

Fig. S2. A close-up stereo of the PP2Ac-PTPA interface surrounding the phosphatase active site. The active site is indicated by two catalytic metal ions (magenta spheres, at M1 and M2 positions) and ATPγS (yellow cylinder). PP2Ac and PTPA are in ribbon and colored blue and orange, respectively. Residues of PP2Ac and PTPA are shown in cylinder and ball-and-stick, and colored cyan and purple, respectively. Arg268 of PP2Ac is highlighted. H-bond interactions are indicated by black dashed lines. Note that mutations to PTPA residues, Phe100, Asp213, and Val209 disrupted PP2A-binding (Figure 6B). The dashed line divides the structural elements of PP2A at the interface with PTPA into two portions: the active site loops connected to the 1<sup>st</sup> β-sheet versus those connected to the  $2^{nd}$  and peripheral β-sheets.