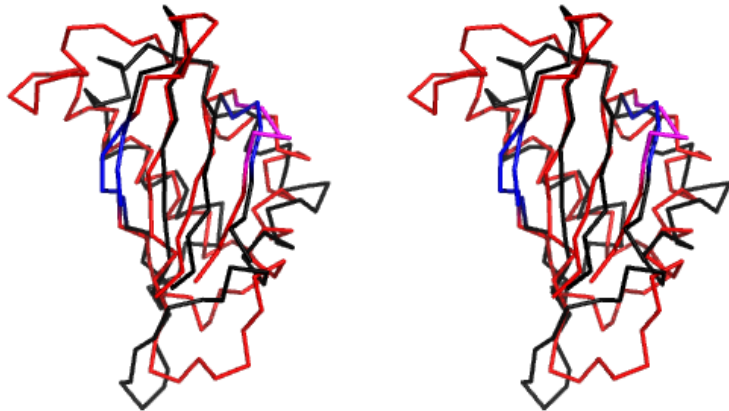
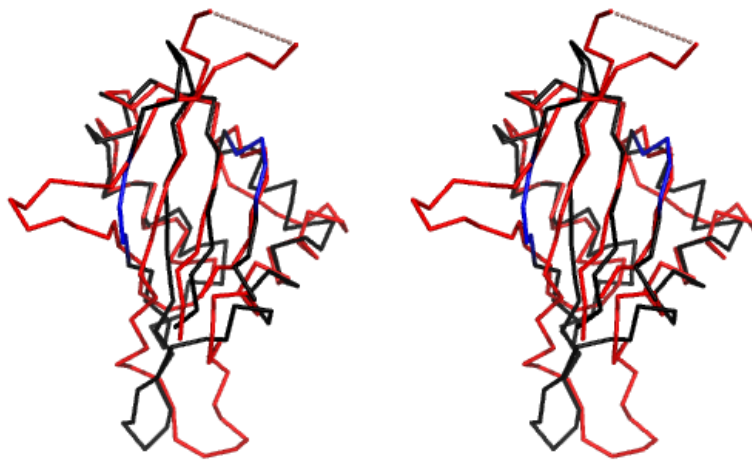


Supplementary Figure S1. Stereo view of superposition of a nucleoporin 54 SEA domain (pdb: 5c2u, black trace) with (A). a canonical SEA domain from Muc16 (pdb: 1ivz, red trace) and (B). a SEA domain from Notch3 (pdb: 4hti, red trace). Beta-bulges with the $\phi x x \phi$ motif are colored blue. The region with the $\phi x x x \phi$ motif in Muc16 is colored magenta.

(A)



(B)



Supplementary Table S2. Phyletic distribution of SEA domain groups. Known and novel SEA domain groups are colored blue and red, respectively.

| SEA domain group | Pfam family | vertebrates | non-vertebrate chordates | non-chordate metazoans | Choano-flagellates | Filasterea | non-Holozoa |
|--|-------------------------------|-------------|--------------------------|------------------------|--------------------|------------|-------------|
| receptor phosphatase R (PTPRR) SEA domains | N/A | ✓ | | | | | |
| EpCAM SEA domains | N/A | ✓ | | | | | |
| CD34 SEA domains | CD34_antigen (PF06365) | ✓ | ✓ | | | | |
| Collectrin SEA domains | Collectrin (PF16959) | ✓ | ✓ | | | | |
| α/ϵ -sarcoglycan SEA domains | Sarcoglycan_2 (PF05510) | ✓ | ✓ | ✓ | | | |
| receptor phosphatase IA-2 SEA domains | Receptor_IA-2 (PF11548) | ✓ | ✓ | ✓ | | | |
| Notch SEA domains | NOD(PF06816) NODP(PF07684) | ✓ | ✓ | ✓ | | | |
| Amnionless SEA domains | Amnionless (PF14828) | ✓ | ✓ | ✓ | | | |
| CELSR/FAT cadherin SEA domains | N/A | ✓ | ✓ | ✓ | | | |
| CDH23/PCDH15/CDHR2 cadherin SEA domains | N/A | ✓ | ✓ | ✓ | ✓ | | |
| Canonical SEA domains | SEA (PF01390) | ✓ | ✓ | ✓ | ✓ | | |
| Nup54 SEA domains | N/A | ✓ | ✓ | ✓ | ✓ | | |
| dystroglycan SEA domains | DAG1 (PF05454) | ✓ | ✓ | ✓ | | ✓ | |
| KIAA0319 SEA domains | N/A | ✓ | ✓ | ✓ | | ✓ | |
| Fibrocystin-like SEA domains | N/A | ✓ | ✓ | ✓ | ✓ | | ✓ |