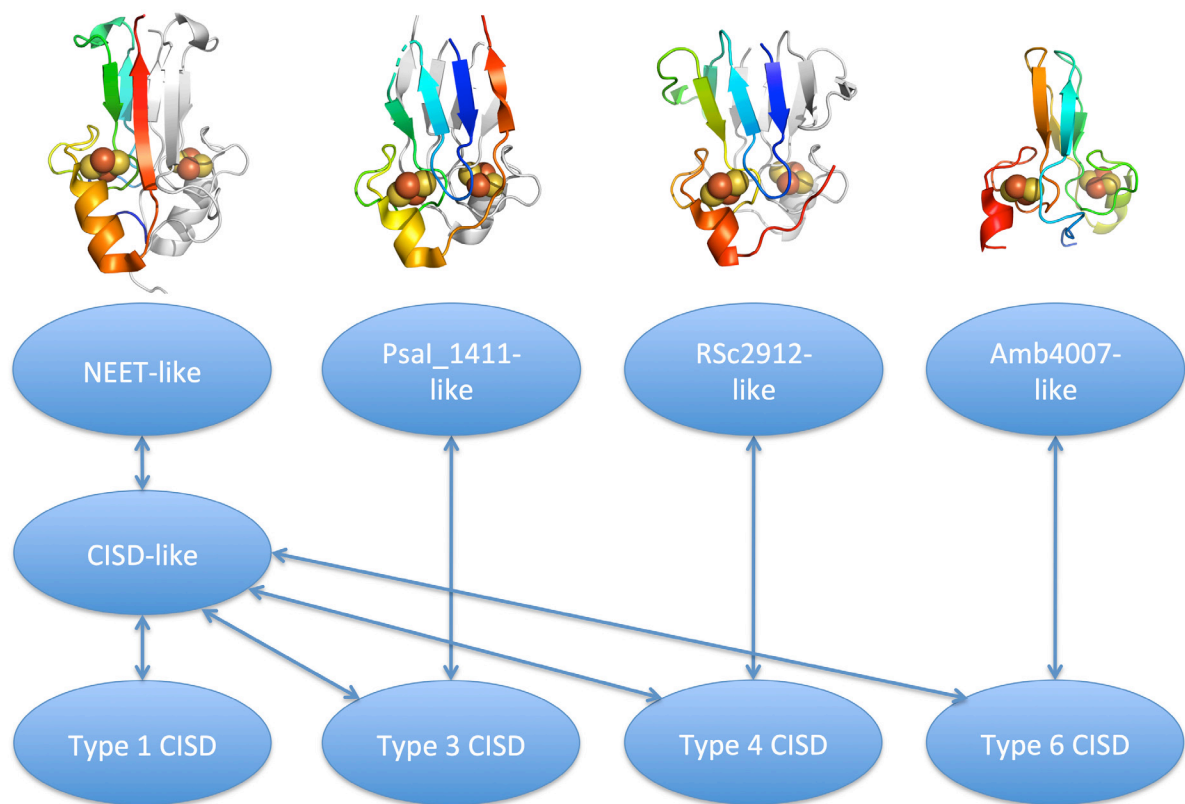
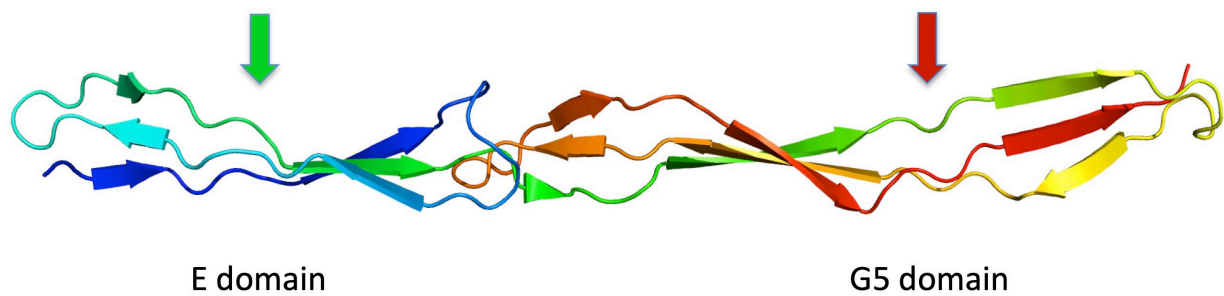


SUPPLEMENTARY MATERIAL



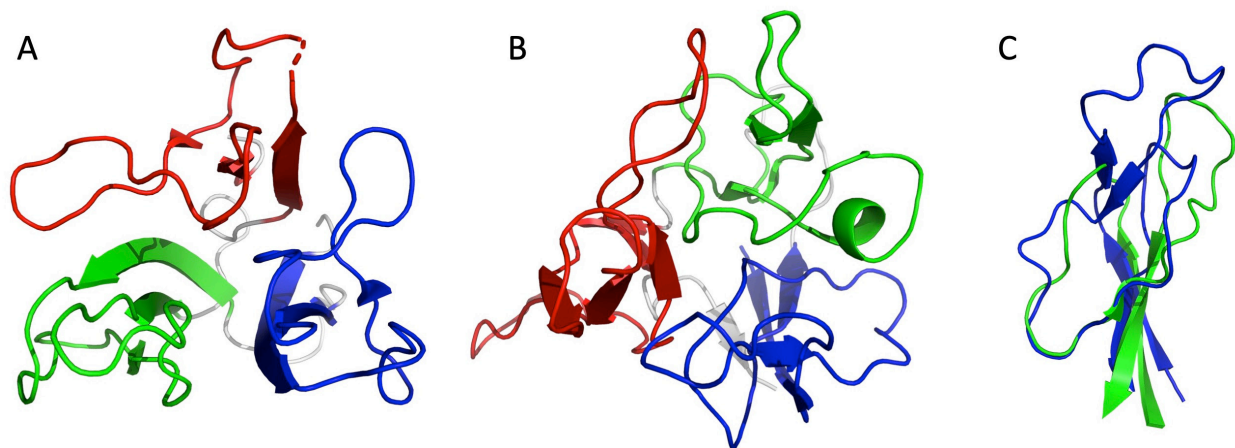
Supplementary Figure 1. Structural and evolutionary relationships of homologous families with different folds.

The CISD families of different types, sharing CDGSH iron sulphur cluster-binding motif, are classified into the same CISD-like superfamily. The fold of the largest type 1 family is selected as representative for this superfamily, whereas each other family is assigned to a different fold. The classification of these families exemplifies a complex scenario of non-hierarchical evolutionary and structural relationships.



Supplementary Figure 2. Novel type of protein architecture in the β -braid fold (SCOP ID 2001419).

This small fold, lacking a hydrophobic core, is made of three interlaced extended segments, capped on both ends by three-stranded β -sheets with different strand orders. This fold is found in the related G5 domain and E domain families, which are present together in Staphylococcal SasG and Aap proteins (*1*), a section of which is shown here as a rainbow-coloured cartoon. Interlacing sections of both domains are indicated by bold arrows coloured green and red, as their C-terminal segments. Before the determination of its structure, the smaller E domain was thought to be unstructured.



Supplementary Figure 3. Intra- and interrelationships of two different new folds

The β -prism III (A; SCOP ID 2001273) and Tricorn (B; SCOP ID 2001279) folds are new folds exhibiting pseudo three fold symmetry. Both folds are composed of three compact motifs shown in different colours: N-terminal in blue, middle in green and C-terminal in red. Individual motifs from the different folds have similar topologies (C; showing the green motif of A superimposed on the blue motif of B), but are assembled differently in different folds. The β -prism III and Tricorn domains are found in the MACPF proteins in the same position C-terminal to the pore-forming domains, suggesting their very remote evolutionary relationship (2, 3)

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