

Table S1: All Families hit by the present Dali search

14-3-3 protein	ALDH-like
1-deoxy-D-xylulose-5-phosphate reductoisomerase, C-terminal domain	Allosteric chorismate mutase
2Fe-2S ferredoxin domains from multidomain proteins	alpha-Amylases, C-terminal beta-sheet domain
3-Methyladenine DNA glycosylase III (MagIII)	alpha-catenin/vinculin
5-carboxymethyl-2-hydroxymuconate isomerase (CHMI)	alpha-D-glucuronidasE-Hyaluronidase catalytic domain
5' nucleotidase-like	alpha-D-glucuronidase, N-terminal domain
5' to 3' exonuclease catalytic domain	Alpha-hemoglobin stabilizing protein AHSP
5' to 3' exonuclease, C-terminal subdomain	alpha-Subunit of urease
6-phosphogluconate dE-Hydrogenase-like, N-terminal domain	alpha-subunit of urease, catalytic domain
ABC transporter ATPase domain-like	Amidase signature (AS) enzymes
Aconitase B, N-terminal domain	A middle domain of Talin 1
Aconitase iron-sulfur domain	Aminoacid dE-Hydrogenase-like, C-terminal domain
Actin/HSP70	Aminoacid dE-Hydrogenases
Acyl-CoA binding protein	Aminoglycoside phosphotransferases
acyl-CoA oxidase C-terminal domains	AmyC C-terminal domain-like
acyl-CoA oxidase N-terminal domains	AmyC N-terminal domain-like
Adapter protein APS, dimerisation domain	Amylase, catalytic domain
Adenylation domain of NAD+-dependent DNA ligase	Animal lipoxigenases
Adenyllyl and guanylyl cyclase catalytic domain	Anticodon-binding domain of a subclass of class I aminoacyl-tRNA synthetases
Adenyllylcyclase toxin (the edema factor)	Antioxidant defense protein AhpD
a domain/subunit of cytochrome bc1 complex (Ubiquinol-cytochrome c reductase)	Anti-sigma factor AsiA
Aerobic respiration control sensor protein, ArcB	Apolipophorin-III
AF0060-like	Apolipoprotein
AF0941-like	Aquaporin-like
AF1104-like	Archaeal DNA-binding protein
AgoG-like	Arfaptin, Rac-binding fragment
Alcohol dE-Hydrogenase-like, C-terminal domain	Arginyl-tRNA synthetase (ArgRS), N-terminal 'additional' domain
Alcohol dE-Hydrogenase-like, N-terminal domain	Aristolochene/pentalenene synthase
AldE-Hyde ferredoxin oxidoreductase, C-terminal domains	Armadillo repeat
AldE-Hyde ferredoxin oxidoreductase, N-terminal domain	Arp2/3 complex 16 kDa subunit ARPC5
	Arylsulfatase

Aspartate/ornithine carbamoyltransferase	Calmodulin-like
Aspartokinase allosteric domain-like	Calpain large subunit, catalytic domain (domain II)
ATP synthase	Calpain large subunit, middle domain (domain III)
ATP synthase (F1-ATPase), gamma subunit	cAMP-binding domain
a tRNA synthase domain	CAPPD, an extracellular domain of amyloid beta A4 protein
Atu0492-like	Cell cycle transcription factor e2f-dp
Avirulence protein AvrPto	Cell division protein ZapA-like
B12-dependent (class II) ribonucleotide reductase	Cellulases catalytic domain
Bacterial dinuclear zinc exopeptidases	Cellulose-binding domain family III
Bacterial exopeptidase dimerisation domain	Centromere-binding
Bacterial GAP domain	Cfr10I/Bse634I
Bacterial glucoamylase C-terminal domain-like	Chaperone J-domain
Bacterial glucoamylase N-terminal domain-like	Chemotaxis phosphatase CheZ
Bacterial photosystem II reaction centre, L and M subunits	Chemotaxis protein CheA P1 domain
Bacterial tryptophan 2,3-dioxygenase	CheW-like
Bacteriophage CII protein	Cholesterol oxidase
Bacteriorhodopsin-like	Choline/Carnitine O-acyltransferase
BAG domain	Circadian clock protein KaiA, C-terminal domain
Band 7/SPFH domain	Class I alpha-1,2-mannosidase, catalytic domain
BAR domain	Class I aminoacyl-tRNA synthetases (RS), catalytic domain
Barrier-to-autointegration factor, BAF	Class II aminoacyl-tRNA synthetase (aaRS)-like, catalytic domain
BAS1536-like	Class-II DAHP synthetase
BC ATP-binding domain-like	Class II glutamine amidotransferases
BC C-terminal domain-like	Class III anaerobic ribonucleotide reductase NRDD subunit
Bcl-2 inhibitors of programmed cell death	clathrin assemblies
BC N-terminal domain-like	Clostridium neurotoxins, catalytic domain
Beta-D-glucan exohydrolase, C-terminal domain	Clostridium neurotoxins, "coiled-coil" domain
beta-Lactamase/D-ala carboxypeptidase	Clostridium neurotoxins, C-terminal domain
beta-Phosphoglucomutase-like	Clostridium neurotoxins, the second last domain
Biotin repressor-like	CMD-like
BRCA2 helical domain	Cobalamin adenosyltransferase
BRCA2 tower domain	Cobalamin (vitamin B12)-binding domain
Bromodomain	CO dE-Hydrogenase flavoprotein C-terminal domain-like
Calcium ATPase, transduction domain A	CO dE-Hydrogenase flavoprotein N-terminal domain-like
Calcium ATPase, transmembrane domain M	

CO dE-Hydrogenase ISP C-domain like	Cytochrome c'-like
CO dE-Hydrogenase molybdoprotein N-domain-like	Cytochrome c oxidase subunit III-like
Coiled-coil domain of nucleotide exchange factor GrpE	Cytochrome c oxidase subunit II-like, transmembrane region
Cold shock DNA-binding domain-like	Cytochrome c oxidase subunit I-like
Colicin E3 receptor domain	Cytochrome P450
Computational models partly based on NMR data	Cytochrome p450 reductase N-terminal domain-like
Conserved hypothetical protein MTH1747	Cytoplasmic domain of inward rectifier potassium channel
CorA soluble domain-like	D-aminoacid aminotransferase-like PLP-dependent enzymes
Coronavirus NSP8-like	DBL homology domain (DH-domain)
Coronavirus S2 glycoprotein	Dcp2 box A domain
COX17-like	Decarboxylase
Creatinase/aminopeptidase	DE-Hydroquinate synthase, DHQS
Creatinase/prolidase N-terminal domain	delta-Endotoxin, C-terminal domain
Crotonase-like	delta-Endotoxin (insecticide), middle domain
Cryptochrome/photolyase FAD-binding domain	delta-Endotoxin (insecticide), N-terminal domain
Cryptochrome/photolyase, N-terminal domain	Designed four-helix bundle protein
CSE2-like	Designed single chain threE-Helix bundle
C-terminal domain of alpha and beta subunits of F1 ATP synthase	DHN aldolase/epimerase
C-terminal domain of class I lysyl-tRNA synthetase	Dihydridipicolinate reductase-like
C-terminal domain of DFF45/ICAD (DFF-C domain)	Dimeric chorismate mutase
C-terminal domain of eukaryotic peptide chain release factor subunit 1, ERF1	Dimerisation domain of CENP-B
C-terminal domain of Ku80	Dimerization-anchoring domain of cAMP-dependent PK regulatory subunit
C-terminal fragment of elongation factor SelB	DinB-like
C-terminal fragment of thermolysin	Diol dE-Hydrtase, gamma subunit
C-terminal UvrC-binding domain of UvrB	DLC
CUE domain	DNA-binding N-terminal domain of transcription activators
Cullin homology domain	DNA-binding protein Mj223
Cullin repeat	DNA damage-inducible protein DinI
Cyclin	DnaK suppressor protein DksA, alpha-hairpin domain
Cyclophilin (peptidylprolyl isomerase)	DNA ligase/mRNA capping enzyme postcatalytic domain
Cytochrome b562	DNA polymerase I
Cytochrome b of cytochrome bc1 complex (Ubiquinol-cytochrome c reductase)	DNA polymerase III clamp loader subunits, C-terminal

domain	Exocyst complex component
DnaQ-like 3'-5' exonuclease	Exodeoxyribonuclease V beta chain (RecC), C-terminal domain
DNA repair protein MutS, domain I	EXOSC10 HRDC domain-like
DNA repair protein MutS, domain II	Extended AAA-ATPase domain
DNA repair protein MutS, domain III	F1F0 ATP synthase subunit A
DNA topoisomerase IV, alpha subunit	F1F0 ATP synthase subunit C
Domain of poly(ADP-ribose) polymerase	FAD-linked oxidases, N-terminal domain
Domain of the SRP/SRP receptor G-proteins	FAD-linked reductases, N-terminal domain
Double Clp-N motif	FAD/NAD-linked reductases, dimerisation (C-terminal) domain
double-SIS domain	FAD/NAD-linked reductases, N-terminal and central domains
E2 regulatory, transactivation domain	FAT domain of focal adhesion kinase
EF2458-like	Fe,Mn superoxide dismutase (SOD), C-terminal domain
EF-hand modules in multidomain proteins	Fe,Mn superoxide dismutase (SOD), N-terminal domain
eIF-2-alpha, C-terminal domain	FemXAB nonribosomal peptidyltransferases
eIF2alpha middle domain-like	Ferredoxin domains from multidomain proteins
Electron transfer flavoprotein-ubiquinone oxidoreductase-like	Ferritin
Elongation factor Ts (EF-Ts), dimerisation domain	Fertilization protein
EntA-Im	FHV B2 protein-like
Enzyme IIa from lactose specific PTS, IIa-lac	Fibrinogen coiled-coil and central regions
Enzyme I of the PEP:sugar phosphotransferase system HPr-binding (sub)domain	FIS-like
EpoxidE-Hydrolase	FKBP12-rapamycin-binding domain of
Epsilon subunit of F1F0-ATP synthase C-terminal domain	FKBP-rapamycin-associated protein (FRAP)
Epsilon subunit of F1F0-ATP synthase N-terminal domain	FKBP immunophilin/proline isomerase
ERP29 C domain-like	Flagellar export chaperone FliS
ERP29 N domain-like	FMN-linked oxidoreductases
ESAT-6 like	Formate dehydrogenase N, cytochrome (gamma) subunit
E-set domains of sugar-utilizing enzymes	Formin homology 2 domain (FH2 domain)
ETF-QO domain-like	Fumarate reductase respiratory complex cytochrome b subunit, FrdC
Eukaryotic DNA topoisomerase I, catalytic core	Fungal zinc peptidase
Eukaryotic DNA topoisomerase I, dispensable insert domain	GABA-aminotransferase-like
Eukaryotic DNA topoisomerase I, N-terminal DNA-binding fragment	GAPDH-like
Eukaryotic type KH-domain (KH-domain type I)	

GAT domain	Heat-inducible transcription repressor HrcA, N-terminal domain
Gated mechanosensitive channel	Heat shock protein 70kD (HSP70), C-terminal subdomain
G domain-linked domain	Heat shock protein 70kD (HSP70), peptide-binding domain
Glutamate–cysteine ligase	Hect, E3 ligase catalytic domain
Glutamyl tRNA-reductase catalytic, N-terminal domain	Helical scaffold and wing domains of SecA
Glutamyl tRNA-reductase dimerization domain	Hemerythrin
Glutathione peroxidase-like	Hepatitis B viral capsid (hbcag)
Glutathione S-transferase (GST), C-terminal domain	Hermes dimerisation domain
Glutathione S-transferase (GST), N-terminal domain	Hermes transposase-like
Glyceraldehyde-3-phosphate dehydrogenase-like, N-terminal domain	HisE-like (PRA-PH)
Glycerol-3-phosphate (1)-acyltransferase	Histidine kinase
Glycerol-3-phosphate dehydrogenase	HlyD-like secretion proteins
(Glycosyl)asparaginase	HMA, heavy metal-associated domain
Glycosyltransferase family 36 C-terminal domain	HMD dimerization domain-like
Glycosyltransferase family 36 N-terminal domain	HMG-box
GMC oxidoreductases	Homeodomain
G proteins	Homodimeric domain of signal transducing histidine kinase
GreA transcript cleavage factor, C-terminal domain	HP1531-like
GreA transcript cleavage protein, N-terminal domain	HR1 repeat
GRIP domain	HrcA C-terminal domain-like
GroEL chaperone, ATPase domain	HRDC domain from helicases
GroEL-like chaperone, apical domain	HSC20 (HSCB), C-terminal oligomerisation domain
GroEL-like chaperone, intermediate domain	Hsp90 co-chaperone CDC37
Group II chaperonin (CCT, TRIC), apical domain	HSP90 C-terminal domain
Group II chaperonin (CCT, TRIC), ATPase domain	Hut operon positive regulatory protein HutP
Group II chaperonin (CCT, TRIC), intermediate domain	Hyaluronate lyase-like catalytic, N-terminal domain
Group I mobile intron endonuclease	Hyaluronate lyase-like, central domain
Group V grass pollen allergen	Hyaluronate lyase-like, C-terminal domain
GTP cyclohydrolase I	Hyaluronidase N-terminal domain-like
half-ferritin	Hyaluronidase post-catalytic domain-like
Haloperoxidase (bromoperoxidase)	Hybrid and chimeric proteins
HAL/PAL-like	Hybrid cluster protein (prismane protein)
HCDH C-domain-like	Hypothetical protein D-63
Head domain of nucleotide exchange factor GrpE	Hypothetical protein MTH393

Hypothetical protein MTH677	domain
Hypothetical protein Ta1238	LeuD-like
Hypothetical protein TM1457	Lipoxygenase N-terminal domain
Hypothetical protein VC0424	Long-chain cytokines
Hypothetical protein YfhH	L-sulfolactate dE-Hydrogenase-like
Hypothetical protein YhaI	Magnesium transport protein CorA, transmembrane region
Hypothetical Protein YjhP	Mago nashi protein
IF2B-like	Malate synthase G
I/LWEQ domain	Malic enzyme N-domain
IMD domain	MarR-like transcriptional regulators
Influenza hemagglutinin (stalk)	Mason-Pfizer monkey virus matrix protein
Inositol	MazG-like
monophosphatase/fructose-1,6-bisphosphatase-like	Mechanosensitive channel protein MscS (YggB), C-terminal domain
Inositol polyphosphate 5-phosphatase (IPPP5)	Mechanosensitive channel protein MscS (YggB), middle domain
Insect pheromone/odorant-binding proteins	Mechanosensitive channel protein MscS (YggB), transmembrane region
Insert subdomain of RNA polymerase alpha subunit	MED7 hinge region
Interferon-induced guanylate-binding protein 1 (GBP1), C-terminal domain	Medium chain acyl-CoA dE-Hydrogenase-like, C-terminal domain
Interferons/interleukin-10 (IL-10)	Medium chain acyl-CoA dE-Hydrogenase, NM (N-terminal and middle) domains
IpaD-like	Membrane ion ATPase
Iron-containing alcohol dE-Hydrogenase	Meta-cation ATPase, catalytic domain P
Isoprenyl diphosphate synthases	Metal cation-transporting ATPase, ATP-binding domain N
ISY1 N-terminal domain-like	Methane monooxygenase-Hydrolase, gamma subunit
KaiB-like	Methicillin resistance protein FemA probable tRNA-binding arm
L27 domain	Methionine synthase domain
Lactate & malate dE-Hydrogenases, C-terminal domain	Methionine synthase SAM-binding domain
Lambda integrase-like, catalytic core	Methionyl-tRNA synthetase (MetRS), Zn-domain
lambda integrase N-terminal domain	Methyl-accepting chemotaxis protein (MCP) signaling domain
Large subunit	Methyl-coenzyme M reductase alpha and beta chain
L-aspartase/fumarase	
LcrE-like	
LDH N-terminal domain-like	
LemA-like	
Lesion bypass DNA polymerase (Y-family), catalytic domain	
Lesion bypass DNA polymerase (Y-family), little finger	

C-terminal domain	NadC N-terminal domain-like
Methyl-coenzyme M reductase alpha and beta chain	NAD+-dependent DNA ligase, domain 3
N-terminal domain	NADH oxidase/flavin reductase
Methylmalonyl-CoA mutase, N-terminal (CoA-binding) domain	NADPH-cytochrome p450 reductase FAD-binding domain-like
Middle domain of eukaryotic peptide chain release factor subunit 1, ERF1	NADPH-cytochrome p450 reductase-like
MIF4G domain-like	NagZ-like
MIF-related	Neurotransmitter-gated ion-channel transmembrane pore
Mismatch glycosylase	NF-kappa-B/REL/DORSAL transcription factors, C-terminal domain
MIT domain	Nickel-containing superoxide dismutase, NiSOD
Mitochondrial ATP synthase coupling factor 6	Nickel-iron hydrogenase, large subunit
Mitochondrial glycoprotein MAM33-like	NifU C-terminal domain-like
Mob1/phoceanin	NifU/IscU domain
modified HD domain	Nitric oxide (NO) synthase oxygenase domain
Molybdenum cofactor-binding domain	Nitrogenase iron protein-like
Molybdopterin synthase subunit MoaE	NKL-like
monodomain cytochrome c	Non-heme 11 kDa protein of cytochrome bc1 complex (Ubiquinol-cytochrome c reductase)
monomeric chorismate mutase	Nonstructural protein ns2, Nep, M1-binding domain
Motor proteins	Nop domain
MPP-like	NSP3 homodimer
mRNA decapping enzyme-like	N-terminal domain of adenylylcyclase associated protein, CAP
MTH1187-like	N-terminal domain of alpha and beta subunits of F1 ATP synthase
Multidrug efflux transporter AcrB pore domain; PN1, PN2, PC1 and PC2 subdomains	N-terminal domain of cbl (N-cbl)
Multidrug efflux transporter AcrB TolC docking domain; DN and DC subdomains	N-terminal domain of enzyme I of the PEP:sugar phosphotransferase system
Multidrug efflux transporter AcrB transmembrane domain	N-terminal domain of eukaryotic peptide chain release factor subunit 1, ERF1
MxiH-like	N-terminal domain of the circadian clock protein KaiA
Myb/SANT domain	N-terminal domain of the delta subunit of the F1F0-ATP synthase
Myosin S1 fragment, N-terminal domain	N-terminal, RNA-binding domain of nonstructural protein
N-acetyl transferase, NAT	
N-acetylglucosamine (NAG) epimerase	
NAD-binding domain of HMG-CoA reductase	
NadC C-terminal domain-like	

NS1	PHBH-like
Nuclear receptor ligand-binding domain	Phenylalanyl-tRNA synthetase (PheRS)
Nucleotide and nucleoside kinases	PhoB-like
NusA extra C-terminal domains	Phosphoinositide 3-kinase (PI3K), catalytic domain
Occludin/ELL domain	Phosphoinositide 3-kinase (PI3K) helical domain
Ohr/OsmC resistance proteins	Phosphate binding protein-like
Oligosaccharide phosphorylase	Phosphoenolpyruvate carboxylase
OmpH-like	PhosphonoacetaldE-HydE-Hydrolase-like
Orbivirus capsid	Phosphorelay protein-like
Orbivirus core	Phosphorelay protein luxU
Outer membrane efflux proteins (OEP)	Phosphoserine phosphatase RsbU, N-terminal domain
Outer surface protein C (OspC)	Photosystem I reaction center subunit XI, PsaL
Oxygen-evolving enhancer protein 3,	Photosystems
P40 nucleoprotein	PhoU-like
PadR-like	PIN domain
Pantothenate synthetase (Pantoate-beta-alanine ligase, PanC)	Plant invertase/pectin methylesterase inhibitor
PAPS sulfotransferase	Plant lipoxygenases
PDEase	PLC-like (P variant)
PE	Pleckstrin-homology domain (PH domain)
Penicillin-binding protein 2x (pbp-2x), c-terminal domain	Poly(ADP-ribose) polymerase, C-terminal domain
Penicillin binding protein dimerisation domain	Poly A polymerase C-terminal region-like
Penta-EF-hand proteins	Poly A polymerase-Head domain-like
PEP carboxykinase C-terminal domain	Polynucleotide phosphorylase/guanosine pentaphosphate synthase (PNPase/GPSI), domain 3
PEP carboxykinase N-terminal domain	Polyphosphate kinase C-terminal domain
Pepsin-like	Potassium channel NAD-binding domain
PepX catalytic domain-like	POU-specific domain
PepX C-terminal domain-like	PPE
Periplasmic domain of cytochrome c oxidase subunit II	PPK middle domain-like
PF1790-like	PPK N-terminal domain-like
PfkB-like kinase	Predicted hydrolases Cof
PFOR PP module	Prefoldin
PFOR Pyr module	Pre-protein crosslinking domain of SecA
PG0816-like	PriB N-terminal domain-like
Phase 1 flagellin	Prion-like

Prokaryotic DksA/TraR C4-type zinc finger	RecG "wedge" domain
Prokaryotic phospholipase A2	Regulator of G-protein signaling, RGS
Prokaryotic type I DNA topoisomerase	RelA/SpoT domain
Prokaryotic type KH domain (KH-domain type II)	Rel/Dorsal transcription factors, DNA-binding domain
Proteasome subunits	Release factor
Proteinase/alpha-amylase inhibitors	Reovirus components
Protein HNS-dependent expression A; HdeA	Restriction endonuclease EcoO109IR
Protein kinases, catalytic subunit	Retrovirus capsid protein C-terminal domain
Protein-L-isoaspartyl O-methyltransferase	Retrovirus capsid protein, N-terminal core domain
Protein prenyltransferase	Ribonucleotide reductase-like
Pseudo ankyrin repeat	Ribosomal protein L19 (L19e)
PTS-regulatory domain, PRD	Ribosomal protein L29 (L29p)
Putative anticodon-binding domain of alanyl-tRNA synthetase (AlaRS)	Ribosomal protein L7/12, C-terminal domain
Putative thiamin/HMP-binding protein YkoF	Ribosomal protein L7/12, oligomerisation (N-terminal) domain
Putative transcriptional regulator TM1602, C-terminal domain	Ribosomal protein S15
PyrH-like	Ribosomal protein S20
Pyrimidine 5'-nucleotidase (UMPH-1)	Ribosome-binding factor A, RbfA
Pyruvate-ferredoxin oxidoreductase, PFOR, domain II	Ribosome complexes
Pyruvate-ferredoxin oxidoreductase, PFOR, domain III	Ribosome recycling factor, RRF
Pyruvate phosphate dikinase, central domain	RING finger domain, C3HC4
Pyruvate phosphate dikinase, C-terminal domain	RNA polymerase
Pyruvate phosphate dikinase, N-terminal domain	RNA polymerase alpha subunit dimerisation domain
R1 subunit of ribonucleotide reductase, C-terminal domain	RNA-polymerase beta
R1 subunit of ribonucleotide reductase, N-terminal domain	RNA-polymerase beta-prime
Rabenosyn-5 Rab-binding domain-like	RNase III catalytic domain-like
Rab geranylgeranyltransferase alpha-subunit, C-terminal domain	Roadblock/LC7 domain
Rab geranylgeranyltransferase alpha-subunit, insert domain	ROK
Rad50 coiled-coil Zn hook	ROK associated domain
RAP domain	ROP protein
Ras-binding domain, RBD	RuBisCo LSMT catalytic domain
RecA protein-like (ATPase-domain)	RuBisCo LSMT C-terminal, substrate-binding domain
RecG, N-terminal domain	Rubredoxin
	RWD domain
	S100 proteins

Saposin B	Succinate dE-Hydrogenase/fumarate reductase
SCF ubiquitin ligase complex WHB domain	flavoprotein C-terminal domain
ScpB/YpuH-like	Succinate dE-Hydrogenase/fumarate reductase
Sec1/munc18-like (SM) proteins	flavoprotein N-terminal domain
Secreted chorismate mutase-like	Succinate dE-Hydrogenase/Fumarate reductase
Serine acetyltransferase	transmembrane subunits (SdhC/FrdC and SdhD/FrdD)
Serum albumin-like	Superantigen MAM
Seryl-tRNA synthetase (SerRS)	Swaposin
SH2 domain	Synatpobrevin N-terminal domain
SH3-domain	T7 RNA polymerase
Short-chain cytokines	Tandem AAA-ATPase domain
Siah interacting protein N terminal domain-like	TAZ domain
Sigma2 domain of RNA polymerase sigma factors	TBP-associated factors, TAFs
Sigma3 domain	TENA/THI-4
Sigma4 domain	Terpene synthases
Signal peptide-binding domain	Terpenoid cyclase C-terminal domain
Single strand DNA-binding domain, SSB	Terpenoid cyclase N-terminal domain
SipA N-terminal domain-like	Tetracyclin repressor-like, C-terminal domain
Siroheme synthase middle domains-like	Tetracyclin repressor-like, N-terminal domain
Siroheme synthase N-terminal domain-like	Tetratricopeptide repeat (TPR)
Small-conductance potassium channel	Thermolysin-like
Small subunit	Tim10/DDP
Smc hinge domain	TK-like PP module
SopE-like GEF domain	TK-like Pyr module
Spectrin repeat	Top domain of virus capsid protein
SPy1572-like	Topoisomerase V catalytic domain-like
SRP alpha N-terminal domain-like	Topoisomerase V repeat domain
Stabilizer of iron transporter SufD	TorD-like
Staphylocoagulase	Transcriptional repressor TraM
STAT	Transcription factor II A (TFIIA), alpha-helical domain
STAT DNA-binding domain	Transcription factor II A (TFIIA), beta-barrel domain
Substrate-binding domain of HMG-CoA reductase	Transcription factor II B (TFIIB), core domain
Subtilases	Transcription factor NusA, N-terminal domain
Succinate dE-Hydrogenase/fumarate reductase	Transcription factor STAT-4 N-domain
flavoprotein, catalytic domain	Transducin (alpha subunit), insertion domain

Transglutaminase core	Virus ectodomain
Transglutaminase N-terminal domain	Voltage-gated potassium channels
Transglutaminase, two C-terminal domains	VPR protein fragments
Transketolase C-terminal domain-like	VPS23 C-terminal domain
Translationally controlled tumor protein TCTP (histamine-releasing factor)	VPS28 C-terminal domain-like
Translin	VPS28 N-terminal domain
Translocated intimin receptor (tir) intimin-binding domain	VPS37 C-terminal domain-like
Transmembrane-Helical fragments	VPS9 domain
Transposase IS200-like	V-type ATP synthase subunit C
Trigger factor ribosome-binding domain	XseB-like
TrkA C-terminal domain-like	YciF-like
TrmB-like	YfiT-like putative metal-dependent hydrolases
Tryptophan synthase beta subunit-like PLP-dependent enzymes	YfmB-like
t-snare proteins	YggX-like
TS-N domain	YhfA-like
Tumor suppressor gene product Apc	YihX-like
TyeA-like	YlxM/p13-like
Type II restriction endonuclease catalytic domain	YppE-like
Type II restriction endonuclease effector domain	Zn metallo-beta-lactamase
Typo IV secretion system protein TraC	14-3-3 protein
TyrA dimerization domain-like	1-deoxy-D-xylulose-5-phosphate reductoisomerase, C-terminal domain
Tyrosine-dependent oxidoreductases	2Fe-2S ferredoxin domains from multidomain proteins
Ubiquitin activating enzymes (UBA)	3-Methyladenine DNA glycosylase III (MagIII)
U-box	5-carboxymethyl-2-hydroxymuconate isomerase (CHMI)
Upper collar protein gp10 (connector protein)	5' nucleotidase-like
Urocanase	5' to 3' exonuclease catalytic domain
Vacuolar ATP synthase subunit C	5' to 3' exonuclease, C-terminal subdomain
Vanabin-like	6-phosphogluconate dehydrogenase-like, N-terminal domain
Vanillyl-alcohol oxidase-like	ABC transporter ATPase domain-like
Variant surface glycoprotein (N-terminal domain)	Aconitase B, N-terminal domain
VBS domain	Aconitase iron-sulfur domain
Vertebrate phospholipase A2	Actin/HSP70
Viral DNA-binding domain	Acyl-CoA binding protein

acyl-CoA oxidase C-terminal domains	Anticodon-binding domain of a subclass of class I aminoacyl-tRNA synthetases
acyl-CoA oxidase N-terminal domains	
Adapter protein APS, dimerisation domain	Antioxidant defense protein AhpD
Adenylation domain of NAD ⁺ -dependent DNA ligase	
Adenylyl and guanylyl cyclase catalytic domain	Anti-sigma factor AsiA
Adenylylcyclase toxin (the edema factor)	Apolipoporphin-III
a domain/subunit of cytochrome bc1 complex (Ubiquinol-cytochrome c reductase)	Apolipoprotein
Aerobic respiration control sensor protein, ArcB	Aquaporin-like
AF0060-like	Archaeal DNA-binding protein
AF0941-like	Arfaptin, Rac-binding fragment
AF1104-like	Arginyl-tRNA synthetase (ArgRS), N-terminal 'additional' domain
AgoG-like	Aristolochene/pentalenene synthase
Alcohol de-Hydrogenase-like, C-terminal domain	Armadillo repeat
Alcohol de-Hydrogenase-like, N-terminal domain	Arp2/3 complex 16 kDa subunit ARPC5
AldE-Hyde ferredoxin oxidoreductase, C-terminal domains	Arylsulfatase
AldE-Hyde ferredoxin oxidoreductase, N-terminal domain	Aspartate/ornithine carbamoyltransferase
ALDH-like	Aspartokinase allosteric domain-like
Allosteric chorismate mutase	ATP synthase
alpha-Amylases, C-terminal beta-sheet domain	ATP synthase (F1-ATPase), gamma subunit
alpha-catenin/vinculin	a tRNA synthase domain
alpha-D-glucuronidasE-Hyaluronidase catalytic domain	Atu0492-like
alpha-D-glucuronidase, N-terminal domain	Avirulence protein AvrPto
Alpha-hemoglobin stabilizing protein AHSP	B12-dependent (class II) ribonucleotide reductase
alpha-Subunit of urease	Bacterial dinuclear zinc exopeptidases
alpha-subunit of urease, catalytic domain	Bacterial exopeptidase dimerisation domain
Amidase signature (AS) enzymes	Bacterial GAP domain
A middle domain of Talin 1	Bacterial glucoamylase C-terminal domain-like
Aminoacid de-Hydrogenase-like, C-terminal domain	Bacterial glucoamylase N-terminal domain-like
Aminoacid de-Hydrogenases	Bacterial photosystem II reaction centre, L and M subunits
Aminoglycoside phosphotransferases	Bacterial tryptophan 2,3-dioxygenase
AmyC C-terminal domain-like	Bacteriophage CII protein
AmyC N-terminal domain-like	Bacteriorhodopsin-like
Amylase, catalytic domain	BAG domain
Animal lipoxigenases	Band 7/SPFH domain
	BAR domain

Barrier-to-autointegration factor, BAF	Class II aminoacyl-tRNA synthetase (aaRS)-like, catalytic domain
BAS1536-like	Class-II DAHP synthetase
BC ATP-binding domain-like	Class II glutamine amidotransferases
BC C-terminal domain-like	Class III anaerobic ribonucleotide reductase NRDD subunit
Bcl-2 inhibitors of programmed cell death	clathrin assemblies
BC N-terminal domain-like	Clostridium neurotoxins, catalytic domain
Beta-D-glucan exohydrolase, C-terminal domain	Clostridium neurotoxins, "coiled-coil" domain
beta-Lactamase/D-ala carboxypeptidase	Clostridium neurotoxins, C-terminal domain
beta-Phosphoglucomutase-like	Clostridium neurotoxins, the second last domain
Biotin repressor-like	CMD-like
BRCA2 helical domain	Cobalamin adenosyltransferase
BRCA2 tower domain	Cobalamin (vitamin B12)-binding domain
Bromodomain	CO dE-Hydrogenase flavoprotein C-terminal domain-like
Calcium ATPase, transduction domain A	CO dE-Hydrogenase flavoprotein N-terminal domain-like
Calcium ATPase, transmembrane domain M	CO dE-Hydrogenase ISP C-domain like
Calmodulin-like	CO dE-Hydrogenase molybdoenzyme N-domain-like
Calpain large subunit, catalytic domain (domain II)	Coiled-coil domain of nucleotide exchange factor GrpE
Calpain large subunit, middle domain (domain III)	Cold shock DNA-binding domain-like
cAMP-binding domain	Colicin E3 receptor domain
CAPPD, an extracellular domain of amyloid beta A4 protein	Computational models partly based on NMR data
Cell cycle transcription factor e2f-dp	Conserved hypothetical protein MTH1747
Cell division protein ZapA-like	CorA soluble domain-like
Cellulases catalytic domain	Coronavirus NSP8-like
Cellulose-binding domain family III	Coronavirus S2 glycoprotein
Centromere-binding	COX17-like
Cfr10I/Bse634I	Creatinase/aminopeptidase
Chaperone J-domain	Creatinase/prolidase N-terminal domain
Chemotaxis phosphatase CheZ	Crotonase-like
Chemotaxis protein CheA P1 domain	Cryptochrome/photolyase FAD-binding domain
CheW-like	Cryptochrome/photolyase, N-terminal domain
Cholesterol oxidase	CSE2-like
Choline/Carnitine O-acyltransferase	C-terminal domain of alpha and beta subunits of F1 ATP synthase
Circadian clock protein KaiA, C-terminal domain	C-terminal domain of class I lysyl-tRNA synthetase
Class I alpha-1;2-mannosidase, catalytic domain	
Class I aminoacyl-tRNA synthetases (RS), catalytic domain	

C-terminal domain of DFF45/ICAD (DFF-C domain)	Dihydrodipicolinate reductase-like
C-terminal domain of eukaryotic peptide chain release factor subunit 1, ERF1	Dimeric chorismate mutase
C-terminal domain of Ku80	Dimerisation domain of CENP-B
C-terminal fragment of elongation factor SelB	Dimerization–anchoring domain of cAMP–dependent PK regulatory subunit
C-terminal fragment of thermolysin	DinB-like
C-terminal UvrC-binding domain of UvrB	Diol dE-Hydrtase, gamma subunit
CUE domain	DLC
Cullin homology domain	DNA-binding N-terminal domain of transcription activators
Cullin repeat	DNA-binding protein Mj223
Cyclin	DNA damage-inducible protein DinI
Cyclophilin (peptidylprolyl isomerase)	DnaK suppressor protein DksA, alpha-hairpin domain
Cytochrome b562	DNA ligase/mRNA capping enzyme postcatalytic domain
Cytochrome b of cytochrome bc1 complex (Ubiquinol-cytochrome c reductase)	DNA polymerase I
Cytochrome c'-like	DNA polymerase III clamp loader subunits, C-terminal domain
Cytochrome c oxidase subunit III-like	DnaQ-like 3'–5' exonuclease
Cytochrome c oxidase subunit II-like, transmembrane region	DNA repair protein MutS, domain I
Cytochrome c oxidase subunit I-like	DNA repair protein MutS, domain II
Cytochrome P450	DNA repair protein MutS, domain III
Cytochrome p450 reductase N-terminal domain-like	DNA topoisomerase IV, alpha subunit
Cytoplasmic domain of inward rectifier potassium channel	Domain of poly(ADP-ribose) polymerase
D-aminoacid aminotransferase-like PLP-dependent enzymes	Domain of the SRP/SRP receptor G-proteins
DBL homology domain (DH-domain)	Double Clp-N motif
Dcp2 box A domain	double-SIS domain
Decarboxylase	E2 regulatory, transactivation domain
DE-Hydroquinate synthase, DHQS	EF2458-like
delta-Endotoxin, C-terminal domain	EF-hand modules in multidomain proteins
delta-Endotoxin (insecticide), middle domain	eIF-2-alpha, C-terminal domain
delta-Endotoxin (insecticide), N-terminal domain	eIF2alpha middle domain-like
Designed four-helix bundle protein	Electron transfer flavoprotein-ubiquinone oxidoreductase-like
Designed single chain threE-Helix bundle	Elongation factor Ts (EF-Ts), dimerisation domain
DHN aldolase/epimerase	EntA-Im
	Enzyme IIa from lactose specific PTS, IIa-lac

Enzyme I of the PEP:sugar phosphotransferase system	FHV B2 protein-like
HPr-binding (sub)domain	Fibrinogen coiled-coil and central regions
EpoxidE-Hydrolase	FIS-like
Epsilon subunit of F1F0-ATP synthase C-terminal domain	FKBP12-rapamycin-binding domain of
Epsilon subunit of F1F0-ATP synthase N-terminal domain	FKBP-rapamycin-associated protein (FRAP)
ERP29 C domain-like	FKBP immunophilin/proline isomerase
ERP29 N domain-like	Flagellar export chaperone FlS
ESAT-6 like	FMN-linked oxidoreductases
E-set domains of sugar-utilizing enzymes	Formate dE-Hydrogenase N, cytochrome (gamma) subunit
ETF-QO domain-like	Formin homology 2 domain (FH2 domain)
Eukaryotic DNA topoisomerase I, catalytic core	Fumarate reductase respiratory complex cytochrome b
Eukaryotic DNA topoisomerase I, dispensable insert domain	subunit, FrdC
Eukaryotic DNA topoisomerase I, N-terminal DNA-binding fragment	Fungal zinc peptidase
Eukaryotic type KH-domain (KH-domain type I)	GABA-aminotransferase-like
Exocyst complex component	GAPDH-like
Exodeoxyribonuclease V beta chain (RecC), C-terminal domain	GAT domain
EXOSC10 HRDC domain-like	Gated mechanosensitive channel
Extended AAA-ATPase domain	G domain-linked domain
F1F0 ATP synthase subunit A	Glutamate-cysteine ligase
F1F0 ATP synthase subunit C	Glutamyl tRNA-reductase catalytic, N-terminal domain
FAD-linked oxidases, N-terminal domain	Glutamyl tRNA-reductase dimerization domain
FAD-linked reductases, N-terminal domain	Glutathione peroxidase-like
FAD/NAD-linked reductases, dimerisation (C-terminal) domain	Glutathione S-transferase (GST), C-terminal domain
FAD/NAD-linked reductases, N-terminal and central domains	Glutathione S-transferase (GST), N-terminal domain
FAT domain of focal adhesion kinase	GlyceralE-Hyde-3-phosphate dE-Hydrogenase-like, N-terminal domain
Fe,Mn superoxide dismutase (SOD), C-terminal domain	Glycerol-3-phosphate (1)-acyltransferase
Fe,Mn superoxide dismutase (SOD), N-terminal domain	Glycerol-3-phosphate dE-Hydrogenase
FemXAB nonribosomal peptidyltransferases	(Glycosyl)asparaginase
Ferredoxin domains from multidomain proteins	Glycosyltransferase family 36 C-terminal domain
Ferritin	Glycosyltransferase family 36 N-terminal domain
Fertilization protein	GMC oxidoreductases
	G proteins
	GreA transcript cleavage factor, C-terminal domain
	GreA transcript cleavage protein, N-terminal domain

GRIP domain	HrcA C-terminal domain-like
GroEL chaperone, ATPase domain	HRDC domain from helicases
GroEL-like chaperone, apical domain	HSC20 (HSCB), C-terminal oligomerisation domain
GroEL-like chaperone, intermediate domain	Hsp90 co-chaperone CDC37
Group II chaperonin (CCT, TRIC), apical domain	HSP90 C-terminal domain
Group II chaperonin (CCT, TRIC), ATPase domain	Hut operon positive regulatory protein HutP
Group II chaperonin (CCT, TRIC), intermediate domain	Hyaluronate lyase-like catalytic, N-terminal domain
Group I mobile intron endonuclease	Hyaluronate lyase-like, central domain
Group V grass pollen allergen	Hyaluronate lyase-like, C-terminal domain
GTP cyclohydrolase I	Hyaluronidase N-terminal domain-like
half-ferritin	Hyaluronidase post-catalytic domain-like
Haloperoxidase (bromoperoxidase)	Hybrid and chimeric proteins
HAL/PAL-like	Hybrid cluster protein (prismane protein)
HCDH C-domain-like	Hypothetical protein D-63
Head domain of nucleotide exchange factor GrpE	Hypothetical protein MTH393
Heat-inducible transcription repressor HrcA, N-terminal domain	Hypothetical protein MTH677
Heat shock protein 70kD (HSP70), C-terminal subdomain	Hypothetical protein Ta1238
Heat shock protein 70kD (HSP70), peptide-binding domain	Hypothetical protein TM1457
Hect, E3 ligase catalytic domain	Hypothetical protein VC0424
Helical scaffold and wing domains of SecA	Hypothetical protein YfhH
Hemerythrin	Hypothetical protein Yhal
Hepatitis B viral capsid (hbcag)	Hypothetical Protein YjhP
Hermes dimerisation domain	IF2B-like
Hermes transposase-like	I/LWEQ domain
HisE-like (PRA-PH)	IMD domain
Histidine kinase	Influenza hemagglutinin (stalk)
HlyD-like secretion proteins	Inositol
HMA, heavy metal-associated domain	monophosphatase/fructose-1,6-bisphosphatase-like
HMD dimerization domain-like	Inositol polyphosphate 5-phosphatase (IPP5)
HMG-box	Insect pheromone/odorant-binding proteins
Homeodomain	Insert subdomain of RNA polymerase alpha subunit
Homodimeric domain of signal transducing histidine kinase	Interferon-induced guanylate-binding protein 1 (GBP1), C-terminal domain
HP1531-like	Interferons/interleukin-10 (IL-10)
HR1 repeat	IpaD-like

Iron-containing alcohol dE-Hydrogenase	domain
Isoprenyl diphosphate synthases	Medium chain acyl-CoA dE-Hydrogenase, NM (N-terminal and middle) domains
ISY1 N-terminal domain-like	
KaiB-like	Membrane ion ATPase
L27 domain	Meta-cation ATPase, catalytic domain P
Lactate & malate dE-Hydrogenases, C-terminal domain	Metal cation-transporting ATPase, ATP-binding domain N
Lambda integrase-like, catalytic core	Methane monooxygenase-Hydrolase, gamma subunit
lambda integrase N-terminal domain	Methicillin resistance protein FemA probable tRNA-binding arm
Large subunit	Methionine synthase domain
L-aspartase/fumarase	Methionine synthase SAM-binding domain
LcrE-like	Methionyl-tRNA synthetase (MetRS), Zn-domain
LDH N-terminal domain-like	Methyl-accepting chemotaxis protein (MCP) signaling domain
LemA-like	Methyl-coenzyme M reductase alpha and beta chain C-terminal domain
Lesion bypass DNA polymerase (Y-family), catalytic domain	Methyl-coenzyme M reductase alpha and beta chain N-terminal domain
Lesion bypass DNA polymerase (Y-family), little finger domain	Methylmalonyl-CoA mutase, N-terminal (CoA-binding) domain
LeuD-like	Middle domain of eukaryotic peptide chain release factor subunit 1, ERF1
Lipoxygenase N-terminal domain	MIF4G domain-like
Long-chain cytokines	MIF-related
L-sulfolactate dE-Hydrogenase-like	Mismatch glycosylase
Magnesium transport protein CorA, transmembrane region	MIT domain
Mago nashi protein	Mitochondrial ATP synthase coupling factor 6
Malate synthase G	Mitochondrial glycoprotein MAM33-like
Malic enzyme N-domain	Mob1/phocein
MarR-like transcriptional regulators	modified HD domain
Mason-Pfizer monkey virus matrix protein	Molybdenum cofactor-binding domain
MazG-like	Molybdopterin synthase subunit MoaE
Mechanosensitive channel protein MscS (YggB), C-terminal domain	monodomain cytochrome c
Mechanosensitive channel protein MscS (YggB), middle domain	monomeric chorismate mutase
Mechanosensitive channel protein MscS (YggB), transmembrane region	Motor proteins
MED7 hinge region	
Medium chain acyl-CoA dE-Hydrogenase-like, C-terminal	

MPP-like	Nop domain
mRNA decapping enzyme-like	NSP3 homodimer
MTH1187-like	N-terminal domain of adenylylcyclase associated protein, CAP
Multidrug efflux transporter AcrB pore domain; PN1, PN2, PC1 and PC2 subdomains	N-terminal domain of alpha and beta subunits of F1 ATP synthase
Multidrug efflux transporter AcrB TolC docking domain; DN and DC subdomains	N-terminal domain of cbl (N-cbl)
Multidrug efflux transporter AcrB transmembrane domain	N-terminal domain of enzyme I of the PEP:sugar phosphotransferase system
MxiH-like	N-terminal domain of eukaryotic peptide chain release factor subunit 1, ERF1
Myb/SANT domain	N-terminal domain of the circadian clock protein KaiA
Myosin S1 fragment, N-terminal domain	N-terminal domain of the delta subunit of the F1F0-ATP synthase
N-acetyl transferase, NAT	N-terminal, RNA-binding domain of nonstructural protein NS1
N-acylglucosamine (NAG) epimerase	Nuclear receptor ligand-binding domain
NAD-binding domain of HMG-CoA reductase	Nucleotide and nucleoside kinases
NadC C-terminal domain-like	NusA extra C-terminal domains
NadC N-terminal domain-like	Occludin/ELL domain
NAD+-dependent DNA ligase, domain 3	Ohr/OsmC resistance proteins
NADH oxidase/flavin reductase	Oligosaccharide phosphorylase
NADPH-cytochrome p450 reductase FAD-binding domain-like	OmpH-like
NADPH-cytochrome p450 reductase-like	Orbivirus capsid
NagZ-like	Orbivirus core
Neurotransmitter-gated ion-channel transmembrane pore	Outer membrane efflux proteins (OEP)
NF-kappa-B/REL/DORSAL transcription factors, C-terminal domain	Outer surface protein C (OspC)
Nickel-containing superoxide dismutase, NiSOD	Oxygen-evolving enhancer protein 3,
Nickel-iron hydrogenase, large subunit	P40 nucleoprotein
NifU C-terminal domain-like	PadR-like
NifU/IscU domain	Pantothenate synthetase (Pantoate-beta-alanine ligase, PanC)
Nitric oxide (NO) synthase oxygenase domain	PAPS sulfotransferase
Nitrogenase iron protein-like	PDEase
NKL-like	PE
Non-heme 11 kDa protein of cytochrome bc1 complex (Ubiquinol-cytochrome c reductase)	
Nonstructural protein ns2, Nep, M1-binding domain	

Penicillin-binding protein 2x (pbp-2x), c-terminal domain	Poly A polymerase C-terminal region-like
Penicillin binding protein dimerisation domain	Poly A polymerase-Head domain-like
Penta-EF-hand proteins	Polynucleotide phosphorylase/guanosine pentaphosphate synthase (PNPase/GPSI), domain 3
PEP carboxykinase C-terminal domain	Polyphosphate kinase C-terminal domain
PEP carboxykinase N-terminal domain	Potassium channel NAD-binding domain
Pepsin-like	POU-specific domain
PepX catalytic domain-like	PPE
PepX C-terminal domain-like	PPK middle domain-like
Periplasmic domain of cytochrome c oxidase subunit II	PPK N-terminal domain-like
PF1790-like	Predicted hydrolases Cof
PfkB-like kinase	Prefoldin
PFOR PP module	Pre-protein crosslinking domain of SecA
PFOR Pyr module	PriB N-terminal domain-like
PG0816-like	Prion-like
Phase 1 flagellin	Prokaryotic DksA/TraR C4-type zinc finger
PHBH-like	Prokaryotic phospholipase A2
Phenylalanyl-tRNA synthetase (PheRS)	Prokaryotic type I DNA topoisomerase
PhoB-like	Prokaryotic type KH domain (KH-domain type II)
Phosphoinositide 3-kinase (PI3K), catalytic domain	Proteasome subunits
Phosphoinositide 3-kinase (PI3K) helical domain	Proteinase/alpha-amylase inhibitors
Phosphate binding protein-like	Protein HNS-dependent expression A; HdeA
Phosphoenolpyruvate carboxylase	Protein kinases, catalytic subunit
PhosphonoacetaldE-HydE-Hydrolase-like	Protein-L-isoaspartyl O-methyltransferase
Phosphorelay protein-like	Protein prenyltransferase
Phosphorelay protein luxU	Pseudo ankyrin repeat
Phosphoserine phosphatase RsbU, N-terminal domain	PTS-regulatory domain, PRD
Photosystem I reaction center subunit XI, PsaL	Putative anticodon-binding domain of alanyl-tRNA synthetase (AlaRS)
Photosystems	Putative thiamin/HMP-binding protein YkoF
PhoU-like	Putative transcriptional regulator TM1602, C-terminal domain
PIN domain	PyrH-like
Plant invertase/pectin methylesterase inhibitor	Pyrimidine 5'-nucleotidase (UMPH-1)
Plant lipoxygenases	Pyruvate-ferredoxin oxidoreductase, PFOR, domain II
PLC-like (P variant)	
Pleckstrin-homology domain (PH domain)	
Poly(ADP-ribose) polymerase, C-terminal domain	

Pyruvate–ferredoxin oxidoreductase, PFOR, domain III	RING finger domain, C3HC4
Pyruvate phosphate dikinase, central domain	RNA polymerase
Pyruvate phosphate dikinase, C-terminal domain	RNA polymerase alpha subunit dimerisation domain
Pyruvate phosphate dikinase, N-terminal domain	RNA–polymerase beta
R1 subunit of ribonucleotide reductase, C-terminal domain	RNA–polymerase beta–prime
R1 subunit of ribonucleotide reductase, N-terminal domain	RNase III catalytic domain–like
Rabenosyn–5 Rab–binding domain–like	Roadblock/LC7 domain
Rab geranylgeranyltransferase alpha–subunit, C-terminal domain	ROK
Rab geranylgeranyltransferase alpha–subunit, insert domain	ROK associated domain
Rad50 coiled-coil Zn hook	ROP protein
RAP domain	RuBisCo LSMT catalytic domain
Ras–binding domain, RBD	RuBisCo LSMT C-terminal, substrate–binding domain
RecA protein–like (ATPase–domain)	Rubredoxin
RecG, N-terminal domain	RWD domain
RecG “wedge” domain	S100 proteins
Regulator of G–protein signaling, RGS	Saposin B
RelA/SpoT domain	SCF ubiquitin ligase complex WHB domain
Rel/Dorsal transcription factors, DNA–binding domain	ScpB/YpuH–like
Release factor	Sec1/munc18–like (SM) proteins
Reovirus components	Secreted chorismate mutase–like
Restriction endonuclease EcoO109IR	Serine acetyltransferase
Retrovirus capsid protein C-terminal domain	Serum albumin–like
Retrovirus capsid protein, N-terminal core domain	Seryl–tRNA synthetase (SerRS)
Ribonucleotide reductase–like	SH2 domain
Ribosomal protein L19 (L19e)	SH3-domain
Ribosomal protein L29 (L29p)	Short–chain cytokines
Ribosomal protein L7/12, C-terminal domain	Siah interacting protein N terminal domain–like
Ribosomal protein L7/12, oligomerisation (N-terminal) domain	Sigma2 domain of RNA polymerase sigma factors
Ribosomal protein S15	Sigma3 domain
Ribosomal protein S20	Sigma4 domain
Ribosome–binding factor A, RbfA	Signal peptide–binding domain
Ribosome complexes	Single strand DNA–binding domain, SSB
Ribosome recycling factor, RRF	SipA N–terminal domain–like
	Siroheme synthase middle domains–like
	Siroheme synthase N-terminal domain–like

Small-conductance potassium channel	Thermolysin-like
Small subunit	Tim10/DDP
Smc hinge domain	TK-like PP module
SopE-like GEF domain	TK-like Pyr module
Spectrin repeat	Top domain of virus capsid protein
SPy1572-like	Topoisomerase V catalytic domain-like
SRP alpha N-terminal domain-like	Topoisomerase V repeat domain
Stabilizer of iron transporter SufD	TorD-like
Staphylocoagulase	Transcriptional repressor TraM
STAT	Transcription factor IIA (TFIIA), alpha-helical domain
STAT DNA-binding domain	Transcription factor IIA (TFIIA), beta-barrel domain
Substrate-binding domain of HMG-CoA reductase	Transcription factor IIB (TFIIB), core domain
Subtilases	Transcription factor NusA, N-terminal domain
Succinate dE-Hydrogenase/fumarate reductase flavoprotein, catalytic domain	Transcription factor STAT-4 N-domain
Succinate dE-Hydrogenase/fumarate reductase flavoprotein C-terminal domain	Transducin (alpha subunit), insertion domain
Succinate dE-Hydrogenase/fumarate reductase flavoprotein N-terminal domain	Transglutaminase core
Succinate dE-Hydrogenase/Fumarate reductase transmembrane subunits (SdhC/FrdC and SdhD/FrdD)	Transglutaminase N-terminal domain
Superantigen MAM	Transglutaminase, two C-terminal domains
Swaposin	Transketolase C-terminal domain-like
Synatpobrevin N-terminal domain	Translationally controlled tumor protein TCTP (histamine-releasing factor)
T7 RNA polymerase	Translin
Tandem AAA-ATPase domain	Translocated intimin receptor (tir) intimin-binding domain
TAZ domain	Transmembrane-Helical fragments
TBP-associated factors, TAFs	Transposase IS200-like
TENA/THI-4	Trigger factor ribosome-binding domain
Terpene synthases	TrkA C-terminal domain-like
Terpenoid cyclase C-terminal domain	TrmB-like
Terpenoid cyclase N-terminal domain	Tryptophan synthase beta subunit-like PLP-dependent enzymes
Tetracyclin repressor-like, C-terminal domain	t-snare proteins
Tetracyclin repressor-like, N-terminal domain	TS-N domain
Tetratricopeptide repeat (TPR)	Tumor suppressor gene product Apc
	TyeA-like
	Type II restriction endonuclease catalytic domain

Type II restriction endonuclease effector domain	VPR protein fragments
Type IV secretion system protein TraC	VPS23 C-terminal domain
TyrA dimerization domain-like	VPS28 C-terminal domain-like
Tyrosine-dependent oxidoreductases	VPS28 N-terminal domain
Ubiquitin activating enzymes (UBA)	VPS37 C-terminal domain-like
U-box	VPS9 domain
Upper collar protein gp10 (connector protein)	V-type ATP synthase subunit C
Urocanase	XseB-like
Vacuolar ATP synthase subunit C	YciF-like
Vanabin-like	YfiT-like putative metal-dependent hydrolases
Vanillyl-alcohol oxidase-like	YfmB-like
Variant surface glycoprotein (N-terminal domain)	YggX-like
VBS domain	YhfA-like
Vertebrate phospholipase A2	YihX-like
Viral DNA-binding domain	YlxM/p13-like
Virus ectodomain	YppE-like
Voltage-gated potassium channels	Zn metallo-beta-lactamase

Figure S1: Alignment of the sequences of 1FSL, and those of 1R8J, 1XL3, 2FM9, 2NP5, and 2P06, respectively, based on the 3D structure alignment produced by Dalilite. A segment with capital letters denotes that the 3D structure of this segment is similar to that of the aligned segment of the query protein. A residue with the mark “†” constitutes a common residue pattern.

1FSL vs. 1R8J Z score = 4.4

E	F	G	H
† † †		† † †	† † †
1FSL -KLTGHAEKLFALVRDSAGQ1kas-GTVVA--caalgsvhAQKAVnDPQFVVVKEALLKTIAAVG--DKWSDeLSRAWEVAYDELAAAIKK-	ayESQKLHQAMOTSRYREIVLSPyFSPnSNLNQsidnfvnmaFPAD-VPVTKVVEIHMEIMDEFAKKLRLveGRSED-ILLDYRLTLIDVIAHLCMyrrsip		
† † †	† † †	† † †	† † †

1FSL vs. 1XL3 Z score = 2.0

E	F	G	H
† † †		† † †	† † †
1FSL kLTGHAEKLFALVRDSAGQ1kas-gtvvadaalgsvhAQKAVnDPQFVVVKEALLKTIAAVGdkNSDELSRAWEVAYDELAAAIKK-----a	nPLQPLRDTYRDAVMGYQG-----iyaiwsdlqkrfpngIDSVILFLQKALSADLQSO---QSGSGREKLGIVISDLQKLXEFsvsdqvxqfwqffs		
† † †	† † †	† † †	† † †

1FSL vs. 2FM9 Z score = 2.9

E	F	G	H
† † †		† † †	† † †
1FSL KLTGHAEKLFALVRDSAGQ1kas-gtvvadaalgsvhAQKAVnDPQFVVVKEALLKTIAAVGDK-wsDELSRAWEVAYDELAAAIK-----	FPALIKQASLDALFKCGKD-----nealkevfTNsNNVAGKKAIIMEFAGLFRSALNATSDSpeAKTLLMKVGAEYTAQIIKDGlkeksafgpwlpetkkaeaklenlekqlld		
† † †	† † †	† † †	† † †
1FSL -----ka	2FM9 iiknnntggelsklstnlvmqevmpyiasciehnfgctldpltrsnlthlvdkaaakavealdmchqkhlemqtlipllrnrvfaqipa		

1FSL vs. 2NP5 Z score = 4.4

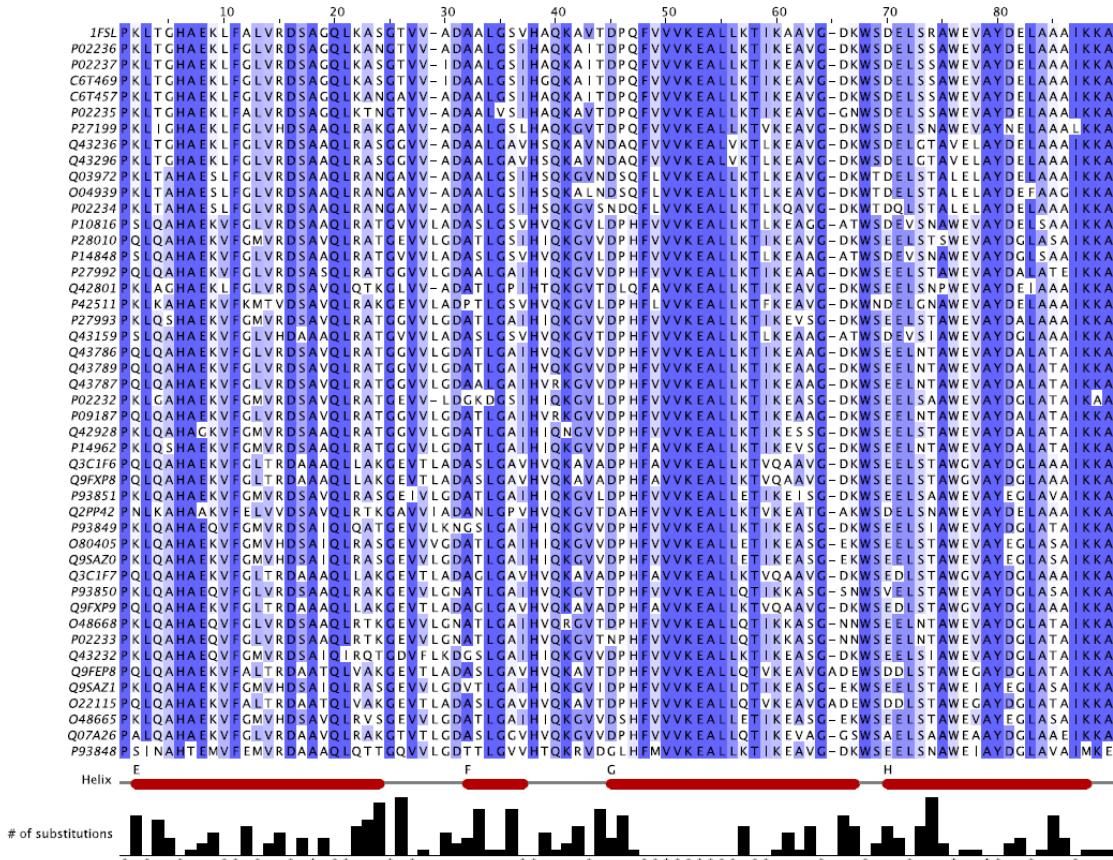
E	F	G	H
† †		†	†
1FSL KLTGHAE-----k1f1LVRD-----sagqlkas-gtvvadaalgsvhAQKAVnDPQFVVVKEALLKTIAAVG--DKWSDeLSRAWE	2NP5 KLLARLSeverggdparALFaamsql1pldearsreahvxaafavraatspslaeirrktltfirtglsav1IGIG--tPEAETRAALLIATVDGLALDAIspALVPEYLEHAL		
† †	† † †	† † †	†
1FSL VAYDELAAAIKK-----	2NP5 DIQIGMIIQGADVvp		
† †			

1FSL vs. 2P06 Z score = 3.2

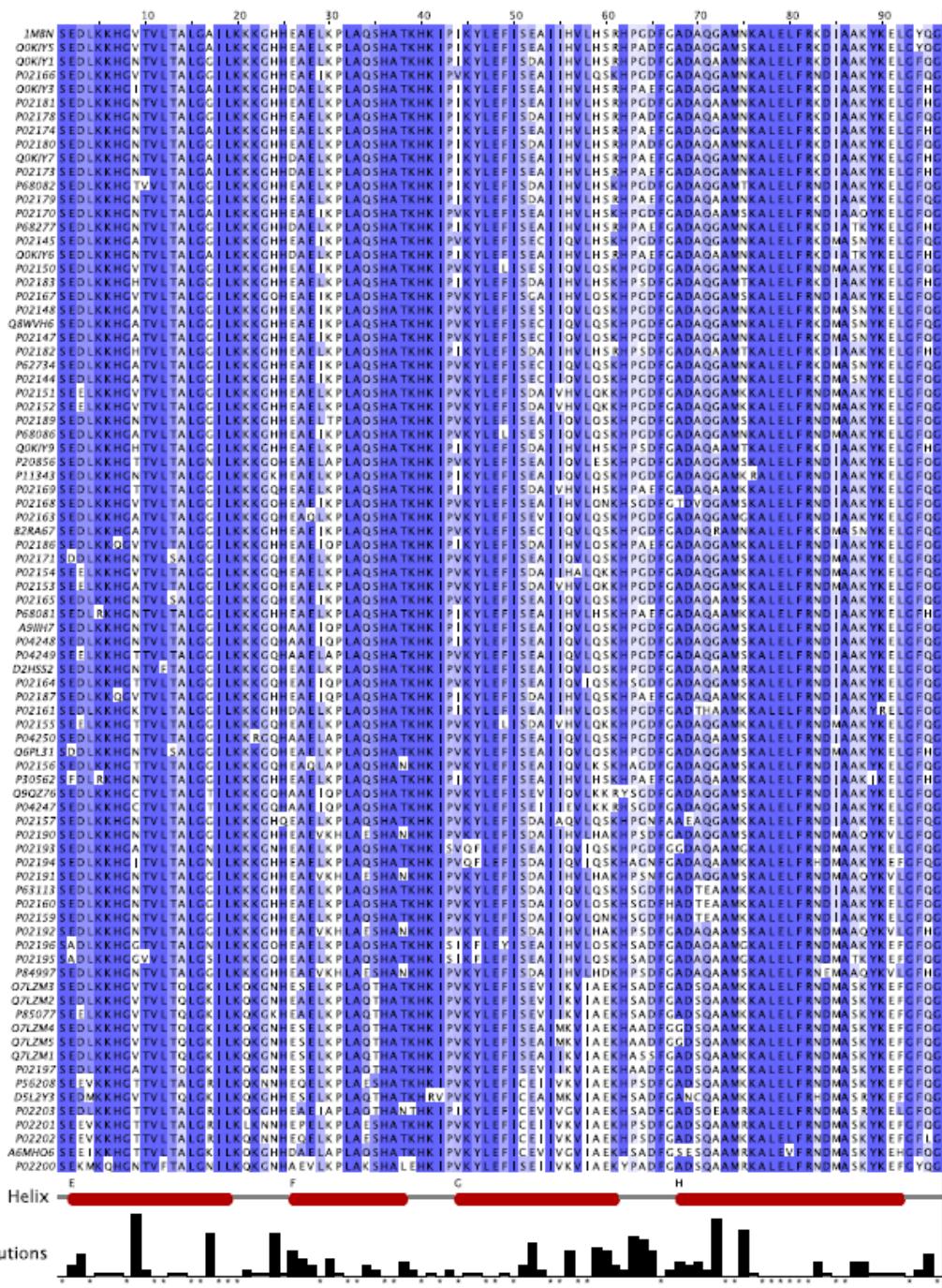
E	F	G	H
† † †		† † †	† † †
1FSL kltghaeklfalvrdsAGQLK---as-gtvvadaalgsvhAQKAVnDPQFVVVKEALLKTIAAVGDKW--sDELSRAWEVAYDELAAAIKK-	2P06 -----Mc yfrlaeKFIRemhakymkrvsrpgntrpwfDESERILLSRLFEEXDELREAVEKEDweNLRDELLDWANFCMYLWGKLSVK		
† †	†	† † †	† † †

Figure S2: Multiple alignment of each protein and its homologues. The accession numbers of homologues are presented in the right side of each figure. The histogram at the bottom of each figure denotes the number of substitutions of each residue. A red bar means a helix.

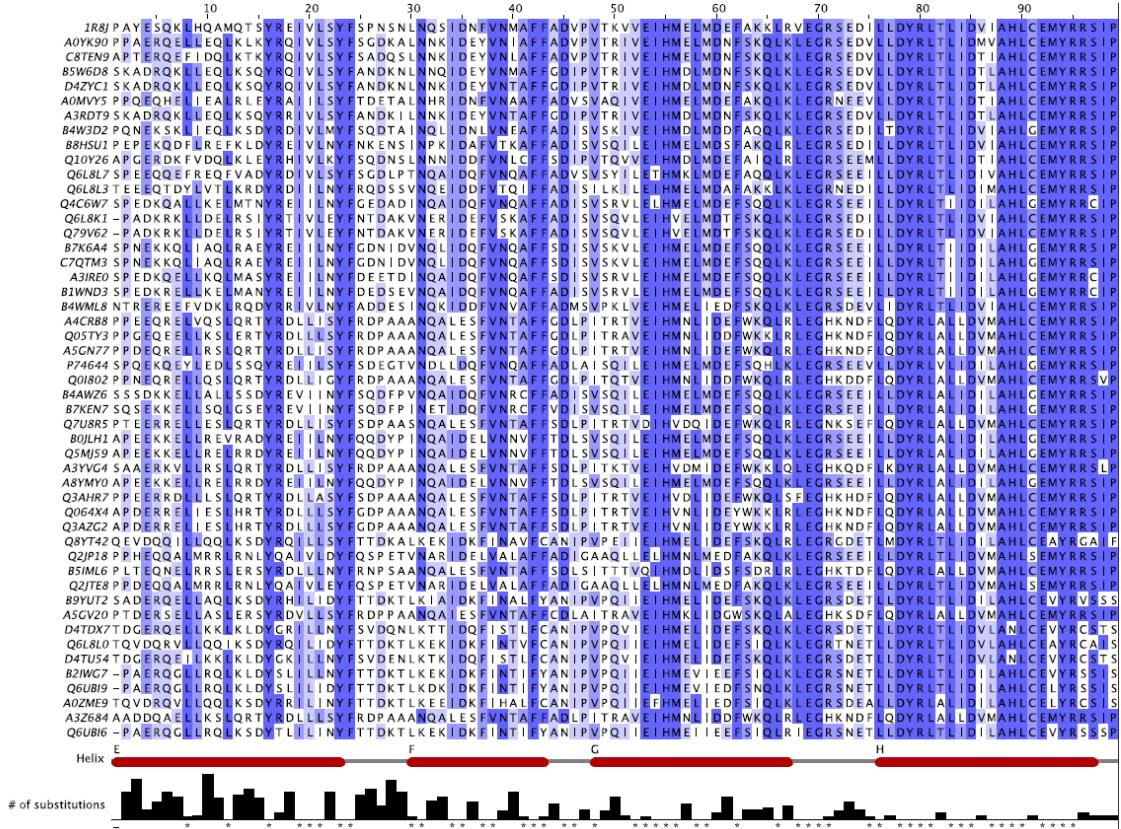
(a) Multiple alignment of the sequences of 1FSL and its homologues.



(b) Multiple alignment of the sequences of 1MBN and its homologues.



(c) Multiple alignment of the sequences of 1R8J and its homologues.



(d) Multiple alignment of the sequences of 1XL3 and its homologues.

