Vps4 Structures

As expected, the Vps4 structures reported here resemble published structures of human VPS4B$_{\Delta MIT}$-SO_4[25], yeast (His)$_6$Vps4$_{\Delta MIT}$[27], and yeast Vps4$_{\Delta MIT}$-ADP[28]. For example, the ATPase cassettes of our yeast Vps4$_{\Delta MIT}$-SO_4 and human VPS4B$_{\Delta MIT}$-SO_4 structures overlap with a Cα root mean square deviation (RMSD) between ordered residues of just 1.2 Å (Fig. 1c). Nevertheless, our two new structures have several ordered loops that have not been seen in previous structures, and the new structures extend the existing ranges of bound ligands, interdomain angles, and intermolecular packing interactions.

As in other AAA ATPases, the ATPase cassette of Vps4 is composed of two domains. The larger amino-terminal domain has six α-helices (helices 1-5 and 10) that pack on either side of a six-stranded β sheet. The first strand of the sheet (β'), which is found in only a subset of AAA ATPases, runs antiparallel to the remaining five strands (strands 1-5). The smaller carboxyl terminal domain is an antiparallel four-helix bundle (helices 6-9) (Fig. 1b). The two domains are structurally distinct, although the final helix extends away from the smaller domain to pack along one edge of the large domain sheet. Vps4 is unique amongst known AAA ATPases in that a three-stranded β-sheet, called the β domain, is inserted between helices 8 and 9 of the four-helix bundle. The β domain contributes to Vta1 binding[25] and enzyme assembly[39].

Both of our Vps4 crystal forms were grown in the presence of ATPγS, and two of the three molecules in crystal form 2 (A and B) show clear electron density for bound