Structure *18*

Supplemental Information

Insights from the Structure of a Smallpox Virus Topoisomerase-DNA Transition State Mimic

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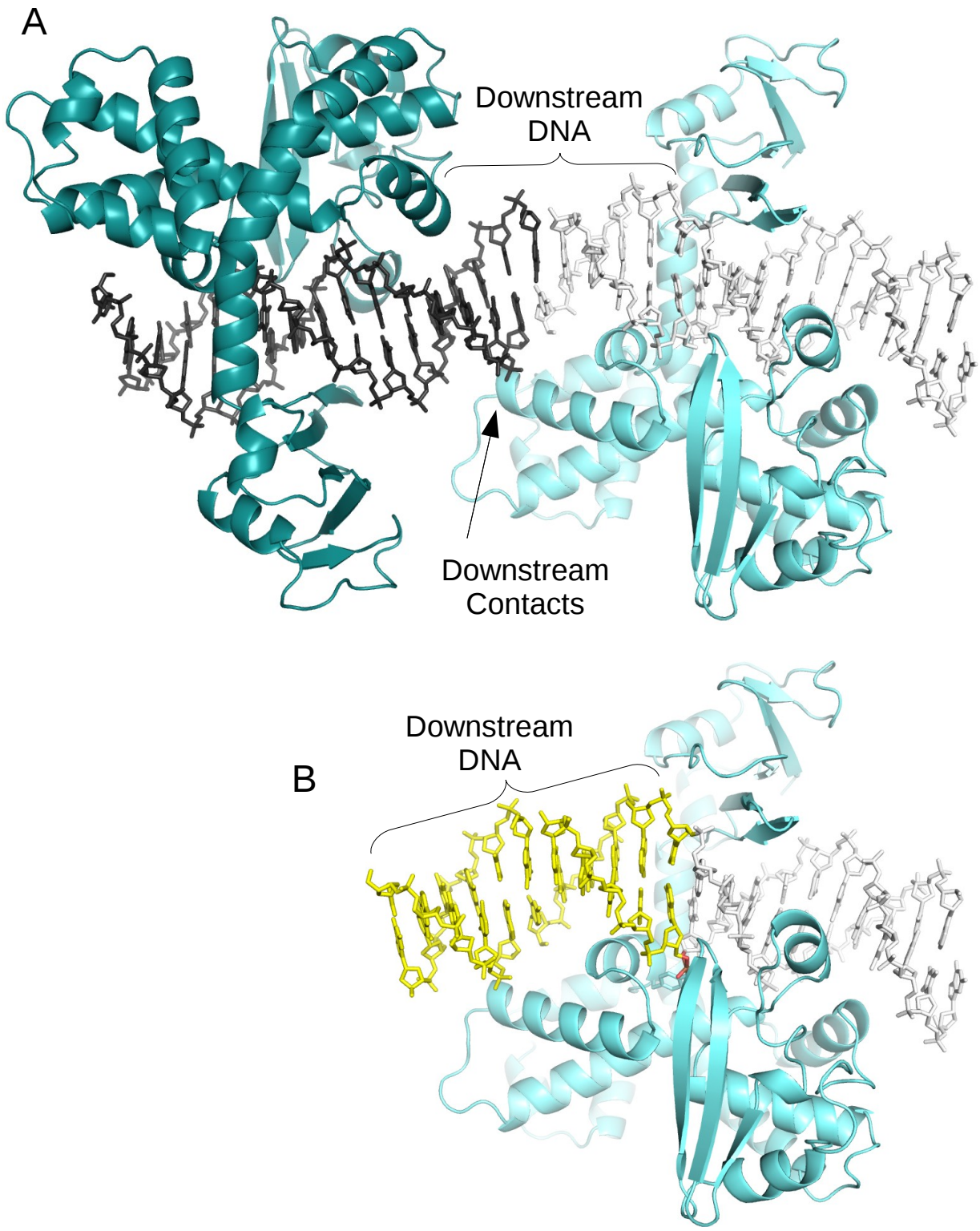

Figure S1. Formation of an extended vTopIB-DNA interface in the crystal. (A) Two adjacent vTopIB/DNA complexes in the crystal lattice. The DNA duplexes form a continuous helix in the crystal, where adjacent duplexes are 180 degrees out of phase. Each vTopIB molecule contacts two DNA duplexes, allowing an extended protein-DNA interaction surface that is longer than the individual duplexes that make up the lattice. Note that there are no interactions between adjacent proteins along the DNA helix and adjacent proteins do not compete for the same binding site. The darker shaded subunit makes downstream contacts to the next DNA duplex extended to the left (not shown). (B) The vTopIB/DNA complex as shown in Figures 2 & 3 in the main text, where base pairs downstream of the cleavage site are colored yellow. As indicated above, this region includes DNA from adjacent duplex segments in the crystal.

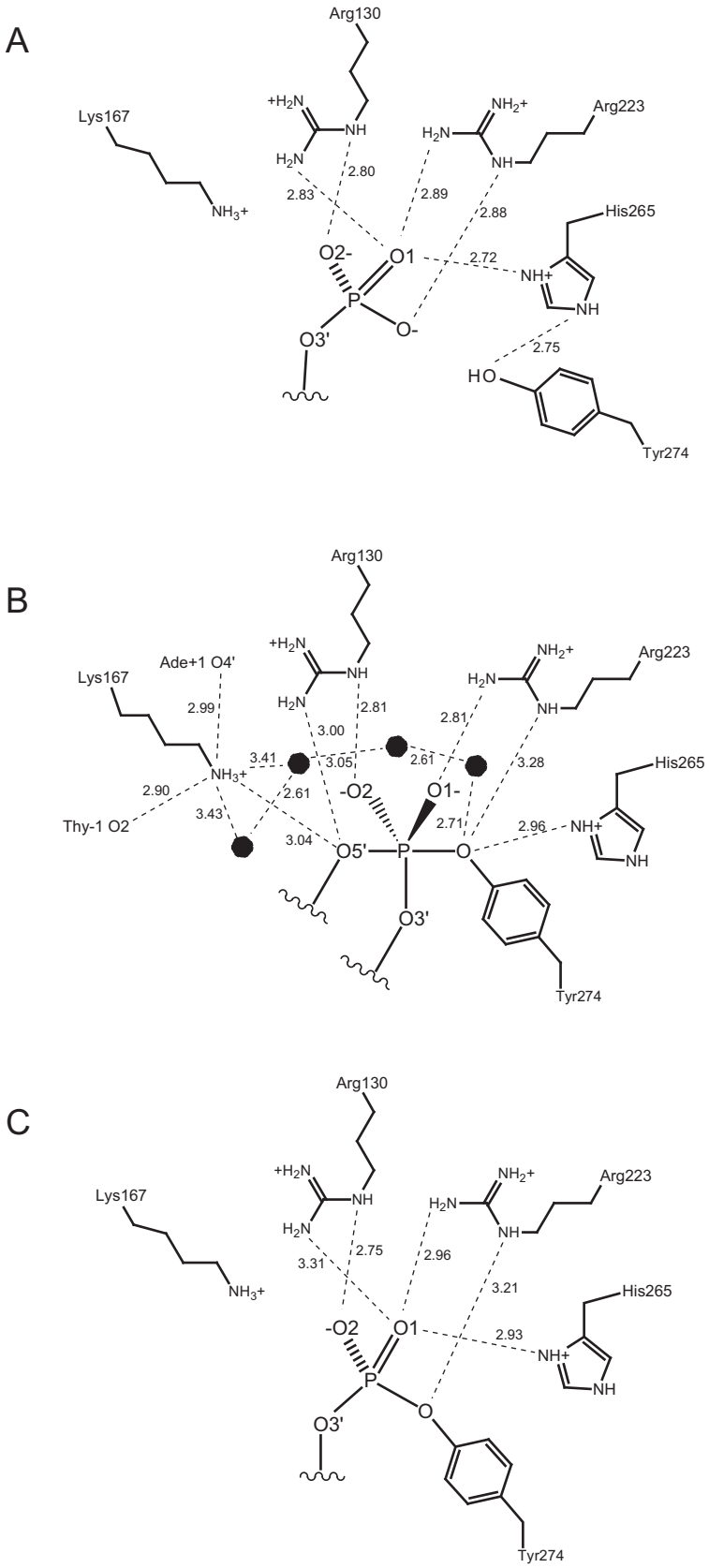

Figure S2. Hydrogen bonding distances in the active sites of vvTopIB structures. A. The non-covalent intermediate (pdb code 2H7F). B. The vanadate transition state mimic (this work). C. The covalent intermediate (2H7F). Note that the non-covalent intermediate in (A) is not a good representation of the pre-cleavage intermediate because the terminal 3'-phosphate has rotated to place the third oxygen atom in position to mimic the tyrosine hydroxyl group as observed in (C). This figure supplements the active site shown in Figure 4 of the main text.