



Fig. 3. (Chaojiang Gu et al.) Comparison of structures of VPg1 bound to WT and four mutant RdRps. a) Ribbon representation of the protein primer VPg1 produced by high-resolution *de novo* structure prediction. b-f) Front-back views of the polymerase molecule showing the trajectory of the VPg protein in the WT RdRp–VPg complex and the mutant RdRp–VPg complexes, respectively. The polymerase domains: fingers, palm, and thumb are colored in sky-blue, magenta, and green-cyan, respectively. In all panels, for clarity, the 3D sub-structure of the thumb domain and some residues at the top of the NTP tunnel (from 163 to 180) are omitted to better show the VPg protein. In detail, panel (b) shows the trajectory of the VPg protein in the structure of the WT RdRp–RNA template–VPg primer complex. The trajectory of the VPg protein in the structure of the L123F RdRp–RNA template–VPg primer complex is presented in (c), the L123F/F244L RdRp–RNA template–VPg primer complex is presented in (d), the T381A RdRp–RNA template–VPg primer complex is presented in (e), and the T291I/T381I RdRp–RNA template–VPg primer complex is presented in (f). The VPg in all panels is shown as a green stick representation and its critical Tyr3 residue is in red. The short RNA template is displayed in a yellow stick form.