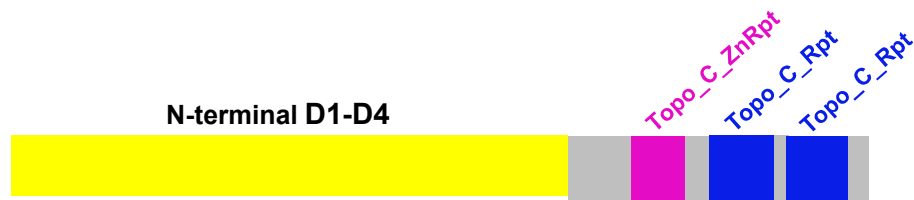


Figure S1. Sunburst illustration of species with Topo_C_Rpt. n=4235 (from http://pfam.xfam.org/family/Toprim_C_rpt#tabview=tab7). Color assignments: Green – Bacteria, Purple – Eukaryota.



Figure S2. Sunburst illustration of species with Topo_C_ZnRpt. n=5401 (from http://pfam.xfam.org/family/zf-C4_Topoiso#tabview=tab7). Color assignments: Green – Bacteria, Purple – Eukaryota, Orange - Archea.



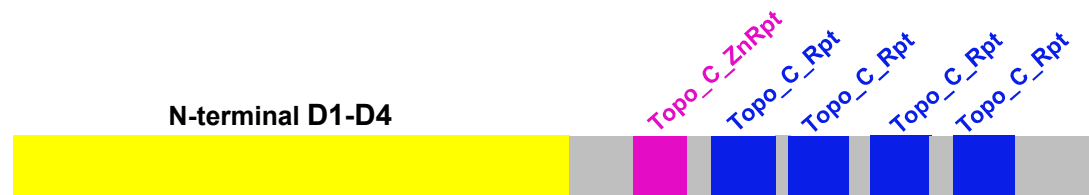
TopA with one Topo_C_ZnRpt followed by two Topo_C_Rpt domains

Examples of bacterial species: *Rickettsia bellii*, *Candidatus Phycorickettsia trachydisci*



TopA with one Topo_C_ZnRpt followed by three Topo_C_Rpt domains

Examples of bacterial species: *Caulobacter crescentus*, *Gallionella capsiferriformans*



TopA with one Topo_C_ZnRpt followed by four Topo_C_Rpt domains

Examples of bacterial species: *Methylocapsa palsarum*, *Roseiarcus fermentans*

Figure S3. Arrangements of Topo_C_ZnRpt and Topo_C_Rpt C-terminal domains in TopA from bacterial species found to have both types of C-terminal domains

Human Top3A

Topo_C_ZnRpt domains

653 EPIRKCPQCNKDMVLKTKKN-----GGFYLS~~CMGF~~PECRSAVWLPDSVLEAS
700 RDSSVCPV~~CQ~~PHPVYRLKLFKRGSLPPTMPLE~~FVCC~~IGGCDDTLREILDLRFS

Zf-GRE domains

807 ESNSVT~~CN~~CGQEAVLLTVRKEGPNRGRQFFK~~CN~~GGSCNFFLWADSPNP
891 SGSGTS~~CL~~CSQPSVTRTVQKDGP~~NCGRQ~~FHTCAKPREQQCGFFQWVDENTAP

CCHC domain

979 KKPRKCSLCHQPGHTRPFCPQNR

Human Top3B

C4-type zinc fingers

615 AATGKPLSR~~CGK~~CHRFMKYIQ-----AKPSRLH~~CSH~~CDETYTLPQNGTIKLYKELR~~C~~PLDD
679 GSRGKSYPLCPY~~CYN~~HPPFRD-----MKKGMGCNE~~C~~THPSCQH
717 SLSMLGIGQCVE~~CE~~SGVLVLDPTS-----GPKWKV~~CNK~~CNVVAH~~C~~FENA
762 HRVRVSADTCSV~~CE~~AALLDVDFNKA~~SPL~~PGDETQHMGCVF~~C~~DPVFQELVELKHAAS~~C~~HPMH

RGG motif

824 RGGPGRRQGRGRARRPPGKPNRRPK

Figure S4. C-terminal domains in human type IA topoisomerases. The RGG motif in Top3B is important for RNA binding.

Bacteria	Topo_C_ZnRpt	Topo_C_Rpt
Cyanobacteria		
▣ <u>Gloeocapsa sp. PCC 7428</u>	0	3
▣ <u>Synechococcus elongatus PCC 7942 = FACHB-805</u>	0	4
Bacteroidetes		
▣ <u>Rhodocytophaga rosea</u>	0	3
Flavobacteriaceae		
▣ <u>Formosa sp. Hel1_31_208</u>	0	2
▣ <u>Spongiivirga citrea</u>	0	2
▣ <u>Aurantibacter aestuarii</u>	0	2
▣ <u>Mangrovimonas yunxiaonensis</u>	0	2
▣ <u>Flavobacterium fontis</u>	0	2
▣ <u>Winogradskyella sp. PG-2</u>	0	2
▣ <u>Rhodothermus marinus DSM 4252</u>	0	3
Chlamydia		
▣ <u>Chlamydia pneumoniae</u>	3	0
▣ <u>Chlamydia trachomatis D/UW-3/CX</u>	3	0
Actinobacteria		
▣ <u>Berryella intestinalis</u>	3	0
Actinomycetia		
▣ <u>Streptomyces</u>		
▣ <u>Streptomyces inhibens</u>	0	4
▣ <u>Streptomyces coelicolor A3(2)</u>	0	4
▣ <u>Mycobacterium</u>		
▣ <u>Mycobacterium avium subsp. avium 2285 (R)</u>	0	1
▣ <u>Mycobacterium tuberculosis H37Rv</u>	0	4
Proteobacteria		
Alphaproteobacteria		
▣ <u>Candidatus Cytothobacter primus</u>	1	2
Rhodospirillales		
▣ <u>Caenispirillum bisanense</u>	1	3
▣ <u>Roseomonas cervicalis ATCC 49957</u>	1	3
Rhodobacterales		
▣ <u>Albimonas donghaensis</u>	1	3
Roseobacteraceae		
▣ <u>Sulfitobacter mediterraneus</u>	1	3
▣ <u>Rubellimicrobium mesophilum DSM 19309</u>	1	3
Hyphomicrobiales		
Beijerinckia		
▣ <u>Beijerinckia sp. 28-YEA-48</u>	1	4
▣ <u>Methylocapsa palsarum</u>	1	4
▣ <u>Roseiarcus fermentans</u>	1	4
Methylocystaceae		
▣ <u>Methylosinus sp. R-45379</u>	1	4
▣ <u>Methylocystis sp. SC2</u>	1	4
▣ <u>Aquamicrobium defluvii</u>	1	3
▣ <u>Agrobacterium fabrum str. C58</u>	1	3
▣ <u>Rickettsia bellii RML369-C</u>	1	2
▣ <u>Zymomonas mobilis subsp. mobilis ZM4 = ATCC 31821</u>	1	3
▣ <u>Caulobacter vibrioides CB15</u>	1	3
▣ <u>Helicobacter pylori 26695</u>	3	0
Gammaproteobacteria		
▣ <u>Xylella fastidiosa 9a5c</u>	0	3
▣ <u>Escherichia coli K-12</u>	3	0
Firmicutes		
Bacilli		
Lactobacillales		
▣ <u>Lactiplantibacillus plantarum</u>	2	0
▣ <u>Enterococcus faecalis</u>	3	0
▣ <u>Streptococcus pneumoniae</u>	3	0
Bacillales		
▣ <u>Listeria monocytogenes serotype 4b str. LL195</u>	3	0
Bacillaceae		
▣ <u>Halalkalibacterium halodurans C-125</u>	3	0
▣ <u>Bacillus subtilis subsp. subtilis str. 168</u>	3	0
▣ <u>Staphylococcus aureus subsp. aureus NCTC 8325</u>	3	0
Eubacteriales		
▣ <u>Sulfolobus acidophilus DSM 10332</u>	3	0
▣ <u>Clostridioides difficile 630</u>	3	0
▣ <u>Caldilinea aerophila DSM 14535 = NBRC 104270</u>	0	3
▣ <u>Thermotoga maritima MSB8</u>	1	0
▣ <u>Deinococcus radiodurans R1</u>	0	4
▣ <u>Borrelia burgdorferi B31</u>	0	1
▣ <u>Aquifex aeolicus VF5</u>	0	0

Figure S5. Taxonomy common tree of select bacterial species to illustrate the distribution of Topo_C_ZnRpt and Topo_C_Rpt repeats in bacterial topoisomerase I. The number of the repeats found in the TopA C-terminal region are indicated next to the species.

Fungi	zf-GRF 3	zf-CCHC 1
▣ Rozeella allomyces CSF55		
Microsporidia		
▣ Nematocida parisii ERTm1	2	0
Enterocytozoonidae		
▣ Enterospora canceri	1	0
▣ Hepatospora eriocheir	0	0
▣ Enterocytozoon hepatopenaei	1	0
▣ Nosema bombycis CQ1	2	0
Ascomycota		
Leotiomycetes		
▣ Pseudogymnoascus verrucosus	0	0
▣ Blumeria hordei DH14	0	0
▣ Botrytis cinerea B05.10	0	0
Saccharomycetales		
▣ [Candida] auris	0	0
▣ Cyberlindnera jadinii NRRL Y-1542	0	0
▣ Saccharomyces cerevisiae S288C	0	0
▣ Scheffersomyces stipitis CBS 6054	0	0
▣ Protomyces lactucae-debilis	0	0
Hypocreales		
▣ Metarhizium rileyi	0	0
▣ Fusarium oxysporum f. sp. cubense	0	0
Dothideomycetes		
▣ Lasiodiplodia theobromae	0	0
▣ Bipolaris victoriae FI3	0	0
▣ Zymoseptoria tritici IPO323	0	0
Aspergillaceae		
▣ Penicillium brasilianum	0	0
▣ Monascus purpureus	0	0
Aspergillus		
▣ Aspergillus niger CBS 513.88	0	0
▣ Aspergillus flavus NRRL3357	0	0
▣ Aspergillus fumigatus Af293	0	0
▣ Xylona heveae TC161	0	0
Pneumocystis		
▣ Pneumocystis jirovecii RU7	0	0
▣ Pneumocystis murina B123	0	0
Orbiliaceae		
▣ Dactylellina haptotyla CBS 200.50	0	0
▣ Orbilia oligospora ATCC 24927	0	0
Pezizales		
▣ Pyronema omphalodes CBS 100304	0	0
▣ Tuber melanosporum Mel28	0	0
▣ Schizosaccharomyces pombe 972h-	0	0
Chytridiomycota		
▣ Neocallimastix californiae	0	0
Chytridiomycetes		
▣ Batrachochytrium dendrobatidis JEL423	2	0
▣ Spizellomyces punctatus DAOM BR117	1	0
▣ Gonapodya prolifera JEL478	2	0
Mucoromycota		
Mucorales		
▣ Choanephora cucurbitarum	2	0
▣ Rhizopus azygosporus	2	0
▣ Rhizophagus irregularis DAOM 181602=DAOM 197198	0	0
Basidiomycota		
Dacrymycetaceae		
▣ Dacryopinax primogenitus	2	0
▣ Calocera viscosa TUFC12733	0	0
Malassezia		
▣ Malassezia vespertilionis	0	0
▣ Malassezia sympodialis ATCC 42132	1	1
▣ Malassezia globosa CBS 7966	0	0
▣ Malassezia restricta CBS 7877	0	0
Tremellomycetes		
Tremellales		
▣ Saitozyma podzolica	2	1
▣ Cryptococcus neoformans var. neoformans JEC21	2	1
▣ Aniotrachium porosum	1	0
Agaricomycetes		
▣ Hypsizygus marmoreus	2	0
Polyporales		
▣ Steccherinum ochraceum	1	3
▣ Grifola frondosa	1	2
Microbotryomycetes		
▣ Leucosporidium creatinivorum	2	2
Sporidiobolaceae		
▣ Sporidiobolus salmonicolor	1	0
▣ Rhodotorula graminis WP1	2	3
▣ Wallemia ichthyophaga EXF-994	1	1
▣ Mixia osmundae IAM 14324	2	0
Ustilaginaceae		
▣ Sporisorium reilianum SRZ2	2	2
▣ Ustilago maydis 521	2	2
▣ Puccinia graminis f. sp. tritici	2	3
Zoopagomycota		
▣ Basidiobolus meristosporus CBS 931.73	0	0
▣ Conidiobolus coronatus NRRL 28638	0	0
▣ Coemansia reversa NRRL 1564	2	1
▣ Allomyces macrogynus ATCC 38327	1	0

Figure S6. Taxonomy common tree of select fungi species to illustrate the distribution of zf-GRF and zf-CCHC repeats in fungal topoisomerase III. The number of the repeats found in the Top3 C-terminal region are indicated next to the species.