SUPPLEMENTARY MATERIAL

The coordinates for our model of the Pol γ holoenzyme with docked primer-template are provided as supplementary material in .pdb format. Primer-template was docked via the alignment shown in Figure S1, *top panel.*

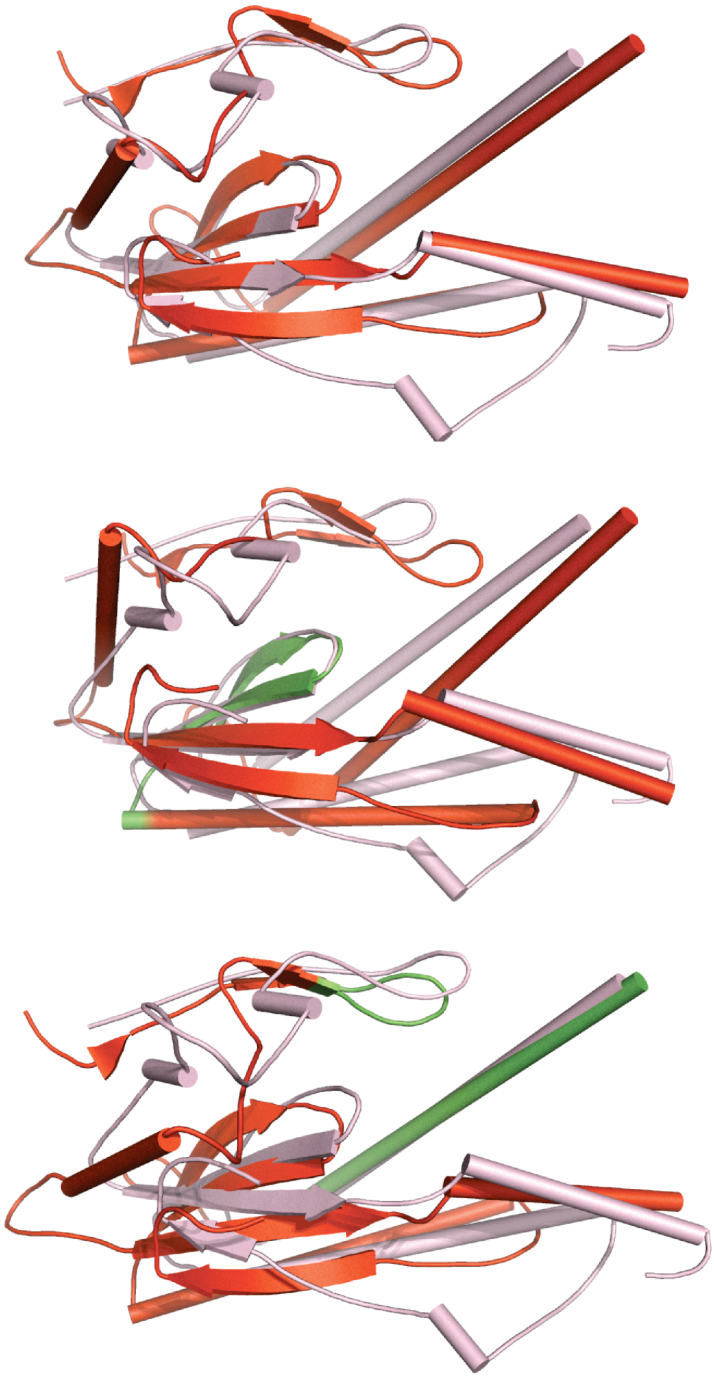

Figure S1. Alignments used for docking DNA onto the *Hs* Pol γ holoenzyme structure (3IKM). Panels display the palm subdomain of the T7 Pol (1T8E) closed ternary complex (red) superimposed on the palm subdomain of Pol γ (pink). *Top panel,* alignment of the palm of T7 Pol (residues 409-487, 611-704) to the palm of Pol γ (815-910, 1095-1239); *middle panel*, alignment of T7 Pol residues 646-663 (green) to Pol γ residues 1127-1144; lower panel, alignment of T7 Pol residues 606-635 and 422-431 (green) to Pol γ residues 1093-1122 (Q-helix) and 846-855 (RR-loop). Alignments were performed in Pymol.

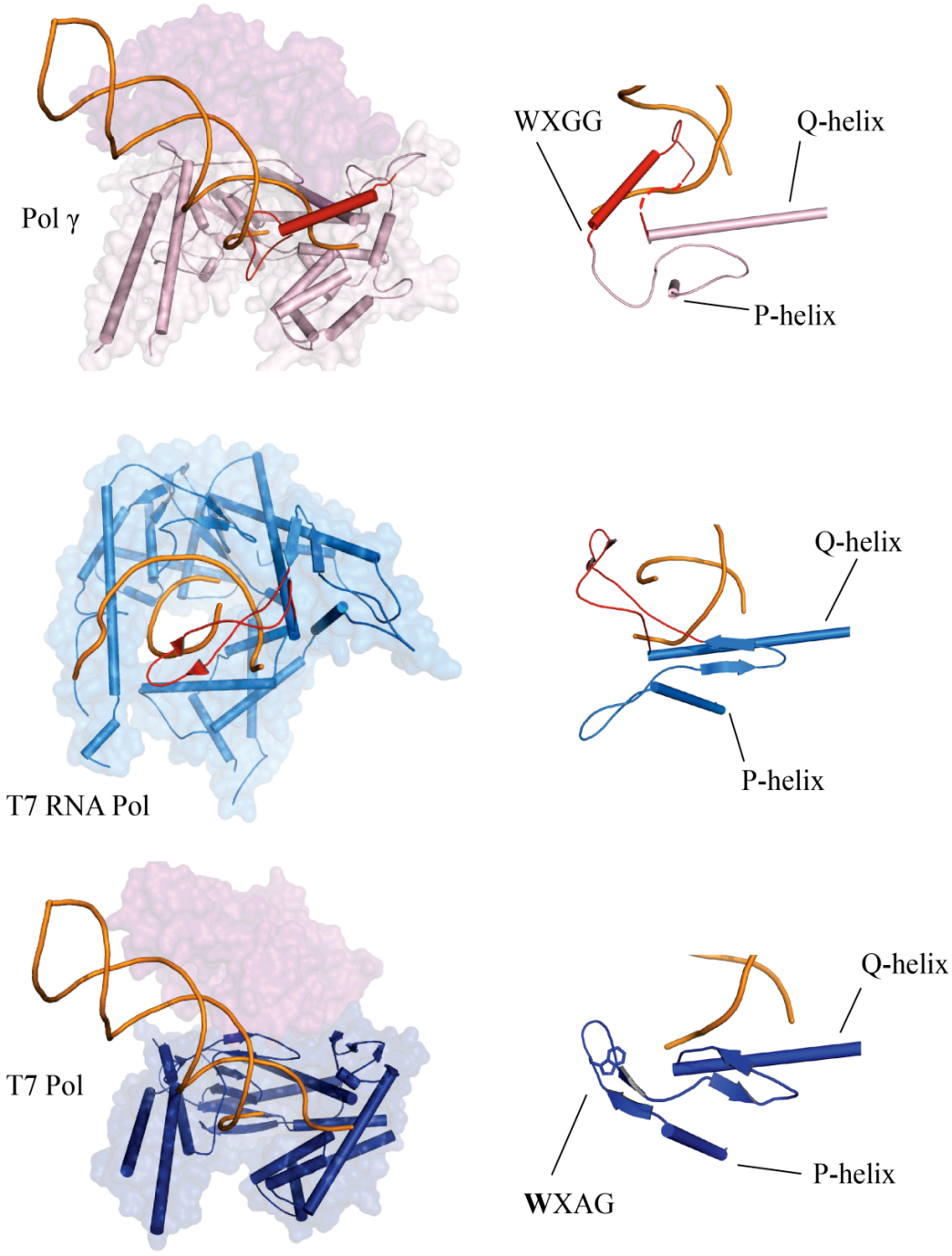


Figure S2. Comparative alignments of *Hs* Pol γ, T7 Pol and T7 RNA Pol illustrating the structural variations in the region between the P-helix and the Q-helix in the pol domain. Panels *at left* display the complete pol domain in complex with DNA, and those *at right* show a close up view of the of the region between the Q-helix and P-helix. *Top panel,* the Pol γ (3IKM) pol domain is shown as pink cartoon and its partitioning loop in red,

with its disordered region indicated as a dashed red line. Transparent surfaces of the exo (purple) and pol (pink) domains are also shown *at left*. DNA docked by alignment with T7 Pol (see Fig. S1, top panel) is shown in orange; *middle panel,* the Pol domain of the T7 RNA Pol elongation complex (1H38) is shown as light blue cartoon and its specificity loop in red; *lower panel,* the T7 Pol (1T8E) pol domain is shown as blue cartoon, and transparent surfaces of its exo (purple) and pol (blue) domains are shown to highlight a similar architecture as in Pol γ. WXGG and WXAG are the amino acid sequence motifs in Pol γ and T7 Pol, respectively, which are discussed in the text.

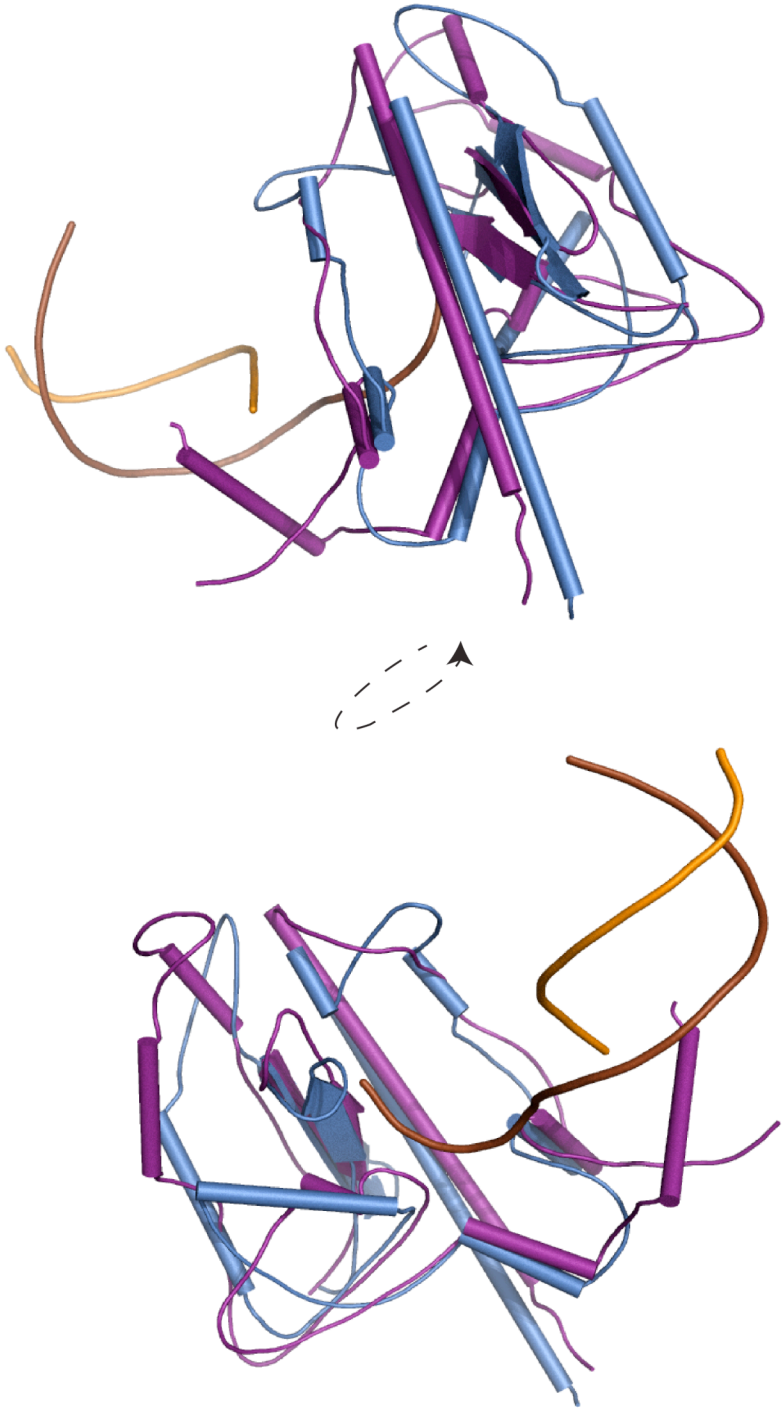

Figure S3. Structural alignment of the exo domain of Klenow editing complex (PDB code 1KLN, residues 324-518, displayed as blue cartoon) with the exo domain of human Pol γ (PDB code 3IKM, residues 170-440, displayed as purple cartoon). This alignment was used to predict the editing complex of Pol γ by docking of the frayed primer template (primer strand in chocolate, template strand in orange) onto the apoholoenzyme structure, which we display in Figure 4B.