

Table S1. Common features of the proteins from several structural superfamilies

(Supplementary material to the review by M.Y. Galperin and E.V. Koonin “Divergence and convergence in enzyme evolution”, submitted for publication in the *Journal of Biological Chemistry*, 2011)

Superfamily name	Member enzymes (PDB code and/or EC number, where available)	Common traits of the superfamily members	References
ATP-grasp	<p>Glutathione synthetase (1gsh, 2hgs, EC 6.3.2.3), D-ala-D-ala ligase (1ioy, EC 6.3.2.4), D-ala-D-lactate ligase (1e4e, EC 6.1.2.1), biotin carboxylase (1dv1, EC 6.3.4.14), carbamoyl phosphate synthase (1jdb, EC 6.3.5.5), pyruvate phosphate dikinase (1dik, EC 2.7.9.1), phosphoribosyl-amine-glycine ligase PurD (1gso, EC 6.3.4.13), phosphoribosyl glycinamide formyltransferase PurT (1eyz, EC 2.1.2.-), N⁵-carboxyaminoimidazole ribonucleotide synthase PurK (1b6s, EC 6.3.4.18), 5-formaminoimidazole-4-carboxamide ribonucleotide synthase PurP (2r7k, EC 6.3.4.-), tubulin-tyrosine ligase (EC 6.3.2.25), tubulin glycyase (EC 6.3.2.-), tubulin polyglutamylase, ribosomal protein S6-glutamate ligase RimK, succinate-CoA ligase (1jki, EC 6.2.1.5), ATP-citrate synthase (3mwd, EC 2.3.3.8), malate-CoA ligase (EC 6.2.1.9), synapsin (1aux), α-aminoadipate-LysW ligase LysX (1uc9, EC 6.3.2.n4), glutathionylspermidine synthetase GspS, (2io9, EC 6.3.1.8), D-aspartate ligase Asl_{fm} (EC 6.3.1.12), carnosine synthase (EC 6.3.2.11), γ-F420-2:α-L-glutamate ligase CofF (EC 6.3.2.32), tetrahydromethanopterin:α-L-glutamate ligase MptN (EC 6.3.2.33), alanine-anticapsin ligase BacD/YwfE (EC 6.3.2.28), L-amino acid ligase (EC 6.3.2.28), N-acetylasparylglutamate synthase, β-citrylglutamate synthase, nikkomycin biosynthesis carboxylase SanS, inositol 1,3,4-trisphosphate 5/6-kinase (1z2n, EC 2.7.1.134), mycosporine glycine synthetase Ava_3856</p>	<p>Conserved structural core (≤ 4.3 Å Cα RMSD on ≥ 230 aa); common ATP-binding residues, which include two conserved Lys/Arg residues that bind α- and β-phosphates of ATP, a Glx/Asp that interacts with adenine amino group and the N⁶ atom, hydrophobic residues that bind the adenine ring, and three Glx/Asx residues that coordinate Mg²⁺ ions; a common catalytic mechanism that includes formation of a phosphoacyl intermediate</p>	<ol style="list-style-type: none"> Superfamily descriptions; Structures of the superfamily members; Descriptions of new superfamily members
Alkaline phosphatase	<p>Alkaline phosphatase (1alk, EC 3.1.3.1), phosphoglycerate mutase (1o98, EC 5.4.2.1), phosphopentomutase (3ot9, EC 5.4.2.7), acid phosphatase (2d1g, EC 3.1.3.2), nucleotide pyrophosphatase/phosphodiesterase (2gso, EC 3.1.4.39), arylsulfatase (1auk, EC 3.1.6.1), N-acetylgalactosamine 4-sulfatase (1fsu, EC 3.1.6.12), steryl-sulfatase (1p49, EC 3.1.6.2), phosphonoacetate hydrolase (1ei6, EC 3.11.1.2), phosphonopyruvate hydrolase (EC 3.11.1.3), phosphoglycerol transferase MdoB (EC 2.7.8.20), phosphonate monoester hydrolase/phosphodiesterase (2vqr), archaeal phosphoglycerate mutase (3kd8, EC 5.4.2.1), GPI phosphoethanolamine transferase PIG-N/Mcd4, LPS:phosphoethanolamine transferase EptB, polyglycerol phosphate lipoteichoic acid synthase LtaS (2w8d, EC 2.7.8.-), pilin phospho-form transferase PptA, inorganic pyrophosphatase (EC 3.6.1.1)</p>	<p>Conserved structural core (≤ 3.6 Å Cα RMSD on ≥ 220 aa), conserved metal (Zn²⁺, Mn²⁺, or Mg²⁺)-binding His and Asp residues; common catalytic mechanism that includes phosphorylation (sulfatation) of the active-site Ser/Thr/fGly residue</p>	<ol style="list-style-type: none"> Superfamily descriptions; Structures of the superfamily members; Descriptions of new superfamily members

Cupin	<p>Oxalate oxidase (1fi2, EC 1.2.3.4), oxalate decarboxylase (1uw8, EC 4.1.1.2), gentisate 1,2-dioxygenase (2d40, EC 1.13.11.4), homogentisate 1,2-dioxygenase (1ey2, EC 1.13.11.5), 3-hydroxyanthranilate 3,4-dioxygenase (1yfu, EC 1.13.11.6), cysteine dioxygenase (3eln, EC 1.13.11.20), quercetin 2,3-dioxygenase (1juh, EC 1.13.11.24), acetylaceton dioxygenase Dke1 (3bal, EC 1.13.11.50), 1,2-dihydroxy-3-keto-5-methylthiopentene (acireductone) dioxygenase (1vr3, EC 1.13.11.-), 1-hydroxy-2-naphthoate dioxygenase (EC 1.13.11.38), phosphomannose isomerase (1pmi, EC 5.3.1.8), glucose-6-phosphate isomerase (1qy4, EC 5.3.1.9), dTDP-4-dehydrorhamnose 3,5-epimerase RmlC (1dzt, EC 5.1.3.13), lyxose isomerase (3mpb, EC 5.3.1.15), 5-keto-4-deoxyuronate isomerase Kdul (1xru, 5.3.1.17), dTDP-4-keto-6-deoxy-glucose-5-epimerase EvaD (1oi6), dTDP-6-deoxy-3,4-keto-hexulose isomerase FdtA (2pa7), ectoine synthase EctC (EC 4.2.1.108), ureidoglycolate hydrolase AIIA (1yqc, EC 3.5.3.19), hydroxypropylphosphonic acid epoxidase (2bnm), dimethylsulfoniopropionate lyase DddL (EC 4.4.1.3), phaseolin (2phl), canavalin (2cau), pirin (1j1l), auxin-binding protein (1lrh), ethanolamine utilization protein EutQ (2pyt), polyketide cyclase RemF (3ht1), bacilysin biosynthesis protein BacB (3h7j), cuproprotein CuaA (2xla), vitamin K-dependent gamma-carboxylase</p>	<p>Conserved structural core (<4.6 Å Cα RMSD on >99 aa), partly conserved metal (Mn²⁺, Fe²⁺, Cu²⁺, Ni²⁺, or Zn²⁺)-binding His residues that often form Gx₅HxHx_{3,4}Ex₆G and GDx₄PxGx₂Hx₃N motifs; common catalytic mechanism includes binding of dioxygen to the metal atom and the substrate with the formation of a peroxidic intermediate</p>	<ol style="list-style-type: none"> Superfamily descriptions; Structures of the superfamily members; Descriptions of new superfamily members
HD-domain phosphohydrolases	<p>3',5'-cAMP/cGMP phosphodiesterase (2hd1, EC 3.1.4.17), ppGpp hydrolase (1vj7, EC 3.1.7.2), exopolyphosphatase (1u6z, EC 3.6.1.11), dNMP 5'-nucleotidase YfbR (2par, EC 3.1.3.5), dNTP triphosphohydrolase (2dqb, EC 3.1.5.-), dGTPase (3bg2, EC 3.1.5.1), cyanamide hydratase (EC 4.2.1.69), 2',3'-cAMP/cGMP hydrolase (EC 3.1.4.16), 3'-5' exoribonuclease YhaM, c-di-GMP phosphodiesterase (EC 3.1.4.52), 7,8-dihydro-D-neopterin 2',3'-cyclic phosphate phosphodiesterase, uridylyl-removing enzyme GlnD, myo-inositol oxygenase MioX (2huo, EC 1.13.99.1)</p>	<p>Conserved structural core (<3.6 Å Cα RMSD on >105 aa), conserved metal (Mn²⁺, Mg²⁺, Co²⁺, or Fe²⁺)-binding His and Asp residues organized into the Hx₂₀₋₅₀HDx₆₀₋₁₄₀D motif</p>	<ol style="list-style-type: none"> Superfamily description; Descriptions of the superfamily members
Ntn-hydrolases	<p>Penicillin acylase (1pnl, EC 3.5.1.11), glutamine 5-phosphoribosyl-1-pyrophosphate amidotransferase (1ecc, EC 2.4.2.14), proteasome subunit (1pma, EC 3.4.99.46), glucosamine 6-phosphate synthase (1xff, EC 2.6.1.16), protease HslV (1m4y, EC 3.4.25.-), aspartylglucosaminidase (1apy, EC 3.5.1.26), γ-glutamyltranspeptidase (2dg5, EC 2.3.2.2), asparagine synthetase (1ct9, EC 6.3.5.4), β-lactam synthetase (1jgt, EC 6.3.3.4), glutamate synthase (1ea0, EC 1.4.1.13), L-asparaginase (2gez, EC 3.5.1.1), threonine aspartase (2a8i, EC 3.4.25.-), acyl-CoA: isopenicillin N acyltransferase (2x1c, EC 2.3.1.164), bile salt hydrolase (2hez, EC 3.5.1.24), N-acyl homoserine lactone acylase PvdQ (2wyb, EC 3.5.1.97), acid ceramidase (EC 3.5.1.23), <i>IMP cyclohydrolase PuroO</i> (2ntk, EC 3.5.4.10)</p>	<p>Common structural core (<4.1 Å Cα RMSD on >96 aa) decorated with a variety of structural elements; sequence conservation is limited to the N-terminal β-hairpin that contains the catalytic Ser, Cys or Thr residue</p>	<ol style="list-style-type: none"> Superfamily descriptions; Structures of the superfamily members; Descriptions of new superfamily members

Root mean square deviation (RMSD) values of Cα traces were taken from [Dali](#) and [MMDB](#) databases