Supporting Information

Modeling the binding mechanism of Remdesvir, Favilavir, and Ribavirin to SARS-CoV-2 RNA-dependent RNA polymerase

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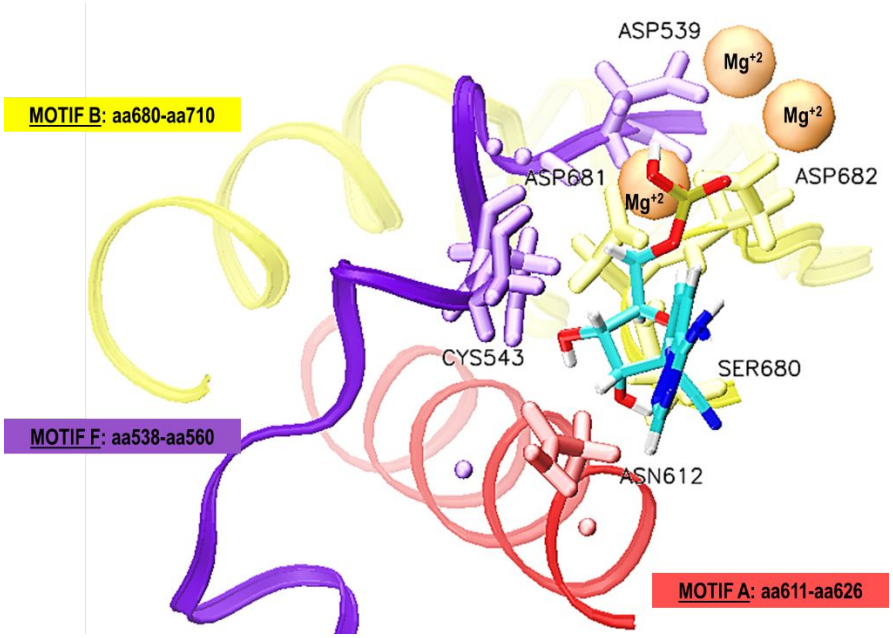

Figure S1. Interactions among the non-natural nucleotide remdesivir and nsp12 conserve motifs located at the enzyme catalytic site: the ligand mainly interact with the conserved motif A (red), B (yellow) and F (violet) trough Asn612, Ser680, Cys543 and Lys543 residues. Asp539, Asp681 and Asp682 belonging to motif B and F coordinate the Mg^{+2} ions.

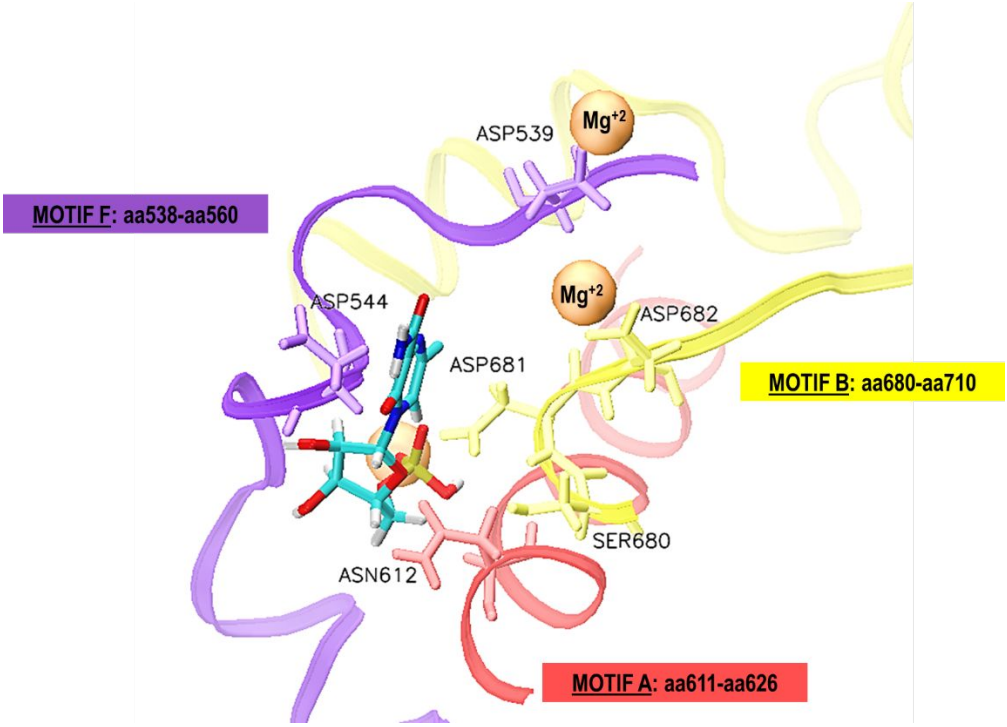

Figure S2. Interactions among the non-natural nucleotide favilavir and nsp12 conserve motifs located at the enzyme catalytic site: the ligand mainly interact with the conserved motif A (red), and B (yellow) trough Asn612 and Ser680. Asp539, Asp681 and Asp682 belonging to motif B and F coordinate the Mg^{+2} ions.

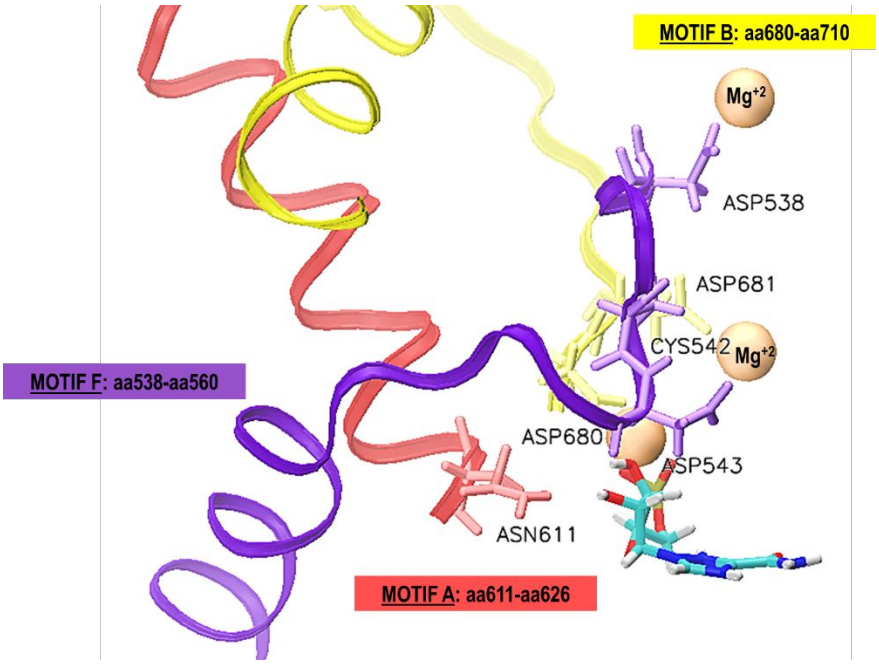

Figure S3. Interactions among the non-natural nucleotide ribavirin and nsp12 conserve motifs located at the enzyme catalytic site: the ligand mainly interact with the conserved motif A (red), and B (yellow) trough Asn611 and Ser680. Asp539, Asp681, Cys542 and Asp682 belonging to motif B and F coordinate the Mg^{+2} ions.

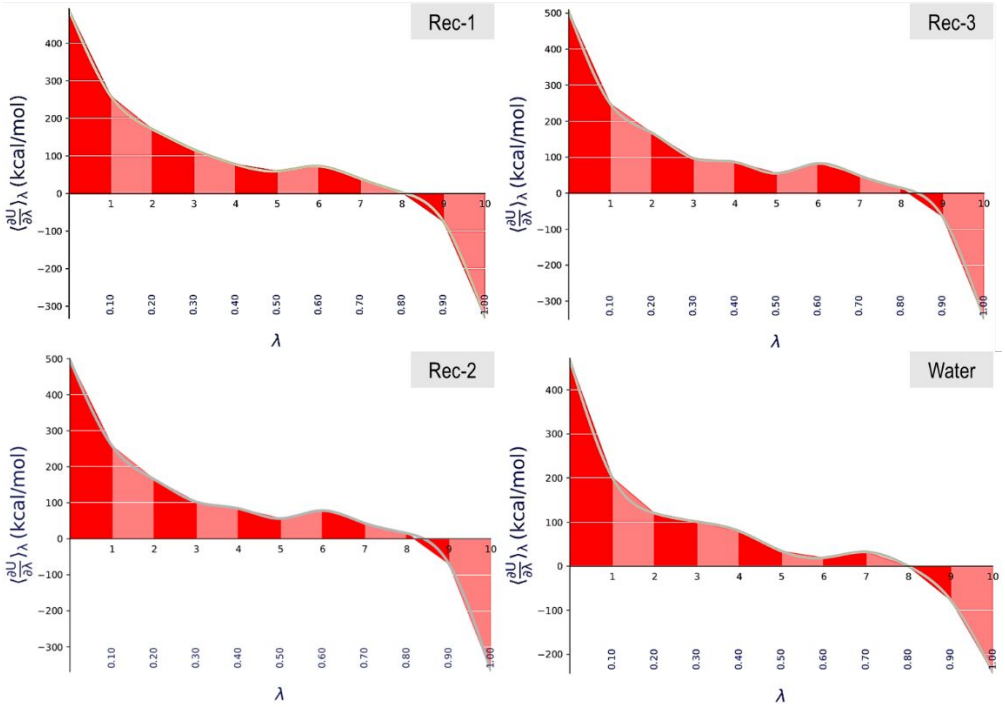

Figure S4. The thermodynamic force as a function of lambda for three independent replicas of the non-natural nucleotide **Favilavir** at the nsp12 protein active site (Rec-1, Rec-2 and Rec-3), as well as, the ligand in water media (Water).

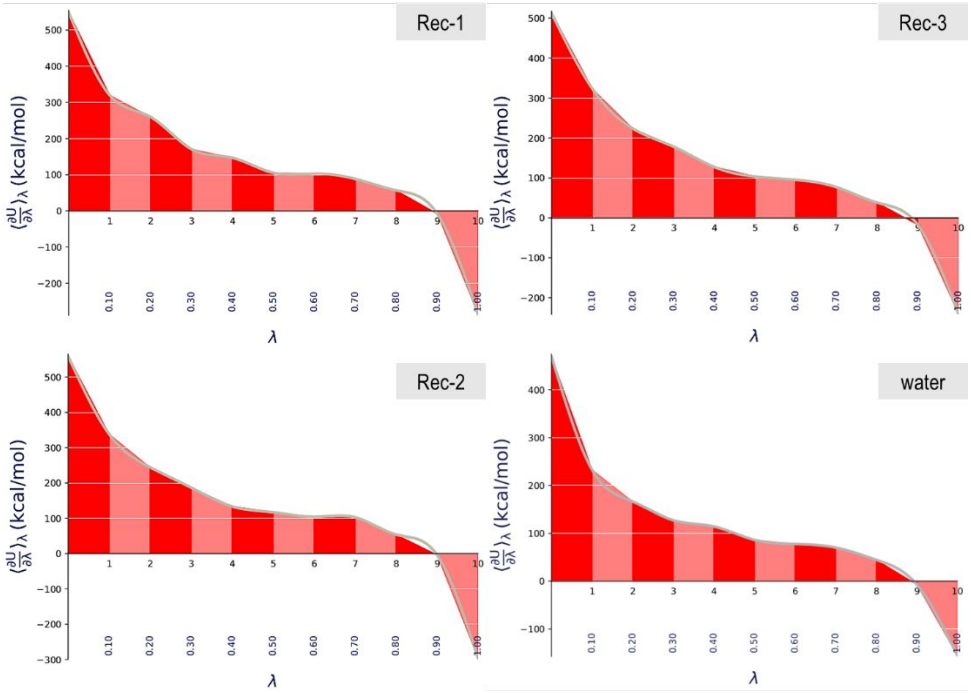

Figure S5. The thermodynamic force as a function of lambda for three independent replicas of the non-natural nucleotide R**ibavirin** at the nsp12 protein active site (Rec-1, Rec-2 and Rec-3), as well as, the ligand in water media (Water).

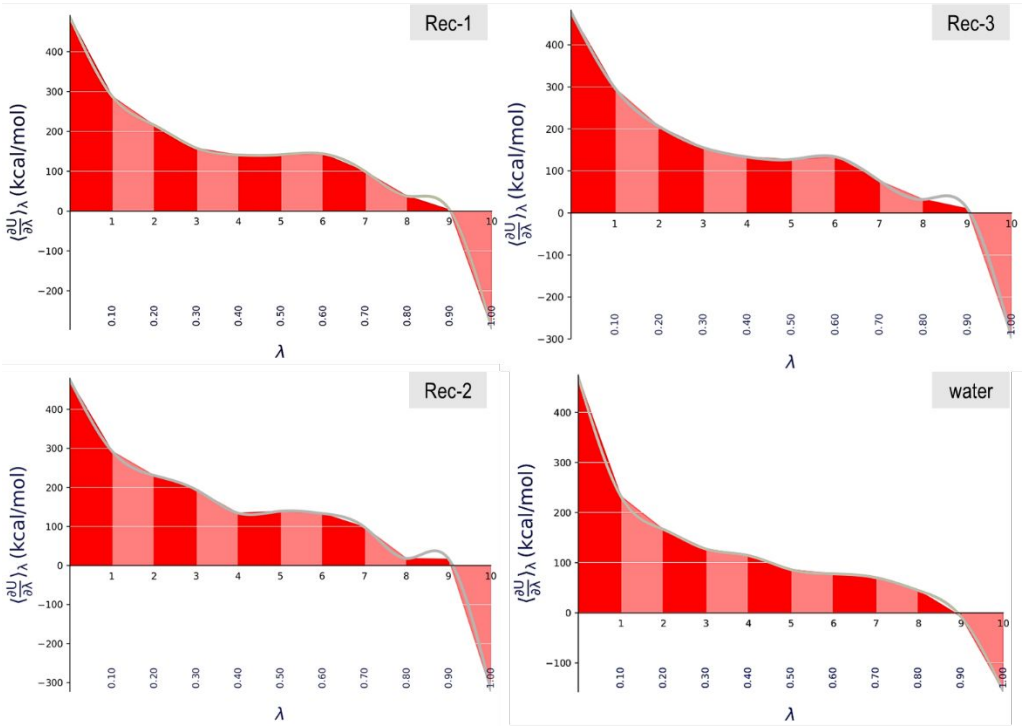

Figure S6. The thermodynamic force as a function of lambda for three independent replicas of the non-natural nucleotide **Remdesivir** at the nsp12 protein active site (Rec-1, Rec-2 and Rec-3), as well as, the ligand in water media (Water).