





**Supplemental Figure S3 (contd.)** Amino acid sequence alignment of VSP orthologues and human PTEN. The residue, which is made disulfide bond with Cys363, is shown in cyan. The residues interacted with Tyr522, Asp523 and Asn524 of CBR3 loop are in green. The secondary-structural elements of the cytoplasmic region of Ci-VSP are indicated above the alignment as a spiral ( $\alpha$ -helix) or an arrow ( $\beta$ -sheet). Those of human PTEN (PDB ID 1D5R) are indicated below the alignment. The abbreviations used are: Ci: *Ciona intestinalis*; Dr: *Danio rerio*; Xl: *Xenopus laevis*; Hs-TPIP: *Homo sapiens* TPTE and PTEN homologous inositol lipid phosphatase; Mm: *Mus musculus*; Gg: *Gallus gallus*.