

Supplementary Figure S1 – The prediction accuracy and robustness of the HMM identifications. The ROC curves were illustrated, and AROC values were calculated for the self-consistency (Curves & triangles in blue) and LOO (Curves & diamonds in red) validations of 8 families, respectively.

Supplementary Figure S2 – From the results of sequence alignment, the profiles of UBC and UEV domains are very similar, while the active site cysteine residue responsible for ubiquitin coupling is not presented in UEV proteins (18).

Supplementary Figure S3 – Although BTB protein can interact with Cul3 in other strategies, the appearance of 3-box following BTB domains can strengthen the Cullin binding (36). By sequence alignment, we observed that 3-boxes are conserved with an asparagine residue at +3 positions. The HMM profile for 3-boxes was constructed. Thus, we separated BTB proteins into two families, and proteins predicted with both BTB domain and 3-box motif were classified into the BTB_3-box family.

Supplementary Table S1 – From the scientific literature, we collected 26 E1s, 105 E2s, 1,003 E3s and 148 DUBs for ubiquitin and ubiquitin-like conjugation systems. The gene name and UniProt accession number and for each protein were provided. The Ensembl IDs were present if available. The classification and organism information was also shown. a. Other database, the known enzymes collected in SCUD (15) and hUbiquitome (17) were indicated and fully covered by UUCD.

Supplementary Table S2 – The cut-off values of 1, 1, 15 and 6 HMM profiles for E1s, E2s, E3s and DUBs at the family level, respectively.

Supplementary Table S3 – The detailed classifications of E1s, E2s, E3s and DUBs in 70 eukaryotes. The numbers of characterized enzymes were shown.

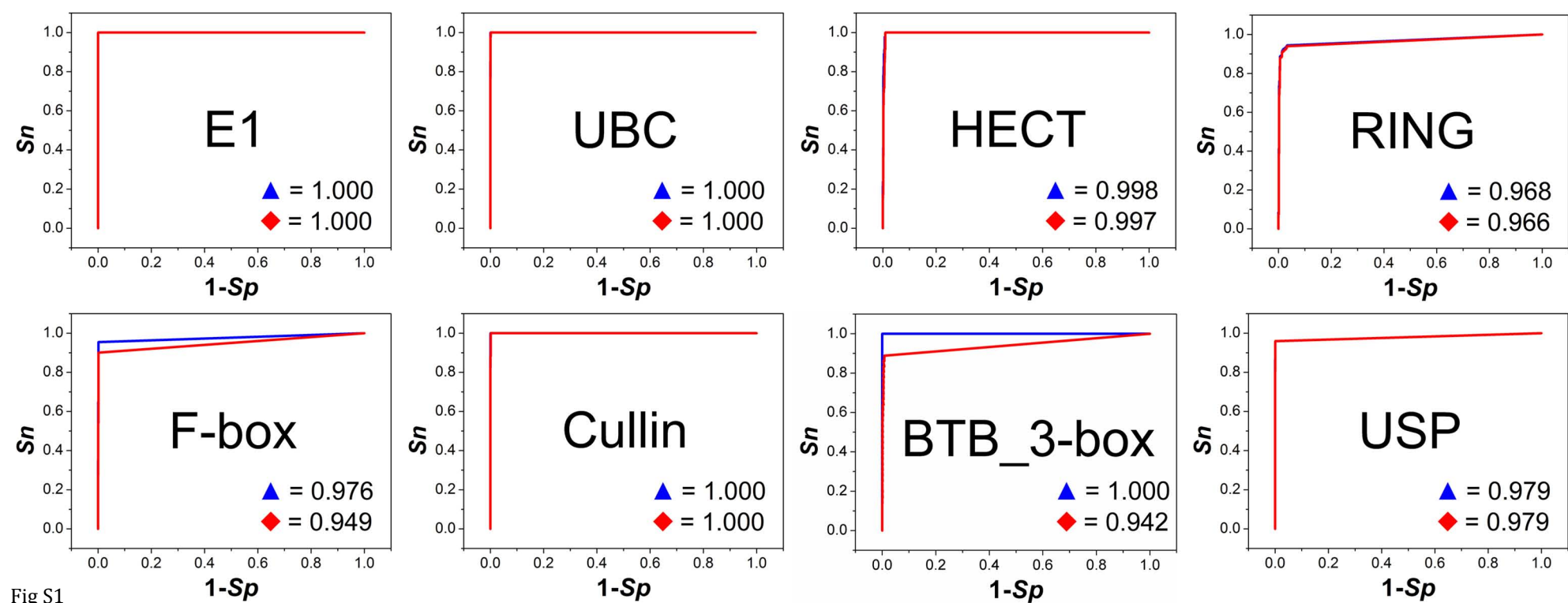
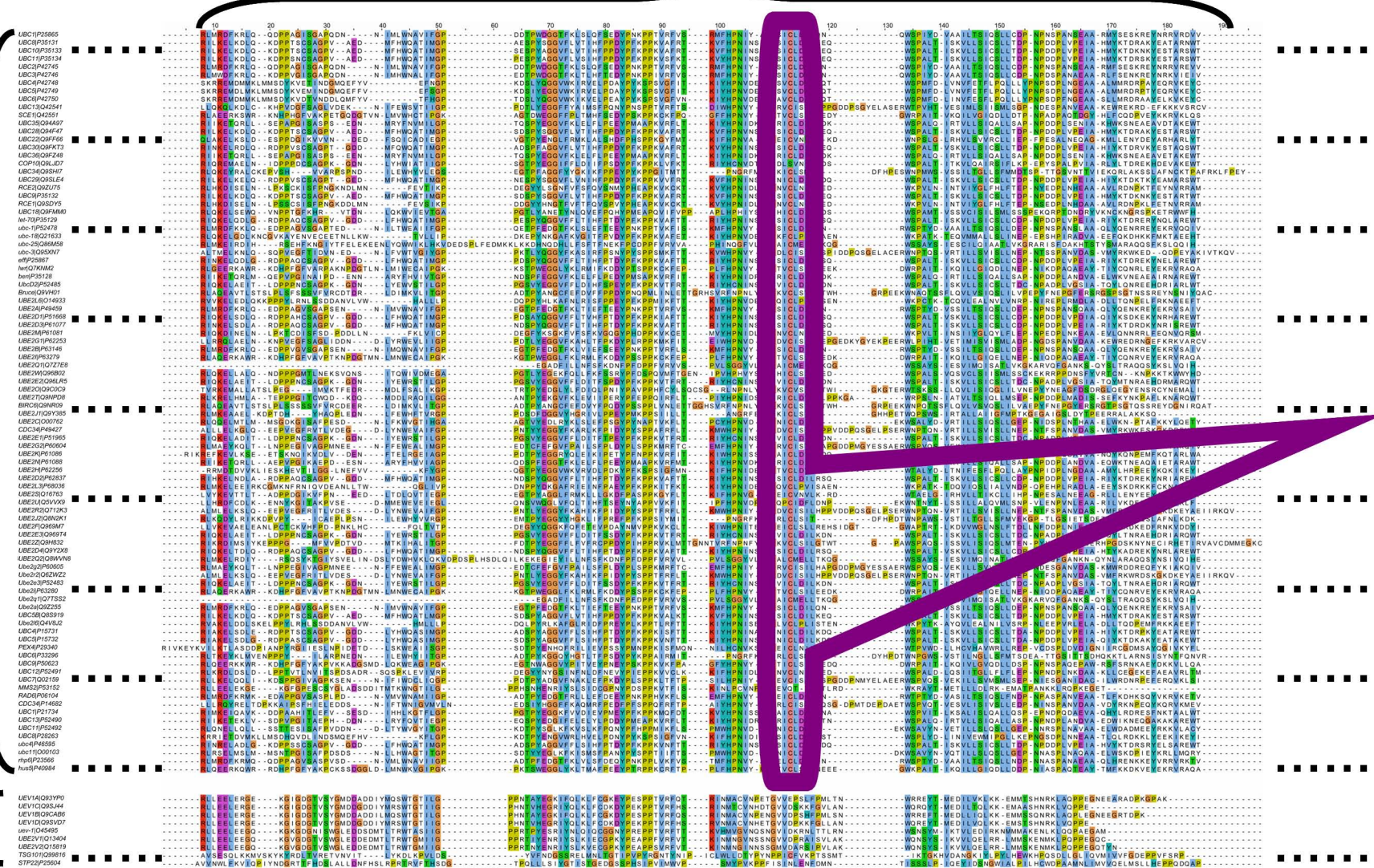


Fig S1

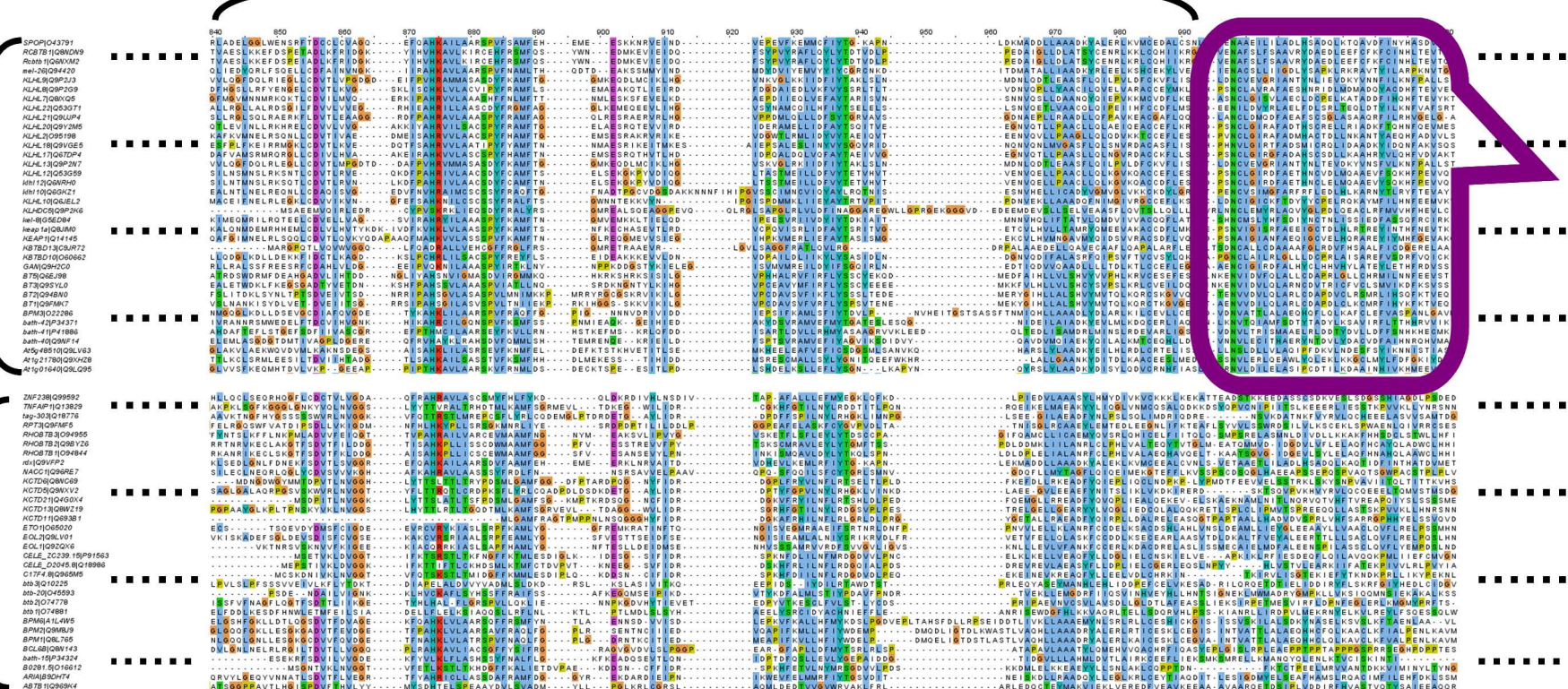
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Conserved Cysteine



BTB_Other BTB_3-box

BTR domain



3-box