeba histolytica*, Strain HM-1:IMSS, version 1.0

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[Show Pathway Evidence Report](#)

[Show Pathway Hole Report](#)

Replicon	Total Genes	Protein Genes	RNA Genes	Pseudogenes	Size (bp)
449 Unassigned Contigs	1946	1946	0	0	16,997,779
Total:	1946	1946	0	0	16,997,779

Pathways:	81
Enzymatic Reactions:	628
Transport Reactions:	12
Polypeptides:	1955
Protein Complexes:	0
Enzymes:	1783
Transporters:	52
Compounds:	513
Transcription Units:	0
tRNAs:	0

Taxonomic lineage: [cellular organisms](#), [Eukaryota](#), [Entamoebidae](#), [Entamoeba](#), [Entamoeba histolytica](#), [Entamoeba histolytica HM-1:IMSS](#)

J. Craig Venter

I N S T I T U T E

Comparative analysis

The comparative analysis feature lets the user compare pathways, reactions, compounds, orthologs or transporters and generate summary tables that compute statistics across one or more selected organism databases.

For example, one can view statistics on the transported substrates of one organism, or compare the transported substrates of several organisms.

Table 1: Transporters

This table presents statistics on the number of transport proteins present in each organism.

Transporters	E. dispar SAW760	E. histolytica HM-1:IMSS	E. invadens IP1
Uptake transporters	21	21	19
Efflux transporters	30	29	28
Transporters assigned to transport reactions	53	52	53
Genes assigned to transport proteins	53	52	53
Genes classified in MultiFun as transport genes	0	0	0

Table 2: Substrate Uptake

This table identifies compounds transported into the cell, and categorizes these compounds further by their metabolic role.

Substrate uptake	E. dispar SAW760	E. histolytica HM-1:IMSS	E. invadens IP1
Compounds transported into the cell	2	1	1
Compounds transported into the cell that are pathway inputs	1	1	1
Compounds transported into the cell that are pathway intermediates	0	0	0
Compounds transported into the cell that are enzyme cofactors	0	0	0
Compounds that are neither pathway inputs, pathway intermediates nor enzyme cofactors	1	0	0

Table 3: Substrate Efflux

This table identifies compounds transported out of the cell, and categorizes these compounds further by their metabolic role.

Substrate efflux	E. dispar SAW760	E. histolytica HM-1:IMSS	E. invadens IP1
Compounds transported out of cell	4	5	4

Omics Viewer

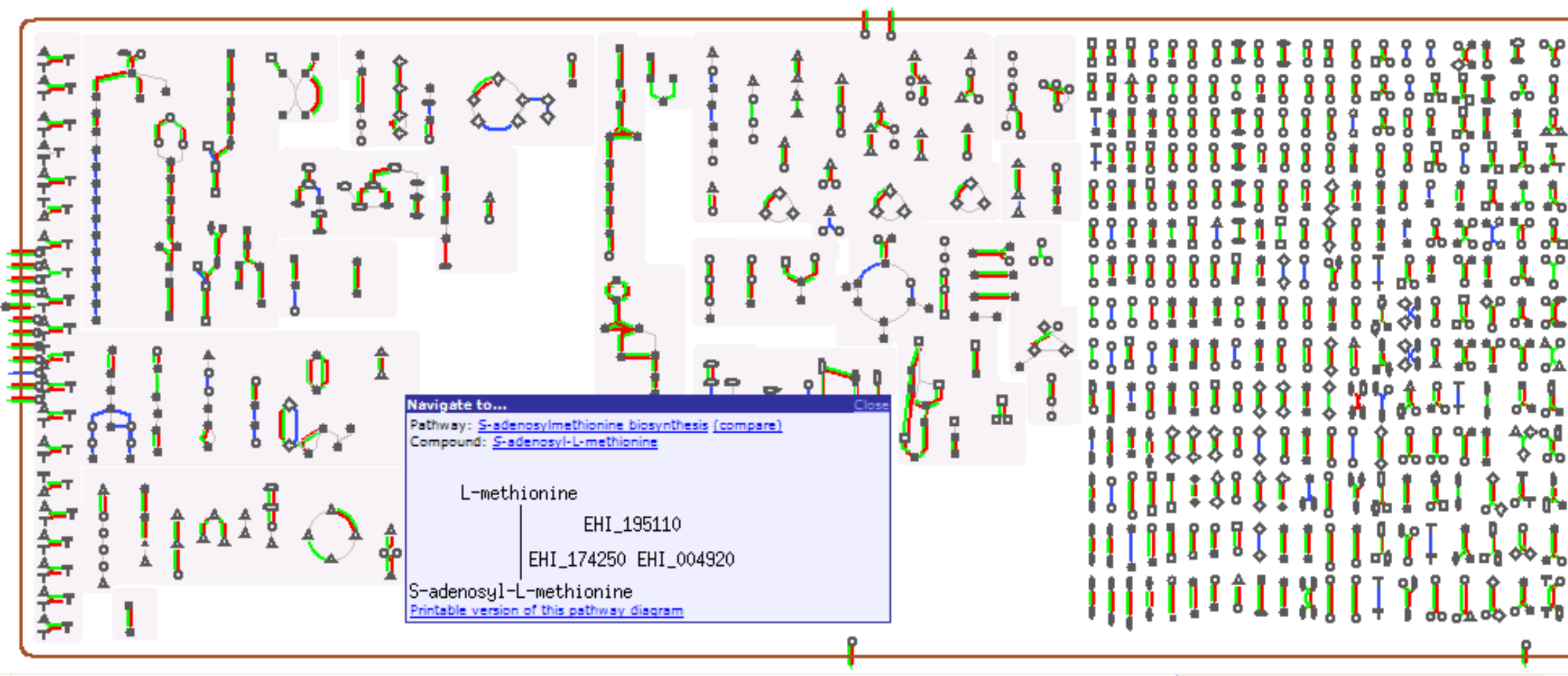
Schematic representation of all pathways in the genome

Overview of the *E. histolytica* Metabolic Map

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This diagram provides a schematic of all pathways of *E. histolytica* metabolism in the ehacyc database. Nodes represent metabolites, with shape indicating class of metabolite (see key to right). Lines represent reactions. Move the mouse over a metabolite icon to identify it. Click on a metabolite icon to navigate to the metabolite page or a related pathway page.

- [Instructions](#)
- [Pathway Tools query page](#)
- [Omics Viewer: Paint omics data onto this diagram](#)
- [Species Comparison: Highlight reactions shared with other organisms](#)



Searches at KEGG

(Kyoto Encyclopedia of Genes and Genomes)



KEGG PATHWAY Database

Wiring diagrams of molecular interactions, reactions, and relations

Direct searches can be performed at KEGG

KEGG2 ATLAS PATHWAY BRITE KO GENES SSDB LIGAND DBGET

Enter map number (Example) hsa05210

Pathway map

Pathway entry

Clear

<http://www.genome.jp/kegg/>

Pathway Maps

KEGG PATHWAY is a collection of manually drawn pathway maps representing our knowledge on the molecular interaction and reaction networks for:

1. Metabolism

Carbohydrate Energy Lipid Nucleotide Amino acid Other amino acid
Glycan PK/NRP Cofactor/vitamin Secondary metabolite Xenobiotics

2. Genetic Information Processing

3. Environmental Information Processing

4. Cellular Processes

5. Human Diseases

and also on the structure relationships (KEGG drug structure maps) in:

6. Drug Development

Pathway Modules

KEGG pathway display at JCVI's pathema page

Highlights pathway steps based on the presence /absence of supporting EC evidence



Pathema - Entamoeba

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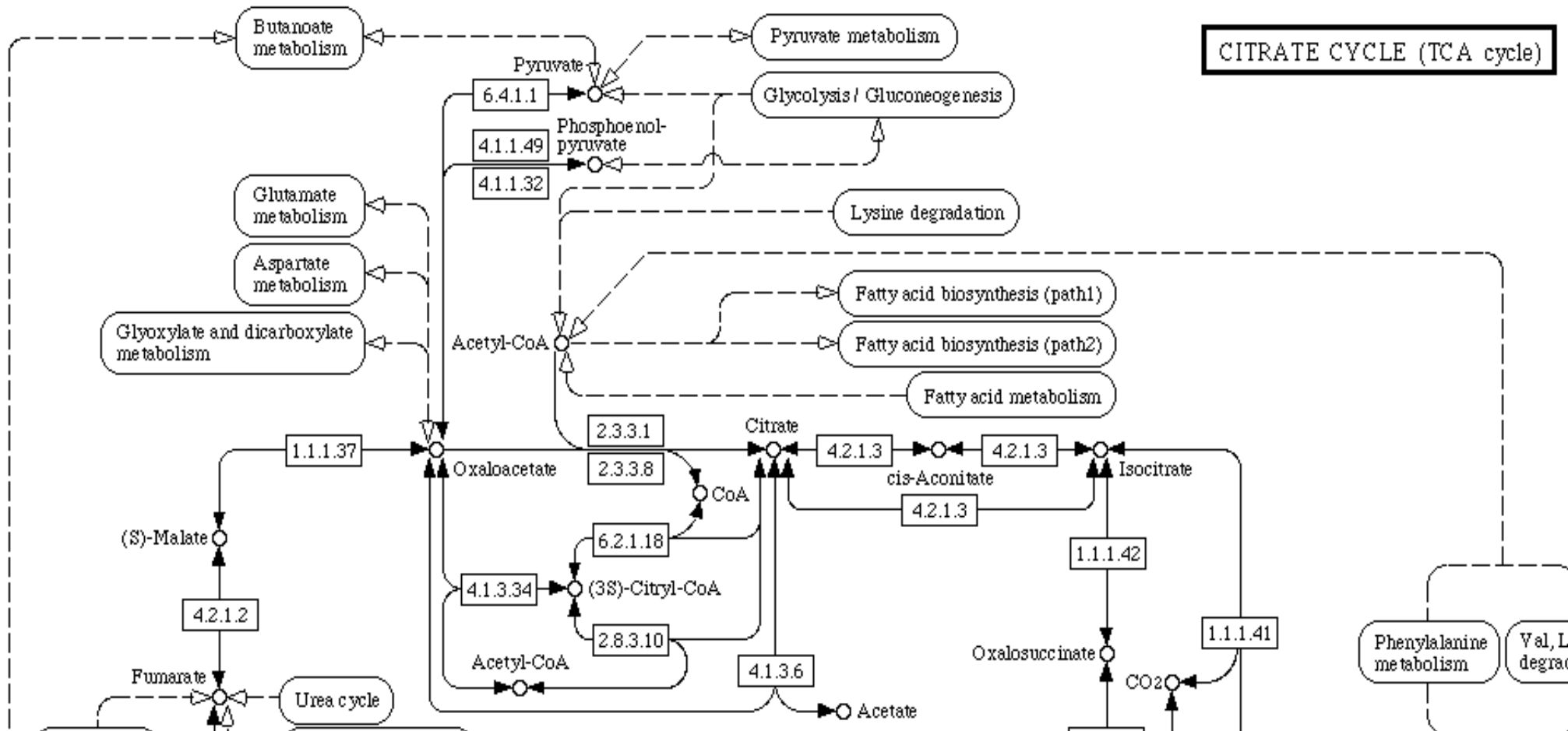
Carts

Entamoeba Manual | Home > Comparative Tools > KEGG Pathway Query Page > KEGG Pathway Viewer Results

Organism Menu

KEGG Pathway Viewer

Entamoeba histolytica HM-1:IMSS



Links

SRI's pathway tools

<http://bioinformatics.ai.sri.com/ptools/>

KEGG

<http://www.genome.jp/kegg/pathway.html>