

**Supp. Fig. 1.** *I domains exist in multiple conformations.* MIDAS bound cation is shown as a pink sphere in each crystal structure. The conserved phenylalanine and MIDAS threonine are shown in blue and red, respectively. (A)  $\alpha$ M integrin I domain crystal structures of inactive and active conformations (PDB ID codes 1JLM and 1IDO, respectively, (46, 47)). Upon transition from the inactive to active state, F302 is flipped out and exposed to the aqueous milieu while T209 shifts from an indirect coordination of the MIDAS cation to a direct one. (B) Top down view of (A). (C) The sANTXR2 crystal structure (PDB ID code 1SHU, (27)) most closely resembles the  $\alpha$ M I domain active conformation. (D) Top down view of sANTXR2 bound to PA (PDB ID code 1TZN (16)) showing the conserved phenylalanine (F203) and threonine (T118) residues are removed from direct binding interactions with PA.