

1 **Title:**

2 **Classification of the treble clef zinc finger: noteworthy lessons for structure and function**
3 **evolution**

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14 **Supplementary Figures.**

15 **Figure S1. Structural variations of the treble clef fold.** The observed structural variations to the
16 core TC fold are shown using the ribbon diagrams for the respective domains. Colouring scheme: as
17 in Fig. 1, mercury: gray. Large insertions in the core and disordered regions in the structures are
18 represented by dotted lines.

19
20 **Figure S2: Insertions and extensions to the core of the treble clef zinc finger fold.** Colouring
21 scheme and representation: as in Fig. 1. The additional α -helix and β -strands of the FYVE are
22 coloured in a lighter tint. 3_{10} -helices are represented as rectangles with serrated edges. Additional
23 loops regions between the knuckles are shown as loop-like protrusions. The SSEs in brackets ('[]')
24 are not conserved in all the structurally characterised members.

25
26 **Figure S3: Topology diagrams of treble clef domains.** SSEs of the TC are coloured and
27 represented as in Fig. 1. β -strands that are placed closely are involved in hydrogen bonding and form
28 β -hairpins/ β -sheets. In some proteins such as RPB10, hypothetical protein ORF126, prolyl-RS, etc.,
29 few SSEs are boxed in different colours because their topological connections are such that they could
30 be independently structurally-related to other protein folds (as mentioned in the figure), but, none-the-
31 less the overall zinc-binding site resembles a TC motif. In MerB (PDBid 3F0P_A1) and ZF of E6
32 oncoprotein TC2 (PDBid 4GIZ_C), the knuckle- β -hairpin forms a β -sheet by hydrogen bonding with
33 the primary β -hairpin and for these, the α -helix is shown behind the plane of the β -sheet.

FIGURE S1

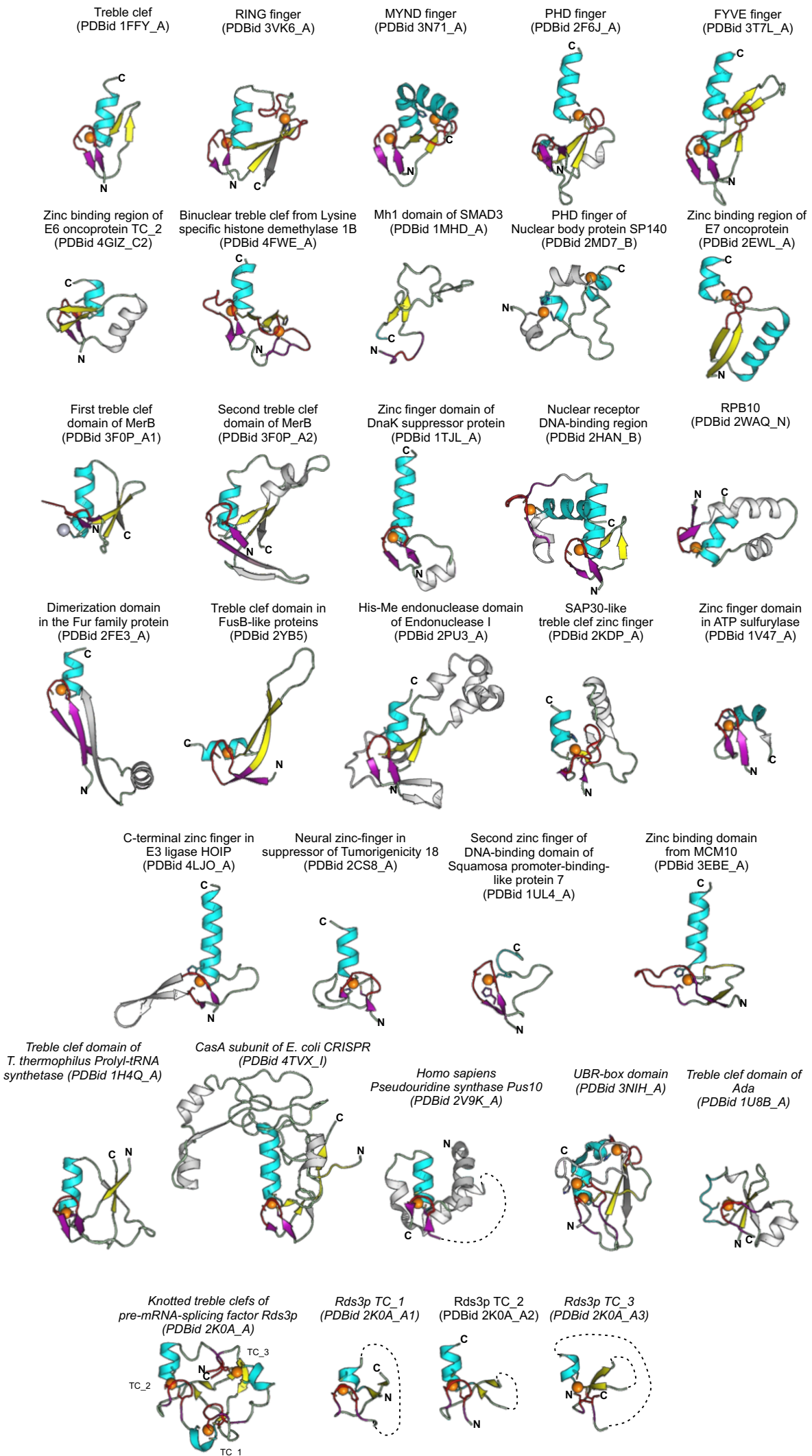


FIGURE S2

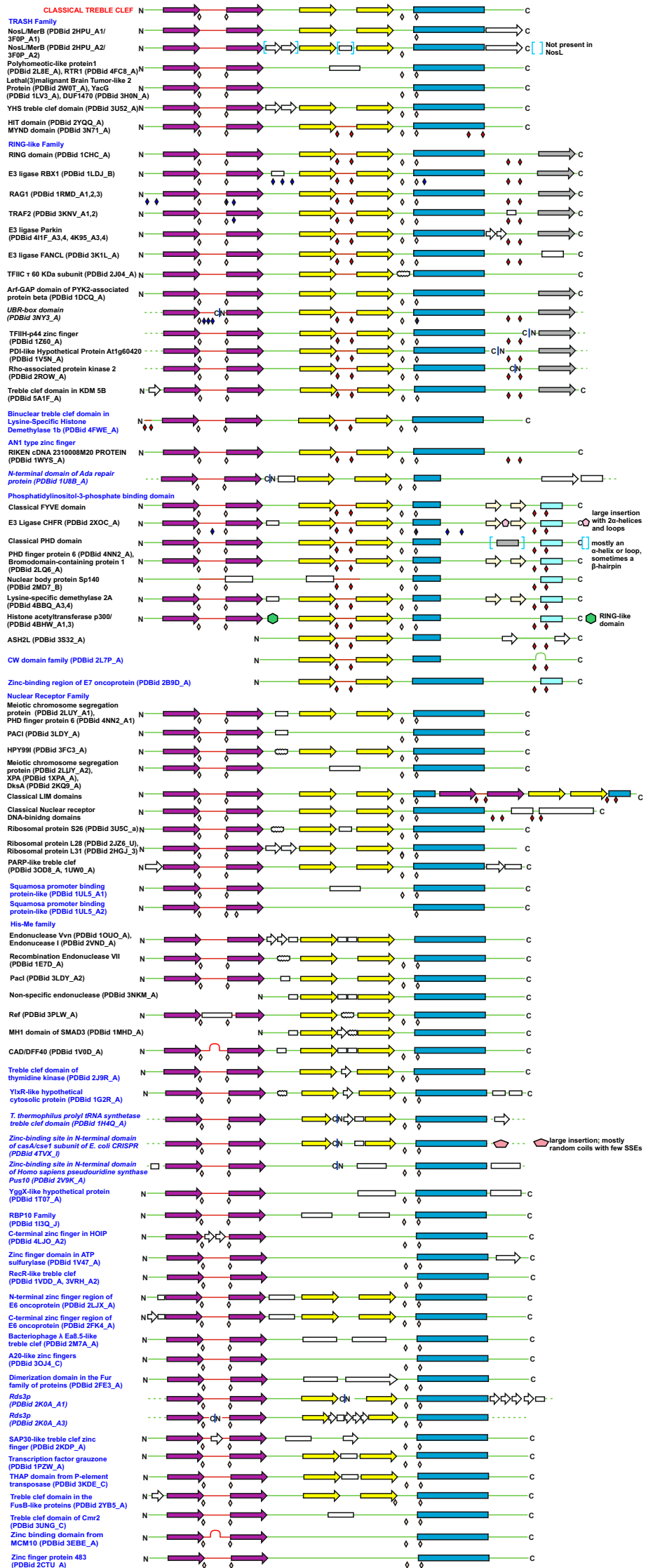
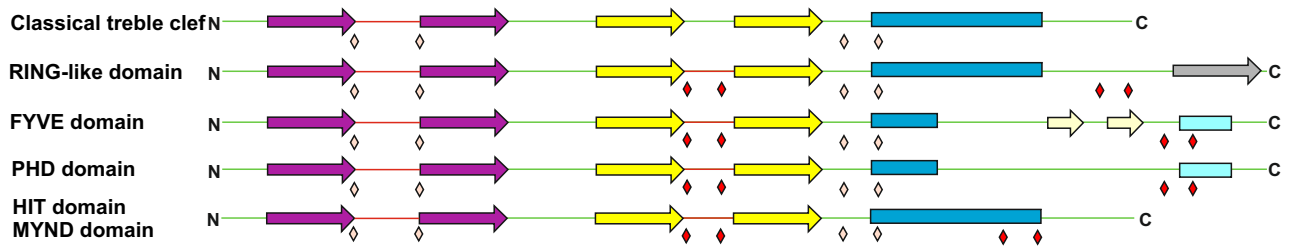
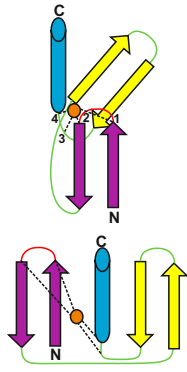


FIGURE S3

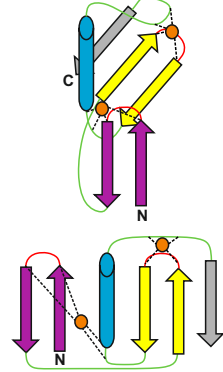
GENERAL TOPOLOGIES



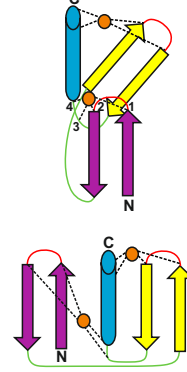
Ribosomal protein L24 (PDBid 3U5E_W)



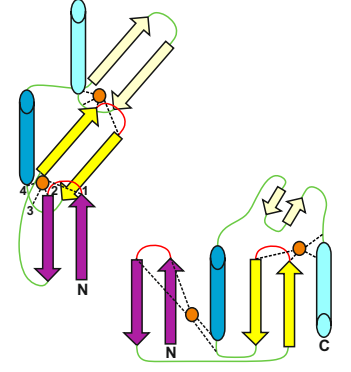
RING-like domain (PDBid 1CHC_A)



HIT domain (PDBid 2YQQ_A)
MYND domain (PDBid 3N71_A)

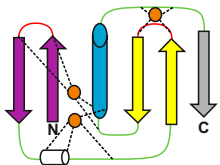


FYVE domain (PDBid 1VFY_A)

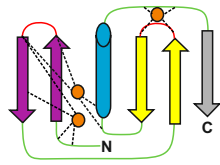


SPECIFIC VARIATIONS OBSERVED

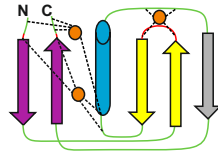
E3 ligase RBX1 (PDBid 1LDJ_B)



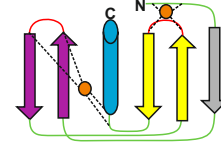
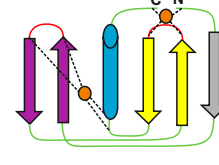
RAG1 (PDBid 1RMD_A1,2,3)



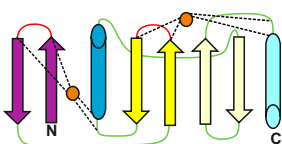
UBR-box domain (PDBid 3NY3_A)



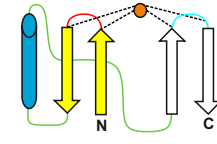
C1 domain of Rho-associated protein kinase 2 (PDBid 2ROW_A)
PDI-like Hypothetical Protein At1g60420 (PDBid 1V5N_A)



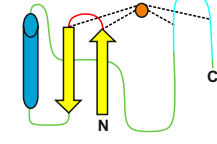
Lysine-specific demethylase 2A (PDBid 4BBQ_A3,4)



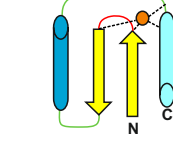
ASH2L (PDBid 3S32_A; N-terminal first zinc-binding site deteriorated in structure)



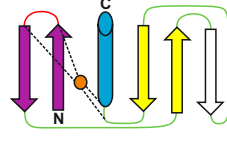
CW domain (PDBid 2L7P_A)



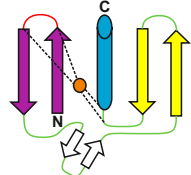
Zinc-binding region of E7 oncoprotein (PDBid 2EWL_A)



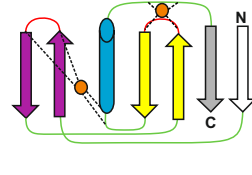
Treble clef of thymidine kinase (PDBid 2J9R_A)



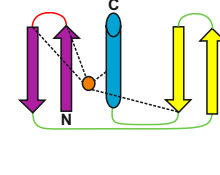
YHS domain (PDBid 3U52_A)



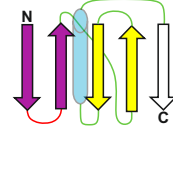
Treble clef in KDM 5B (PDBid 5A1F_A)



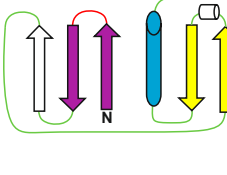
Treble clef in FusB-like proteins (PDBid 2YB5)



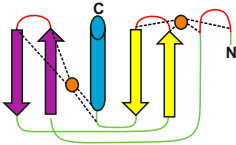
MerB (PDBid 3F0P_A1)



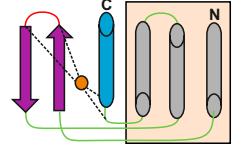
MerB (PDBid 3F0P_A2)



Binuclear treble clef domain in Lysine-Specific Histone Demethylase 1b (PDBid 4FWE_A1,2)

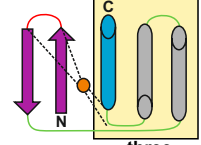


Bacteriophage λ Ea8.5-like treble clef (PDBid 2M7A_A)



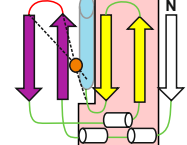
Homeodomain

RBP10 (PDBid 1I3Q_J)



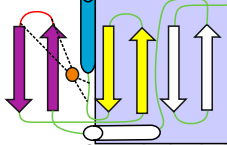
three helical bundle

Zinc finger region of E6 oncoprotein TC_2 (PDBid 4GIZ_C2)



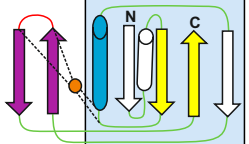
lambda cro repressor fold

Hypothetical protein ORF126 (PDBid 2X5R_A)



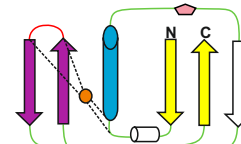
C-terminal sub-domain of ATP-grasp fold

T. thermophilus prolyl tRNA synthetase treble clef (PDBid 1H4Q_A)



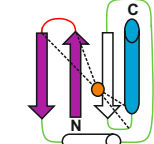
IF3-like fold

Zinc-binding site in N-terminal domain of CasA/Cse1 subunit of *E. coli* CRISPR (PDBid 4TVX_I)

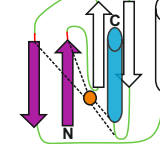


large insertion; mostly random coils with few SSEs

Dimerization domain in the Fur family (PDBid 2FE3_A)



SAP30-like treble clef (PDBid 2KDP_A)



PARP-like treble clef (PDBid 3OD8_A)

