

Table S1. An update to the 1998 listing of analogous enzymes

This listing was originally prepared as a web supplement to the article by M.Y. Galperin, D.R. Walker and E.V. Koonin

["Analogous enzymes: Independent inventions in enzyme evolution"](#), published in 1998 in *Genome Research* **8**: 779-790. [Free full text.](#)

This updated version lists the same 105 EC nodes as the original one and is Supplementary Table S1 to the manuscript by M.V. Omelchenko, M.Y. Galperin, Y.I. Wolf and E.V. Koonin **"Analogous enzymes: A systematic analysis of alternative solutions in enzyme evolution"**, submitted for publication in January 2010.

No.	EC no.	Enzyme name	Example	PDB	SCOP fold	Family (Pfam)	Ref.	Comments
1	1.1.1.1	Alcohol dehydrogenase (NAD ⁺)	ADH1B_HUMAN	1HDY	GroES-like & Rossmann-fold	Zinc-containing alcohol dehydrogenase	9802210, 8201622	Three distinct structural folds
	1.1.1.1	Alcohol dehydrogenase (NAD ⁺)	ADH4_YEAST	2BI4	Dehydroquinase synthase-like	Iron-containing alcohol dehydrogenase	3282541, 2823079	
	1.1.1.1	Alcohol dehydrogenase (NAD ⁺)	ADH_DROME	1MG5	Rossmann-fold	Short chain dehydrogenase	15016358, 11669613	
2	1.1.1.2	Alcohol dehydrogenase (NADP ⁺)	ADHC_MYCBO	1YQD	GroES-like & Rossmann-fold	Zinc-containing alcohol dehydrogenase	1427101, 15829607	Three distinct structural folds
	1.1.1.2	Alcohol dehydrogenase (NADP ⁺)	AK1A1_HUMAN	2ALR	TIM beta/alpha-barrel	Aldo/keto reductase	15299353, 10486210	
	1.1.1.2	Alcohol dehydrogenase (NADP ⁺)	ADH4_SCHPO	1O2D	Dehydroquinase synthase-like	Iron-containing alcohol dehydrogenase	15327949, 14705036	
3	1.1.1.27	L-lactate dehydrogenase	LDHA_HUMAN	1EZ4	Rossmann-fold & LDH C-terminal domain	Lactate & malate dehydrogenases	PubMed	Two distinct structural folds
	1.1.1.27	L-lactate dehydrogenase	LDH_RALEH	1VBI	L-sulfolactate dehydrogenase-like	Malate/L-Lactate dehydrogenases	8405966	
4	1.1.1.28	D-lactate dehydrogenase	LDHD_ECOLI	2DLD	Rossmann-fold & Flavodoxin-like	Formate/glycerate dehydrogenases	9025293	Two distinct structural folds

	1.1.1.28	D-lactate dehydrogenase	DLD_ECOLI	1F0X	FAD-binding domain & Ferredoxin-like	D-lactate dehydrogenase	10944213	
5	1.1.1.37	Malate dehydrogenase	MDH_HALMA	2J5K	Rossmann-fold & LDH C-terminal domain	L-lactate/malate dehydrogenases	8476859 , 10653643	Two distinct structural folds
	1.1.1.37	Malate dehydrogenase	MDH_METFE	2G8Y	L-sulfolactate dehydrogenase-like	Malate/L-Lactate dehydrogenases	2110059 , 10850983	
6	1.1.1.42	Isocitrate dehydrogenase (NADP+)	IDH_ECOLI	1IDC	Isocitrate/ Isopropylmalate dehydrogenase-like	Isocitrate/ isopropylmalate dehydrogenase	1888729	Same fold, same superfamily
	1.1.1.42	Isocitrate dehydrogenase (NADP+)	IDH_AZOVI	1ITW	Isocitrate/ Isopropylmalate dehydrogenase-like	Monomeric isocitrate dehydrogenase	4149369	
7	1.1.1.47	Glucose 1-dehydrogenase	DHG_BACSU	1GCO	Rossmann-fold	Short chain dehydrogenase	3082854	Two distinct structural folds
	1.1.1.47	Glucose 1-dehydrogenase	DHG_THEAC	1HDZ	GroES-like	Alcohol dehydrogenase GroES-like domain	2803257 , 8436115	
8	1.1.1.50	3alpha-hydroxysteroid dehydrogenase	Q9ZFY9_COMTE	1FJH	Rossmann-fold	Short chain dehydrogenase	10833462	Two distinct structural folds
	1.1.1.50	3alpha-hydroxysteroid dehydrogenase	AK1C4_HUMAN	2FVL	TIM beta/alpha barrel	Aldo/keto reductase	1530633 , 11158055	
9	1.1.1.62	Estradiol 17 β -dehydrogenase	DHB1_HUMAN	1FDS	Rossmann-fold	Short chain dehydrogenase	2846351 , 7663947	Two distinct structural folds
	1.1.1.62	Estradiol 17 β -dehydrogenase	DHB5_MOUSE	1Q5M	TIM beta/alpha barrel	Aldo/keto reductase	PubMed	

10	1.2.1.2	Formate dehydrogenase	FDHF_ECOLI	1FDI	Formate dehydrogenase/ DMSO reductase	Molybdopterin-containing oxidoreductases	9036855	Two distinct structural folds
	1.2.1.2	Formate dehydrogenase	FDH_PESER	2NAC	Rossmann-fold & Flavodoxin-like	2-hydroxyacid dehydrogenases	1597184, 8484798	
11	1.2.99.2	Carbon-monoxide dehydrogenase	DCML_OLICO	1N60	CO dehydrogenase ISP C-domain like and others		10482497, 12475995	Two distinct structural folds
	1.2.99.2	Carbon-monoxide dehydrogenase	COOS_RHORU	1JQK	Prismane protein-like	Prismane/CO dehydrogenase family	8561463, 11593006	
12	1.3.1.33	Protochlorophyllide reductase	BCHN_RHOCA	3MIN	Nitrogenase Fe-Mo fold	Protochlorophyllide reductase	10811655	The two forms use different electron donors
	1.3.1.33	Protochlorophyllide reductase	PORB_ARATH	1hdu	Rossmann-fold	Short chain dehydrogenase	7659751	
13	1.5.1.3	Dihydrofolate reductase	DYR_BACSU	1MVS	Dihydrofolate reductase-like	Dihydrofolate reductases	1731871	Two distinct structural folds
	1.5.1.3	Dihydrofolate reductase	FOLM_ECOLI	3edm	Rossmann-fold	Short chain dehydrogenase	14617668	
14	1.6.99.3	NADH dehydrogenase	DHNA_BACYN	1XHC	FAD/NAD(P)-binding domain	NADH dehydrogenase	1917890	Two distinct structural folds
	1.6.99.3	NADH dehydrogenase	NDUS1_HUMAN	2FUG	Formate dehydrogenase/ DMSO reductase	Complex I 75 kDa subunit family	1935949	
15	1.10.3.1	Catechol oxidase	DXA2_DROME	N/A	Corrected to PSMD3_DROME , 26S proteasome regulatory subunit 3		1909680	Misassignment corrected
	1.10.3.1	Diphenol oxidase	PPO_SPIOL	1BT1	Di-copper centre-containing domain		7794929	

16	1.11.1.5	Cytochrome-c peroxidase	CCPR_PSEAE	1EB7	Cytochrome c	Di-heme cytochrome c peroxidase	7781769, 1657179, 8591033	Two distinct structural folds
	1.11.1.5	Cytochrome-c peroxidase	CCPR_YEAST	1EBE	Heme-dependent peroxidases	Peroxidase	2169873, 6092361	
17	1.11.1.6	Catalase	CATA_HUMAN	1QQW	Heme-dependent catalase	Heme-dependent catalase	10666617, 3755525	Three distinct structural folds
	1.11.1.6	Catalase	CATA_ECOLI	2FXG	Heme-dependent peroxidases	Peroxidase	374409, 2670897, 8508796	
	1.11.1.6	Catalase	MCAT_LACPL	1JKU	Ferritin-like	Manganese catalase	8939876	
18	1.11.1.7	Peroxidase	PRDX6_MOUSE	1PRX	Thioredoxin	Thioredoxin	9291135, 10395907, 9587003	Three distinct structural folds
	1.11.1.7	Peroxidase	PERM_HUMAN	1MYP	Heme-dependent peroxidases	Animal heme peroxidase	2154223	
	1.11.1.7	Peroxidase	YCDB_ECOLI	2D3Q	Ferredoxin-like	Dyp-type peroxidase-like	16551627, 14684913	
19	1.11.1.10	Chloride peroxidase	PRXC_PSEPY	1A88	Alpha/beta-hydrolases	Haloperoxidase	8344520	Three distinct structural folds
	1.11.1.10	Chloride peroxidase	PRXC_CURIN	1VNC	Acid phosphatase	Type 2 phosphatidic acid phosphatase (PAP2)	9165086	
	1.11.1.10	Chloride peroxidase	PRXC_CALFU	2CPO	EF Hand-like	Cloroperoxidase	8747463, 11278701	
20	1.14.15.3	Alkane 1-monooxygenase	ALKB_PSEOL	1AFR	Ferritin-like (predicted)	Fatty acid desaturase	2647718	Two distinct structural folds
	1.14.15.3	Alkane 1-monooxygenase	CP4AM_HUMAN	1TQN	Cytochrome P450	Cytochrome P450	PubMed	

21	1.15.1.1	Superoxide dismutase	SODF_ECOLI	1ISA	Fe,Mn superoxide dismutase	Fe,Mn superoxide dismutase	2447093	Three distinct structural folds
	1.15.1.1	Superoxide dismutase	SODC_ECOLI	1ESO	Immunoglobulin-like beta-sandwich	Cu,Zn superoxide dismutase	9405149	
	1.15.1.1	Superoxide dismutase	SODN_STRSO	1Q0D	Four-helical up-and-down bundle	Nickel-containing superoxide dismutase	8836134, 15173586	
22	1.17.4.2	Ribonucleoside-triphosphate reductase	NRDD_ECOLI	1H7A	PFL-like glycy radical enzymes	Anaerobic ribonucleotide reductase	7852304, 12655046	Same fold, same superfamily
	1.17.4.2	Ribonucleoside-triphosphate reductase	RTPR_LACLE	1L1L	PFL-like glycy radical enzymes	B12-dependent (class II) ribonucleotide reductase	11875520	
23	1.18.99.1	Hydrogenase (now EC 1.12.2.1)	PHNL_DESGI	1FRV	HydA/Nqo6-like & HydB/Nqo4-like	Ni-Fe hydrogenase	2651421, 7854413	Two distinct structural folds
	1.18.99.1	Hydrogenase (now EC 1.12.7.2)	PHF1_CLOPA	1FEH	Fe-only hydrogenase	Iron-only hydrogenase	1911757, 9836629	
24	2.1.1.17	Phosphatidylethanolamine N-methyltransferase	PMTA_RHOSH	3DH0	SAM-dependent methyltransferases	SAM-dependent methyltransferase	8340421	Two distinct structural folds
	2.1.1.17	Phosphatidylethanolamine N-methyltransferase	PEM1_YEAST	N/A	Integral membrane protein		2445736	
25	2.3.1.15	Glycerol-3-phosphate O-acyltransferase	PLSB_ECOLI	N/A		Acyltransferase	6350296	Same catalytic domain
	2.3.1.15	Glycerol-3-phosphate O-acyltransferase	PLSB_CUCMO	1K30	Glycerol-3-phosphate 1-acyltransferase	Glycerol-3-phosphate 1-acyltransferase	11377195	
26	2.3.1.28	Chloramphenicol O-acetyltransferase	CAT4_AGRTU	1XAT	Single-stranded left-handed beta-helix	Galactoside acetyltransferase	2013403, 9578552	Two distinct structural folds
	2.3.1.28	Chloramphenicol O-acetyltransferase	CAT3_ECOLX	3CLA	CoA-dependent acyltransferases	Chloramphenicol acetyltransferase	2187098	

27	2.3.1.43	Phosphatidylcholine-sterol O-acyltransferase	LCAT_HUMAN	1ex9	Alpha/beta hydrolase fold (predicted)		2823898	Two distinct structural folds
	2.3.1.43	Phosphatidylcholine-sterol O-acyltransferase	GCAT_AERHY	1vig	Eukaryotic type KH-domain (predicted)		3280033	
28	2.3.2.13	Protein-glutamine gamma-glutamyltransferase	F13A_HUMAN TGAS_STRMB	1FIE 1IU4	Cysteine proteinases	Transglutaminase, microbial transglutaminase	9839945 , 2901091 , 2877456	Two distinct structural folds
	2.3.2.13	Protein-glutamine gamma-glutamyltransferase	TGL_BACSU	1ssq	Single-stranded left-handed beta-helix (predicted)		9692191	
29	2.4.1.25	4-a-glucanotransferase	MALQ_ECOLI	1FP8	TIM beta/alpha-barrel	Glycosyl hydrolase family 77	2845225	Two distinct structural folds
	2.4.1.25	4-a-glucanotransferase	MALQ_THELI	1K1X	7-stranded beta/alpha barrel	Glycosyl hydrolase family 57	12618437	
30	2.5.1.18	Glutathione S-transferase	GST_ECOLI GSTK1_HUMAN	1A0F 1R4W	Thioredoxin & GST C-terminal domain	Glutathione S-transferase, class beta, class kappa	2185038 , 16081649 , 14717589	Three distinct structural folds
	2.5.1.18	Glutathione S-transferase	MGST1_HUMAN	2H8A	MAPEG domain	MAPEG family	8812420 , 9278457 , 10091672 , 16806268	
	2.5.1.18	Glutathione S-transferase	FOSA_SERMA	1NPB	Glyoxalase/ Bleomycin resistance protein	Antibiotic resistance proteins	15075406 , 9115979	
31	2.6.1.44	Alanine-glyoxylate aminotransferase	SPYA_HUMAN	1H0C	PLP-dependent transferases	Cystathionine synthase-like	2253628 , 12899834	Same fold, same superfamily
	2.6.1.44	Alanine-glyoxylate aminotransferase	AGT2_RAT	1Z3Z	PLP-dependent transferases	GABA-aminotransferase	7592550	

32	2.7.1.2	Glucose kinase	GLK_ECOLI	1SZ2	Ribonuclease H-like motif	Glucokinase	9023215	Same fold, same superfamily
	2.7.1.2	Glucose kinase	GLK_STRCO	1WOK	Ribonuclease H-like motif	ROK family	1435260	
	2.7.1.2	Glucose kinase	HXK1_HUMAN	1DGK	Ribonuclease H-like motif	Hexokinase	1637300, 9735292	
33	2.7.1.4	Fructokinase	SCRK_ECOLX	1TZ6	Ribokinase-like	PfkB family carbohydrate kinase	8278523	Two distinct structural folds
	2.7.1.4	Fructokinase	SCRK_STRMU	1XC3	Ribonuclease H-like motif	Actin-like ATPase domain	8336109	
34	2.7.1.11	6-Phosphofructokinase	K6PF1_ECOLI	1PFK	Phosphofructokinase	Phosphofructokinase	2975709	Two distinct structural folds
	2.7.1.11	6-Phosphofructokinase	K6PF2_ECOLI	3CQD	Ribokinase-like	PfkB family carbohydrate kinase	18762190, 6310120	
35	2.7.1.12	Gluconokinase	GNTK_ECOLI	1KNQ	P-loop NTPases	Gluconate kinase	8655507, 11468405	Two distinct structural folds
	2.7.1.12	Gluconokinase	GNTK_BACSU	2ITM	Ribonuclease H-like motif	Glycerol kinase	3020045	
36	2.7.1.107	Diacylglycerol kinase	KDGL_ECOLI	N/A	Integral membrane protein	Prokaryotic diacylglycerol kinase	2984194, 8071224, 18611377	Two distinct structural folds
	2.7.1.107	Diacylglycerol kinase	DGKG_HUMAN	2qv7	NAD kinase (predicted)	Diacylglycerol kinase catalytic domain	8034597	
37	2.7.4.3	Adenylate kinase	KAD_ECOLI	1AKE	P-loop NTPases	Adenylate kinase	9715904	Same structural family
	2.7.4.3	Adenylate kinase	KADA_METVO	1NKS	P-loop NTPases	Archaeal adenylate kinase	7768791, 9055821, 9733648	

38	2.7.7.2	FAD synthetase	FAD1_YEAST	3G5A	Adenine nucleotide alpha hydrolase (predicted)	PAPS reductase	7799934, 19375431	Same fold, different superfamilies, discussed in Huerta et al.
	2.7.7.2	FAD synthetase	RIBF_CORAM	1S4M	Adenine nucleotide alpha hydrolase	FAD synthetase	3023344, 9454067	
39	2.7.7.4	Sulfate adenylyltransferase	CYSN_ECOLI CYSD_ECOLI	1ZUN	P-loop NTPases and Adenine nucleotide alpha hydrolase		2828368	CysD and MET3 belong to the same superfamily
	2.7.7.4	Sulfate adenylyltransferase	MET3_YEAST	1JEE	Adenine nucleotide alpha hydrolase	ATP-sulfurylase	11157739	
40	2.7.7.9	UTP-glucose-1-phosphate uridylyltransferase	GALU_ECOLI	2E3D	Nucleotide-diphospho-sugar transferases	Nucleotidyl transferase	7961613, 17322528	Two distinct structural folds
	2.7.7.9	UTP-glucose-1-phosphate uridylyltransferase	UGPA_HUMAN	2icy	Single-stranded left-handed beta-helix	UTP-glucose-1-phosphate uridylyltransferase	8354390, 17178129	
41	2.7.7.12	Galactose-1-phosphate uridylyltransferase	GAL7_ECOLI	1GUP	HIT-like	Galactose-1-phosphate uridylyltransferase 1	321007, 7669762	Same fold, same superfamily
	2.7.7.12	Galactose-1-phosphate uridylyltransferase	GALT_LACHE	1gup	HIT-like (predicted)	Galactose-1-phosphate uridylyltransferase 2	2066342	
42	2.7.7.19	Polynucleotide adenylyltransferase	PCNB_ECOLI	1MIY	Nucleotidyltransferase & Poly A polymerase C-terminal region-like	Poly A polymerase C-terminal region-like	10361280	Same fold, same superfamily (catalytic domain)
	2.7.7.19	Polynucleotide adenylyltransferase	PAP_HUMAN	1Q78	Nucleotidyltransferase & PAP/OAS1 substrate-binding domain & Ferredoxin-like	Poly(A) polymerase, PAP, middle domain&	9061026	

43	2.7.7.25	tRNA adenylyltransferase	CCA_ECOLI	1VFG	Nucleotidyltransferase & Poly A polymerase C-terminal region-like	Bacterial CCA-adding enzyme type 1	2204621	Same fold, same superfamily (catalytic domain)
	2.7.7.25	tRNA adenylyltransferase	CCA_SULSH	1UET	Nucleotidyltransferase & PAP/OAS1 substrate-binding domain & Ferredoxin-like	Archaeal tRNA CCA-adding enzyme substrate-binding domain	8809016 , 15590678	
44	2.7.8.8	CDP-diacylglycerol--serine O-phosphatidyltransferase	PSS_ECOLI	1BYR	Phospholipase D/nuclease	Phospholipase D Active site motif	1323044 , 10074947	Two distinct structural folds
	2.7.8.8	CDP-diacylglycerol--serine O-phosphatidyltransferase	PSS_YEAST	N/A	Integral membrane protein	CDP-alcohol phosphatidyltransferase	3040403	
45	3.1.2.15	Ubiquitin thiolesterase	UBP5_HUMAN	2G43	Cysteine proteinases	Ubiquitin carboxyl-terminal hydrolase	7498549	Different activities: cleave polyubiquitin chains linked, respectively, to Lys-48 and Lys-63
	3.1.2.15	Ubiquitin thiolesterase	STALP_HUMAN	2ZNR	Cytidine deaminase-like (predicted)	JAB1/MPN/Mov34 metalloenzyme	15314065 , 18758443	
46	3.1.3.48	Protein-tyrosine-phosphatase	PTPA_STRCO	1D1P	Phosphotyrosine protein phosphatases I-like	Low-molecular-weight phosphotyrosine protein phosphatases	8550407 , 1304913	Five distinct structural folds
	3.1.3.48	Protein-tyrosine-phosphatase	PTPRD_HUMAN	1LAR	Phosphotyrosine protein phosphatases II	Higher-molecular-weight phosphotyrosine protein phosphatases	2170109 , 8833149	
	3.1.3.48	Protein-tyrosine-phosphatase	MPIP3_HUMAN	1QB0	Rhodanese/Cell cycle control phosphatase	Cell cycle control phosphatase	8276463	
	3.1.3.48	Protein-tyrosine-phosphatase	YWQE_BACSU	2ANU	7-stranded beta/alpha barrel	PHP domain	15866923	

	3.1.3.48	Protein-tyrosine-phosphatase	EYA3_MOUSE	1JUD	HAD-like	HAD-like hydrolase	14628042, 14628052	
47	3.2.1.1	Alpha-amylase	AMY1_ECOLI	1EA9	TIM beta/alpha-barrel & Glycosyl hydrolase	Alpha-amylase	9268356	Two distinct structural folds
	3.2.1.1	Alpha-amylase	AMYA_PYRFU	1K1X	7-stranded beta/alpha barrel	Glycosyl hydrolase family 57	8226990	
48	3.2.1.4	Cellulase	GUNA_PSEFL	1UT9	Alpha/alpha toroid	Glycosyl hydrolase family 9 (cellulase E)	2851699	At least four distinct structural folds
	3.2.1.4	Cellulase	GUNA_CLOCE	1EDG	TIM beta/alpha-barrel	Beta-glycanases	1744052, 8535787	
	3.2.1.4	Cellulase	GUN1_STRHA	2BOD	7-stranded beta/alpha barrel	Glycosyl hydrolase family 6	1400190	
	3.2.1.4	Cellulase	GUNM_CLOTM	2FVG	Phosphorylase/hydrolase	Cellulase M	GenBank	
	3.2.1.4	Cellulase	GUN_ASPAC	1KS4	Concanavalin A-like lectins/glucanases	Glycosyl hydrolase family 11 (cellulase G)	2249253, 7586029, 2379837	
	3.2.1.4	Cellulase	GUNE_RUMFL	1LOH	Acyl carrier protein-like (predicted)		8360615	
	3.2.1.4	Cellulase	GUNA_PAELA	2EQD	TIM beta/alpha-barrel (predicted)		17905739	
49	3.2.1.8	Endo-1,4- β -xylanase	XYNA_BUTFI	1XAS	TIM beta/alpha-barrel	beta-glycanases	2198249, 1909424	Two distinct structural folds
	3.2.1.8	Endo-1,4- β -xylanase	XYNA2_CLOSR	1QH6	Concanavalin A-like lectins/ glucanases	Glycosyl hydrolase family 11 (cellulase G)	7763496	
50	3.2.1.11	Dextranase	DEXT_STRDO	N/A			8021165	Two distinct structural folds

	3.2.1.11	Dextranase	DEXT_PENMI	1OGM	Single-stranded right-handed beta-helix	Glycosyl hydrolase family 28	8905923, 12962629	
51	3.2.1.14	Chitinase	CHIA_SERMA	1RD6	TIM beta/alpha barrel	Type II chitinase	PubMed	Two distinct structural folds
	3.2.1.14	Chitinase	CHI1_ORYSA	2BAA	Lysozyme-like	Family 19 glycosidase	1893114	
52	3.2.1.17	Lysozyme	LYS_CLOAB	1JFX	TIM beta/alpha barrel	1,4-beta-N-acetylmuraminidase	1599233, 7649184	Two distinct structural folds
	3.2.1.17	Lysozyme	LYS_BPP1	1XJT	Lysozyme-like	Phage lysozyme	8576044, 9514719	
	3.2.1.17	Lysozyme	ACMA_LACLM	2ZYC	Lysozyme-like	Glycosyl hydrolase family 73	7883712, 10049388, 19351587	
	3.2.1.17	Lysozyme	LYB_BACSU	N/A	N/A		3148618	
53	3.2.1.20	Alpha-glucosidase	MALT_CANAL	1J11	TIM beta/alpha barrel & Glycosyl-hydrolase domain	Glycosyl hydrolase family 13	1400249	Two distinct structural folds
	3.2.1.20	Alpha-glucosidase	AGLA_THEMA	1OBB	Rossmann-fold & LDH C-terminal domain	Glycosyl hydrolase family 4	12062450, 10972187	
54	3.2.1.21	Beta-glucosidase	BGLA_THEMA	1OIF	TIM beta/alpha barrel	Glycosyl hydrolase family 1	8277941, 14624580	Same fold, same superfamily
	3.2.1.21	Beta-glucosidase	BGLS_BUTFI	1X38	TIM beta/alpha barrel	Glycosyl hydrolase family 3	2262790	
55	3.2.1.22	Alpha-galactosidase	AGAL_STRMU	1ZY9	TIM beta/alpha barrel	Glycosyl hydrolase family 36	1649890	Two distinct structural folds
	3.2.1.22	Alpha-galactosidase	AGAL_ECOLI	1OBB	Rossmann-fold & LDH C-terminal domain	Glycosyl hydrolase family 4	2831880	

56	3.2.1.23	Beta-galactosidase	BGAL_ECOLI	1BGL	TIM beta/alpha-barrel	Glycosyl hydrolase family 2	11732897	Same fold, same superfamily
	3.2.1.23	Beta-galactosidase	BGAL_SULAC		TIM beta/alpha-barrel	Glycosyl hydrolase family 1	2508066	
57	3.2.1.28	Alpha,alpha-trehalase	TREA_ECOLI	2JG0	Alpha/alpha toroid	Glycosyl hydrolase family 37	2820965, 17455176	Same fold, same superfamily
	3.2.1.28	Alpha,alpha-trehalase	TREA_EMENI	1H54	Alpha/alpha toroid (predicted)	Glycosyl hydrolase family 65	9140977	
58	3.2.1.35	Hyaluronidase	HYAL2_HUMAN	1FCU	TIM beta/alpha barrel	Glycosyl hydrolase family 56	9712871, 17503783	Two distinct structural folds
	3.2.1.35	Hyaluronidase	HYLP2_BPH45	2PK1	Triple-stranded beta-helix	Hyaluronidase_1	7622224	
	3.2.1.35	Hyaluronidase	HEMO_PIG	1HXN	4-bladed beta-propeller	Hemopexin domain	7798203, 8590016	Most likely a mistake
59	3.2.1.37	Xylan 1,4- β -xylosidase	XYNB_BACPU	1YIF	5-bladed beta-propeller	Glycosyl hydrolase family 43	2440680, 7766665	Three distinct structural folds
	3.2.1.37	Xylan 1,4- β -xylosidase	XYNB_THESA	1PX8	TIM beta/alpha barrel	Glycosyl hydrolase family 39	8612648	
	3.2.1.37	Xylan 1,4- β -xylosidase	XYLA1_BACST	N/A	N/A	Glycosyl hydrolase family 52	8074507, 11322943	
60	3.2.1.39	Glucan endo-1,3- β -D-glucosidase	E13A_ARATH	2CYG	TIM beta/alpha barrel	Glycosyl hydrolase family 17	11405630, 16421930	Three distinct structural folds
	3.2.1.39	Glucan endo-1,3- β -D-glucosidase	E13B_BACCI	1UPS	Concanavalin A-like lectins/ glucanases	Glycosyl hydrolase family 16	2311931	
	3.2.1.39	Glucan endo-1,3- β -D-glucosidase	E13B_CELCE	N/A	N/A	Glycosyl hydrolase family 64	1985933	

61	3.2.1.55	Alpha-N-arabinofuranosidase	ABFA_STRLI	2C7F	TIM beta/alpha barrel	Glycosyl hydrolase family 51	8092996, 16336192	Three distinct structural folds
	3.2.1.55	Alpha-N-arabinofuranosidase	XYLB_BUTFI	1YRZ	Concanavalin A-like lectins/glucanases & 5-bladed beta-propeller	Glycosyl hydrolase family 43	1905520, 18980579	
	3.2.1.55	Alpha-N-arabinofuranosidase	XYNC_PSEFL	N/A	<i>5-bladed beta-propeller (predicted)</i>	Glycosyl hydrolase family 62	2125205	
62	3.2.1.58	Glucan 1,3- β -glucosidase	EXG_CANAL	2PB1	TIM beta/alpha barrel	Glycosyl hydrolase family 5 (cellulase A)	8436950, 10610795	Two distinct structural folds
	3.2.1.58	Glucan 1,3- β -glucosidase	EXG1_COCCA	3EQO	<i>Single-stranded right-handed beta-helix</i>	Glycosyl hydrolase family 55	8135518	
63	3.2.1.73	Licheninase	GUB_NICPL	2CYG	TIM beta/alpha barrel	Glycosyl hydrolase family 17	PubMed	Three distinct structural folds
	3.2.1.73	Licheninase	GUB_BACSU	1GBG	Concanavalin A-like lectins/glucanases	Glycosyl hydrolase family 16	1740123	
	3.2.1.73	Licheninase	GUB_BACCI	1V5C	Alpha/alpha toroid	Glycosyl hydrolase family 8 (cellulase D)	2377467	
64	3.2.1.78	Mannan endo-1,4- β -mannosidase	MANA_PSEFL	1GW1	TIM beta/alpha barrel	Glycosyl hydrolase family 26	7848261, 12203498	Same fold, same superfamily
	3.2.1.78	Mannan endo-1,4- β -mannosidase	MANB_CALSA	1BQC	TIM beta/alpha barrel	Glycosyl hydrolase family 5	1476429	
65	3.2.1.81	β -agarase	AGAR_STRCO	1QOX	TIM beta/alpha barrel	Glycosyl hydrolase family 1	3034860	Predicted two distinct structural folds
	3.2.1.81	β -agarase	AGAA_VIBS7	N/A	N/A	Glycosyl hydrolase family 50	8285681	
	3.2.1.81	β -agarase	AGAR_ALTAT	N/A	N/A	Glycosyl hydrolase family 86	2914859	

66	3.2.1.86	6-phospho- β -glucosidase	BGLB_ECOLI	1QOX	TIM beta/alpha barrel	Glycosyl hydrolase family 1	3034860	Two distinct structural folds
	3.2.1.86	6-phospho- β -glucosidase	CHBF_ECOLI	1S6Y	Rossmann-fold & LDH C-terminal domain	Glycosyl hydrolase family 4	10572139	
67	3.2.2.21	DNA-3-methyladenine glycosylase	3MG2_ECOLI	1MPG	DNA-glycosylase & TBP-like		6389535	Two distinct structural folds
	3.2.2.21	DNA-3-methyladenine glycosylase	3MG_HUMAN	1F4R	FMT C-terminal domain-like		8589517, 1645538	
68	3.5.1.1	Asparaginase	ASPG1_YEAST	1HFW	Glutaminase/Asparaginase	Glutaminase/Asparaginase	8026756	At least two distinct structural folds
	3.5.1.1	Asparaginase	ASPG_HUMAN	1APY	Ntn_hydrolase-like	(Glycosyl)asparaginase	1840528	
	3.5.1.1	Asparaginase	Q9RFN5_RHIET	N/A	N/A	L-asparaginase II	10930734	
69	3.5.1.4	Amidase	AMID_PSECL	1OCK	Amidase signature	Amidase	2013568	Two distinct structural folds
	3.5.1.4	Amidase	AMIE_PSEAE	2UXY	Carbon-nitrogen hydrolase	Carbon-nitrogen hydrolase	87219101	
70	3.5.1.11	Penicillin acylase	PAC_ECOLX	1PNL	Ntn hydrolase-like	Penicillin amidase	9292993, 7816145	Same fold, same supefamily
	3.5.1.11	Penicillin acylase	PAC_BACSH	2PVA	Ntn hydrolase-like	Linear amide C-N hydrolases	10331865	
71	3.5.1.28	N-acetylmuramoyl-L-alanine amidase	AMPD_ECOLI	1J3G	N-acetylmuramoyl-L-alanine amidase-like	N-acetylmuramoyl-L-alanine amidase-like	12654266	Two distinct structural folds
	3.5.1.28	N-acetylmuramoyl-L-alanine amidase	AMIB_ECOLI	1JWQ	Phosphorylase/hydrolase-like	Zn-dependent exopeptidases	7511774	
72	3.5.2.6	β -Lactamase	AMPC_ECOLI	2BLS	Beta-lactamase/transpeptidase-like	Beta-lactamase	6795623	Two distinct structural folds

	3.5.2.6	β -Lactamase	BLAB_BACCE	1BC2	Metallo-hydrolase/ oxidoreductase	Zn metallo-beta-lactamase	9730812	
73	3.6.1.1	Inorganic diphosphatase	IPYR_ARATH	1TWL	OB-fold	Pyrophosphatase	654155	Four distinct structural folds
	3.6.1.1	Inorganic diphosphatase	AVP1_ARATH	N/A	Integral membrane protein	Inorganic H+ pyrophosphatase	9268385	
	3.6.1.1	Inorganic diphosphatase	PPAC_BACSU	1WPM	DHH phosphoesterases	DHH hydrolase	9845334, 11697905	
	3.6.1.1	Inorganic diphosphatase	PPAX_BACSU	2HDO	HAD-like	HAD-like hydrolase	12359880	
74	3.6.1.5	Apyrase	APY_AEDAE	1HP1	5-nucleotidase & Metallo-dependent phosphatases	5'-nucleotidase	2173922	Three distinct structural folds
	3.6.1.5	Apyrase	ENTP3_HUMAN	1T6C	Ribonuclease H-like	Actin-like ATPase domain	9675246, 8955160	
	3.6.1.5	Apyrase	APY_CIMLE	2H2N	5-bladed beta-propeller	Apyrase	9804829, 15006348	
75	3.6.1.11	Exopolyphosphatase	PPX_ECOLI	1U6Z	HD-domain/PDEase-like & Ribonuclease H-like	Ppx associated domain	8212131	Two distinct structural folds
	3.6.1.11	Exopolyphosphatase	PPX1_YEAST	1K20	DHH phosphoesterases	Mn-dependent inorganic pyrophosphatase	7860598	
76	3.6.1.17	Bis(5'-nucleosyl) - tetraphosphatase (asymmetrical)	APH1_SCHPO	1FHI	HIT-like	HIT family	8554540	Three distinct structural folds
	3.6.1.17	Bis(5'-nucleosyl) - tetraphosphatase (asymmetrical)	AP4A_HUMAN	1XSA	Nudix	MutT-like	7487923	

	3.6.1.17	Bis(5'-nucleosyl) - tetraphosphatase (asymmetrical)	PRPE_BACSU	1G5B	Metallo-dependent phosphatases	Protein serine/ threonine phosphatase	12059787	
77	3.8.1.2	2-Haloalkanoate dehalogenase	HAD1_PSEUC	1QQ5	HAD-like	HAD-like hydrolase	1556080, 10521454	Different stereospecificity
	3.8.1.9	2-Haloalkanoate dehalogenase	HADD_PSEPU	3BJX	N/A	Haloacid dehalogenase DehI	1556080, 18353360	
78	3.8.1.3	Haloacetate dehalogenase	DEH1_MORSB	1G5F	Alpha/beta-hydrolases	Alpha/beta hydrolase_1	1512562, 11939779	Two distinct structural folds
	3.8.1.3	Haloacetate dehalogenase	DEH2_MORSB	1JUD	HAD-like	HAD-like hydrolase	8702766	
79	4.1.1.17	Ornithine decarboxylase	DCOS_ECOLI	1ORD	PLP-dependent transferase	Orn/Lys/Arg decarboxylase, class I	7563080	Two distinct structural folds
	4.1.1.17	Ornithine decarboxylase	DCOR_HUMAN	1D7K	TIM beta/alpha barrel	Orn/Lys/Arg decarboxylase class II	2587220, 2318872	
80	4.1.1.19	Arginine decarboxylase	ADIA_ECOLI	2VYC	PLP-dependent transferase	Orn/Lys/Arg decarboxylase, class I	8383109, 19298070	Three distinct structural folds
	4.1.1.19	Arginine decarboxylase	SPEA_ECOLI	1TWI	TIM beta/alpha barrel	Orn/Lys/Arg decarboxylase class II	4571773	
	4.1.1.19	Arginine decarboxylase	PDAD_METJA	1N2M	Pyruvoyl-dependent histidine and arginine decarboxylases	Pyruvoyl-dependent ArgDC	11980912	
81	4.1.1.22	Histidine decarboxylase	DCHS_ENTAE	1JS3	PLP-dependent transferase	Pyridoxal-dependent decarboxylase	2033044	Two distinct structural folds
	4.1.1.22	Histidine decarboxylase	DCHS_LACS3	1HQ6	Pyruvoyl-dependent histidine and arginine decarboxylases	Histidine decarboxylase	2857718	

82	4.1.1.50	S-adenosylmethionine decarboxylase	SPED_ECOLI	1TLU	S-adenosylmethionine decarboxylase	SAM decarboxylase	3546296, 17567041	Same fold, same superfamily
	4.1.1.50	S-adenosylmethionine decarboxylase	DCAM_HUMAN	1MSV	S-adenosylmethionine decarboxylase	SAM decarboxylase	10378277	
83	4.1.2.13	Fructose 1,6-bisphosphate aldolase	ALF_ECOLI	1DOS	TIM beta/alpha barrel	Fructose-bisphosphate aldolase class II	8436219, 8836102	Same fold, same superfamily
	4.1.2.13	Fructose 1,6-bisphosphate aldolase	ALDOA_HUMAN	1ALD	TIM beta/alpha barrel	Fructose-bisphosphate aldolase class I	3355497, 2335208	
84	4.1.2.15	Phospho-2-keto-3-deoxyheptonate aldolase	AROG_ECOLI	1GG1	TIM beta/alpha barrel	DAHP synthetase I	10425687	Same fold, same superfamily
	4.1.2.15	Phospho-2-keto-3-deoxyheptonate aldolase	AROF_STRCO	2B7O	TIM beta/alpha barrel	Class-II DAHP synthetase	8760910, 16288916	
85	4.1.2.40	Tagatose 1,6-bisphosphate aldolase	KBAY_ECOLI	1GVF	TIM beta/alpha barrel	Fructose-bisphosphate aldolase class II	11940603	Same fold, same superfamily
	4.1.2.40	Tagatose 1,6-bisphosphate aldolase	LACD_LACLA	1TO3	TIM beta/alpha barrel	DeoC/LacD family aldolase	1901863	
86	4.2.1.1	Carbonate dehydratase	CYNT_ECOLI	1EKJ	Resolvase-like	beta-carbonic anhydrase	1740425	Three distinct structural folds
	4.2.1.1	Carbonate dehydratase	CAH1_HUMAN	2FOY	Carbonic anhydrase		804171, 4207120	
	4.2.1.1	Carbonate dehydratase	CAH_METTE	1QQ0	Single-stranded left-handed beta-helix	gamma-carbonic anhydrase-like	8041719	
87	4.2.1.2	Fumarate hydratase	FUMA_ECOLI	2ISB	The swivelling beta/beta/alpha domain	Class I fumarase family	1917897	Two distinct structural folds
	4.2.1.2	Fumarate hydratase	FUMC_ECOLI	1FUO	L-aspartase-like	L-aspartase/fumarase	8909293, 3282546	

88	4.2.1.10	3-dehydroquinate dehydratase	AROQ_ACTPL	1UQR	Flavodoxin-like	Type II 3-dehydroquinate dehydratase	PubMed	Two distinct structural folds
	4.2.1.10	3-dehydroquinate dehydratase	AROD_ECOLI	1QFE	TIM beta/alpha barrel	Class I aldolase	3541912	
89	4.2.1.13	L-serine ammonia-lyase (now EC 4.3.1.17)	SDHL_ECOLI	2IQQ	FwdE/GAPDH domain	FeS-dependent L-serine dehydratase	2504697	Two distinct structural folds
	4.2.1.13	L-serine ammonia-lyase (now EC 4.3.1.17)	SDHL_HUMAN	1PWH	Tryptophan synthase beta subunit-like PLP-dependent enzymes	DeoC/LacD family aldolase	14596599	
90	4.2.1.51	Prephenate dehydratase	PHEA_ECOLI	2QMW	Periplasmic binding protein-like II	Prephenate dehydratase	18171624	Same fold, same superfamily
	4.2.1.51	Prephenate dehydratase	PHEC_PSEAE	1XT8	Periplasmic binding protein-like II	Bacterial extracellular solute-binding proteins	92129331	
91	4.2.2.2	Pectate lyase	PEL3_ERWCA	1PLU	Single-stranded right-handed beta-helix	Pectate lyase C	12226275	Two distinct structural folds, different families
	4.2.2.2	Pectate lyase	PELP_PECCC	2V8K	Alpha/alpha toroid	Periplasmic pectate lyase	2695748, 17881361	
	4.2.2.2	Pectate lyase	PELL_ERWCH	1RU4	Single-stranded right-handed beta-helix	Polysaccharide lyase family 9	14670977	
	4.2.2.2	Pectate lyase	Q47471_ERWCA	3B4N	Single-stranded right-handed beta-helix	Pectate lyase (transeliminase)	7756691	
92	4.2.2.3	Poly(β -D-mannuronate) lyase	ALGL_PSEFL	1QAZ	Alpha/alpha toroid	Chondroitin AC/alginate lyase	12775688	Three distinct structural folds
	4.2.2.3	Poly(β -D-mannuronate) lyase	ALYA_KLEPN	1VAV	Concanavalin A-like lectins/glucanases	Concanavalin A-like lectins/glucanases	8200539	
	4.2.2.3	Poly(β -D-mannuronate) lyase	ALYP_PESO	1OFM	Single-stranded right-handed beta-helix		8336113, 8319887	

93	4.2.99.18	DNA-(apurinic or apyrimidinic site) lyase	END3_ECOLI	2ABK	DNA-glycosylase	Endonuclease III	2669955	Four distinct structural folds
	4.2.99.18	DNA-(apurinic or apyrimidinic site) lyase	APEX1_HUMAN	1E9N	DNase I-like	DNase I-like	1383925 , 1380694	
	4.2.99.18	DNA-(apurinic or apyrimidinic site) lyase	APN1_YEAST	1QTW	TIM beta/alpha barrel	Endonuclease IV	3056935	
	4.2.99.18	DNA-(apurinic or apyrimidinic site) lyase	FPG_ECOLI	1K82	MutM-like DNA repair proteins	MutM-like DNA repair proteins	11106507 , 14607836 , 11912217	
94	4.6.1.1	Adenylate cyclase	CYAA_ECOLI	N/A	N/A	Adenylate cyclase class I	6344011 , 92011391	Four distinct structural folds
	4.6.1.1	Adenylate cyclase	CYAA_BORPE	1YRU	EF-hand-like	Anthrax toxin LF (class II AC)	2897067 , 16138079	
	4.6.1.1	Adenylate cyclase	CYA1_HUMAN	1CS4	Ferrodoxin-like	Adenylate/guanylate cyclase (class III AC)	8314585	
	4.6.1.1	Adenylate cyclase	O69199_AERHY	2FJT	CYTH-like phosphatases	CYTH domain (class IV AC)	9642185 , 16905149	
95	5.2.1.8	Peptidylprolyl isomerase	PPIA_ECOLI	1CLH	Cyclophilin-like	Cyclophilin	9501079 , 17909185	Two distinct structural folds
	5.2.1.8	Peptidylprolyl isomerase	FKBA_ECOLI	1Q6H	FKBP-like	FKBP-type PPIase	1379319	
96	5.3.1.8	Mannose-6-phosphate isomerase	MANA_STRMU	1QWR	Double-stranded beta-helix	RmlC-like cupins	8293960	Three distinct structural folds
	5.3.1.8	Mannose-6-phosphate isomerase	MANA_RHIME	2GZ6	Six-hairpin glycosidases	GlcNAc 2-epimerase	1452036	
	5.3.1.8	Mannose-6-phosphate isomerase	PGMI_SULAC	1TZB	SIS domain	SIS_domain	14551194	

97	5.4.2.1	Phosphoglycerate mutase	GPMA_ECOLI	1E59	Phosphoglycerate mutase	Phosphoglycerate mutase	11038361	Two distinct structural folds
	5.4.2.1	Phosphoglycerate mutase	GPMI_PSESM	1EJJ	Alkaline phosphatase-like	2,3-BPG-independent phosphoglycerate mutase	12076796	
98	5.4.2.8	Phosphomannomutase	RFBK_SALTY	1K2Y	Phosphoglucomutase	Phosphoglucomutase	PubMed	Two distinct structural folds
	5.4.2.8	Phosphomannomutase	PMM1_HUMAN	2FUC	HAD-like	Eukaryotic phosphomannomutase	9119384	
99	5.4.99.5	Chorismate mutase	CHMU_ENTAG	2AO2	Chorismate mutase II	Secreted chorismate mutase-like	8335631, 9497350, 7496534	Two distinct structural folds
	5.4.99.5	Chorismate mutase	CHMU_BACSU	1COM	Bacillus chorismate mutase-like	Chorismate mutase	8378335, 8046752	
100	5.5.1.1	Muconate cycloisomerase	CATB_PSEPU	1MUC	TIM beta/alpha barrel & Enolase N-terminal domain	D-glucarate dehydratase-like	3609743, 3612800	Two distinct structural folds
	5.5.1.1	Muconate cycloisomerase	MLE_TRICU	1JOF	7-bladed beta-propeller	WD40/YVTN repeat	8110801, 11937053	
101	5.99.1.2	DNA topoisomerase	TOP1_ECOLI	1CY1	Prokaryotic type I DNA topoisomerase	Prokaryotic type I DNA topoisomerase	PubMed	Two distinct structural folds
	5.99.1.2	DNA topoisomerase	TOP1_HUMAN	1LPQ	DNA-breaking-rejoining enzymes	Eukaryotic DNA topoisomerase I	98155246, 8747458, 16352556	
102	6.1.1.6	Lysine-tRNA ligase	SYK1_ECOLI	1BBU	Class II aaRS and biotin synthetases	Class II aminoacyl-tRNA synthetase	7735833, 11887185	Two distinct structural folds
	6.1.1.6	Lysine-tRNA ligase	SYK_PYRHO	1IRX	Adenine nucleotide alpha hydrolase	Class I lysyl-tRNA synthetase	9353192, 11887185	

103	<u>6.1.1.14</u>	Glycine-tRNA ligase	<u>SYGA_ECOLI</u> <u>SYGB_ECOLI</u>	<u>1J5W</u>	<u>Class II aaRS and biotin synthetases</u>	Glycyl-tRNA synthetase, alpha and beta subunits	<u>6309809</u>	Same fold, same superfamily
	<u>6.1.1.14</u>	Glycine-tRNA ligase	<u>SYG_HUMAN</u>	<u>1ATI</u>	<u>Class II aaRS and biotin synthetases</u>	Class-II aminoacyl-tRNA synthetase	<u>7753621</u>	
104	<u>6.3.2.2</u>	Glutamate-cysteine ligase	<u>GSH1_ECOLI</u>	<u>1VA6</u>	<u>Glutamine synthetase/guanido kinase</u>	<u>Glutamate-cysteine ligase</u>	<u>86232579</u>	Predicted same fold
	<u>6.3.2.2</u>	Glutamate-cysteine ligase	<u>GSH1_HUMAN</u>	N/A	<i>Glutamine synthetase (predicted)</i>	<u>Glutamate-cysteine ligase</u>	<u>12663448,</u> <u>9675072</u>	
105	<u>6.3.2.3</u>	Glutathione synthase	<u>GSHB_ECOLI</u>	<u>1GSA</u>	<u>PreATP-grasp domain & ATP-grasp</u>	Prokaryotic glutathione synthetase	<u>9010922</u>	Same fold, same superfamily, circular permutation
	<u>6.3.2.3</u>	Glutathione synthase	<u>GSHB_HUMAN</u>	<u>2HGS</u>	<u>PreATP-grasp domain & ATP-grasp</u>	Eukaryotic glutathione synthetase	<u>10369661</u>	