DOCKING REPORT.

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Molecular docking was done using crystal structure with PDB code **5RED** (Main protease of SARS-CoV2)[1] given the crystal parameters shown in figure 1.

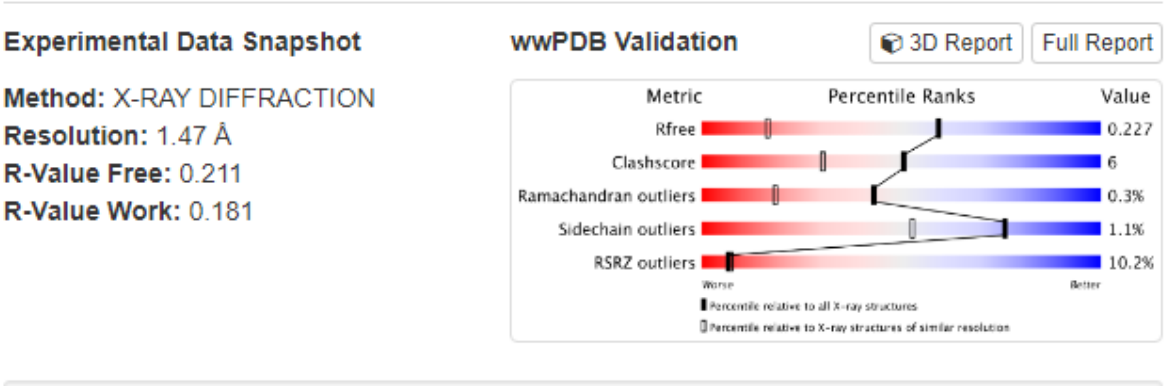
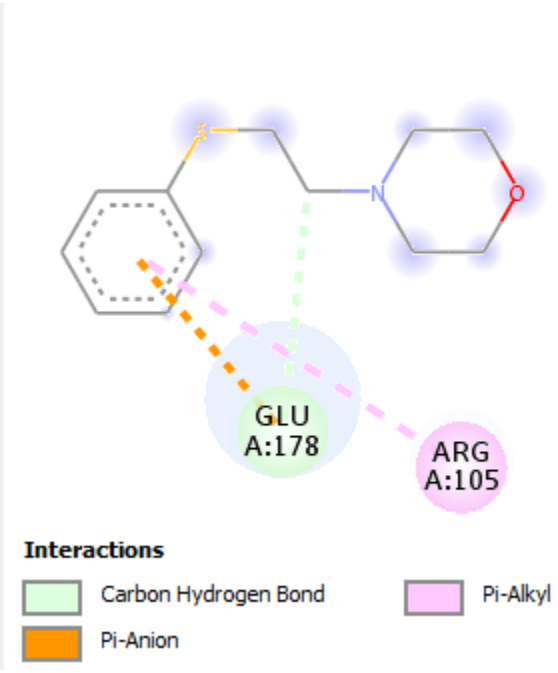


Figure 1. Parameters of crystal 5RED.

Mentioned enzime was co-crystallized with morpholine named in this document as compound **M1** (Interactions enzyme – M1 are shown in scheme 1). Redocking of this compound was done in AutoDock Tools 1.5.6. with grid parameters shown in figure 2; these were found centering the box in co-crystallized ligand. With this calculation, new interactions in more stable conformation were found in addition to those displayed by X-ray diffraction analysis (Scheme 2).

[1] https://www.rcsb.org/3d-view/5RED?preset=ligandInteraction&sele=JJG Revisado el 25-03-2020 a las 11:03.



Scheme 1. Interactions of compound **M1** with main protease of SARS-CoV2 observed in crystal Structure.

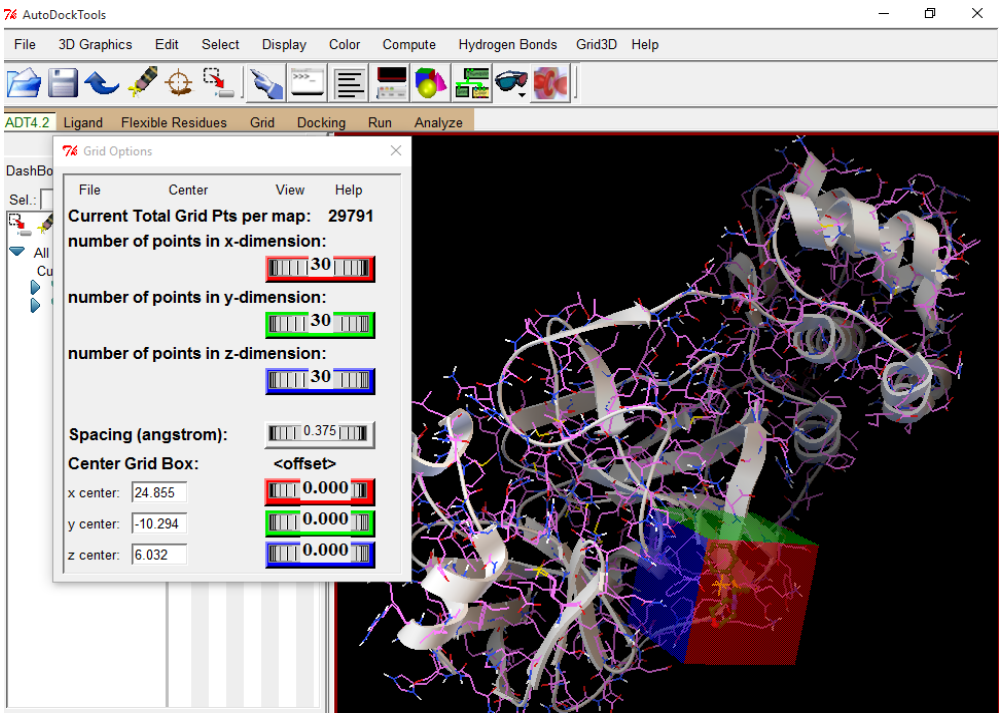
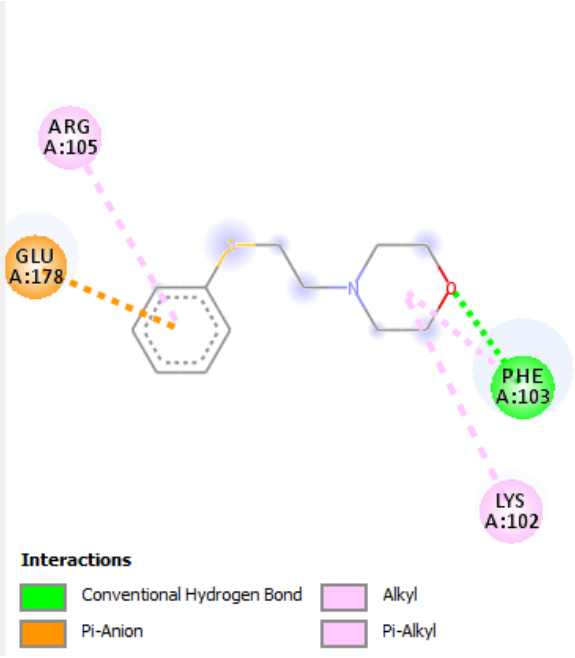


Figure 2. Grid parameters.



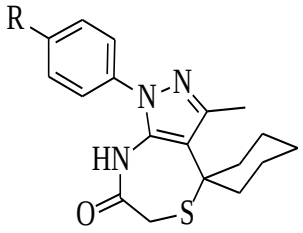
Scheme 2. Interactions of compound **M1** found by re-docking.

Molecular docking of proposed molecules was done given the inclusion of a sulfur- and nitrogen-containing heterocycle, including the spiro-fused fragment based on a ring closure strategy inspired in co-crystallized ligand **M1**; given this, four molecules will be submitted in collaboration project link[2], in addition to the fact that synthesis is already made and reported[3].

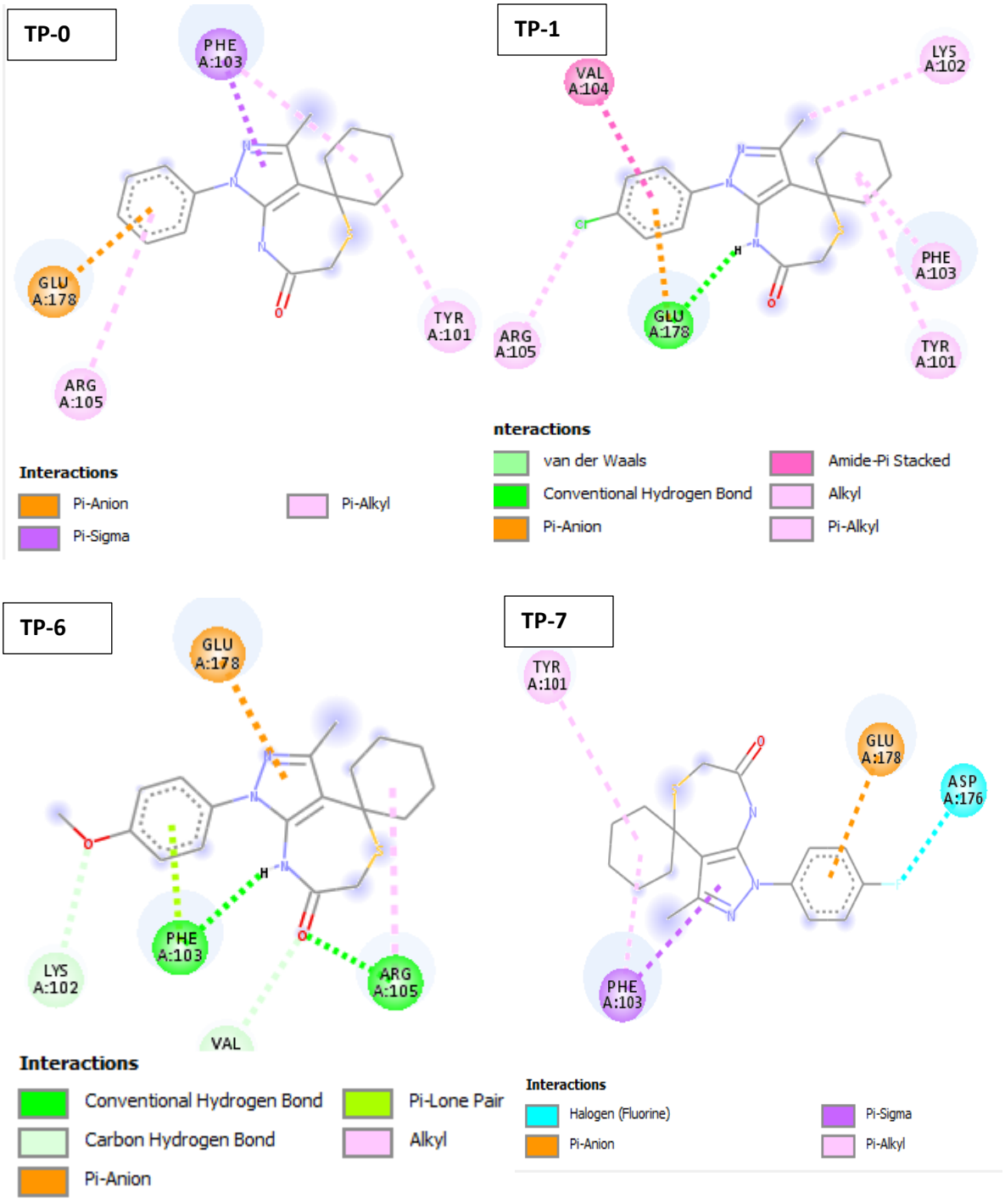
Screening was performed and qualified by energy, considering also predicted inhibition constant in comparison with other compounds such as reported peptide-mimetic **13b**[4], Favipiravir and Chloroquine (Table 1).

[2] https://covid.postera.ai/covid
[3] Becerra-Rivas, C; Cuervo-Prado, P; Orozco-Lopez, F. *Synthetic Communications* 49(3) 367 – 376 (**2019**).
[4] Zhang, L. *et al., Science, 10.1126/science.abb3405* (**2020**).

Table 1. Results of molecular docking for proposed molecules and some reported compounds



Code	R-	Energy (kCal/mol)	Ki
M1	-	-4.41	587.87 uM
Peptide-mimetic 13b	-	-2.86	7.96 mM
Favipiravir	-	-3.38	3.32 mM
Chloroquine	-	-5.26	139.33 uM
TP-0	H-	-6.07	35.32 uM
TP-1	Cl-	-5.81	55.21 uM
TP-6	MeO-	-5.87	49.94 uM
TP-7	F-	-5.76	60.36 uM



Scheme 3. Interactions predicted by molecular docking for proposed molecules.