

Tutorial for KEGG Online Database

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Thanks to Dr. Peter Abuja for his expert knowledge in the area of methabolisms and pathways.

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This document is available at:

<http://www.icg.tu-graz.ac.at/research/CGIS/GENVIEW/>

<http://www.genome.jp/kegg/pathway.html> visited 17-08-2006

visited 17-08-2006

[illegible]

Figure 1

Klick on [2.5.1.48] opens this:



ENZYME: 2.5.1.48

Help

Entry

EC
2.5.1.48 Enzyme

Name

cystathionine gamma-synthase;
O-succinyl-L-homoserine succinate-lyase (adding cysteine);
O-succinylhomoserine (thiol)-lyase;
homoserine O-transsuccinylase;
O-succinylhomoserine synthase;
O-succinylhomoserine synthetase;
cystathionine synthase;
cystathionine synthetase;
homoserine transsuccinylase

Class

Transferases
Transferring alkyl or aryl groups, other than methyl groups
Transferring alkyl or aryl groups, other than methyl groups

Sysname

O4-succinyl-L-homoserine:L-cysteine
S-(3-amino-3-carboxypropyl)transferase

Reaction

O-succinyl-L-homoserine + L-cysteine = L-cystathionine + succinate
[RN:[R00999](#) [R01288](#) [R02508](#) [R03132](#) [R03260](#) [R04944](#) [R04945](#) [R04946](#)]

Substrate

O-Succinyl-L-homoserine [CPD:[C01118](#)];
L-Cysteine [CPD:[C00097](#)]

Product

L-Cystathionine [CPD:[C02291](#)];
Succinate [CPD:[C00042](#)]

Cofactor

Pyridoxal phosphate [CPD:[C00018](#)]

Comment

A pyridoxal-phosphate protein. Also reacts with hydrogen sulfide and methanethiol as replacing agents, producing homocysteine and methionine, respectively. In the absence of thiol, can also catalyse beta,gamma-elimination to form 2-oxobutanoate, succinate and ammonia.

Pathway

PATH: [map00271](#) Methionine metabolism
PATH: [map00272](#) Cysteine metabolism
PATH: [map00450](#) Selenoamino acid metabolism
PATH: [map00920](#) Sulfur metabolism

Ortholog

KO: [K01739](#) cystathionine gamma-synthase

Genes

XLA: [494673](#) (LOC494673)
XTR: [394634](#) (MGC75946)
ATH: [At3g01120](#) (T4P13.19)
CME: [CMF156C](#)
SCE: [YJR130C](#) (STR2) [YML082W](#)
AGO: [AER164C](#) (AER164Cp)
CAL: [orf19.1033](#) (STR2) [orf19.7297](#)
SPO: [SPBC15D4.09c](#)
CNE: [CNC01220](#)
LMA: [LmjF35.3230](#)
EHI: [132.t00018](#) [389.t00003](#) [395.t00003](#)
ECO: [b3939](#) (metB)
ECJ: [JW3910](#) (metB)
...: reduced the list of 191 gene in total

Reference

1 [PMID:[5340123](#)]

Flavin M, Slaughter C.
 Enzymatic synthesis of homocysteine or methionine directly from
 O-succinyl-homoserine.
 Biochim. Biophys. Acta. 132 (1967) 400-5.
 2 [PMID:[5922970](#)]
 Kaplan MM, Flavin M.
 Cystathionine gamma-synthetase of Salmonella. Catalytic properties
 of a new enzyme in bacterial methionine biosynthesis.
 J. Biol. Chem. 241 (1966) 4463-71.
 3 [PMID:[6016326](#)]
 Wiebers JL, Garner HR.
 Homocysteine and cysteine synthetases of Neurospora crassa.
 Purification, properties, and feedback control of activity.
 J. Biol. Chem. 242 (1967) 12-23.
 4
 Wiebers, J.L. and Garner, H.R. Acyl derivatives of homoserine as
 substrates for homocysteine synthesis in Neurospora crassa, yeast,
 and Escherichia coli. J. Biol. Chem. 242 (1967) 5644-5649.
 5 [PMID:[9843488](#)]
 Clausen T, Huber R, Prade L, Wahl MC, Messerschmidt A.
 Crystal structure of Escherichia coli cystathionine gamma-synthase
 at 1.5 Å resolution.
 EMBO. J. 17 (1998) 6827-38.
 6 [PMID:[9531508](#)]
 Ravanel S, Gakiere B, Job D, Douce R.
 Cystathionine gamma-synthase from Arabidopsis thaliana:
 purification
 and biochemical characterization of the recombinant enzyme
 overexpressed in Escherichia coli.
 Biochem. J. 331 (Pt 2) (1998) 639-48.

Other DBs IUBMB Enzyme Nomenclature: [2.5.1.48](#)
 ExpASY - ENZYME nomenclature database: [2.5.1.48](#)
 ERGO genome analysis and discovery system: [2.5.1.48](#)
 BRENDA, the Enzyme Database: [2.5.1.48](#)
 CAS: 9030-70-0

LinkDB

[All DBs](#)

=> [Original format](#)

[DBGET](#) integrated database retrieval system, [GenomeNet](#)

Figure 2

[illegible]

Figure 3

Klick on Cystathionine opens this page:



COMPOUND: C02291

Help

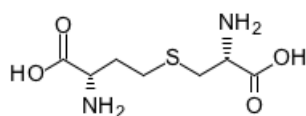
Entry C02291 Compound

Name L-Cystathionine

Formula C₇H₁₄N₂O₄S

Mass 222.0674

Structure



C02291

Mol file

KCF file

DB search

Reaction [R01001](#) [R01286](#) [R01290](#) [R03217](#) [R03260](#)

Pathway PATH: [map00260](#) Glycine, serine and threonine metabolism
PATH: [map00271](#) Methionine metabolism

Enzyme [2.5.1.48](#) [2.5.1.49](#) [4.2.1.22](#) [4.4.1.1](#)
[4.4.1.8](#)

Other DBs CAS: 56-88-2
PubChem: [5347](#)
ChEBI: [17482](#)

LinkDB [All DBs](#)

KCF data [Show](#)

=> [Original format](#)

[DBGET](#) integrated database retrieval system, [GenomeNet](#)

Figure 4

Example for a reaction:



REACTION: R00999

Help

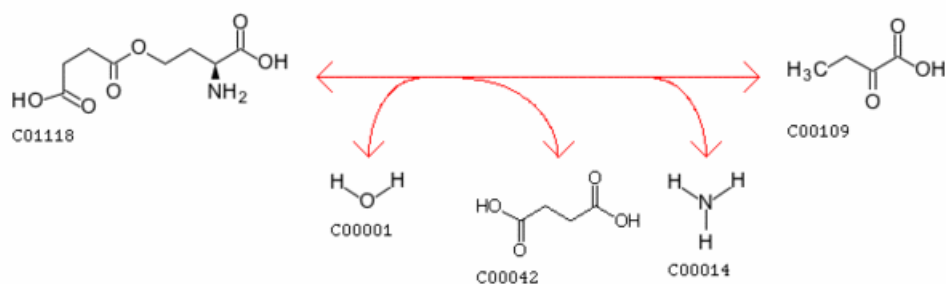
Entry R00999

Reaction

Name O-Succinyl-L-homoserine succinate-lyase (adding cysteine)

Definition O-Succinyl-L-homoserine + H₂O \rightleftharpoons 2-Oxobutanoate + Succinate + NH₃

Equation [C01118](#) + [C00001](#) \rightleftharpoons [C00109](#) + [C00042](#) + [C00014](#)



RPair RP: [A00132](#) C00042_C01118 main
RP: [A01229](#) C00109_C01118 main

Pathway PATH: [rn00271](#) Methionine metabolism

Enzyme [2.5.1.48](#)

Ortholog KO: [K01739](#) cystathionine gamma-synthase

LinkDB [All DBs](#)

=> [Original format](#)

[DBGET](#) integrated database retrieval system, [GenomeNet](#)

Figure 5

Flow Charts:

Enzyme:

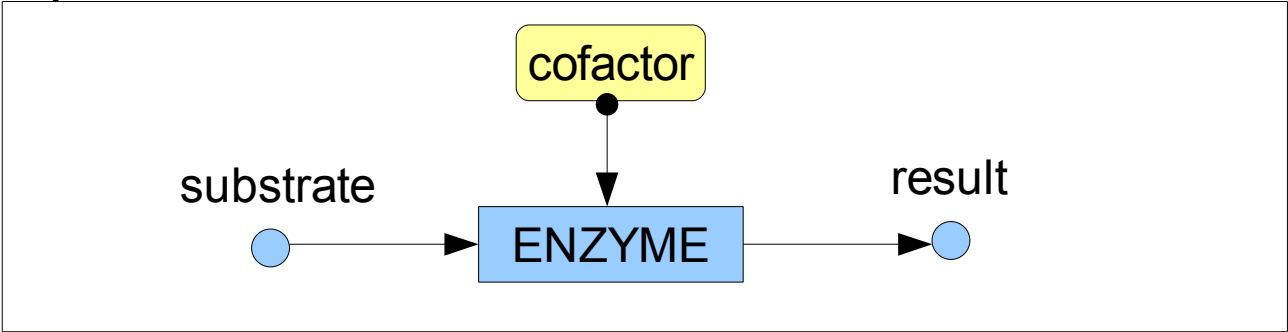


Figure 6

Regulation of enzymes and metabolism

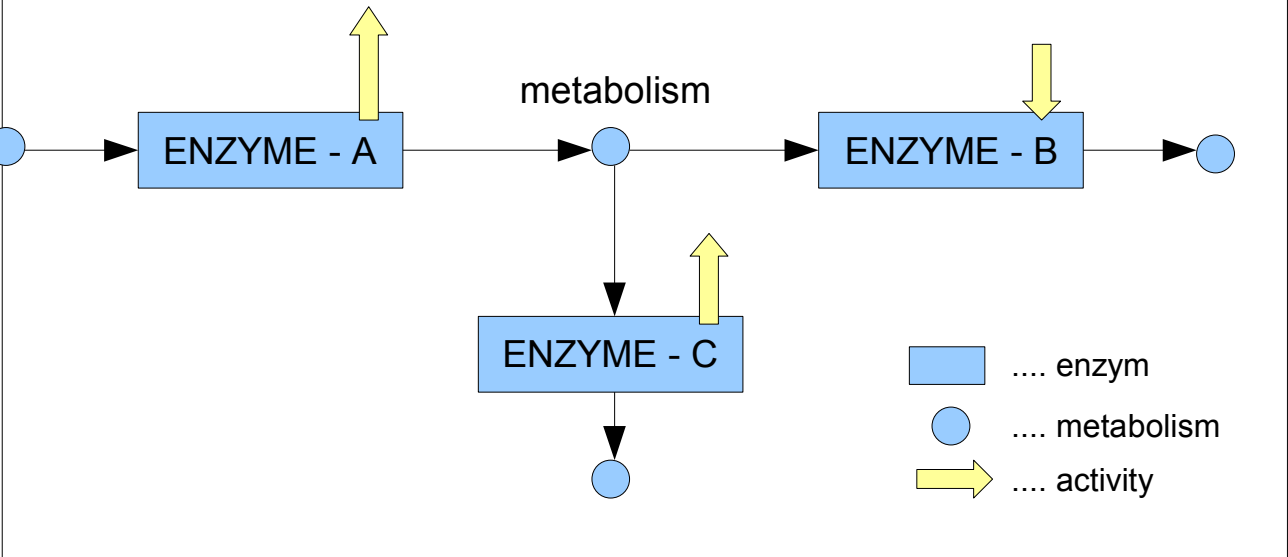


Figure 7

Concepts:

- Inside pathway: 2 step, 3 step relations inside the graph from a given Protein or Methabolit
- Take connectivity of methabolit into account
- Use connectivity of methabolit as wight for its importance
- Interrelations/ interaction:
 - Kinese ==> Proteine
 - Protein <==> Protein interrelations

- Visualize flows from:

Substrate ==>
(Enzyme/ Protein) <-- using cofactor ==>
Methabolit A ==>
(Enzym / Protein) ==>
Methabolit B

- Semantic Zooming:
 - hide / show methabolits
 - collapse proteins
 - collapse pathway inside another pathway
 - magic lense for sematic zooming
- Messure activity of Methobilids:
required for detailed analysis, but not done within Micro Array analysis
- Position of enzyme inside cell
- Compartments the enzyme is present in
- Handle enzyme casscades ==> if top element of enzyme-casscade is active, the casscade might be active to. Thus only the result of the casscade is active, but not its intermediate enzymes.

- Important fields of „Enzymes“ in KEGG (see figure 2):

Entry: unique international standardized identifier

Name: known names for this molecule and aliases for it

Reaction: chemical reaction

Substrate: Input to the Enzyme

Product: Output of the Enzyme

Cofactor: if set, it is necessary to activate the Enzyme

Pathway: shows only active pathways linked to one Enzyme but not pathways influenced by this enzyme!

Ortholog: ???

Genes: ???

- Important fields of „Compounds“ in KEGG (see figure 4):

Entry: unique code (used by KEGG? Only or also international unique?)

Name: known names for this molecule and aliases for it

Mass: mass of this molecule (mass unit?)

Structure: chemical structure of this molecule

Reaction: chemical reaction, where this compound is part of

Pathway: list of active pathways, where this compound can be found

Enzyme: list of enzymes capable of handling this compound, either as input or as output; also known as „Substrate“ and „Product“

- Important fields of „Reaction“ in KEGG (see figure 5):

Entry: unique name (probably only in KEGG)

Name: name that defines this reaction

Definition: define this reaction

Equation: link to compounds of this reaction

Rpair: ??

Pathway: list of pathways where this reaction is part of

Enzyme: list of enzymes that do this reaction

Ortholog: ???

Other databases aside from KEGG:

(suggested by Dr. Abuja)

Biomodal DB: <http://www.ebi.ac.uk/biomodals/>

Reactome „A curated knowledgebase of biological pathways“ <http://www.reactome.org/>

Brookhaven Protein Database
for structure of enzymes <http://cds.dl.ac.uk/cds/pdb.html>

EMBL „European Molecular Biology Laboratory“ <http://www.embl.org/>

EMBO „European Molecular Biology Organization“ <http://www.embo.org/>

Other important websides:

RCSB „Research Collaboratory for Structural Bioinformatics“ <http://home.rcsb.org/>

RCSB PDB Protein Data Base <http://www.rcsb.org/pdb/>

Software we should look at:

- „Panther“ (Applied Biosoftware)
- google: „Pathway“ as well as „Pathway Heatmap“

Books:

David Fell, „Regulation of Metabolism“ („Kinetische Regulation“)

Homepage of David Fell:

<http://www.brookes.ac.uk/bms/research/fell.html>

Glossary:

Inhibitor: ??

Effektor: ??

Substrate: ??

Kinese: wirken auf andere Proteine / Aminosäuren
?phosphorisierte Kinese?

Kinetische Regulation: