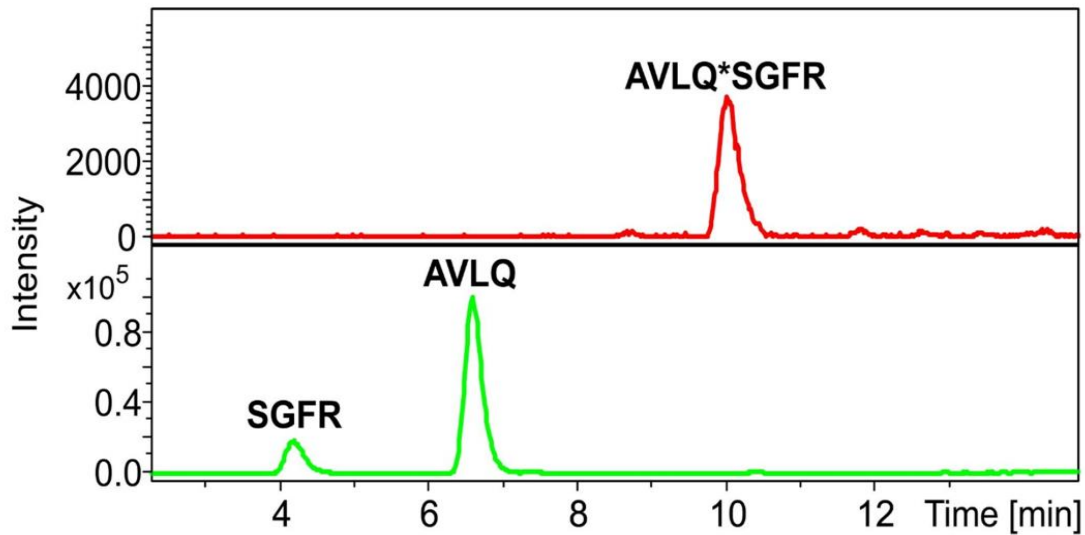


Supplementary figure 1. Determination of substrate cleavage and position of the cleavage products by SARS-CoV-2 M^{pro}. His₆-tagged purified M^{pro} was incubated with the substrate representing the AVLQ*SGFR cleavage site of SARS-CoV-2 PP1ab. High-performance liquid chromatography coupled to electrospray ionization time-of-flight mass spectrometry (HPLC-ESI-TOF MS) was then used to identify the cleavage products.



Supplementary table 1. Data compiled from the literature regarding the *in silico* screening of inhibitors against SARS-CoV-2 M^{pro}. Based on the scoring used in the given studies, efficacies of the tested HIV PIs were determined. The inhibitors predicted to be most effective out of the tested ones are shown in grey background. The values determined in the given studies are not fully comparable, as different methods were applied for the calculations. “-“ indicates that the given inhibitor was not included in the study or the obtained value was not reported.

Reference	Value	Amprenavir	Atazanavir	Darunavir	Fosamprenavir	Indinavir	Lopinavir	Nelfinavir	Ritonavir	Saquinavir	Tipranavir
Ortega et al., 2020	Binding energy (kcal/mol)	-7.6	-7.2	-8.2	-	-	-9.1	-	-6.9	-9.6	-8.7
Sang et al., 2020	Binding energy (kJ/mol)	-	-	-10.24	-	-10.02	-5.49	-	-2.34	-8.26	-5.8
Calligari et al., 2020	Vina scoring (kcal/mol)	-7.7	-8.0	-7.6	-7.2	-8.7	-8.1	-7.9	-8.1	-9.3	-8.6
Pant et al., 2020	Docking score	-	-	-7.21	-	-7.35	-8.36	-7.44	-8.30	-8.64	-
Shah et al., 2020	dock score (5R81)	-6.583	>-6.5	>-6.5	>-6.5	-6.834	-8.44	>-6.5	-6.764	-7.632	>-6.5
Beck et al., 2020	predicted K _d (nM)	-	94.94	-	-	-	-	-	204.05	-	-
Fisher et al., 2020	binding energy (kcal/mol)	-66.5	-	-	-	-	-	-80.6	-	-71.5	-