

Table S1. Homology detection results of OB-fold structures

SCOP Superfamily	SCOP family	PDB structure	New homologs	NCBI annotation
Nucleic acid-binding proteins	anticodon-binding domain	1eovA, 104-202	15615731	DNA polymerase III alpha subunit
		1b8aA: 1-102	3914638	DNA helicase recG
		1c0aA: 1-106	12846238	acyl-CoA thioester hydrolase *
		1g51A: 1-104	15669348	replication factor A related protein
			15789450	replication A related protein
		1bbuA: 64-151	14195653	DNA polymerase III alpha subunit
			15594924	DNA polymerase III, subunit alpha
			15669348	replication factor A related protein
			15615731	DNA polymerase III alpha subunit
		1e1oA, 64-148	14195653	DNA polymerase III alpha subunit
			15594924	DNA polymerase III, subunit alpha
		1qvcA, 1-114	6468242	putative hydrolase *
			14972484	HemK protein *
		1fguA, 181-298	15221815	hypothetical protein
			15615731	DNA polymerase III alpha subunit
			6166145	DNA polymerase III alpha subunit
		1quqB, 3-89; 1quqA, 62-152; 1otcA, 37-152; 1otcA, 210-303; 1otcA, 366-494; 1otcB, 36-126; 1b7yB, 39-151; 1fl0A; 1cuk, 1-64		
	cold shock DNA-binding domain like	1mjc	15619842	30S ribosomal protein S1
			8100800	cold shock protein
		1csp	15619842	30S ribosomal protein S1
		1sro	14039811	Y-box binding protein
			1477478	Y-box binding protein
			15671999	HYPOTHETICAL PROTEIN
		1d7qA	11231164	Sucrose-phosphate synthase *
		2eifA, 73-132	15615362	translation elongation factor EF-P
		1bkb, 75-139; 1rl2; 1c09A 1ffk; 1ah9; 1a62, 48-125		
	DNA ligase/mRNA capping enzyme, domain 2	1ckmA, 238-302		
		1a0i, 241-349	10955735	DNA ligase homolog
			10955937	unknown
		1fviA, 190-293		
		1dgsA, 315-400		
	Phage ssDNA-binding proteins	1gvp		
		1pfs		
		1gpc		
	RNA polymerase subunit RBP8	1a1d		

SCOP Superfamily	SCOP family	PDB structure	New homologs	NCBI annotation
Staphylococcal nuclease	Staphylococcal nuclease	1eyd		
Bacterial enterotoxins	bacterial AB5 toxins, B units	1tiiD, 3chbD 1c4qA, 1prtB: 90-192 1prtD, 1prtF		
	superantigen toxins	1an8, 19-94		
TIMP-like	tissue inhibitor of metalloproteases	1ueaB, 14-106		
Inorganic pyrophosphatase	Inorganic pyrophosphatase	2prd		
MOP-like	BiMOP, duplicated molybdate-binding domain	1b9mA, 127-262		
Histidine kinase CheA, C-terminal domain	Histidine kinase CheA, C-terminal domain	1b3qA, 540-671		

* putative false positives as assessed by manual inspection.

Table S2. Homology detection result for 1mjc

Method	Weight	Number of accepted Steps	Designed Sequence added	#hits 15619842 ribosomal S1	#hits 9366840 <i>T.brucei</i> hypothetical
Z-score design	0.91	34	70	100/100*	3/100
	0.91	67	70	100/100	25/100
	0.91	100	70	95/100	52/100
	0.91	34	35	99/100	7/100
	0.91	67	35	96/100	32/100
	0.91	100	35	70/100	42/100
	0.91	34	140	100/100	1/100
	0.91	67	140	100/100	14/100
	0.91	100	140	100/100	38/100
Dayhoff PAM1 mutation	NA	34	70	0/20	0/20
	NA	67	70	0/20	0/20
	NA	100	70	0/20	0/20

* 100 different seeds for random number generation were tried.