



Figure S4. Interaction networks of the high-IS residues of membrane protein transporters. Red circle represents cavity residues and blue circle indicates non-cavity residues. (A) Chloride pump halorhodopsin (PDB ID: 1E12), (B) Sulfate/molybdate ABC transporter (PDB ID: 3D31), (C) KvAP voltage-gated K<sup>+</sup> channel (PDB ID: 1ORQ), and (D) P-type Ca<sup>2+</sup> ATPase (PDB ID: 1WPG).