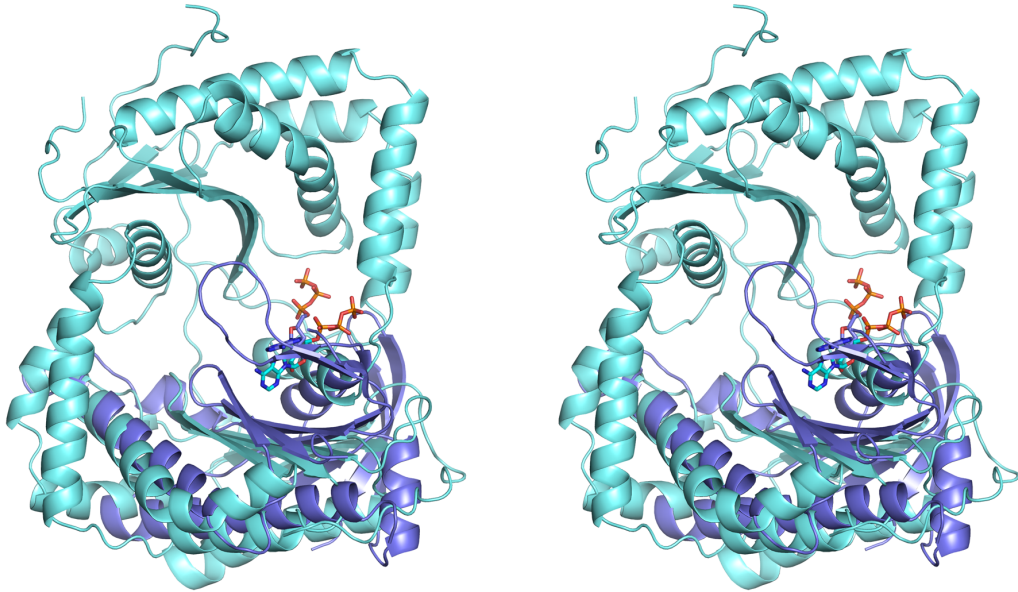
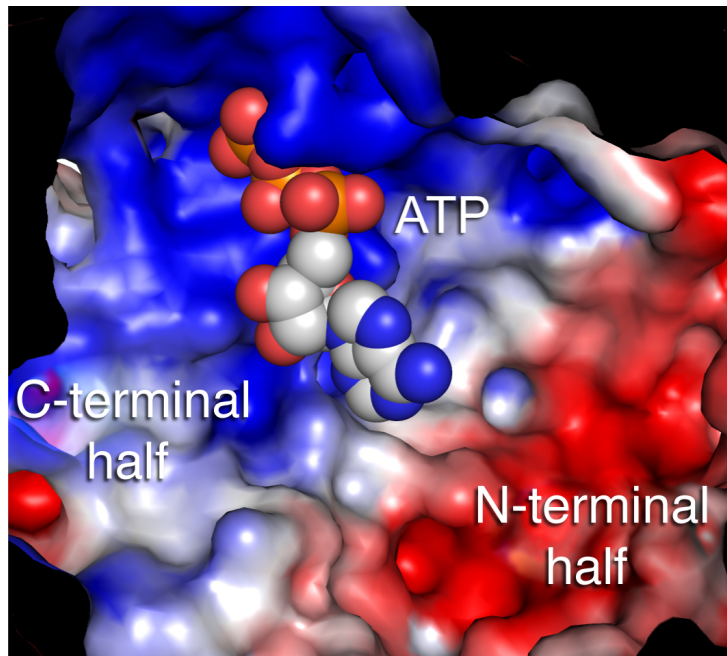


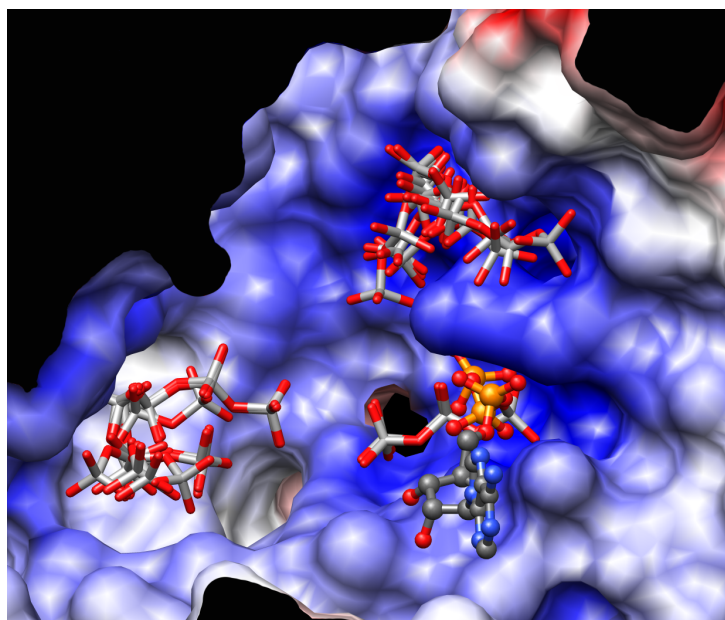
A



B



C



**Figure S3. Structural relationship of the proposed IDE ATP/polyanion binding fold to palm domain containing enzymes, surface electrostatics, and alternative binding sites.** *A*, Stereo view of a ribbons representation of domains 3 and 4 of IDE is shown (cyan) superimposed with the C<sub>1a</sub> domain of adenyl cyclase (purple; Tesmer et al., 1999; PDB entry 1CJU). ATP ligands for both molecules are shown in stick representation with carbon atom colors matching the corresponding ribbon model. IDE is oriented as viewed from the substrate-binding chamber of the enzyme with domain 4 at the top of the figure. *B*, Surface electrostatic potential on the walls of the substrate-binding chamber. The molecular surface is colored according to electrostatic potential (*blue*, positive; *red*, negative) with modeled ATP shown in a sphere representation and the N-terminal and C-terminal halves of IDE indicated. *C*, Positively charged surface containing the identified ATP binding site. The inner surface from domains 3 and 4 of IDE is shown with triphosphate molecules docked by the program Autodock Vina (47) in stick representations (light gray phosphorous). The bound ATP ligand from the crystal structure is shown in a ball and stick representation (orange phosphorous). The electrostatic potential at the surface is indicated by color (blue positive, red negative) with +/- 10 kT cutoff values.