

The Enzyme List

Class 6 — Ligases

Nomenclature Committee
of the
International Union of Biochemistry and Molecular Biology
(NC-IUBMB)

Generated from the [ExplorEnz](#) database, September 2010

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EC 6.1 Forming carbon-oxygen bonds

This subclass contains a single sub-subclass for enzymes that acylate a tRNA with the corresponding amino acid, forming a carbon-oxygen bond (amino-acid—tRNA ligases; EC 6.1.1).

EC 6.1.1 Ligases forming aminoacyl-tRNA and related compounds

EC 6.1.1.1

Accepted name: tyrosine—tRNA ligase

Reaction: $\text{ATP} + \text{L-tyrosine} + \text{tRNA}^{\text{Tyr}} = \text{AMP} + \text{diphosphate} + \text{L-tyrosyl-tRNA}^{\text{Tyr}}$
Systematic name: L-tyrosine:tRNA^{Tyr} ligase (AMP-forming)
References: [5, 49, 103, 246, 34]

[EC 6.1.1.1 created 1961, modified 2002]

EC 6.1.1.2

Accepted name: tryptophan—tRNA ligase
Reaction: $\text{ATP} + \text{L-tryptophan} + \text{tRNA}^{\text{Trp}} = \text{AMP} + \text{diphosphate} + \text{L-tryptophyl-tRNA}^{\text{Trp}}$
Other name(s): tryptophanyl-tRNA synthetase; L-tryptophan-tRNA^{Trp} ligase (AMP-forming); tryptophanyl-transfer ribonucleate synthetase; tryptophanyl-transfer ribonucleic acid synthetase; tryptophanyl-transfer RNA synthetase; tryptophanyl ribonucleic synthetase; tryptophanyl-transfer ribonucleic synthetase; tryptophanyl-tRNA synthase; tryptophan translase; TrpRS
Systematic name: L-tryptophan:tRNA^{Trp} ligase (AMP-forming)
References: [54, 214, 296]

[EC 6.1.1.2 created 1961, modified 2002]

EC 6.1.1.3

Accepted name: threonine—tRNA ligase
Reaction: $\text{ATP} + \text{L-threonine} + \text{tRNA}^{\text{Thr}} = \text{AMP} + \text{diphosphate} + \text{L-threonyl-tRNA}^{\text{Thr}}$
Other name(s): threonyl-tRNA synthetase; threonyl-transfer ribonucleate synthetase; threonyl-transfer RNA synthetase; threonyl-transfer ribonucleic acid synthetase; threonyl ribonucleic synthetase; threonine-transfer ribonucleate synthetase; threonine translase; threonyl-tRNA synthetase; TRS
Systematic name: L-threonine:tRNA^{Thr} ligase (AMP-forming)
References: [5, 103]

[EC 6.1.1.3 created 1961]

EC 6.1.1.4

Accepted name: leucine—tRNA ligase
Reaction: $\text{ATP} + \text{L-leucine} + \text{tRNA}^{\text{Leu}} = \text{AMP} + \text{diphosphate} + \text{L-leucyl-tRNA}^{\text{Leu}}$
Other name(s): leucyl-tRNA synthetase; leucyl-transfer ribonucleate synthetase; leucyl-transfer RNA synthetase; leucyl-transfer ribonucleic acid synthetase; leucine-tRNA synthetase; leucine translase
Systematic name: L-leucine:tRNA^{Leu} ligase (AMP-forming)
References: [5, 26, 27]

[EC 6.1.1.4 created 1961]

EC 6.1.1.5

Accepted name: isoleucine—tRNA ligase
Reaction: $\text{ATP} + \text{L-isoleucine} + \text{tRNA}^{\text{Ile}} = \text{AMP} + \text{diphosphate} + \text{L-isoleucyl-tRNA}^{\text{Ile}}$
Other name(s): isoleucyl-tRNA synthetase; isoleucyl-transfer ribonucleate synthetase; isoleucyl-transfer RNA synthetase; isoleucine-transfer RNA ligase; isoleucine-tRNA synthetase; isoleucine translase
Systematic name: L-isoleucine:tRNA^{Ile} ligase (AMP-forming)
References: [5, 26, 27]

[EC 6.1.1.5 created 1961]

EC 6.1.1.6

Accepted name: lysine—tRNA ligase
Reaction: $\text{ATP} + \text{L-lysine} + \text{tRNA}^{\text{Lys}} = \text{AMP} + \text{diphosphate} + \text{L-lysyl-tRNA}^{\text{Lys}}$

Other name(s): lysyl-tRNA synthetase; lysyl-transfer ribonucleate synthetase; lysyl-transfer RNA synthetase; L-lysine-transfer RNA ligase; lysine-tRNA synthetase; lysine transase
Systematic name: L-lysine:tRNA^{Lys} ligase (AMP-forming)
References: [5, 43, 138, 262]

[EC 6.1.1.6 created 1961]

EC 6.1.1.7

Accepted name: alanine—tRNA ligase
Reaction: ATP + L-alanine + tRNA^{Ala} = AMP + diphosphate + L-alanyl-tRNA^{Ala}
Other name(s): alanyl-tRNA synthetase; alanyl-transfer ribonucleate synthetase; alanyl-transfer RNA synthetase; alanyl-transfer ribonucleic acid synthetase; alanine-transfer RNA ligase; alanine transfer RNA synthetase; alanine tRNA synthetase; alanine transase; alanyl-transfer ribonucleate synthase; AlaRS; Ala-tRNA synthetase
Systematic name: L-alanine:tRNA^{Ala} ligase (AMP-forming)
References: [104, 286]

[EC 6.1.1.7 created 1961]

[6.1.1.8 Deleted entry. D-alanine-sRNA synthetase]

[EC 6.1.1.8 created 1961, deleted 1965]

EC 6.1.1.9

Accepted name: valine—tRNA ligase
Reaction: ATP + L-valine + tRNA^{Val} = AMP + diphosphate + L-valyl-tRNA^{Val}
Other name(s): valyl-tRNA synthetase; valyl-transfer ribonucleate synthetase; valyl-transfer RNA synthetase; valyl-transfer ribonucleic acid synthetase; valine transfer ribonucleate ligase; valine transase
Systematic name: L-valine:tRNA^{Val} ligase (AMP-forming)
References: [26, 27]

[EC 6.1.1.9 created 1961]

EC 6.1.1.10

Accepted name: methionine—tRNA ligase
Reaction: ATP + L-methionine + tRNA^{Met} = AMP + diphosphate + L-methionyl-tRNA^{Met}
Other name(s): methionyl-tRNA synthetase; methionyl-transfer ribonucleic acid synthetase; methionyl-transfer ribonucleate synthetase; methionyl-transfer RNA synthetase; methionine transase; MetRS
Systematic name: L-methionine:tRNA^{Met} ligase (AMP-forming)
Comments: In those organisms producing *N*-formylmethionyl-tRNA^{Met} for translation initiation, this enzyme also recognizes the initiator tRNA^{Met} and catalyses the formation of L-methionyl-tRNA^{Met}, the substrate for EC 2.1.2.9, methionyl-tRNA formyltransferase.
References: [27, 146]

[EC 6.1.1.10 created 1961, modified 2002]

EC 6.1.1.11

Accepted name: serine—tRNA ligase
Reaction: ATP + L-serine + tRNA^{Ser} = AMP + diphosphate + L-seryl-tRNA^{Ser}
Other name(s): seryl-tRNA synthetase; SerRS; seryl-transfer ribonucleate synthetase; seryl-transfer RNA synthetase; seryl-transfer ribonucleic acid synthetase; serine transase
Systematic name: L-serine:tRNA^{Ser} ligase (AMP-forming)
Comments: This enzyme also recognizes tRNA^{Sec}, the special tRNA for selenocysteine, and catalyses the formation of L-seryl-tRNA^{Sec}, the substrate for EC 2.9.1.1, L-seryl-tRNA^{Sec} selenium transferase.

References: [124, 164, 288, 207]

[EC 6.1.1.11 created 1961, modified 2002]

EC 6.1.1.12

Accepted name: aspartate—tRNA ligase
Reaction: $\text{ATP} + \text{L-aspartate} + \text{tRNA}^{\text{Asp}} = \text{AMP} + \text{diphosphate} + \text{L-aspartyl-tRNA}^{\text{Asp}}$
Other name(s): aspartyl-tRNA synthetase; aspartyl ribonucleic synthetase; aspartyl-transfer RNA synthetase; aspartic acid translase; aspartyl-transfer ribonucleic acid synthetase; aspartyl ribonucleate synthetase
Systematic name: L-aspartate:tRNA^{Asp} ligase (AMP-forming)
References: [80, 205]

[EC 6.1.1.12 created 1965]

EC 6.1.1.13

Accepted name: D-alanine—poly(phosphoribitol) ligase
Reaction: $\text{ATP} + \text{D-alanine} + \text{poly(ribitol phosphate)} = \text{AMP} + \text{diphosphate} + \text{O-D-alanyl-poly(ribitol phosphate)}$
Other name(s): D-alanyl-poly(phosphoribitol) synthetase; D-alanine: membrane acceptor ligase; D-alanine-D-alanyl carrier protein ligase; D-alanine-membrane acceptor ligase; D-alanine-activating enzyme
Systematic name: D-alanine:poly(phosphoribitol) ligase (AMP-forming)
Comments: A thioester bond is formed transiently between D-alanine and the sulfhydryl group of the 4'-phosphopantetheine prosthetic group of D-alanyl carrier protein during the activation of the alanine. Involved in the synthesis of teichoic acids.
References: [17, 227, 210, 97, 57]

[EC 6.1.1.13 created 1965, modified 2001]

EC 6.1.1.14

Accepted name: glycine—tRNA ligase
Reaction: $\text{ATP} + \text{glycine} + \text{tRNA}^{\text{Gly}} = \text{AMP} + \text{diphosphate} + \text{glycyl-tRNA}^{\text{Gly}}$
Other name(s): glycyl-tRNA synthetase; glycyl-transfer ribonucleate synthetase; glycyl-transfer RNA synthetase; glycyl-transfer ribonucleic acid synthetase; glycyl translase
Systematic name: glycine:tRNA^{Gly} ligase (AMP-forming)
References: [75, 202]

[EC 6.1.1.14 created 1972]

EC 6.1.1.15

Accepted name: proline—tRNA ligase
Reaction: $\text{ATP} + \text{L-proline} + \text{tRNA}^{\text{Pro}} = \text{AMP} + \text{diphosphate} + \text{L-prolyl-tRNA}^{\text{Pro}}$
Other name(s): prolyl-tRNA synthetase; prolyl-transfer RNA synthetase; prolyl-transfer ribonucleate synthetase; proline translase; prolyl-transfer ribonucleic acid synthetase; prolyl-s-RNA synthetase; prolinyl-tRNA ligase
Systematic name: L-proline:tRNA^{Pro} ligase (AMP-forming)
References: [204, 211]

[EC 6.1.1.15 created 1972]

EC 6.1.1.16

Accepted name: cysteine—tRNA ligase
Reaction: $\text{ATP} + \text{L-cysteine} + \text{tRNA}^{\text{Cys}} = \text{AMP} + \text{diphosphate} + \text{L-cysteinyl-tRNA}^{\text{Cys}}$

Other name(s): cysteinyl-tRNA synthetase; cysteinyl-transferRNA synthetase; cysteinyl-transfer ribonucleate synthetase; cysteine transase
Systematic name: L-cysteine:tRNA^{Cys} ligase (AMP-forming)
References: [175]

[EC 6.1.1.16 created 1972]

EC 6.1.1.17

Accepted name: glutamate—tRNA ligase
Reaction: ATP + L-glutamate + tRNA^{Glu} = AMP + diphosphate + L-glutamyl-tRNA^{Glu}
Other name(s): glutamyl-tRNA synthetase; glutamyl-transfer ribonucleate synthetase; glutamyl-transfer RNA synthetase; glutamyl-transfer ribonucleic acid synthetase; glutamate-tRNA synthetase; glutamic acid transase
Systematic name: L-glutamate:tRNA^{Glu} ligase (AMP-forming)
References: [223]

[EC 6.1.1.17 created 1972]

EC 6.1.1.18

Accepted name: glutamine—tRNA ligase
Reaction: ATP + L-glutamine + tRNA^{Gln} = AMP + diphosphate + L-glutamyl-tRNA^{Gln}
Other name(s): glutaminyl-tRNA synthetase; glutaminyl-transfer RNA synthetase; glutaminyl-transfer ribonucleate synthetase; glutamine-tRNA synthetase; glutamine transase; glutamate-tRNA ligase; glutaminyl ribonucleic acid; GlnRS
Systematic name: L-glutamine:tRNA^{Gln} ligase (AMP-forming)
References: [223]

[EC 6.1.1.18 created 1972]

EC 6.1.1.19

Accepted name: arginine—tRNA ligase
Reaction: ATP + L-arginine + tRNA^{Arg} = AMP + diphosphate + L-arginyl-tRNA^{Arg}
Other name(s): arginyl-tRNA synthetase; arginyl-transfer ribonucleate synthetase; arginyl-transfer RNA synthetase; arginyl transfer ribonucleic acid synthetase; arginine-tRNA synthetase; arginine transase
Systematic name: L-arginine:tRNA^{Arg} ligase (AMP-forming)
References: [7, 178, 187]

[EC 6.1.1.19 created 1972]

EC 6.1.1.20

Accepted name: phenylalanine—tRNA ligase
Reaction: ATP + L-phenylalanine + tRNA^{Phe} = AMP + diphosphate + L-phenylalanyl-tRNA^{Phe}
Other name(s): phenylalanyl-tRNA synthetase; phenylalanyl-transfer ribonucleate synthetase; phenylalanine-tRNA synthetase; phenylalanyl-transfer RNA synthetase; phenylalanyl-tRNA ligase; phenylalanyl-transfer RNA ligase; L-phenylalanyl-tRNA synthetase; phenylalanine transase
Systematic name: L-phenylalanine:tRNA^{Phe} ligase (AMP-forming)
References: [264]

[EC 6.1.1.20 created 1972]

EC 6.1.1.21

Accepted name: histidine—tRNA ligase

Reaction: $\text{ATP} + \text{L-histidine} + \text{tRNA}^{\text{His}} = \text{AMP} + \text{diphosphate} + \text{L-histidyl-tRNA}^{\text{His}}$
Other name(s): histidyl-tRNA synthetase; histidyl-transfer ribonucleate synthetase; histidine transase
Systematic name: L-histidine:tRNA^{His} ligase (AMP-forming)
References: [272]

[EC 6.1.1.21 created 1972]

EC 6.1.1.22

Accepted name: asparagine—tRNA ligase
Reaction: $\text{ATP} + \text{L-asparagine} + \text{tRNA}^{\text{Asn}} = \text{AMP} + \text{diphosphate} + \text{L-asparaginyl-tRNA}^{\text{Asn}}$
Other name(s): asparaginyl-tRNA synthetase; asparaginyl-transfer ribonucleate synthetase; asparaginyl transfer RNA synthetase; asparaginyl transfer ribonucleic acid synthetase; asparagyl-transfer RNA synthetase; asparagine transase
Systematic name: L-asparagine:tRNA^{Asn} ligase (AMP-forming)
References: [55]

[EC 6.1.1.22 created 1976]

EC 6.1.1.23

Accepted name: aspartate—tRNA^{Asn} ligase
Reaction: $\text{ATP} + \text{L-aspartate} + \text{tRNA}^{\text{Asx}} = \text{AMP} + \text{diphosphate} + \text{aspartyl-tRNA}^{\text{Asx}}$
Other name(s): nondiscriminating aspartyl-tRNA synthetase
Systematic name: L-aspartate:tRNA^{Asx} ligase (AMP-forming)
Comments: When this enzyme acts on tRNA^{Asp}, it catalyses the same reaction as EC 6.1.1.12, aspartate—tRNA ligase. It has, however, diminished discrimination, so that it can also form aspartyl-tRNA^{Asn}. This relaxation of specificity has been found to result from the absence of a loop in the tRNA that specifically recognizes the third position of the anticodon [111]. This accounts for the ability of this enzyme in, for example, *Thermus thermophilus*, to recognize both tRNA^{Asp} (GUC anticodon) and tRNA^{Asn} (GUU anticodon). The aspartyl-tRNA^{Asn} is not used in protein synthesis until it is converted by EC 6.3.5.6, asparaginyl-tRNA synthase (glutamine-hydrolysing), into asparaginyl-tRNA^{Asn}.
References: [111, 244, 20]

[EC 6.1.1.23 created 2002]

EC 6.1.1.24

Accepted name: glutamate—tRNA^{Gln} ligase
Reaction: $\text{ATP} + \text{L-glutamate} + \text{tRNA}^{\text{Glx}} = \text{AMP} + \text{diphosphate} + \text{glutamyl-tRNA}^{\text{Glx}}$
Other name(s): nondiscriminating glutamyl-tRNA synthetase
Systematic name: L-glutamate:tRNA^{Glx} ligase (AMP-forming)
Comments: When this enzyme acts on tRNA^{Glu}, it catalyses the same reaction as EC 6.1.1.17, glutamate—tRNA ligase. It has, however, diminished discrimination, so that it can also form glutamyl-tRNA^{Gln}. This relaxation of specificity has been found to result from the absence of a loop in the tRNA that specifically recognizes the third position of the anticodon [111]. This accounts for the ability of this enzyme in, for example, *Bacillus subtilis*, to recognize both tRNA^{1Gln} (UUG anticodon) and tRNA^{Glu} (UUC anticodon) but not tRNA^{2Gln} (CUG anticodon). The ability of this enzyme to recognize both tRNA^{Glu} and one of the tRNA^{Gln} isoacceptors derives from their sharing a major identity element, a hypermodified derivative of U34 (5-methylaminomethyl-2-thiouridine). The glutamyl-tRNA^{Gln} is not used in protein synthesis until it is converted by EC 6.3.5.7, glutaminyl-tRNA synthase (glutamine-hydrolysing), into glutaminyl-tRNA^{Gln}.
References: [111, 244, 129]

[EC 6.1.1.24 created 2002]

EC 6.1.1.25

- Accepted name:** lysine—tRNA^{Pyl} ligase
Reaction: ATP + L-lysine + tRNA^{Pyl} = AMP + diphosphate + L-lysyl-tRNA^{Pyl}
Systematic name: L-lysine:tRNA^{Pyl} ligase (AMP-forming)
Comments: In organisms such as *Methanosarcina barkeri* that incorporate the modified amino acid pyrrolysine (Pyl) into certain methylamine methyltransferases, an unusual tRNA^{Pyl}, with a CUA anticodon, is charged with lysine by this class II aminoacyl—tRNA ligase. The tRNA and the ligase are encoded within the same gene cluster, and the ligase does not appear to be closely related to EC 6.1.1.6, lysine—tRNA ligase.
References: [256, 93]

[EC 6.1.1.25 created 2002]

EC 6.1.1.26

- Accepted name:** pyrrolysine—tRNA^{Pyl} ligase
Reaction: ATP + L-pyrrolysine + tRNA^{Pyl} = AMP + diphosphate + L-pyrrolysyl-tRNA^{Pyl}
Other name(s): PylS; pyrrolysyl-tRNA synthetase
Systematic name: L-pyrrolysine:tRNA^{Pyl} ligase (AMP-forming)
Comments: In organisms such as *Methanosarcina barkeri* that incorporate the modified amino acid pyrrolysine (Pyl) into certain methylamine methyltransferases, an unusual tRNA^{Pyl}, with a CUA anticodon, can be charged directly with pyrrolysine by this class II aminoacyl—tRNA ligase. The enzyme is specific for pyrrolysine as substrate as it cannot be replaced by lysine or any of the other natural amino acids [30].
References: [30, 212, 242]

[EC 6.1.1.26 created 2007]

EC 6.1.1.27

- Accepted name:** *O*-phospho-L-serine—tRNA ligase
Reaction: ATP + *O*-phospho-L-serine + tRNA^{Cys} = AMP + diphosphate + *O*-phospho-L-seryl-tRNA^{Cys}
Other name(s): *O*-phosphoseryl-tRNA ligase; non-canonical *O*-phosphoseryl-tRNA synthetase; SepRS
Systematic name: *O*-phospho-L-serine:tRNA^{Cys} ligase (AMP-forming)
Comments: In organisms like *Archaeoglobus fulgidus* lacking EC 6.1.1.16 (cysteine—tRNA ligase) for the direct Cys-tRNA^{Cys} formation, Cys-tRNA^{Cys} is produced by an indirect pathway, in which EC 6.1.1.27 (*O*-phosphoseryl-tRNA ligase) ligates *O*-phosphoserine to tRNA^{Cys}, and EC 2.5.1.73 (*O*-phospho-L-seryl-tRNA: Cys-tRNA synthase) converts the produced *O*-phospho-L-seryl-tRNA^{Cys} to Cys-tRNA^{Cys}. The SepRS/SepCysS pathway is the sole route for cysteine biosynthesis in the organism [78]. *Methanosarcina mazei* can use both pathways, the direct route using EC 6.1.1.16 (cysteine—tRNA ligase) and the indirect pathway with EC 6.1.1.27 and EC 2.5.1.73 (*O*-phospho-L-seryl-tRNA: Cys-tRNA synthase) [96].
References: [78, 96]

[EC 6.1.1.27 created 2009]

EC 6.2 Forming carbon-sulfur bonds

This subclass contains a single sub-subclass for enzymes that synthesize acyl-CoA derivatives by forming a carbon-sulfur bond (acid-thiol ligases; EC 6.2.1).

EC 6.2.1 Acid-thiol ligases

EC 6.2.1.1

Accepted name: acetate—CoA ligase
Reaction: $\text{ATP} + \text{acetate} + \text{CoA} = \text{AMP} + \text{diphosphate} + \text{acetyl-CoA}$
Other name(s): acetyl-CoA synthetase; acetyl activating enzyme; acetate thiokinase; acyl-activating enzyme; acetyl coenzyme A synthetase; acetic thiokinase; acetyl CoA ligase; acetyl CoA synthase; acetyl-coenzyme A synthase; short chain fatty acyl-CoA synthetase; short-chain acyl-coenzyme A synthetase; ACS
Systematic name: acetate:CoA ligase (AMP-forming)
Comments: Also acts on propanoate and propenoate.
References: [44, 66, 99, 185]

[EC 6.2.1.1 created 1961]

EC 6.2.1.2

Accepted name: butyrate—CoA ligase
Reaction: $\text{ATP} + \text{an acid} + \text{CoA} = \text{AMP} + \text{diphosphate} + \text{an acyl-CoA}$
Other name(s): butyryl-CoA synthetase; fatty acid thiokinase (medium chain); acyl-activating enzyme; fatty acid elongase; fatty acid activating enzyme; fatty acyl coenzyme A synthetase; medium chain acyl-CoA synthetase; butyryl-coenzyme A synthetase; L-(+)-3-hydroxybutyryl CoA ligase; short-chain acyl-CoA synthetase
Systematic name: butanoate:CoA ligase (AMP-forming)
Comments: Acts on acids from C₄ to C₁₁ and on the corresponding 3-hydroxy- and 2,3- or 3,4-unsaturated acids.
References: [163, 169, 289]

[EC 6.2.1.2 created 1961]

EC 6.2.1.3

Accepted name: long-chain-fatty-acid—CoA ligase
Reaction: $\text{ATP} + \text{a long-chain carboxylic acid} + \text{CoA} = \text{AMP} + \text{diphosphate} + \text{an acyl-CoA}$
Other name(s): acyl-CoA synthetase; fatty acid thiokinase (long chain); acyl-activating enzyme; palmitoyl-CoA synthase; lignoceroyl-CoA synthase; arachidonyl-CoA synthetase; acyl coenzyme A synthetase; acyl-CoA ligase; palmitoyl coenzyme A synthetase; thiokinase; palmitoyl-CoA ligase; acyl-coenzyme A ligase; fatty acid CoA ligase; long-chain fatty acyl coenzyme A synthetase; oleoyl-CoA synthetase; stearoyl-CoA synthetase; long chain fatty acyl-CoA synthetase; long-chain acyl CoA synthetase; fatty acid elongase; LCFA synthetase; pristanoyl-CoA synthetase; ACS3; long-chain acyl-CoA synthetase I; long-chain acyl-CoA synthetase II; fatty acyl-coenzyme A synthetase; long-chain acyl-coenzyme A synthetase; FAA1
Systematic name: acid:CoA ligase (AMP-forming)
Comments: Acts on a wide range of long-chain saturated and unsaturated fatty acids, but the enzymes from different tissues show some variation in specificity. The liver enzyme acts on acids from C₆ to C₂₀; that from brain shows high activity up to C₂₄.
References: [18, 107, 196, 267]

[EC 6.2.1.3 created 1961, modified 1989]

EC 6.2.1.4

Accepted name: succinate—CoA ligase (GDP-forming)
Reaction: $\text{GTP} + \text{succinate} + \text{CoA} = \text{GDP} + \text{phosphate} + \text{succinyl-CoA}$
Other name(s): succinyl-CoA synthetase (GDP-forming); succinyl coenzyme A synthetase (guanosine diphosphate-forming); succinate thiokinase; succinic thiokinase; succinyl coenzyme A synthetase; succinate-phosphorylating enzyme; P-enzyme; SCS; G-STK; succinyl coenzyme A synthetase (GDP-forming); succinyl CoA synthetase; succinyl coenzyme A synthetase
Systematic name: succinate:CoA ligase (GDP-forming)
Comments: Itaconate can act instead of succinate, and ITP instead of GTP.
References: [92, 127, 173, 236]

[EC 6.2.1.4 created 1961]

EC 6.2.1.5

Accepted name: succinate—CoA ligase (ADP-forming)
Reaction: $\text{ATP} + \text{succinate} + \text{CoA} = \text{ADP} + \text{phosphate} + \text{succinyl-CoA}$
Other name(s): succinyl-CoA synthetase (ADP-forming); succinic thiokinase; succinate thiokinase; succinyl-CoA synthetase; succinyl coenzyme A synthetase (adenosine diphosphate-forming); succinyl coenzyme A synthetase; A-STK (adenin nucleotide-linked succinate thiokinase); STK; A-SCS
Systematic name: succinate:CoA ligase (ADP-forming)
References: [92, 125, 126]

[EC 6.2.1.5 created 1961]

EC 6.2.1.6

Accepted name: glutarate—CoA ligase
Reaction: $\text{ATP} + \text{glutarate} + \text{CoA} = \text{ADP} + \text{phosphate} + \text{glutaryl-CoA}$
Other name(s): glutaryl-CoA synthetase; glutaryl coenzyme A synthetase
Systematic name: glutarate:CoA ligase (ADP-forming)
Comments: GTP or ITP can act instead of ATP.
References: [181]

[EC 6.2.1.6 created 1961]

EC 6.2.1.7

Accepted name: cholate—CoA ligase
Reaction: (1) $\text{ATP} + \text{cholate} + \text{CoA} = \text{AMP} + \text{diphosphate} + \text{choloyl-CoA}$
(2) $\text{ATP} + (25R)\text{-}3\alpha,7\alpha,12\alpha\text{-trihydroxy-}5\beta\text{-cholestan-}26\text{-oate} + \text{CoA} = \text{AMP} + \text{diphosphate} + (25R)\text{-}3\alpha,7\alpha,12\alpha\text{-trihydroxy-}5\beta\text{-cholestanoyl-CoA}$
Other name(s): BAL; bile acid CoA ligase; bile acid coenzyme A ligase; choloyl-CoA synthetase; choloyl coenzyme A synthetase; cholic thiokinase; cholate thiokinase; cholic acid:CoA ligase; $3\alpha,7\alpha,12\alpha\text{-trihydroxy-}5\beta\text{-cholestanoyl coenzyme A synthetase}$; $3\alpha,7\alpha,12\alpha\text{-trihydroxy-}5\beta\text{-cholestanoate-CoA ligase}$; $3\alpha,7\alpha,12\alpha\text{-trihydroxy-}5\beta\text{-cholestanoate-CoA synthetase}$; THCA-CoA ligase; $3\alpha,7\alpha,12\alpha\text{-trihydroxy-}5\beta\text{-cholestanate-CoA ligase}$; $3\alpha,7\alpha,12\alpha\text{-trihydroxy-}5\beta\text{-cholestanate:CoA ligase (AMP-forming)}$; cholyl-CoA synthetase; trihydroxycoprostanoyl-CoA synthetase
Systematic name: cholate:CoA ligase (AMP-forming)
Comments: Requires Mg^{2+} for activity. This membrane-bound enzyme catalyses the first step in the conjugation of bile acids with amino acids, converting bile acids into their acyl-CoA thioesters. The second step involves EC 2.3.1.65, bile acid-CoA:amino acid *N*-acyltransferase and converts the acyl-CoA thioester into the corresponding *N*-acyl amidate by conjugation with glycine or taurine [292]. Chenodeoxycholate, deoxycholate, lithocholate and trihydroxycoprostanate can also act as substrates [71].
References: [68, 69, 215, 241, 292, 71]

[EC 6.2.1.7 created 1961 (EC 6.2.1.29 created 1992, incorporated 2005), modified 2005]

EC 6.2.1.8

Accepted name: oxalate—CoA ligase
Reaction: $\text{ATP} + \text{oxalate} + \text{CoA} = \text{AMP} + \text{diphosphate} + \text{oxalyl-CoA}$
Other name(s): oxalyl-CoA synthetase; oxalyl coenzyme A synthetase
Systematic name: oxalate:CoA ligase (AMP-forming)
References: [83]

[EC 6.2.1.8 created 1972]

EC 6.2.1.9

Accepted name: malate—CoA ligase
Reaction: $\text{ATP} + \text{malate} + \text{CoA} = \text{ADP} + \text{phosphate} + \text{malyl-CoA}$
Other name(s): malyl-CoA synthetase; malyl coenzyme A synthetase; malate thiokinase
Systematic name: malate:CoA ligase (ADP-forming)
References: [193]

[EC 6.2.1.9 created 1972]

EC 6.2.1.10

Accepted name: acid—CoA ligase (GDP-forming)
Reaction: $\text{GTP} + \text{an acid} + \text{CoA} = \text{GDP} + \text{phosphate} + \text{acyl-CoA}$
Other name(s): acyl-CoA synthetase (GDP-forming); acyl coenzyme A synthetase (guanosine diphosphate forming)
Systematic name: acid:CoA ligase (GDP-forming)
References: [234]

[EC 6.2.1.10 created 1972]

EC 6.2.1.11

Accepted name: biotin—CoA ligase
Reaction: $\text{ATP} + \text{biotin} + \text{CoA} = \text{AMP} + \text{diphosphate} + \text{biotinyl-CoA}$
Other name(s): biotinyl-CoA synthetase; biotin CoA synthetase; biotinyl coenzyme A synthetase
Systematic name: biotin:CoA ligase (AMP-forming)
References: [45]

[EC 6.2.1.11 created 1972]

EC 6.2.1.12

Accepted name: 4-coumarate—CoA ligase
Reaction: $\text{ATP} + 4\text{-coumarate} + \text{CoA} = \text{AMP} + \text{diphosphate} + 4\text{-coumaroyl-CoA}$
Other name(s): 4-coumaroyl-CoA synthetase; *p*-coumaroyl CoA ligase; *p*-coumaryl coenzyme A synthetase; *p*-coumaryl-CoA synthetase; *p*-coumaryl-CoA ligase; feruloyl CoA ligase; hydroxycinnamoyl CoA synthetase; 4-coumarate:coenzyme A ligase; caffeoyl coenzyme A synthetase; *p*-hydroxycinnamoyl coenzyme A synthetase; feruloyl coenzyme A synthetase; sinapoyl coenzyme A synthetase; 4-coumaryl-CoA synthetase; hydroxycinnamate:CoA ligase; *p*-coumaryl-CoA ligase; *p*-hydroxycinnamic acid:CoA ligase; 4CL
Systematic name: 4-coumarate:CoA ligase (AMP-forming)
References: [88, 154]

[EC 6.2.1.12 created 1976]

EC 6.2.1.13

Accepted name: acetate—CoA ligase (ADP-forming)
Reaction: $\text{ATP} + \text{acetate} + \text{CoA} = \text{ADP} + \text{phosphate} + \text{acetyl-CoA}$
Other name(s): acetyl-CoA synthetase (ADP-forming); acetyl coenzyme A synthetase (adenosine diphosphate-forming); acetate thiokinase
Systematic name: acetate:CoA ligase (ADP-forming)
Comments: Also acts on propanoate and, very slowly, on butanoate.
References: [225]

[EC 6.2.1.13 created 1978]

EC 6.2.1.14

Accepted name: 6-carboxyhexanoate—CoA ligase
Reaction: ATP + 6-carboxyhexanoate + CoA = AMP + diphosphate + 6-carboxyhexanoyl-CoA
Other name(s): 6-carboxyhexanoyl-CoA synthetase; pimelyl-CoA synthetase
Systematic name: 6-carboxyhexanoate:CoA ligase (AMP-forming)
References: [116, 117]

[EC 6.2.1.14 created 1983]

EC 6.2.1.15

Accepted name: arachidonate—CoA ligase
Reaction: ATP + arachidonate + CoA = AMP + diphosphate + arachidonoyl-CoA
Other name(s): arachidonoyl-CoA synthetase
Systematic name: arachidonate:CoA ligase (AMP-forming)
Comments: Not identical with EC 6.2.1.3 long-chain-fatty-acid—CoA ligase. Icosa-8,11,14-trienoate, but not the other long-chain fatty acids, can act in place of arachidonate.
References: [294]

[EC 6.2.1.15 created 1984]

EC 6.2.1.16

Accepted name: acetoacetate—CoA ligase
Reaction: ATP + acetoacetate + CoA = AMP + diphosphate + acetoacetyl-CoA
Other name(s): acetoacetyl-CoA synthetase
Systematic name: acetoacetate:CoA ligase (AMP-forming)
Comments: Also acts, more slowly, on L-3-hydroxybutanoate.
References: [77]

[EC 6.2.1.16 created 1984]

EC 6.2.1.17

Accepted name: propionate—CoA ligase
Reaction: ATP + propanoate + CoA = AMP + diphosphate + propanoyl-CoA
Other name(s): propionyl-CoA synthetase
Systematic name: propanoate:CoA ligase (AMP-forming)
Comments: Propenoate can act instead of propanoate. Not identical with EC 6.2.1.1 (acetate—CoA ligase) or EC 6.2.1.2 (butyrate—CoA ligase).
References: [229]

[EC 6.2.1.17 created 1984]

EC 6.2.1.18

Accepted name: citrate—CoA ligase
Reaction: ATP + citrate + CoA = ADP + phosphate + (3S)-citryl-CoA
Other name(s): citryl-CoA synthetase; citrate:CoA ligase; citrate thiokinase
Systematic name: citrate:CoA ligase (ADP-forming)
Comments: The enzyme is a component of EC 2.3.3.8 ATP citrate synthase.
References: [153, 14]

[EC 6.2.1.18 created 1986]

EC 6.2.1.19

Accepted name: long-chain-fatty-acid—luciferin-component ligase
Reaction: ATP + an acid + protein = AMP + diphosphate + an acyl-protein thioester
Other name(s): acyl-protein synthetase
Systematic name: long-chain-fatty-acid:protein ligase (AMP-forming)
Comments: Together with EC 1.2.1.50 long-chain-fatty-acyl-CoA reductase, enzyme forms a fatty acid reductase system that produces the substrate of EC 1.14.14.3 alkanal monooxygenase (FMN-linked), thus being a component of the bacterial luciferase system.
References: [230, 284]

[EC 6.2.1.19 created 1986]

EC 6.2.1.20

Accepted name: long-chain-fatty-acid—[acyl-carrier-protein] ligase
Reaction: ATP + an acid + an [acyl-carrier protein] = AMP + diphosphate + an acyl-[acyl-carrier protein]
Other name(s): acyl-[acyl-carrier-protein] synthetase; acyl-[acyl carrier protein] synthetase; acyl-ACP synthetase; acyl-[acyl-carrier-protein]synthetase; stearyl-ACP synthetase; acyl-acyl carrier protein synthetase; long-chain-fatty-acid:[acyl-carrier-protein] ligase (AMP-forming)
Systematic name: long-chain-fatty-acid:[acyl-carrier protein] ligase (AMP-forming)
Comments: Not identical with EC 6.2.1.3 long-chain-fatty-acid—CoA ligase.
References: [273]

[EC 6.2.1.20 created 1986]

[6.2.1.21 Deleted entry. phenylacetate—CoA ligase. Activity covered by EC 6.2.1.30, phenylacetate—CoA ligase]

[EC 6.2.1.21 created 1986, deleted 2001]

EC 6.2.1.22

Accepted name: [citrate (*pro*-3*S*)-lyase] ligase
Reaction: ATP + acetate + [citrate (*pro*-3*S*)-lyase](thiol form) = AMP + diphosphate + [citrate (*pro*-3*S*)-lyase](acetyl form)
Other name(s): citrate lyase ligase; citrate lyase synthetase; acetate: SH-[acyl-carrier-protein] enzyme ligase (AMP); acetate:HS-citrate lyase ligase; acetate:citrate-(*pro*-3*S*)-lyase(thiol-form) ligase (AMP-forming)
Systematic name: acetate:[citrate-(*pro*-3*S*)-lyase](thiol-form) ligase (AMP-forming)
Comments: Both this enzyme and EC 2.3.1.49,deacetyl-[citrate-(*pro*-3*S*)-lyase] *S*-acetyltransferase, acetylate and activate EC 4.1.3.6, citrate (*pro*-3*S*)-lyase.
References: [10, 11, 216, 243]

[EC 6.2.1.22 created 1989]

EC 6.2.1.23

Accepted name: dicarboxylate—CoA ligase
Reaction: ATP + an $\alpha\omega$ -dicarboxylic acid + CoA = AMP + diphosphate + an ω -carboxyacyl-CoA
Other name(s): carboxylyl-CoA synthetase; dicarboxylyl-CoA synthetase
Systematic name: ω -dicarboxylate:CoA ligase (AMP-forming)
Comments: Acts on dicarboxylic acids of chain length C₅ to C₁₆; the best substrate is dodecanedioic acid.
References: [279]

[EC 6.2.1.23 created 1989]

EC 6.2.1.24

Accepted name: phytanate—CoA ligase
Reaction: ATP + phytanate + CoA = AMP + diphosphate + phytanoyl-CoA
Other name(s): phytanoyl-CoA ligase

Systematic name: phytanate:CoA ligase (AMP-forming)
Comments: Not identical with EC 6.2.1.20 long-chain-fatty-acid—[acyl-carrier-protein] ligase.
References: [195]

[EC 6.2.1.24 created 1989]

EC 6.2.1.25

Accepted name: benzoate—CoA ligase
Reaction: ATP + benzoate + CoA = AMP + diphosphate + benzoyl-CoA
Other name(s): benzoate—coenzyme A ligase; benzoyl-coenzyme A synthetase; benzoyl CoA synthetase (AMP forming)
Systematic name: benzoate:CoA ligase (AMP-forming)
Comments: Also acts on 2-, 3- and 4-fluorobenzoate, but only very slowly on the corresponding chlorobenzoates.
References: [109, 240]

[EC 6.2.1.25 created 1989]

EC 6.2.1.26

Accepted name: *o*-succinylbenzoate—CoA ligase
Reaction: ATP + 2-succinylbenzoate + CoA = AMP + diphosphate + 4-(2-carboxyphenyl)-4-oxobutanoyl-CoA
Other name(s): *o*-succinylbenzoyl-coenzyme A synthetase; *o*-succinylbenzoate:CoA ligase (AMP-forming)
Systematic name: 2-succinylbenzoate:CoA ligase (AMP-forming)
References: [98, 132, 177]

[EC 6.2.1.26 created 1992]

EC 6.2.1.27

Accepted name: 4-hydroxybenzoate—CoA ligase
Reaction: ATP + 4-hydroxybenzoate + CoA = AMP + diphosphate + 4-hydroxybenzoyl-CoA
Other name(s): 4-hydroxybenzoate-CoA synthetase; 4-hydroxybenzoate—coenzyme A ligase (AMP-forming); 4-hydroxybenzoyl coenzyme A synthetase; 4-hydroxybenzoyl-CoA ligase
Systematic name: 4-hydroxybenzoate:CoA ligase (AMP-forming)
References: [182]

[EC 6.2.1.27 created 1992]

EC 6.2.1.28

Accepted name: 3 α ,7 α -dihydroxy-5 β -cholestanate—CoA ligase
Reaction: ATP + (25*R*)-3 α ,7 α -dihydroxy-5 β -cholestan-26-oate + CoA = AMP + diphosphate + (25*R*)-3 α ,7 α -dihydroxy-5 β -cholestanoyl-CoA
Other name(s): 3 α ,7 α -dihydroxy-5 β -cholestanoyl coenzyme A synthetase; DHCA-CoA ligase; 3 α ,7 α -dihydroxy-5 β -cholestanate:CoA ligase (AMP-forming)
Systematic name: (25*R*)-3 α ,7 α -dihydroxy-5 β -cholestan-26-oate:CoA ligase (AMP-forming)
References: [215]

[EC 6.2.1.28 created 1992]

[6.2.1.29 Deleted entry. 3 α ,7 α ,12 α -trihydroxy-5 β -cholestanate—CoA ligase. The enzyme is identical to EC 6.2.1.7, cholate—CoA ligase]

[EC 6.2.1.29 created 1992, deleted 2005]

EC 6.2.1.30

Accepted name: phenylacetate—CoA ligase
Reaction: ATP + phenylacetate + CoA = AMP + diphosphate + phenylacetyl-CoA
Other name(s): phenacyl coenzyme A synthetase; phenylacetyl-CoA ligase; PA-CoA ligase; phenylacetyl-CoA ligase (AMP-forming)
Systematic name: phenylacetate:CoA ligase (AMP-forming)
Comments: Also acts, more slowly, on acetate, propanoate and butanoate, but not on hydroxy derivatives of phenylacetate and related compounds.
References: [168]

[EC 6.2.1.30 created 1992 (EC 6.2.1.21 created 1986, incorporated 2001)]

EC 6.2.1.31

Accepted name: 2-furoate—CoA ligase
Reaction: ATP + 2-furoate + CoA = AMP + diphosphate + 2-furoyl-CoA
Other name(s): 2-furoyl coenzyme A synthetase
Systematic name: 2-furoate:CoA ligase (AMP-forming)
References: [131]

[EC 6.2.1.31 created 1992]

EC 6.2.1.32

Accepted name: anthranilate—CoA ligase
Reaction: ATP + anthranilate + CoA = AMP + diphosphate + anthranilyl-CoA
Other name(s): anthraniloyl coenzyme A synthetase; 2-aminobenzoate—CoA ligase; 2-aminobenzoate—coenzyme A ligase; 2-aminobenzoate coenzyme A ligase
Systematic name: anthranilate:CoA ligase (AMP-forming)
References: [8]

[EC 6.2.1.32 created 1992]

EC 6.2.1.33

Accepted name: 4-chlorobenzoate—CoA ligase
Reaction: 4-chlorobenzoate + CoA + ATP = 4-chlorobenzoyl-CoA + AMP + diphosphate
Systematic name: 4-chlorobenzoate:CoA ligase
Comments: Requires Mg²⁺. This enzyme is part of the bacterial 2,4-dichlorobenzoate degradation pathway.
References: [64, 155, 39]

[EC 6.2.1.33 created 1999]

EC 6.2.1.34

Accepted name: *trans*-feruloyl-CoA synthase
Reaction: ferulic acid + CoA + ATP = feruloyl-CoA + products of ATP breakdown
Other name(s): *trans*-feruloyl-CoA synthetase; *trans*-ferulate:CoASH ligase (ATP-hydrolysing); ferulate:CoASH ligase (ATP-hydrolysing)
Systematic name: ferulate:CoA ligase (ATP-hydrolysing)
Comments: Requires Mg²⁺. It has not yet been established whether AMP + diphosphate or ADP + phosphate are formed in this reaction.
References: [198, 213]

[EC 6.2.1.34 created 2000]

EC 6.2.1.35

Accepted name: ACP-SH:acetate ligase
Reaction: ATP + acetate + an [acyl-carrier protein] = AMP + diphosphate + an acetyl-[acyl-carrier protein]
Other name(s): HS-acyl-carrier protein:acetate ligase; [acyl-carrier protein]:acetate ligase; MadH
Systematic name: acetate:[acyl-carrier-protein] ligase (AMP-forming)
Comments: This enzyme, from the anaerobic bacterium *Malonomonas rubra*, is a component of the multienzyme complex EC 4.1.1.89, biotin-dependent malonate decarboxylase. The enzyme uses the energy from hydrolysis of ATP to convert the thiol group of the acyl-carrier-protein-bound 2'-(5-phosphoribosyl)-3'-dephospho-CoA prosthetic group into its acetyl thioester [24].
References: [101, 24, 25, 61]

[EC 6.2.1.35 created 2008]

EC 6.2.1.36

Accepted name: 3-hydroxypropionyl-CoA synthase
Reaction: 3-hydroxypropionate + ATP + coenzyme A = 3-hydroxypropionyl-CoA + AMP + diphosphate
Other name(s): 3-hydroxypropionyl-CoA synthetase (AMP-forming); 3-hydroxypropionate—CoA ligase
Systematic name: hydroxypropionate:CoA ligase (AMP-forming)
Comments: Catalyses a step in the 3-hydroxypropionate/4-hydroxybutyrate cycle, an autotrophic CO₂ fixation pathway found in some thermoacidophilic archaea [23, 4]. The enzymes from *Metallosphaera sedula* and *Sulfolobus tokodaii* can also use propionate, acrylate, acetate, and butanoate as substrates [4], and are thus different from EC 6.2.1.17 (propionate—CoA ligase), which does not accept acetate or butanoate.
References: [23, 4]

[EC 6.2.1.36 created 2009]

EC 6.3 Forming carbon-nitrogen bonds

This subclass contains enzymes that form carbon-nitrogen bonds. Sub-subclasses are: acid—ammonia (or amine) ligases (amide synthases; EC 6.3.1), acid—amino-acid ligases (peptide synthases; EC 6.3.2), enzymes forming heterocyclic rings (cyclo-ligases; EC 6.3.3), enzymes using glutamine as amido-N-donor (EC 6.3.5) and other carbon-nitrogen ligases (EC 6.3.4).

EC 6.3.1 Acid—ammonia (or amine) ligases (amide synthases)

EC 6.3.1.1

Accepted name: aspartate—ammonia ligase
Reaction: ATP + L-aspartate + NH₃ = AMP + diphosphate + L-asparagine
Other name(s): asparagine synthetase; L-asparagine synthetase
Systematic name: L-aspartate:ammonia ligase (AMP-forming)
References: [222, 287]

[EC 6.3.1.1 created 1961]

EC 6.3.1.2

Accepted name: glutamate—ammonia ligase
Reaction: ATP + L-glutamate + NH₃ = ADP + phosphate + L-glutamine
Other name(s): glutamine synthetase; glutamylhydroxamic synthetase; L-glutamine synthetase
Systematic name: L-glutamate:ammonia ligase (ADP-forming)
Comments: Also acts, more slowly, on 4-methylene-L-glutamate (*cf.* EC 6.3.1.7 4-methyleneglutamate—ammonia ligase).
References: [67, 76, 139, 179, 297]

[EC 6.3.1.2 created 1961]

[6.3.1.3 *Transferred entry. phosphoribosyl-glycinamide synthetase. Now EC 6.3.4.13, phosphoribosylamine—glycine ligase*]

[EC 6.3.1.3 created 1961, deleted 1972]

EC 6.3.1.4

Accepted name: aspartate—ammonia ligase (ADP-forming)
Reaction: $\text{ATP} + \text{L-aspartate} + \text{NH}_3 = \text{ADP} + \text{phosphate} + \text{L-asparagine}$
Other name(s): asparagine synthetase (ADP-forming); asparagine synthetase (adenosine diphosphate-forming)
Systematic name: L-aspartate:ammonia ligase (ADP-forming)
References: [197]

[EC 6.3.1.4 created 1972]

EC 6.3.1.5

Accepted name: NAD^+ synthase
Reaction: $\text{ATP} + \text{deamido-NAD}^+ + \text{NH}_3 = \text{AMP} + \text{diphosphate} + \text{NAD}^+$
Other name(s): NAD synthetase; NAD synthase; nicotinamide adenine dinucleotide synthetase; diphosphopyridine nucleotide synthetase
Systematic name: deamido- NAD^+ :ammonia ligase (AMP-forming)
Comments: L-Glutamine also acts, more slowly, as amido-donor [*cf.* EC 6.3.5.1].
References: [255]

[EC 6.3.1.5 created 1972]

EC 6.3.1.6

Accepted name: glutamate—ethylamine ligase
Reaction: $\text{ATP} + \text{L-glutamate} + \text{ethylamine} = \text{ADP} + \text{phosphate} + \text{N}^5\text{-ethyl-L-glutamine}$
Other name(s): N^5 -ethyl-L-glutamine synthetase; theanine synthetase; N^5 -ethylglutamine synthetase
Systematic name: L-glutamate:ethylamine ligase (ADP-forming)
References: [237, 238, 239]

[EC 6.3.1.6 created 1976]

EC 6.3.1.7

Accepted name: 4-methyleneglutamate—ammonia ligase
Reaction: $\text{ATP} + 4\text{-methylene-L-glutamate} + \text{NH}_3 = \text{AMP} + \text{diphosphate} + 4\text{-methylene-L-glutamine}$
Other name(s): 4-methyleneglutamine synthetase
Systematic name: 4-methylene-L-glutamate:ammonia ligase (AMP-forming)
Comments: Glutamine can act instead of NH_3 , but more slowly.
References: [295]

[EC 6.3.1.7 created 1986]

EC 6.3.1.8

Accepted name: glutathionylspermidine synthase
Reaction: glutathione + spermidine + ATP = glutathionylspermidine + ADP + phosphate
Other name(s): glutathione:spermidine ligase (ADP-forming)
Systematic name: γ -L-glutamyl-L-cysteinyl-glycine:spermidine ligase (ADP-forming) [spermidine is numbered so that atom *N*-1 is in the amino group of the aminopropyl part of the molecule]

Comments: Requires magnesium ions. Involved in the synthesis of trypanothione in trypanosomatids. The enzyme from *Escherichia coli* is bifunctional and also catalyses the glutathionylspermidine amidase (EC 3.5.1.78) reaction, resulting in a net hydrolysis of ATP.

References: [253, 33]

[EC 6.3.1.8 created 1999]

EC 6.3.1.9

Accepted name: trypanothione synthase

Reaction: glutathione + glutathionylspermidine + ATP = N^1, N^8 -bis(glutathionyl)spermidine + ADP + phosphate

Systematic name: glutathionylspermidine:glutathione ligase (ADP-forming)

Comments: Involved in the synthesis of trypanothione in trypanosomatids

References: [253]

[EC 6.3.1.9 created 1999]

EC 6.3.1.10

Accepted name: adenosylcobinamide-phosphate synthase

Reaction: (1) ATP + adenosylcobyrinic acid + (*R*)-1-aminopropan-2-yl phosphate = ADP + phosphate + adenosylcobinamide phosphate
(2) ATP + adenosylcobyrinic acid + (*R*)-1-aminopropan-2-ol = ADP + phosphate + adenosylcobinamide

Other name(s): CbiB

Systematic name: adenosylcobyrinic acid:(*R*)-1-aminopropan-2-yl phosphate ligase (ADP-forming)

Comments: One of the substrates for this reaction, (*R*)-1-aminopropan-2-yl phosphate, is produced by CobD (EC 4.1.1.81, threonine-phosphate decarboxylase).

References: [41, 285]

[EC 6.3.1.10 created 2004]

EC 6.3.1.11

Accepted name: glutamate—putrescine ligase

Reaction: ATP + L-glutamate + putrescine = ADP + phosphate + γ -L-glutamylputrescine

Other name(s): γ -glutamylputrescine synthetase; YcjK

Systematic name: L-glutamate:putrescine ligase (ADP-forming)

Comments: Forms part of a novel bacterial putrescine utilization pathway in *Escherichia coli*.

References: [136]

[EC 6.3.1.11 created 2005]

EC 6.3.1.12

Accepted name: D-aspartate ligase

Reaction: ATP + D-aspartate + [β -GlcNAc-(1 \rightarrow 4)-Mur2Ac(oyl-L-Ala- γ -D-Glu-L-Lys-D-Ala-D-Ala)]_n = [β -GlcNAc-(1 \rightarrow 4)-Mur2Ac(oyl-L-Ala- γ -D-Glu-6-*N*-(β -D-Asp)-L-Lys-D-Ala-D-Ala)]_n + ADP + phosphate

Other name(s): Asl_f_m; UDP-MurNAc-pentapeptide:D-aspartate ligase; D-aspartic acid-activating enzyme

Systematic name: D-aspartate:[β -GlcNAc-(1 \rightarrow 4)-Mur2Ac(oyl-L-Ala- γ -D-Glu-L-Lys-D-Ala-D-Ala)]_n ligase (ADP-forming)

Comments: This enzyme forms part of the peptidoglycan assembly pathway of Gram-positive bacteria grown in medium containing D-Asp. Normally, the side chains the acylate the 6-amino group of the L-lysine residue contain L-Ala-L-Ala but these amino acids are replaced by D-Asp when D-Asp is included in the medium. Hybrid chains containing L-Ala-D-Asp, L-Ala-L-Ala-D-Asp or D-Asp-L-Ala are not formed [21]. The enzyme belongs in the ATP-grasp protein superfamily [79, 21]. The enzyme is highly specific for D-aspartate, as L-aspartate, D-glutamate, D-alanine, D-iso-asparagine and D-malic acid are not substrates [21]. In *Enterococcus faecium*, the substrate D-aspartate is produced by EC 5.1.1.13, aspartate racemase [21]

References: [258, 259, 79, 21]

[EC 6.3.1.12 created 2006]

EC 6.3.1.13

Accepted name: L-cysteine:1D-*myo*-inositol 2-amino-2-deoxy- α -D-glucopyranoside ligase
Reaction: 1-*O*-(2-amino-2-deoxy- α -D-glucopyranosyl)-1D-*myo*-inositol + L-cysteine + ATP = 1D-*myo*-inositol + 1-*O*-[2-(L-cysteinamido)-2-deoxy- α -D-glucopyranosyl]-1D-*myo*-inositol + AMP + diphosphate
Other name(s): MshC; MshC ligase; Cys:GlcN-Ins ligase; mycothiol ligase
Systematic name: L-cysteine:1-*O*-(2-amino-2-deoxy- α -D-glucopyranosyl)-1D-*myo*-inositol ligase (AMP-forming)
Comments: This enzyme is a key enzyme in the biosynthesis of mycothiol, a small molecular weight thiol found in *Mycobacteria* spp. and other actinomycetes. Mycothiol plays a fundamental role in these organisms by helping to provide protection from the effects of reactive oxygen species and electrophiles, including many antibiotics. The enzyme may represent a novel target for new classes of antituberculars [89]
References: [72, 89, 275]

[EC 6.3.1.13 created 2009]

EC 6.3.2 Acid—amino-acid ligases (peptide synthases)

EC 6.3.2.1

Accepted name: pantoate— β -alanine ligase
Reaction: ATP + (*R*)-pantoate + β -alanine = AMP + diphosphate + (*R*)-pantothenate
Other name(s): pantothenate synthetase; pantoate activating enzyme; pantoic-activating enzyme; D-pantoate: β -alanine ligase (AMP-forming)
Systematic name: (*R*)-pantoate: β -alanine ligase (AMP-forming)
References: [82, 159, 160]

[EC 6.3.2.1 created 1961]

EC 6.3.2.2

Accepted name: glutamate—cysteine ligase
Reaction: ATP + L-glutamate + L-cysteine = ADP + phosphate + γ -L-glutamyl-L-cysteine
Other name(s): γ -glutamylcysteine synthetase; γ -glutamyl-L-cysteine synthetase; γ -glutamylcysteinyl synthetase
Systematic name: L-glutamate:L-cysteine γ -ligase (ADP-forming)
Comments: Can use L-aminohexanoate in place of glutamate.
References: [161, 254, 165]

[EC 6.3.2.2 created 1961]

EC 6.3.2.3

Accepted name: glutathione synthase
Reaction: ATP + γ -L-glutamyl-L-cysteine + glycine = ADP + phosphate + glutathione

Other name(s): glutathione synthetase; GSH synthetase
Systematic name: γ -L-glutamyl-L-cysteine:glycine ligase (ADP-forming)
References: [145, 162]

[EC 6.3.2.3 created 1961]

EC 6.3.2.4

Accepted name: D-alanine—D-alanine ligase
Reaction: ATP + 2 D-alanine = ADP + phosphate + D-alanyl-D-alanine
Other name(s): MurE synthetase [ambiguous]; alanine:alanine ligase (ADP-forming); alanylalanine synthetase
Systematic name: D-alanine:D-alanine ligase (ADP-forming)
Comments: Involved with EC 6.3.2.7 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—L-lysine ligase) or EC 6.3.2.13 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—2,6-diaminopimelate ligase), EC 6.3.2.8 (UDP-*N*-acetylmuramate—L-alanine ligase), EC 6.3.2.9 (UDP-*N*-acetylmuramoyl-L-alanine—D-glutamate ligase) and EC 6.3.2.10 (UDP-*N*-acetylmuramoyl-tripeptide—D-alanyl-D-alanine ligase) in the synthesis of a cell-wall peptide (click here for diagram).
References: [115, 201, 280]

[EC 6.3.2.4 created 1961, modified 2002]

EC 6.3.2.5

Accepted name: phosphopantothenate—cysteine ligase
Reaction: CTP + (*R*)-4'-phosphopantothenate + L-cysteine = CMP + diphosphate + *N*-[(*R*)-4'-phosphopantothenoyl]-L-cysteine
Other name(s): phosphopantothenoylcysteine synthetase
Systematic name: (*R*)-4'-phosphopantothenate:L-cysteine ligase
Comments: Cysteine can be replaced by some of its derivatives.
References: [36, 263, 135]

[EC 6.3.2.5 created 1961, modified 2003]

EC 6.3.2.6

Accepted name: phosphoribosylaminoimidazolesuccinocarboxamide synthase
Reaction: ATP + 5-amino-1-(5-phospho-D-ribosyl)imidazole-4-carboxylate + L-aspartate = ADP + phosphate + (*S*)-2-[5-amino-1-(5-phospho-D-ribosyl)imidazole-4-carboxamido]succinate
Other name(s): phosphoribosylaminoimidazole-succinocarboxamide synthetase; PurC; SAICAR synthetase; 4-(*N*-succinocarboxamide)-5-aminoimidazole synthetase; 4-[(*N*-succinylamino)carbonyl]-5-aminoimidazole ribonucleotide synthetase; SAICARs; phosphoribosylaminoimidazolesuccinocarboxamide synthetase; 5-aminoimidazole-4-*N*-succinocarboxamide ribonucleotide synthetase
Systematic name: 5-amino-1-(5-phospho-D-ribosyl)imidazole-4-carboxylate:L-aspartate ligase (ADP-forming)
Comments: Forms part of the purine biosynthesis pathway.
References: [157, 208, 65, 40, 206, 200]

[EC 6.3.2.6 created 1961, modified 2000, modified 2006]

EC 6.3.2.7

Accepted name: UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—L-lysine ligase
Reaction: ATP + UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate + L-lysine = ADP + phosphate + UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamyl-L-lysine
Other name(s): MurE synthetase; UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamyl-L-lysine synthetase; uridine diphospho-*N*-acetylmuramoylalanyl-D-glutamyllysine synthetase; UPD-MurNAc-L-Ala-D-Glu:L-Lys ligase
Systematic name: UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate:L-lysine γ -ligase (ADP-forming)

Comments: Involved with EC 6.3.2.4 (D-alanine—D-alanine ligase), EC 6.3.2.8 (UDP-*N*-acetylmuramate—L-alanine ligase), EC 6.3.2.9 (UDP-*N*-acetylmuramoyl-L-alanine—D-glutamate ligase) and EC 6.3.2.10 (UDP-*N*-acetylmuramoyl-tripeptide—D-alanyl-D-alanine ligase) in the synthesis of a cell-wall peptide (click here for diagram). This enzyme adds lysine in some Gram-positive organisms; in others and in Gram-negative organisms EC 6.3.2.13 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—2,6-diaminopimelate ligase) adds 2,6-diaminopimelate instead.

References: [114, 280]

[EC 6.3.2.7 created 1961, modified 2002]

EC 6.3.2.8

Accepted name: UDP-*N*-acetylmuramate—L-alanine ligase

Reaction: ATP + UDP-*N*-acetylmuramate + L-alanine = ADP + phosphate + UDP-*N*-acetylmuramoyl-L-alanine

Other name(s): MurC synthetase; UDP-*N*-acetylmuramoyl-L-alanine synthetase; uridine diphospho-*N*-acetylmuramoylalanine synthetase; UDP-*N*-acetylmuramoylalanine synthetase; L-alanine-adding enzyme; UDP-acetylmuramoyl-L-alanine synthetase; UDPMurNAc-L-alanine synthetase; L-Ala ligase; uridine diphosphate *N*-acetylmuramate:L-alanine ligase; uridine 5'-diphosphate-*N*-acetylmuramoyl-L-alanine synthetase; uridine-diphosphate-*N*-acetylmuramate:L-alanine ligase; UDP-MurNAc:L-alanine ligase; alanine-adding enzyme; UDP-*N*-acetylmuramoyl:L-alanine ligase

Systematic name: UDP-*N*-acetylmuramate:L-alanine ligase (ADP-forming)

Comments: Involved with EC 6.3.2.4 (D-alanine—D-alanine ligase), EC 6.3.2.7 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—L-lysine ligase) or EC 6.3.2.13 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—2,6-diaminopimelate ligase), EC 6.3.2.9 (UDP-*N*-acetylmuramoyl-L-alanine—D-glutamate ligase) and EC 6.3.2.10 (UDP-*N*-acetylmuramoyl-tripeptide—D-alanyl-D-alanine ligase) in the synthesis of a cell-wall peptide (click here for diagram).

References: [114, 199, 280]

[EC 6.3.2.8 created 1965, modified 2002]

EC 6.3.2.9

Accepted name: UDP-*N*-acetylmuramoyl-L-alanine—D-glutamate ligase

Reaction: ATP + UDP-*N*-acetylmuramoyl-L-alanine + D-glutamate = ADP + phosphate + UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate

Other name(s): MurD synthetase; UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate synthetase; uridine diphospho-*N*-acetylmuramoylalanyl-D-glutamate synthetase; D-glutamate-adding enzyme; D-glutamate ligase; UDP-Mur-NAC-L-Ala:D-Glu ligase; UDP-*N*-acetylmuramoyl-L-alanine:glutamate ligase (ADP-forming); UDP-*N*-acetylmuramoylalanine—D-glutamate ligase

Systematic name: UDP-*N*-acetylmuramoyl-L-alanine:D-glutamate ligase (ADP-forming)

Comments: Involved with EC 6.3.2.4 (D-alanine—D-alanine ligase), EC 6.3.2.7 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—L-lysine ligase) or EC 6.3.2.13 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—2,6-diaminopimelate ligase), EC 6.3.2.8 (UDP-*N*-acetylmuramate—L-alanine ligase) and EC 6.3.2.10 (UDP-*N*-acetylmuramoyl-tripeptide—D-alanyl-D-alanine ligase) in the synthesis of a cell-wall peptide (click here for diagram).

References: [114, 280]

[EC 6.3.2.9 created 1965, modified 2002]

EC 6.3.2.10

Accepted name: UDP-*N*-acetylmuramoyl-tripeptide—D-alanyl-D-alanine ligase

Reaction: ATP + UDP-*N*-acetylmuramoyl-L-alanyl-γ-D-glutamyl-L-lysine + D-alanyl-D-alanine = ADP + phosphate + UDP-*N*-acetylmuramoyl-L-alanyl-γ-D-glutamyl-L-lysyl-D-alanyl-D-alanine

Other name(s): MurF synthetase; UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamyl-L-lysyl-D-alanyl-D-alanine synthetase; UDP-*N*-acetylmuramoylalanyl-D-glutamyl-L-lysine-D-alanyl-D-alanine ligase; uridine diphosphoacetylmuramoylpentapeptide synthetase; UDPacetylmuramoylpentapeptide synthetase; UDP-MurNAc-L-Ala-D-Glu-L-Lys:D-Ala-D-Ala ligase

Systematic name: UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamyl-L-lysine:D-alanyl-D-alanine ligase (ADP-forming)
Comments: Involved with EC 6.3.2.4 (D-alanine—D-alanine ligase), EC 6.3.2.7 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—L-lysine ligase) or EC 6.3.2.13 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—2,6-diaminopimelate ligase), EC 6.3.2.8 (UDP-*N*-acetylmuramate—L-alanine ligase) and EC 6.3.2.9 (UDP-*N*-acetylmuramoyl-L-alanine—D-glutamate ligase) in the synthesis of a cell-wall peptide (click here) for diagram. This enzyme also catalyses the reaction when the C-terminal residue of the tripeptide is *meso*-2,4-diaminoheptanedioate (acylated at its L-centre), linking the D-Ala-D-Ala to the carboxy group of the L-centre. This activity was previously attributed to EC 6.3.2.15, which has since been deleted.
References: [115, 280]

[EC 6.3.2.10 created 1965, modified 2002]

EC 6.3.2.11

Accepted name: carnosine synthase
Reaction: ATP + L-histidine + β -alanine = ADP + phosphate + carnosine
Other name(s): carnosine synthetase; carnosine-anserine synthetase; homocarnosine-carnosine synthetase; carnosine-homocarnosine synthetase; L-histidine: β -alanine ligase (AMP-forming) (incorrect)
Systematic name: L-histidine: β -alanine ligase (ADP-forming)
Comments: This enzyme was thought to form AMP [122, 261], but studies with highly purified enzyme proved that it forms ADP [63]. Carnosine is a dipeptide that is present at high concentrations in skeletal muscle and the olfactory bulb of vertebrates [51]. It is also found in the skeletal muscle of some invertebrates. The enzyme can also catalyse the formation of homocarnosine from 4-aminobutanoate and L-histidine, with much lower activity [63].
References: [122, 261, 51, 63]

[EC 6.3.2.11 created 1965, modified 2010]

EC 6.3.2.12

Accepted name: dihydrofolate synthase
Reaction: ATP + 7,8-dihydropteroate + L-glutamate = ADP + phosphate + 7,8-dihydropteroylglutamate
Other name(s): dihydrofolate synthetase; 7,8-dihydrofolate synthetase; H₂-folate synthetase; 7,8-dihydropteroate:L-glutamate ligase (ADP); dihydrofolate synthetase-folylpolyglutamate synthetase; folylpoly-(γ -glutamate) synthetase-dihydrofolate synthase; FHFS; FHFS/FPGS; dihydropteroate:L-glutamate ligase (ADP-forming); DHFS
Systematic name: 7,8-dihydropteroate:L-glutamate ligase (ADP-forming)
Comments: In some bacteria, a single protein catalyses both this activity and that of EC 6.3.2.17, tetrahydrofolate synthase [32], the combined activity of which leads to the formation of the coenzyme polyglutamated tetrahydropteroate (H₄PteGlu_{*n*}), i.e. various tetrahydrofolates. In contrast, the activities are located on separate proteins in most eukaryotes studied to date [221]. This enzyme is responsible for attaching the first glutamate residue to dihydropteroate to form dihydrofolate and is present only in those organisms that have the ability to synthesize tetrahydrofolate *de novo*, e.g. plants, most bacteria, fungi and protozoa [221].
References: [87, 32, 221, 42, 48]

[EC 6.3.2.12 created 1972, modified 2005]

EC 6.3.2.13

Accepted name: UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—2,6-diaminopimelate ligase
Reaction: ATP + UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate + *meso*-2,6-diaminoheptanedioate = ADP + phosphate + UDP-*N*-acetylmuramoyl-L-alanyl-D- γ -glutamyl-*meso*-2,6-diaminoheptanedioate
Other name(s): MurE synthetase [ambiguous]; UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate:*meso*-2,6-diaminoheptanedioate ligase (ADP-forming); UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamyl-*meso*-2,6-diaminopimelate synthetase; UDP-*N*-acetylmuramoylalanyl-D-glutamate—2,6-diaminopimelate ligase

Systematic name: UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate:(L)-*meso*-2,6-diaminoheptanedioate γ -ligase (ADP-forming)

Comments: Involved with EC 6.3.2.4 (D-alanine—D-alanine ligase), EC 6.3.2.8 (UDP-*N*-acetylmuramate—L-alanine ligase), EC 6.3.2.9 (UDP-*N*-acetylmuramoyl-L-alanine—D-glutamate ligase) and EC 6.3.2.10 (UDP-*N*-acetylmuramoyl-tripeptide—D-alanyl-D-alanine ligase) in the synthesis of a cell-wall peptide (click here for diagram). This enzyme adds diaminopimelate in Gram-negative organisms and in some Gram-positive organisms; in others EC 6.3.2.7 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—L-lysine ligase) adds lysine instead. It is the amino group of the L-centre of the diaminopimelate that is acylated.

References: [188, 280]

[EC 6.3.2.13 created 1972, modified 2002]

EC 6.3.2.14

Accepted name: 2,3-dihydroxybenzoate—serine ligase

Reaction: ATP + 2,3-dihydroxybenzoate + L-serine = products of ATP breakdown + *N*-(2,3-dihydroxybenzoyl)-L-serine

Other name(s): *N*-(2,3-dihydroxybenzoyl)-serine synthetase; 2,3-dihydroxybenzoylserine synthetase

Systematic name: 2,3-dihydroxybenzoate:L-serine ligase

References: [35]

[EC 6.3.2.14 created 1972]

[6.3.2.15 Deleted entry. UDP-*N*-acetylmuramoylalanyl-D-glutamyl-2,6-diaminopimelate-D-alanyl-D-alanine ligase. The activity observed is due to EC 6.3.2.10, UDP-*N*-acetylmuramoyl-tripeptide—D-alanyl-D-alanine ligase]

[EC 6.3.2.15 created 1976, deleted 2002]

EC 6.3.2.16

Accepted name: D-alanine—alanyl-poly(glycerolphosphate) ligase

Reaction: ATP + D-alanine + alanyl-poly(glycerolphosphate) = ADP + phosphate + D-alanyl-alanyl-poly(glycerolphosphate)

Other name(s): D-alanyl-alanyl-poly(glycerolphosphate) synthetase; D-alanine:membrane-acceptor ligase; D-alanylalanylpoly(phosphoglycerol) synthetase; D-alanyl-poly(phosphoglycerol) synthetase; D-alanine-membrane acceptor-ligase

Systematic name: D-alanine:alanyl-poly(glycerolphosphate) ligase (ADP-forming)

Comments: Involved in the synthesis of teichoic acids.

References: [227]

[EC 6.3.2.16 created 1976]

EC 6.3.2.17

Accepted name: tetrahydrofolate synthase

Reaction: ATP + tetrahydropteroyl- $[\gamma$ -Glu]_{*n*} + L-glutamate = ADP + phosphate + tetrahydropteroyl- $[\gamma$ -Glu]_{*n*+1}

Other name(s): folylpolyglutamate synthase; folate polyglutamate synthetase; formyltetrahydropteroyldiglutamate synthetase; *N*¹⁰-formyltetrahydropteroyldiglutamate synthetase; folylpoly- γ -glutamate synthase; folylpolyglutamyl synthetase; folylpoly(γ -glutamate) synthase; folylpolyglutamate synthetase; folylpoly- γ -glutamate synthetase-dihydrofolate synthetase; FPGS; tetrahydrofolylpolyglutamate synthase; tetrahydrofolate:L-glutamate γ -ligase (ADP-forming); tetrahydropteroyl- $[\gamma$ -Glu]_{*n*}:L-glutamate γ -ligase (ADP-forming)

Systematic name: tetrahydropteroyl- γ -polyglutamate:L-glutamate γ -ligase (ADP-forming)

Comments: In some bacteria, a single protein catalyses both this activity and that of EC 6.3.2.12, dihydrofolate synthase [32], the combined activity of which leads to the formation of the coenzyme polyglutamated tetrahydropterolate ($H_4PteGlu_n$), i.e. various tetrahydrofolates (H_4 folate). In contrast, the activities are located on separate proteins in most eukaryotes studied to date [221]. In *Arabidopsis thaliana*, this enzyme is present as distinct isoforms in the mitochondria, the cytosol and the chloroplast. Each isoform is encoded by a separate gene, a situation that is unique among eukaryotes [221]. As the affinity of folate-dependent enzymes increases markedly with the number of glutamic residues, the tetrahydropteroyl polyglutamates are the preferred coenzymes of C1 metabolism. (reviewed in [48]). The enzymes from different sources (particularly eukaryotes versus prokaryotes) have different substrate specificities with regard to one-carbon substituents and the number of glutamate residues present on the tetrahydrofolates.

References: [46, 176, 32, 221, 48, 42]

[EC 6.3.2.17 created 1984, modified 2003, modified 2005]

EC 6.3.2.18

Accepted name: γ -glutamylhistamine synthase
Reaction: ATP + L-glutamate + histamine = products of ATP breakdown + N^α - γ -L-glutamylhistamine
Other name(s): γ -glutaminyhistamine synthetase; γ -GHA synthetase
Systematic name: L-glutamate:histamine ligase
References: [260]

[EC 6.3.2.18 created 1986]

EC 6.3.2.19

Accepted name: ubiquitin—protein ligase
Reaction: ATP + ubiquitin + protein lysine = AMP + diphosphate + protein *N*-ubiquityllysine
Other name(s): ubiquitin-activating enzyme
Systematic name: ubiquitin:protein-lysine *N*-ligase (AMP-forming)
Comments: Ubiquitin is coupled to protein by a peptide bond between the C-terminal glycine of ubiquitin and ϵ -amino groups of lysine residues in the protein. An intermediate in the reaction contains one ubiquitin residue bound as a thioester to the enzyme, and a residue of ubiquitin adenylate non-covalently bound to the enzyme.
References: [47, 90, 91, 100]

[EC 6.3.2.19 created 1986]

EC 6.3.2.20

Accepted name: indoleacetate—lysine synthetase
Reaction: ATP + (indol-3-yl)acetate + L-lysine = ADP + phosphate + N^6 -[(indol-3-yl)acetyl]-L-lysine
Other name(s): indoleacetate:L-lysine ligase (ADP-forming)
Systematic name: (indol-3-yl)acetate:L-lysine ligase (ADP-forming)
References: [84, 110]

[EC 6.3.2.20 created 1989]

EC 6.3.2.21

Accepted name: ubiquitin—calmodulin ligase
Reaction: n ATP + calmodulin + n ubiquitin = n AMP + n diphosphate + (ubiquitin) $_n$ -calmodulin
Other name(s): ubiquityl-calmodulin synthase; ubiquitin-calmodulin synthetase; ubiquityl-calmodulin synthetase; uCaM-synthetase
Systematic name: calmodulin:ubiquitin ligase (AMP-forming)
Comments: Specific for Ca^{2+} -calmodulin from vertebrates. At least three ubiquitin molecules can be coupled to lysine residues in calmodulin.

References: [119, 302]

[EC 6.3.2.21 created 1990]

EC 6.3.2.22

Accepted name: diphthine—ammonia ligase
Reaction: ATP + diphthine + NH₃ = ADP + phosphate + diphthamide
Other name(s): diphthamide synthase; diphthamide synthetase
Systematic name: diphthine:ammonia ligase (ADP-forming)
References: [189, 190]

[EC 6.3.2.22 created 1990]

EC 6.3.2.23

Accepted name: homoglutathione synthase
Reaction: ATP + γ -L-glutamyl-L-cysteine + β -alanine = ADP + phosphate + γ -L-glutamyl-L-cysteinyl- β -alanine
Other name(s): homoglutathione synthetase; β -alanine specific hGSH synthetase
Systematic name: γ -L-glutamyl-L-cysteine: β -alanine ligase (ADP-forming)
Comments: Not identical with EC 6.3.2.3 glutathione synthase.
References: [162]

[EC 6.3.2.23 created 1990]

EC 6.3.2.24

Accepted name: tyrosine—arginine ligase
Reaction: ATP + L-tyrosine + L-arginine = AMP + diphosphate + L-tyrosyl-L-arginine
Other name(s): tyrosyl-arginine synthase; kyotorphin synthase; kyotorphin-synthesizing enzyme; kyotorphin synthetase
Systematic name: L-tyrosine:L-arginine ligase (AMP-forming)
References: [276]

[EC 6.3.2.24 created 1992]

EC 6.3.2.25

Accepted name: tubulin—tyrosine ligase
Reaction: ATP + detyrosinated α -tubulin + L-tyrosine = α -tubulin + ADP + phosphate
Systematic name: α -tubulin:L-tyrosine ligase (ADP-forming)
Comments: L-Tyrosine is linked via a peptide bond to the C-terminus of de-tyrosinated α -tubulin (des-Tyr⁰- α -tubulin). The enzyme is highly specific for α -tubulin and moderately specific for ATP and L-tyrosine. L-Phenylalanine and 3,4-dihydroxy-L-phenylalanine are transferred but with higher *K*_m values.
References: [290, 235]

[EC 6.3.2.25 created 1999]

EC 6.3.2.26

Accepted name: *N*-(5-amino-5-carboxypentanoyl)-L-cysteinyl-D-valine synthase
Reaction: 3 ATP + L-2-aminohexanedioate + L-cysteine + L-valine + H₂O = 3 AMP + 3 diphosphate + *N*-[L-5-amino-5-carboxypentanoyl]-L-cysteinyl-D-valine
Other name(s): L- δ -(α -aminoadipoyl)-L-cysteinyl-D-valine synthetase; ACV synthetase; L- α -aminoadipyl-cysteinyl-valine synthetase;
Systematic name: L-2-aminohexanedioate:L-cysteine:L-valine ligase (AMP-forming, valine-inverting)
Comments: Requires Mg²⁺. The enzyme contains 4'-phosphopantetheine, which may be involved in the mechanism of the reaction. Forms part of the penicillin biosynthesis pathway (for pathway, click here).

References: [37, 269]

[EC 6.3.2.26 created 2002]

EC 6.3.2.27

Accepted name: aerobactin synthase
Reaction: $4 \text{ ATP} + \text{citrate} + 2 \text{ N}^6\text{-acetyl-N}^6\text{-hydroxy-L-lysine} + 2 \text{ H}_2\text{O} = 4 \text{ ADP} + 4 \text{ phosphate} + \text{aerobactin}$
Other name(s): citrate:6-*N*-acetyl-6-*N*-hydroxy-L-lysine ligase (ADP-forming)
Systematic name: citrate:*N*⁶-acetyl-*N*⁶-hydroxy-L-lysine ligase (ADP-forming)
Comments: Requires Mg²⁺. Aerobactin is one of a group of high-affinity iron chelators known as siderophores and is produced under conditions of iron deprivation [38]. It is a dihydroxamate comprising two molecules of *N*⁶-acetyl-*N*⁶-hydroxylysine and one molecule of citric acid. This is the last of the three enzymes involved in its synthesis, the others being EC 1.14.13.59, L-lysine 6-monooxygenase (NADPH) and EC 2.3.1.102, *N*⁶-hydroxylysine *O*-acetyltransferase [172].
References: [15, 81, 172, 56, 38]

[EC 6.3.2.27 created 2002, modified 2006]

EC 6.3.2.28

Accepted name: L-amino-acid α-ligase
Reaction: ATP + an L-amino acid + an L-amino acid = ADP + phosphate + L-aminoacyl-L-amino acid
Other name(s): L-amino acid α-ligase; bacilysin synthetase; YwfE; L-amino acid ligase
Systematic name: L-amino acid:L-amino acid ligase (ADP-forming)
Comments: The enzyme from *Bacillus* sp. requires Mg²⁺ or Mn²⁺ for activity. While the enzyme has extremely broad substrate specificity, it does not accept highly charged amino acids, such as Lys, Arg, Glu and Asp, nor does it react with secondary amines such as Pro. The N-terminal residue of the α-dipeptide formed seems to be limited to Ala, Gly, Ser, Thr and Met (with Ala and Ser being the most preferred), whereas the C-terminal residue seems to allow for a wider variety of amino acids (but with a preference for Met and Phe). However, not all combinations or dipeptides are formed. For example, while Ser is acceptable for the N-terminus and Thr for the C-terminus, a Ser-Thr dipeptide is not formed. D-Ala, D-Ser and D-Phe are not substrates. Belongs in the ATP-dependent carboxylate-amine/thiol ligase superfamily.
References: [266]

[EC 6.3.2.28 created 2006]

EC 6.3.2.29

Accepted name: cyanophycin synthase (L-aspartate-adding)
Reaction: ATP + [L-Asp(4-L-Arg)]_n + L-Asp = ADP + phosphate + [L-Asp(4-L-Arg)]_n-L-Asp
Other name(s): CphA (ambiguous); CphA1 (ambiguous); CphA2 (ambiguous); cyanophycin synthetase (ambiguous); multi-L-arginyl-poly-L-aspartate synthase (ambiguous)
Systematic name: cyanophycin:L-aspartate ligase (ADP-forming)
Comments: Requires Mg²⁺ for activity. Both this enzyme and EC 6.3.2.30, cyanophycin synthase (L-arginine-adding), are required for the elongation of cyanophycin, which is a protein-like cell inclusion that is unique to cyanobacteria and acts as a temporary nitrogen store [2]. Both enzymes are found in the same protein but have different active sites [2, 22]. Both L-Asp and L-Arg must be present before either enzyme will display significant activity [2].
References: [1, 2, 6, 22, 303, 304]

[EC 6.3.2.29 created 2007]

EC 6.3.2.30

Accepted name: cyanophycin synthase (L-arginine-adding)

Reaction: $\text{ATP} + [\text{L-Asp}(4\text{-L-Arg})]_n\text{-L-Asp} + \text{L-Arg} = \text{ADP} + \text{phosphate} + [\text{L-Asp}(4\text{-L-Arg})]_{n+1}$
Other name(s): CphA (ambiguous); CphA1 (ambiguous); CphA2 (ambiguous); cyanophycin synthetase (ambiguous); multi-L-arginyl-poly-L-aspartate synthase (ambiguous)
Systematic name: cyanophycin:L-arginine ligase (ADP-forming)
Comments: Requires Mg^{2+} for activity. Both this enzyme and EC 6.3.2.29, cyanophycin synthase (L-aspartate-adding), are required for the elongation of cyanophycin, which is a protein-like cell inclusion that is unique to cyanobacteria and acts as a temporary nitrogen store [2]. Both enzymes are found in the same protein but have different active sites [2, 22]. Both L-Asp and L-Arg must be present before either enzyme will display significant activity [2]. Canavanine and lysine can be incorporated into the polymer instead of arginine [2].
References: [1, 2, 6, 22, 303, 304]

[EC 6.3.2.30 created 2007]

EC 6.3.2.31

Accepted name: coenzyme $\text{F}_{420}\text{-0}$:L-glutamate ligase
Reaction: $\text{GTP} + \text{coenzyme F}_{420}\text{-0} + \text{L-glutamate} = \text{GDP} + \text{phosphate} + \text{coenzyme F}_{420}\text{-1}$
Other name(s): CofE-AF; MJ0768; CofE
Systematic name: L-glutamate:coenzyme $\text{F}_{420}\text{-0}$ ligase (GDP-forming)
Comments: This protein catalyses the successive addition of two glutamate residues to cofactor F_{420} by two distinct and independent reactions. In the reaction described here the enzyme attaches a glutamate via its α -amine group to $\text{F}_{420}\text{-0}$. In the second reaction (EC 6.3.2.34, coenzyme $\text{F}_{420}\text{-1}$ — γ -L-glutamate ligase) it catalyses the addition of a second L-glutamate residue to the γ -carboxyl of the first glutamate.
References: [149, 203]

[EC 6.3.2.31 created 2010]

EC 6.3.2.32

Accepted name: coenzyme $\gamma\text{-F}_{420}\text{-2}$: α -L-glutamate ligase
Reaction: $\text{ATP} + \text{coenzyme } \gamma\text{-F}_{420}\text{-2} + \text{L-glutamate} = \text{ADP} + \text{phosphate} + \text{coenzyme } \alpha\text{-F}_{420}\text{-3}$
Other name(s): MJ1001; CofF protein; $\gamma\text{-F}_{420}\text{-2}$: α -L-glutamate ligase
Systematic name: L-glutamate:coenzyme $\gamma\text{-F}_{420}\text{-2}$ (ADP-forming)
Comments: The enzyme caps the γ -glutamyl tail of the hydride carrier coenzyme F_{420} [150].
References: [150]

[EC 6.3.2.32 created 2010]

EC 6.3.2.33

Accepted name: tetrahydrosarcinapterin synthase
Reaction: $\text{ATP} + \text{tetrahydromethanopterin} + \text{L-glutamate} = \text{ADP} + \text{phosphate} + 5,6,7,8\text{-tetrahydrosarcinapterin}$
Other name(s): $\text{H}_4\text{MPT}:\alpha\text{-L-glutamate}$ ligase; MJ0620; MptN protein
Systematic name: tetrahydromethanopterin: $\alpha\text{-L-glutamate}$ ligase (ADP-forming)
Comments: This enzyme catalyses the biosynthesis of 5,6,7,8-tetrahydrosarcinapterin, a modified form of tetrahydromethanopterin found in the Methanosarcinales. It does not require K^+ , and does not discriminate between ATP and GTP [150].
References: [150]

[EC 6.3.2.33 created 2010]

EC 6.3.2.34

Accepted name: coenzyme $\text{F}_{420}\text{-1}$: γ -L-glutamate ligase
Reaction: $\text{GTP} + \text{coenzyme F}_{420}\text{-1} + \text{L-glutamate} = \text{GDP} + \text{phosphate} + \text{coenzyme } \gamma\text{-F}_{420}\text{-2}$
Other name(s): $\text{F}_{420}:\gamma\text{-glutamyl}$ ligase; CofE-AF; MJ0768; CofE

Systematic name: L-glutamate:coenzyme F₄₂₀-1 ligase (GDP-forming)
Comments: This protein catalyses the successive addition of two glutamate residues to cofactor F₄₂₀ by two distinct and independent reactions. In the first reaction (EC 6.3.2.31, coenzyme F₄₂₀-0—L-glutamate ligase) the enzyme attaches a glutamate via its α-amine group to F₄₂₀-0. In the second reaction, which is described here, the enzyme catalyses the addition of a second L-glutamate residue to the γ-carboxyl of the first glutamate.
References: [149, 203]

[EC 6.3.2.34 created 2010]

EC 6.3.3 Cyclo-ligases

EC 6.3.3.1

Accepted name: phosphoribosylformylglycinamide cyclo-ligase
Reaction: ATP + 2-(formamido)-N¹-(5-phospho-D-ribosyl)acetamide = ADP + phosphate + 5-amino-1-(5-phospho-D-ribosyl)imidazole
Other name(s): phosphoribosylaminoimidazole synthetase; AIR synthetase; 5'-aminoimidazole ribonucleotide synthetase; 2-(formamido)-1-N-(5-phosphoribosyl)acetamide cyclo-ligase (ADP-forming)
Systematic name: 2-(formamido)-N¹-(5-phosphoribosyl)acetamide cyclo-ligase (ADP-forming)
References: [148, 147]

[EC 6.3.3.1 created 1961, modified 2000]

EC 6.3.3.2

Accepted name: 5-formyltetrahydrofolate cyclo-ligase
Reaction: ATP + 5-formyltetrahydrofolate = ADP + phosphate + 5,10-methenyltetrahydrofolate
Other name(s): 5,10-methenyltetrahydrofolate synthetase; formyltetrahydrofolic cyclodehydrase; 5-formyltetrahydrofolate cyclodehydrase
Systematic name: 5-formyltetrahydrofolate cyclo-ligase (ADP-forming)
References: [86]

[EC 6.3.3.2 created 1972]

EC 6.3.3.3

Accepted name: dethiobiotin synthase
Reaction: ATP + 7,8-diaminononanoate + CO₂ = ADP + phosphate + dethiobiotin
Other name(s): dethiobiotin synthase
Systematic name: 7,8-diaminononanoate:carbon-dioxide cyclo-ligase (ADP-forming)
Comments: CTP has half the activity of ATP.
References: [133, 298]

[EC 6.3.3.3 created 1976]

EC 6.3.3.4

Accepted name: (carboxyethyl)arginine β-lactam-synthase
Reaction: ATP + L-N²-(2-carboxyethyl)arginine = AMP + diphosphate + deoxyamidinoproclavaminatate
Other name(s): L-2-N-(2-carboxyethyl)arginine cyclo-ligase (AMP-forming)
Systematic name: L-N²-(2-carboxyethyl)arginine cyclo-ligase (AMP-forming)
Comments: Forms part of the pathway for the biosynthesis of the β-lactamase inhibitor clavulanate in *Streptomyces clavuligerus*. It has been proposed [16] that L-N²-(2-carboxyethyl)arginine is first converted into an acyl-AMP by reaction with ATP and loss of diphosphate, and that the β-lactam ring is then formed by the intramolecular attack of the β-nitrogen on the activated carboxy group.
References: [301, 274, 16]

[EC 6.3.3.4 created 2003]

EC 6.3.4 Other carbon-nitrogen ligases

EC 6.3.4.1

Accepted name: GMP synthase
Reaction: $\text{ATP} + \text{xanthosine } 5'\text{-phosphate} + \text{NH}_3 = \text{AMP} + \text{diphosphate} + \text{GMP}$
Other name(s): xanthosine-5'-phosphate—ammonia ligase; guanylate synthetase; XMP aminase; xanthosine 5'-monophosphate aminase
Systematic name: xanthosine-5'-phosphate:ammonia ligase (AMP-forming)
References: [192]

[EC 6.3.4.1 created 1961]

EC 6.3.4.2

Accepted name: CTP synthase
Reaction: $\text{ATP} + \text{UTP} + \text{NH}_3 = \text{ADP} + \text{phosphate} + \text{CTP}$
Other name(s): UTP—ammonia ligase; cytidine triphosphate synthetase; uridine triphosphate aminase; cytidine 5'-triphosphate synthetase
Systematic name: UTP:ammonia ligase (ADP-forming)
Comments: Glutamine can replace NH_3 .
References: [151, 156]

[EC 6.3.4.2 created 1961]

EC 6.3.4.3

Accepted name: formate—tetrahydrofolate ligase
Reaction: $\text{ATP} + \text{formate} + \text{tetrahydrofolate} = \text{ADP} + \text{phosphate} + 10\text{-formyltetrahydrofolate}$
Other name(s): formyltetrahydrofolate synthetase; 10-formyltetrahydrofolate synthetase; tetrahydrofolic formylase; tetrahydrofolate formylase
Systematic name: formate:tetrahydrofolate ligase (ADP-forming)
Comments: In eukaryotes occurs as a trifunctional enzyme also having methylenetetrahydrofolate dehydrogenase (NADP^+) (EC 1.5.1.5) and methenyltetrahydrofolate cyclohydrolase (EC 3.5.4.9) activity.
References: [118, 156, 217, 293]

[EC 6.3.4.3 created 1961]

EC 6.3.4.4

Accepted name: adenylosuccinate synthase
Reaction: $\text{GTP} + \text{IMP} + \text{L-aspartate} = \text{GDP} + \text{phosphate} + N^6\text{-(1,2-dicarboxyethyl)-AMP}$
Other name(s): IMP—aspartate ligase; adenylosuccinate synthetase; succinoadenylic kinosynthetase; succino-AMP synthetase
Systematic name: IMP:L-aspartate ligase (GDP-forming)
References: [53, 152, 299]

[EC 6.3.4.4 created 1961]

EC 6.3.4.5

Accepted name: argininosuccinate synthase
Reaction: $\text{ATP} + \text{L-citrulline} + \text{L-aspartate} = \text{AMP} + \text{diphosphate} + 2\text{-(}N^0\text{-L-arginino)succinate}$
Other name(s): citrulline—aspartate ligase; argininosuccinate synthetase; arginine succinate synthetase; argininosuccinic acid synthetase; arginosuccinate synthetase

Systematic name: L-citrulline:L-aspartate ligase (AMP-forming)
References: [218, 245]

[EC 6.3.4.5 created 1961]

EC 6.3.4.6

Accepted name: urea carboxylase
Reaction: $\text{ATP} + \text{urea} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + \text{urea-1-carboxylate}$
Other name(s): urease (ATP-hydrolysing); urea carboxylase (hydrolysing); ATP—urea amidolyase; urea amidolyase; UALase; UCA
Systematic name: urea:carbon-dioxide ligase (ADP-forming)
Comments: A biotinyl-protein. The yeast enzyme (but not that from green algae) also catalyses the reaction of EC 3.5.1.54 allophanate hydrolase, thus bringing about the hydrolysis of urea to CO_2 and NH_3 . Previously also listed as EC 3.5.1.45. The enzyme from the prokaryotic bacterium *Oleomonas sagaranensis* can also use acetamide and formamide as substrates [123].
References: [232, 233, 265, 123]

[EC 6.3.4.6 created 1972, modified 1986 (EC 3.5.1.45 created 1978, incorporated 1986)]

EC 6.3.4.7

Accepted name: ribose-5-phosphate—ammonia ligase
Reaction: $\text{ATP} + \text{ribose 5-phosphate} + \text{NH}_3 = \text{ADP} + \text{phosphate} + \text{5-phosphoribosylamine}$
Other name(s): 5-phosphoribosylamine synthetase; ribose 5-phosphate aminotransferase; ammonia-ribose 5-phosphate aminotransferase
Systematic name: ribose-5-phosphate:ammonia ligase (ADP-forming)
References: [224]

[EC 6.3.4.7 created 1972]

EC 6.3.4.8

Accepted name: imidazoleacetate—phosphoribosyldiphosphate ligase
Reaction: $\text{ATP} + \text{imidazole-4-acetate} + \text{5-phosphoribosyl diphosphate} = \text{ADP} + \text{phosphate} + \text{1-(5-phosphoribosyl)imidazole-4-acetate} + \text{diphosphate}$
Other name(s): 5-phosphoribosylimidazoleacetate synthetase
Systematic name: imidazoleacetate:5-phosphoribosyl-diphosphate ligase (ADP- and diphosphate-forming)
References: [50]

[EC 6.3.4.8 created 1972]

EC 6.3.4.9

Accepted name: biotin—[methylmalonyl-CoA-carboxyltransferase] ligase
Reaction: $\text{ATP} + \text{biotin} + \text{apo-[methylmalonyl-CoA:pyruvate carboxyltransferase]} = \text{AMP} + \text{diphosphate} + \text{[methylmalonyl-CoA:pyruvate carboxyltransferase]}$
Other name(s): biotin-[methylmalonyl-CoA-carboxyltransferase] synthetase; biotin-methylmalonyl coenzyme A carboxyltransferase synthetase; biotin-transcarboxylase synthetase; methylmalonyl coenzyme A holotranscarboxylase synthetase; biotin—[methylmalonyl-CoA-carboxyltransferase] ligase; biotin:apo[methylmalonyl-CoA:pyruvate carboxyltransferase] ligase (AMP-forming)
Systematic name: biotin:apo[methylmalonyl-CoA:pyruvate carboxyltransferase] ligase (AMP-forming)
References: [142]

[EC 6.3.4.9 created 1972]

EC 6.3.4.10

Accepted name: biotin—[propionyl-CoA-carboxylase (ATP-hydrolysing)] ligase
Reaction: ATP + biotin + apo-[propionyl-CoA:carbon-dioxide ligase (ADP-forming)] = AMP + diphosphate + [propionyl-CoA:carbon-dioxide ligase (ADP-forming)]
Other name(s): biotin-[propionyl-CoA-carboxylase (ATP-hydrolysing)] synthetase; biotin-propionyl coenzyme A carboxylase synthetase; propionyl coenzyme A holocarboxylase synthetase
Systematic name: biotin:apo-[propanoyl-CoA:carbon-dioxide ligase (ADP-forming)] ligase (AMP-forming)
References: [250]

[EC 6.3.4.10 created 1972]

EC 6.3.4.11

Accepted name: biotin—[methylcrotonoyl-CoA-carboxylase] ligase
Reaction: ATP + biotin + apo-[3-methylcrotonoyl-CoA:carbon-dioxide ligase (ADP-forming)] = AMP + diphosphate + [3-methylcrotonoyl-CoA:carbon-dioxide ligase (ADP-forming)]
Other name(s): biotin-[methylcrotonoyl-CoA-carboxylase] synthetase; biotin- β -methylcrotonyl coenzyme A carboxylase synthetase; β -methylcrotonyl coenzyme A holocarboxylase synthetase; holocarboxylase-synthetase
Systematic name: biotin:apo-[3-methylcrotonoyl-CoA:carbon-dioxide ligase (ADP-forming)] ligase (AMP-forming)
References: [105]

[EC 6.3.4.11 created 1972]

EC 6.3.4.12

Accepted name: glutamate—methylamine ligase
Reaction: ATP + L-glutamate + methylamine = ADP + phosphate + N^5 -methyl-L-glutamine
Other name(s): γ -glutamylmethylamide synthetase
Systematic name: L-glutamate:methylamine ligase (ADP-forming)
References: [134]

[EC 6.3.4.12 created 1972]

EC 6.3.4.13

Accepted name: phosphoribosylamine—glycine ligase
Reaction: ATP + 5-phospho-D-ribosylamine + glycine = ADP + phosphate + N^1 -(5-phospho-D-ribosyl)glycinamide
Other name(s): phosphoribosylglycinamide synthetase; glycinamide ribonucleotide synthetase; phosphoribosyl-glycineamide synthetase; glycineamide ribonucleotide synthetase; 2-amino-*N*-ribosylacetamide 5'-phosphate kinosynthase; 5'-phosphoribosylglycinamide synthetase; GAR
Systematic name: 5-phospho-D-ribosylamine:glycine ligase (ADP-forming)
References: [85, 94]

[EC 6.3.4.13 created 1961 as EC 6.3.1.3, transferred 1972 to EC 6.3.4.13, modified 2000]

EC 6.3.4.14

Accepted name: biotin carboxylase
Reaction: ATP + biotin-carboxyl-carrier protein + CO₂ = ADP + phosphate + carboxybiotin-carboxyl-carrier protein
Other name(s): biotin carboxylase (component of acetyl CoA carboxylase)
Systematic name: biotin-carboxyl-carrier-protein:carbon-dioxide ligase (ADP-forming)
References: [60]

[EC 6.3.4.14 created 1976]

EC 6.3.4.15

Accepted name: biotin—[acetyl-CoA-carboxylase] ligase
Reaction: ATP + biotin + apo-[acetyl-CoA:carbon-dioxide ligase (ADP-forming)] = AMP + diphosphate + [acetyl-CoA:carbon-dioxide ligase (ADP-forming)]
Other name(s): biotin-[acetyl-CoA carboxylase] synthetase; biotin-[acetyl coenzyme A carboxylase] synthetase; acetyl coenzyme A holocarboxylase synthetase; acetyl CoA holocarboxylase synthetase; biotin:apocarboxylase ligase; Biotin holoenzyme synthetase; HCS
Systematic name: biotin:apo-[acetyl-CoA:carbon-dioxide ligase (ADP-forming)] ligase (AMP-forming)
References: [140]

[EC 6.3.4.15 created 1978]

EC 6.3.4.16

Accepted name: carbamoyl-phosphate synthase (ammonia)
Reaction: 2 ATP + NH₃ + CO₂ + H₂O = 2 ADP + phosphate + carbamoyl phosphate
Other name(s): carbon-dioxide—ammonia ligase; carbamoylphosphate synthase; carbamylphosphate synthetase; carbamoylphosphate synthase (ammonia); carbamoylphosphate synthetase; carbamylphosphate synthetase I
Systematic name: carbon-dioxide:ammonia ligase (ADP-forming, carbamate-phosphorylating)
References: [70, 120, 166, 167]

[EC 6.3.4.16 created 1965 as EC 2.7.2.5, transferred 1978 to EC 6.3.4.16]

EC 6.3.4.17

Accepted name: formate—dihydrofolate ligase
Reaction: ATP + formate + dihydrofolate = ADP + phosphate + 10-formyldihydrofolate
Other name(s): formyltransferase, dihydrofolate; dihydrofolate formyltransferase; formyl dihydrofolate synthase
Systematic name: formate:dihydrofolate ligase (ADP-forming)
Comments: Not identical with EC 6.3.4.3 (formate—tetrahydrofolate ligase).
References: [62]

[EC 6.3.4.17 created 1992]

EC 6.3.4.18

Accepted name: 5-(carboxyamino)imidazole ribonucleotide synthase
Reaction: ATP + 5-amino-1-(5-phospho-D-ribosyl)imidazole + HCO₃⁻ = ADP + phosphate + 5-carboxyamino-1-(5-phospho-D-ribosyl)imidazole
Other name(s): N⁵-CAIR synthetase; N⁵-carboxyaminoimidazole ribonucleotide synthetase; PurK
Systematic name: 5-amino-1-(5-phospho-D-ribosyl)imidazole:carbon-dioxide ligase (ADP-forming)
Comments: In *Escherichia coli*, this enzyme, along with EC 5.4.99.18, 5-(carboxyamino)imidazole ribonucleotide mutase, is required to carry out the single reaction catalysed by EC 4.1.1.21, phosphoribosylaminoimidazole carboxylase, in vertebrates. Belongs to the ATP grasp protein superfamily [271]. Carboxyphosphate is the putative acyl phosphate intermediate. Involved in the late stages of purine biosynthesis.
References: [183, 194, 271]

[EC 6.3.4.18 created 2006]

EC 6.3.5 Carbon-nitrogen ligases with glutamine as amido-N-donor

EC 6.3.5.1

Accepted name: NAD⁺ synthase (glutamine-hydrolysing)

Reaction: $\text{ATP} + \text{deamido-NAD}^+ + \text{L-glutamine} + \text{H}_2\text{O} = \text{AMP} + \text{diphosphate} + \text{NAD}^+ + \text{L-glutamate}$
Other name(s): NAD synthetase (glutamine-hydrolysing); nicotinamide adenine dinucleotide synthetase (glutamine); desamidonicotinamide adenine dinucleotide amidotransferase; DPN synthetase
Systematic name: deamido-NAD⁺:L-glutamine amido-ligase (AMP-forming)
Comments: NH₃ can act instead of glutamine (*cf.* EC 6.3.1.5 NAD⁺ synthase).
References: [112, 113]

[EC 6.3.5.1 created 1961]

EC 6.3.5.2

Accepted name: GMP synthase (glutamine-hydrolysing)
Reaction: $\text{ATP} + \text{xanthosine } 5'\text{-phosphate} + \text{L-glutamine} + \text{H}_2\text{O} = \text{AMP} + \text{diphosphate} + \text{GMP} + \text{L-glutamate}$
Other name(s): GMP synthetase (glutamine-hydrolysing); guanylate synthetase (glutamine-hydrolyzing); guanosine monophosphate synthetase (glutamine-hydrolyzing); xanthosine 5'-phosphate amidotransferase; guanosine 5'-monophosphate synthetase
Systematic name: xanthosine-5'-phosphate:L-glutamine amido-ligase (AMP-forming)
References: [3, 137]

[EC 6.3.5.2 created 1961]

EC 6.3.5.3

Accepted name: phosphoribosylformylglycinamide synthase
Reaction: $\text{ATP} + N^2\text{-formyl-}N^1\text{-(5-phospho-D-ribose)glycinamide} + \text{L-glutamine} + \text{H}_2\text{O} = \text{ADP} + \text{phosphate} + 2\text{-(formamido)-}N^1\text{-(5-phospho-D-ribose)acetamide} + \text{L-glutamate}$
Other name(s): phosphoribosylformylglycinamide synthetase; formylglycinamide ribonucleotide amidotransferase; phosphoribosylformylglycineamidase synthetase; FGAM synthetase; FGAR amidotransferase; 5'-phosphoribosylformylglycinamide:L-glutamine amido-ligase (ADP-forming); 2-N-formyl-1-N-(5-phospho-D-ribose)glycinamide:L-glutamine amido-ligase (ADP-forming)
Systematic name: N²-formyl-N¹-(5-phospho-D-ribose)glycinamide:L-glutamine amido-ligase (ADP-forming)
References: [180]

[EC 6.3.5.3 created 1961, modified 2000]

EC 6.3.5.4

Accepted name: asparagine synthase (glutamine-hydrolysing)
Reaction: $\text{ATP} + \text{L-aspartate} + \text{L-glutamine} + \text{H}_2\text{O} = \text{AMP} + \text{diphosphate} + \text{L-asparagine} + \text{L-glutamate}$
(1a) $\text{L-glutamine} + \text{H}_2\text{O} = \text{L-glutamate} + \text{NH}_3$
(1b) $\text{ATP} + \text{L-aspartate} + \text{NH}_3 = \text{AMP} + \text{diphosphate} + \text{L-asparagine}$
Other name(s): asparagine synthetase (glutamine-hydrolysing); glutamine-dependent asparagine synthetase; asparagine synthetase B; AS; AS-B
Systematic name: L-aspartate:L-glutamine amido-ligase (AMP-forming)
Comments: The enzyme from *Escherichia coli* has two active sites [143] that are connected by an intramolecular ammonia tunnel [108, 268]. The enzyme catalyses three distinct chemical reactions: glutamine hydrolysis to yield ammonia takes place in the N-terminal domain. The C-terminal active site mediates both the synthesis of a β-aspartyl-AMP intermediate and its subsequent reaction with ammonia. The ammonia released is channeled to the other active site to yield asparagine [268].
References: [209, 31, 228, 143, 144, 108, 268]

[EC 6.3.5.4 created 1972, modified 2006]

EC 6.3.5.5

Accepted name: carbamoyl-phosphate synthase (glutamine-hydrolysing)
Reaction: $2 \text{ATP} + \text{L-glutamine} + \text{HCO}_3^- + \text{H}_2\text{O} = 2 \text{ADP} + \text{phosphate} + \text{L-glutamate} + \text{carbamoyl phosphate}$

(1) L-glutamine + H₂O = L-glutamate + NH₃
(2) 2 ATP + HCO₃⁻ = 2 ADP + phosphate + carbamoyl phosphate

Other name(s): carbamoyl-phosphate synthetase (glutamine-hydrolysing); carbamyl phosphate synthetase (glutamine); carbamoylphosphate synthetase II; glutamine-dependent carbamyl phosphate synthetase; carbamoyl phosphate synthetase; CPS; carbon-dioxide:L-glutamine amido-ligase (ADP-forming, carbamate-phosphorylating)

Systematic name: hydrogen-carbonate:L-glutamine amido-ligase (ADP-forming, carbamate-phosphorylating)

Comments: The product carbamoyl phosphate is an intermediate in the biosynthesis of arginine and the pyrimidine nucleotides [257]. The enzyme from *Escherichia coli* has three separate active sites, which are connected by a molecular tunnel that is almost 100 Å in length [270]. The amidotransferase domain within the small subunit of the enzyme hydrolyses glutamine to ammonia via a thioester intermediate. The ammonia migrates through the interior of the protein, where it reacts with carboxy phosphate to produce the carbamate intermediate. The carboxy-phosphate intermediate is formed by the phosphorylation of bicarbonate by ATP at a site contained within the N-terminal half of the large subunit. The carbamate intermediate is transported through the interior of the protein to a second site within the C-terminal half of the large subunit, where it is phosphorylated by another ATP to yield the final product, carbamoyl phosphate [220].

References: [9, 121, 300, 257, 102, 220, 219, 270]

[EC 6.3.5.5 created 1972 as EC 2.7.2.9, transferred 1978 to EC 6.3.5.5, modified 2006]

EC 6.3.5.6

Accepted name: asparaginyl-tRNA synthase (glutamine-hydrolysing)

Reaction: ATP + aspartyl-tRNA^{Asn} + L-glutamine = ADP + phosphate + asparaginyl-tRNA^{Asn} + L-glutamate

Other name(s): Asp-AdT; Asp-tRNA^{Asn} amidotransferase; aspartyl-tRNA^{Asn} amidotransferase; Asn-tRNA^{Asn}:L-glutamine amido-ligase (ADP-forming)

Systematic name: aspartyl-tRNA^{Asn}:L-glutamine amido-ligase (ADP-forming)

Comments: This reaction forms part of a two-reaction system for producing asparaginyl-tRNA in *Deinococcus radiodurans* and other organisms lacking a specific enzyme for asparagine synthesis. In the first step, a non-discriminating ligase (EC 6.1.1.23, aspartate—tRNA^{Asn} ligase) mischarges tRNA^{Asn} with aspartate, leading to the formation of Asp-tRNA^{Asn}. The aspartyl-tRNA^{Asn} is not used in protein synthesis until the present enzyme converts it into asparaginyl-tRNA^{Asn} (aspartyl-tRNA^{Asp} is not a substrate for this reaction). Ammonia or asparagine can substitute for the preferred substrate glutamine.

References: [186, 52, 111]

[EC 6.3.5.6 created 2002]

EC 6.3.5.7

Accepted name: glutaminyl-tRNA synthase (glutamine-hydrolysing)

Reaction: ATP + glutamyl-tRNA^{Gln} + L-glutamine = ADP + phosphate + glutaminyl-tRNA^{Gln} + L-glutamate

Other name(s): Glu-AdT; Glu-tRNA^{Gln} amidotransferase; glutamyl-tRNA^{Gln} amidotransferase; Glu-tRNA^{Gln}:L-glutamine amido-ligase (ADP-forming)

Systematic name: glutamyl-tRNA^{Gln}:L-glutamine amido-ligase (ADP-forming)

Comments: In systems lacking discernible glutamine—tRNA ligase (EC 6.1.1.18), glutaminyl-tRNA^{Gln} is formed by a two-enzyme system. In the first step, a nondiscriminating ligase (EC 6.1.1.24, glutamate—tRNA^{Gln} ligase) mischarges tRNA^{Gln} with glutamate, forming glutamyl-tRNA^{Gln}. The glutamyl-tRNA^{Gln} is not used in protein synthesis until the present enzyme converts it into glutaminyl-tRNA^{Gln} (glutamyl-tRNA^{Glu} is not a substrate for this reaction). Ammonia or asparagine can substitute for the preferred substrate glutamine.

References: [106, 52, 111]

[EC 6.3.5.7 created 2002]

[6.3.5.8 Transferred entry. aminodeoxychorismate synthase. Now EC 2.6.1.85, aminodeoxychorismate synthase. As ATP is not hydrolysed during the reaction, the classification of the enzyme as a ligase was incorrect]

[EC 6.3.5.8 created 2003, deleted 2007]

EC 6.3.5.9

Accepted name: hydrogenobyirinic acid *a,c*-diamide synthase (glutamine-hydrolysing)
Reaction: $2 \text{ ATP} + \text{hydrogenobyirinic acid } a,c\text{-diamide} + 2 \text{ L-glutamine} + 2 \text{ H}_2\text{O} = 2 \text{ ADP} + 2 \text{ phosphate} + \text{hydrogenobyirinic acid } a,c\text{-diamide} + 2 \text{ L-glutamate}$
Other name(s): CobB
Systematic name: hydrogenobyirinic-acid:L-glutamine amido-ligase (AMP-forming)
Comments: This step in the aerobic biosynthesis of cobalamin generates hydrogenobyirinic acid *a,c*-diamide, the substrate required by EC 6.6.1.2, cobaltochelataase, which adds cobalt to the macrocycle.
References: [59, 285]

[EC 6.3.5.9 created 2004]

EC 6.3.5.10

Accepted name: adenosylcobyric acid synthase (glutamine-hydrolysing)
Reaction: $4 \text{ ATP} + \text{adenosylcobyric acid } a,c\text{-diamide} + 4 \text{ L-glutamine} + 4 \text{ H}_2\text{O} = 4 \text{ ADP} + 4 \text{ phosphate} + \text{adenosylcobyric acid} + 4 \text{ L-glutamate}$
Other name(s): CobQ; cobyric acid synthase; 5'-deoxy-5'-adenosylcobyirinic-acid-*a,c*-diamide:L-glutamine amido-ligase; Ado-cobyric acid synthase [glutamine hydrolyzing]
Systematic name: adenosylcobyirinic-acid-*a,c*-diamide:L-glutamine amido-ligase (ADP-forming)
Comments: Requires Mg^{2+} . NH_3 can act instead of glutamine. This enzyme catalyses the four-step amidation sequence from cobyirinic acid *a,c*-diamide to cobyric acid via the formation of cobyirinic acid triamide, tetraamide and pentaamide intermediates.
References: [29, 285]

[EC 6.3.5.10 created 2004]

EC 6.4 Forming carbon-carbon bonds

This subclass contains a single sub-subclass (EC 6.4.1) for enzymes that form carbon-carbon bonds. These are the carboxylating enzymes, which are mostly biotinyl-proteins.

EC 6.4.1 Ligases that form carbon-carbon bonds (only sub-subclass identified to date)

EC 6.4.1.1

Accepted name: pyruvate carboxylase
Reaction: $\text{ATP} + \text{pyruvate} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + \text{oxaloacetate}$
Other name(s): pyruvic carboxylase
Systematic name: pyruvate:carbon-dioxide ligase (ADP-forming)
Comments: A biotinyl-protein containing manganese (animal tissues) or zinc (yeast). The animal enzyme requires acetyl-CoA.
References: [174, 247, 249, 277]

[EC 6.4.1.1 created 1961]

EC 6.4.1.2

Accepted name: acetyl-CoA carboxylase
Reaction: $\text{ATP} + \text{acetyl-CoA} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + \text{malonyl-CoA}$
Other name(s): acetyl coenzyme A carboxylase
Systematic name: acetyl-CoA:carbon-dioxide ligase (ADP-forming)

Comments: A biotinyl-protein. Also catalyses transcarboxylation; the plant enzyme also carboxylates propanoyl-CoA and butanoyl-CoA.

References: [95, 170, 171, 278, 281]

[EC 6.4.1.2 created 1961]

EC 6.4.1.3

Accepted name: propionyl-CoA carboxylase

Reaction: $\text{ATP} + \text{propanoyl-CoA} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + (S)\text{-methylmalonyl-CoA}$

Other name(s): propionyl coenzyme A carboxylase

Systematic name: propanoyl-CoA:carbon-dioxide ligase (ADP-forming)

Comments: A biotinyl-protein. Also carboxylates butanoyl-CoA and catalyses transcarboxylation.

References: [128, 141, 184, 191, 278]

[EC 6.4.1.3 created 1961, modified 1983]

EC 6.4.1.4

Accepted name: methylcrotonoyl-CoA carboxylase

Reaction: $\text{ATP} + 3\text{-methylcrotonoyl-CoA} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + 3\text{-methylglutaconyl-CoA}$

Other name(s): methylcrotonyl coenzyme A carboxylase; β -methylcrotonyl coenzyme A carboxylase; β -methylcrotonyl CoA carboxylase; methylcrotonoyl-CoA carboxylase

Systematic name: 3-methylcrotonoyl-CoA:carbon-dioxide ligase (ADP-forming)

Comments: A biotinyl-protein.

References: [130, 158, 231, 278]

[EC 6.4.1.4 created 1961]

EC 6.4.1.5

Accepted name: geranoyl-CoA carboxylase

Reaction: $\text{ATP} + \text{geranoyl-CoA} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + 3\text{-(4-methylpent-3-en-1-yl)pent-2-enediyl-CoA}$

Other name(s): geranoyl coenzyme A carboxylase; geranyl-CoA carboxylase

Systematic name: geranoyl-CoA:carbon-dioxide ligase (ADP-forming)

Comments: A biotinyl-protein. Also carboxylates dimethylpropenoyl-CoA and farnesoyl-CoA.

References: [248]

[EC 6.4.1.5 created 1972]

EC 6.4.1.6

Accepted name: acetone carboxylase

Reaction: $\text{acetone} + \text{CO}_2 + \text{ATP} + 2 \text{H}_2\text{O} = \text{acetoacetate} + \text{AMP} + 2 \text{phosphate}$

Systematic name: acetone:carbon-dioxide ligase (AMP-forming)

Comments: Requires Mg^{2+} and ATP. The enzyme from *Xanthobacter* sp. strain Py2 also carboxylates butan-2-one to 3-oxopentanoate.

References: [252]

[EC 6.4.1.6 created 2001]

EC 6.4.1.7

Accepted name: 2-oxoglutarate carboxylase

Reaction: $\text{ATP} + 2\text{-oxoglutarate} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + \text{oxalosuccinate}$

Other name(s): oxalosuccinate synthetase; carboxylating factor for ICDH (incorrect); CFI; OGC

Comments: A biotin-containing enzyme that requires Mg^{2+} for activity. It was originally thought [13] that this enzyme was a promoting factor for the carboxylation of 2-oxoglutarate by EC 1.1.1.41, isocitrate dehydrogenase (NAD^+), but this has since been disproved [12]. The product of the reaction is unstable and is quickly converted into isocitrate by the action of EC 1.1.1.41 [12].

References: [13, 12]

[EC 6.4.1.7 created 2006]

EC 6.5 Forming phosphoric-ester bonds

This subclass contains enzymes that restore broken phosphodiester bonds in nucleic acids (often called repair enzymes) in a single sub-subclass (EC 6.5.1).

EC 6.5.1 Ligases that form phosphoric-ester bonds (only sub-subclass identified to date)

EC 6.5.1.1

Accepted name: DNA ligase (ATP)
Reaction: $ATP + (\text{deoxyribonucleotide})_n + (\text{deoxyribonucleotide})_m = AMP + \text{diphosphate} + (\text{deoxyribonucleotide})_{n+m}$
Other name(s): polydeoxyribonucleotide synthase (ATP); polynucleotide ligase; sealase; DNA repair enzyme; DNA joinase; DNA ligase; deoxyribonucleic ligase; deoxyribonucleate ligase; DNA-joining enzyme; deoxyribonucleic-joining enzyme; deoxyribonucleic acid-joining enzyme; deoxyribonucleic repair enzyme; deoxyribonucleic joinase; deoxyribonucleic acid ligase; deoxyribonucleic acid joinase; deoxyribonucleic acid repair enzyme
Systematic name: poly(deoxyribonucleotide):poly(deoxyribonucleotide) ligase (AMP-forming)
Comments: Catalyses the formation of a phosphodiester at the site of a single-strand break in duplex DNA. RNA can also act as substrate, to some extent.
References: [19, 28, 291]

[EC 6.5.1.1 created 1972, modified 1976]

EC 6.5.1.2

Accepted name: DNA ligase (NAD^+)
Reaction: $NAD^+ + (\text{deoxyribonucleotide})_n + (\text{deoxyribonucleotide})_m = AMP + \text{nicotinamide nucleotide} + (\text{deoxyribonucleotide})_{n+m}$
Other name(s): polydeoxyribonucleotide synthase (NAD); polynucleotide ligase (NAD); DNA repair enzyme; DNA joinase; DNA ligase (NAD); polynucleotide synthetase (nicotinamide adenine dinucleotide); deoxyribonucleic-joining enzyme; deoxyribonucleic ligase; deoxyribonucleic repair enzyme; deoxyribonucleic joinase; DNA ligase; DNA joinase; deoxyribonucleate ligase; polynucleotide ligase; deoxyribonucleic acid ligase; polynucleotide synthetase; deoxyribonucleic acid joinase; DNA-joining enzyme; deoxyribonucleic joinase; deoxyribonucleic repair enzyme; polynucleotide ligase (nicotinamide adenine dinucleotide); polydeoxyribonucleotide synthase (NAD^+)
Systematic name: poly(deoxyribonucleotide):poly(deoxyribonucleotide) ligase (AMP-forming, NMN-forming)
Comments: Catalyses the formation of a phosphodiester at the site of a single-strand break in duplex DNA. RNA can also act as substrate, to some extent.
References: [305]

[EC 6.5.1.2 created 1972, modified 1976]

EC 6.5.1.3

Accepted name: RNA ligase (ATP)

Reaction: $\text{ATP} + (\text{ribonucleotide})_n + (\text{ribonucleotide})_m = \text{AMP} + \text{diphosphate} + (\text{ribonucleotide})_{n+m}$
Other name(s): polyribonucleotide synthase (ATP); RNA ligase; polyribonucleotide ligase; ribonucleic ligase
Systematic name: poly(ribonucleotide):poly(ribonucleotide) ligase (AMP-forming)
Comments: Converts linear RNA to a circular form by transfer of the 5'-phosphate to the 3'-hydroxy terminus.
References: [251]

[EC 6.5.1.3 created 1976]

EC 6.5.1.4

Accepted name: RNA-3'-phosphate cyclase
Reaction: $\text{ATP} + \text{RNA } 3'\text{-terminal-phosphate} = \text{AMP} + \text{diphosphate} + \text{RNA terminal-2',3'-cyclic-phosphate}$
Other name(s): RNA cyclase
Systematic name: RNA-3'-phosphate:RNA ligase (cyclizing, AMP-forming)
Comments: Adenosine 5'-(γ -thio)triphosphate can act instead of ATP.
References: [73, 226]

[EC 6.5.1.4 created 1986, modified 1989]

EC 6.6 Forming nitrogen—metal bonds

This subclass contains a single sub-subclass for enzymes that form coordination complexes, i.e. form nitrogen—metal bonds (EC 6.6.1).

EC 6.6.1 Forming coordination complexes

EC 6.6.1.1

Accepted name: magnesium chelatase
Reaction: $\text{ATP} + \text{protoporphyrin IX} + \text{Mg}^{2+} + \text{H}_2\text{O} = \text{ADP} + \text{phosphate} + \text{Mg-protoporphyrin IX} + 2 \text{H}^+$
Other name(s): protoporphyrin IX magnesium-chelatase; protoporphyrin IX Mg-chelatase; magnesium-protoporphyrin IX chelatase; magnesium-protoporphyrin chelatase; magnesium-chelatase; Mg-chelatase; Mg-protoporphyrin IX magnesium-lyase
Systematic name: Mg-protoporphyrin IX magnesium-lyase
Comments: This is the first committed step of chlorophyll biosynthesis and is a branchpoint of two major routes in the tetrapyrrole pathway.
References: [282, 283, 74]

[EC 6.6.1.1 created 2003]

EC 6.6.1.2

Accepted name: cobaltochelataase
Reaction: $\text{ATP} + \text{hydrogenobyrrinic acid } a,c\text{-diamide} + \text{Co}^{2+} + \text{H}_2\text{O} = \text{ADP} + \text{phosphate} + \text{cob(II)yrinic acid } a,c\text{-diamide} + \text{H}^+$
Other name(s): hydrogenobyrrinic acid *a,c*-diamide cobaltochelataase; CobNST; CobNCobST
Systematic name: hydrogenobyrrinic-acid-*a,c*-diamide:cobalt cobalt-ligase (ADP-forming)

Comments: This enzyme, which forms part of the aerobic cobalamin biosynthesis pathway, is a type I chelatase, being heterotrimeric and ATP-dependent. It comprises two components, one of which corresponds to CobN and the other is composed of two polypeptides, specified by *cobS* and *cobT* in *Pseudomonas denitrificans*, and named CobST [58]. Hydrogenobyric acid is a very poor substrate. ATP can be replaced by dATP or CTP but the reaction proceeds more slowly. CobN exhibits a high affinity for hydrogenobyric acid *a,c*-diamide. The oligomeric protein CobST possesses at least one sulfhydryl group that is essential for ATP-binding. Once the Co²⁺ is inserted, the next step in the pathway ensures that the cobalt is ligated securely by reducing Co(II) to Co(I). This step is carried out by EC 1.16.8.1, cob(II)yrinic acid *a,c*-diamide reductase.

References: [58, 285]

[EC 6.6.1.2 created 2004]

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