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Supplementary Data

Identification of therapeutic drugs against COVID-19 through computational investigation on drug repurposing and structural modification

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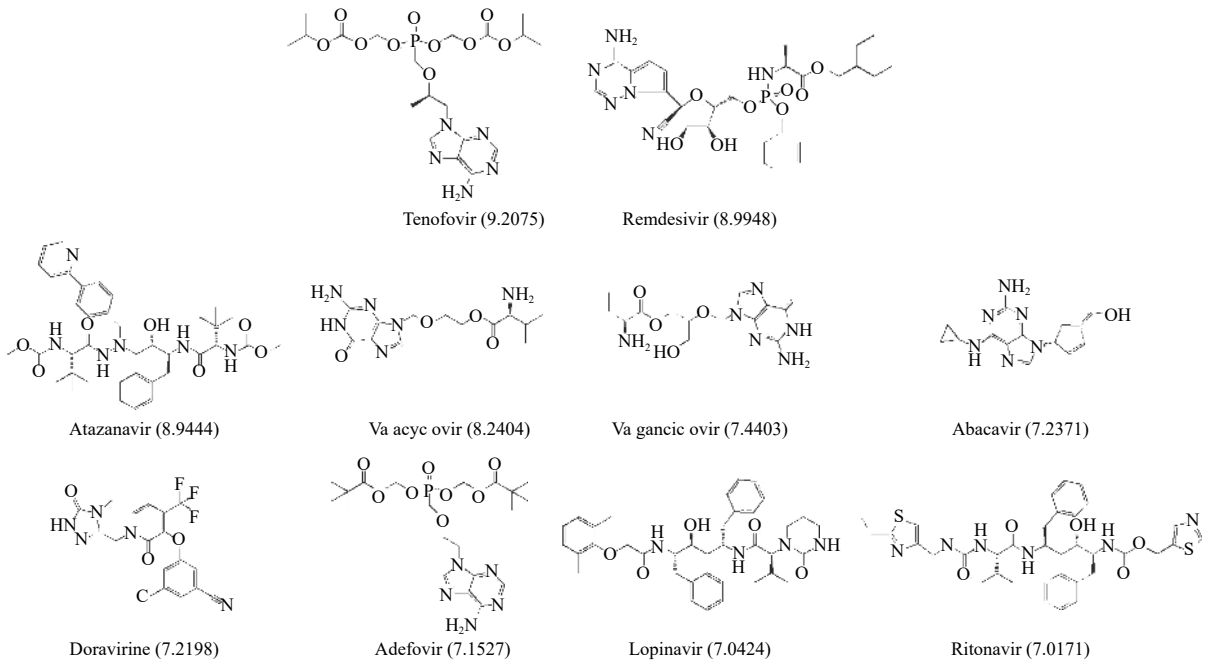

Supplementary Fig. 1 **Structural formulas of the screened antiviral compounds and their docking scores at spike-ACE2 interface.**

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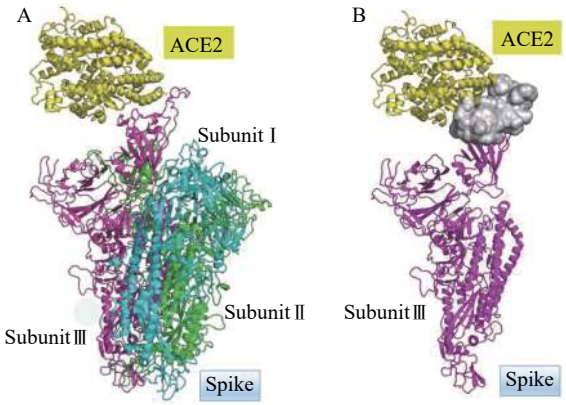
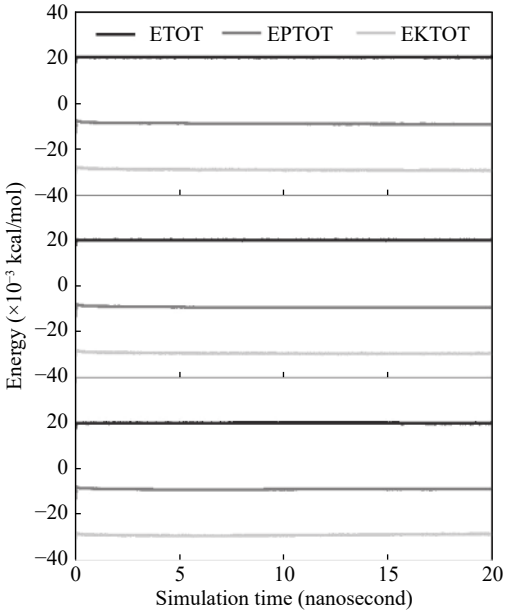
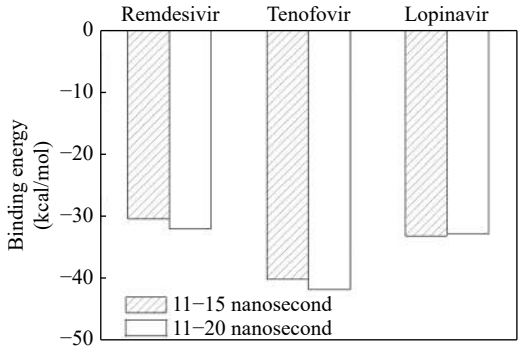


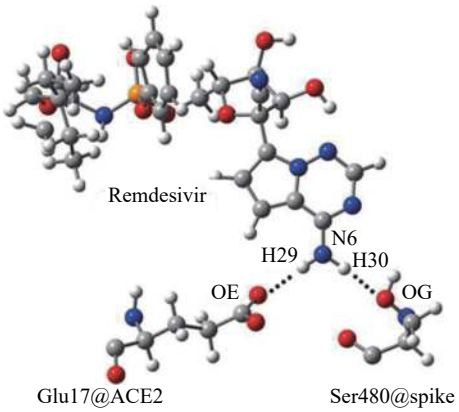
Supplementary Fig. 2 **Three-dimensional structure of spike-ACE2 complex.** A: Spike protein contains three subunits, Ⅰ, Ⅱ, and Ⅲ, which are colored in blue, green, and purple, respectively. B: Only subunit Ⅲ of spike is exhibited and the active pocket locating at the interface between spike and ACE2 is shown in gray.



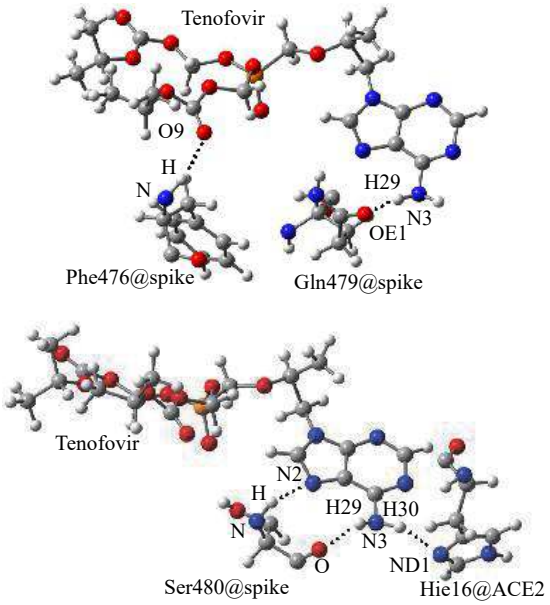
Supplementary Fig. 3 **Fluctuations of total (ETOT), potential energies (EPTOT), and kinetic (EKTOT) of the studied protein-ligand complexes with the simulation time.**



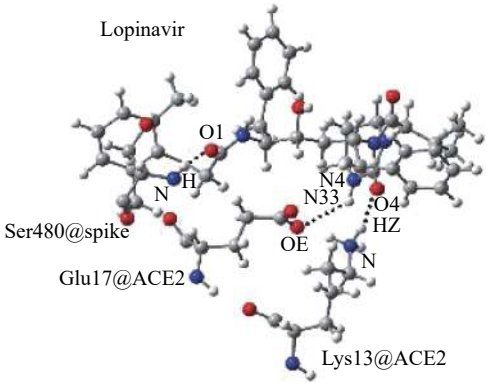
Supplementary Fig. 4 **Binding energies of studied compounds to spike-ACE2 coupling complex calculated from different simulation time.**



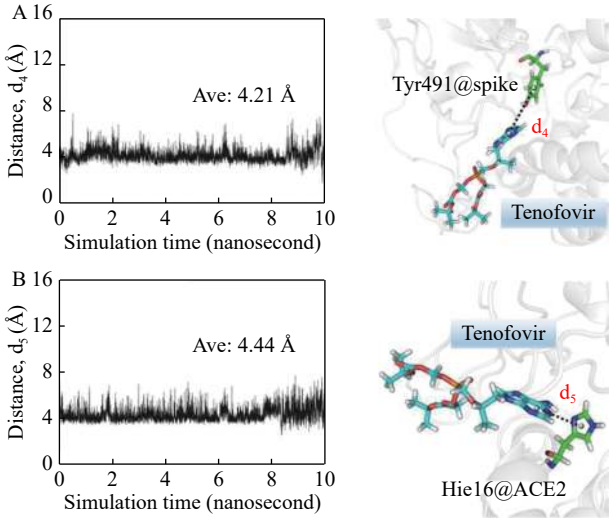
Supplementary Fig. 5 **The atomic index of remdesivir and its interacting residues.**



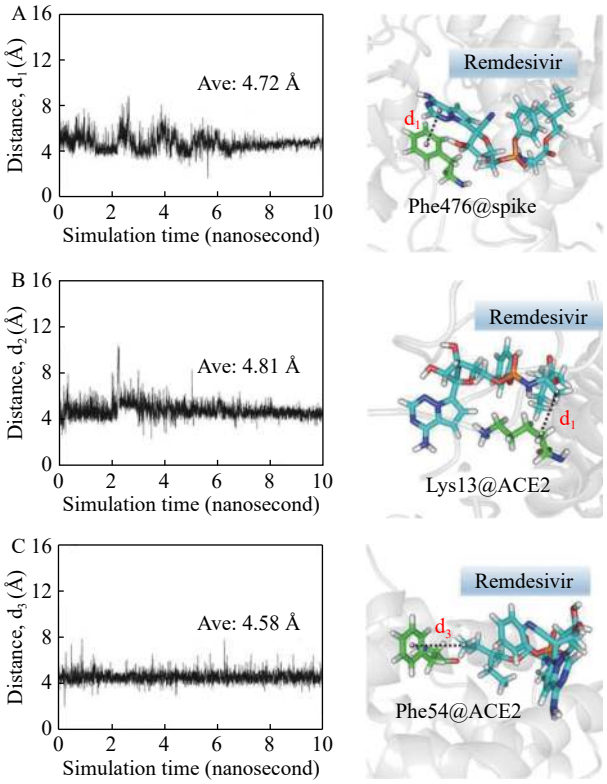
Supplementary Fig. 6 **The atomic index of tenofovir and its interacting residues.**



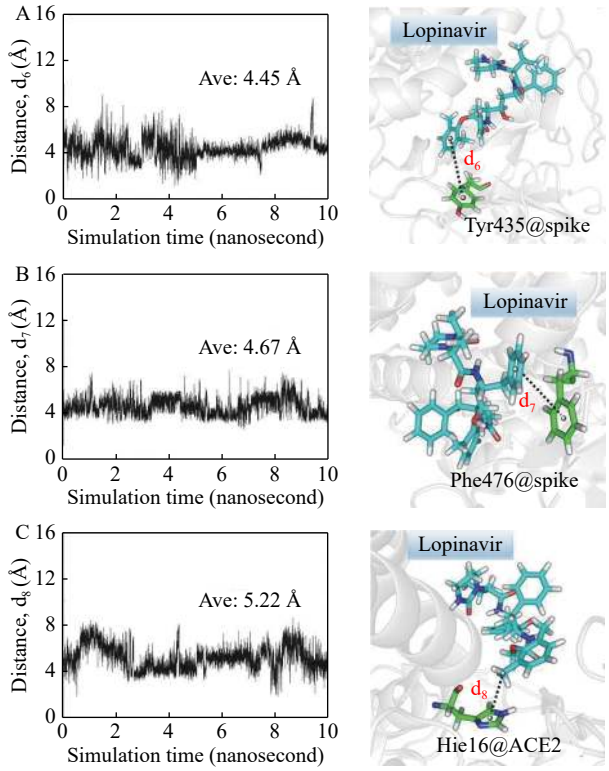
Supplementary Fig. 7 **The atomic index of lopinavir and its interacting residues.**



Supplementary Fig. 9 **Hydrophobic interaction between tenofovir and spike-ACE2.**



Supplementary Fig. 8 **Hydrophobic interaction between remdesivir and spike-ACE2.**



Supplementary Fig. 10 **Hydrophobic interaction between lopinavir and spike-ACE2.**

Supplementary Table 1 **Potential drugs obtained through high-throughput screening**

Name	Score	Name	Score
Tenofovir[a]	9.2075	Abacavir[a]	7.2371
Remdesivir[b]	8.9948	Doravirine[a]	7.2198
Atazanavir[a]	8.9444	Adefovir[a]	7.1527
Valacyclovir[a]	8.2404	Lopinavir[a]	7.0424
Valganciclovir[a]	7.4403	Ritonavir[a]	7.0171
Deferoxamine mesylate	12.8960	Naloxegol oxalate	8.7217
Goserelin acetate	10.6346	Octenidine dihydrochloride	8.6713
Landiolol hydrochloride	10.5632	Ethaverine hydrochloride	8.6713
Roxatidine acetate hydrochloride	10.2444	Carvedilol	8.6469
Bimatoprost	10.0981	Mitoxantrone hydrochloride	8.6327
Orlistat	10.0383	n-docosanol	8.5666
Naringin	10.0295	Tirofiban hydrochloride monohydrate	8.5228
Verapamil hydrochloride	10.0185	Esmolol hydrochloride	8.5129
Daurisoline	9.8525	Ethambutol dihydrochloride	8.4801
Tazemetostat	9.8259	Risedronic acid	8.4645
Leuprolide acetate	9.7606	Tianeptine sodium	8.4628
Coenzyme Q10	9.7268	Risedronate sodium	8.4608
Aspartame	9.7041	Ixazomib	8.4296
Thymopentin	9.4585	Glutathione	8.4278
Miriplatin	9.3745	Miltefosine	8.4256
Atorvastatin calcium	9.3730	Enzastaurin	8.4103
Flunixin meglumine	9.3568	DL-α-tocopherol	8.3863
Dabigatran etexilate	9.2073	Cediranib	8.3650
Batilol	9.1369	Mycophenolic acid	8.3294
Salvianolic acid B	9.0966	Methotrexate	8.3198
Batyl alcohol	9.0465	D-sorbitol	8.3188
Carfilzomib	8.9885	Visomitin	8.3188
Fulvestrant	8.8875	D-Mannitol	8.3188
Azelnidipine	8.8552	Pentagastrin	8.3182
Dronedarone hydrochloride	8.8402	Erythromycin	8.3108
Mitoxantrone	8.8016	Menatetrenone	8.2955
Prostaglandin E1	8.7995	Isavuconazonium sulfate	8.2915
Fingolimod hydrochloride	8.7727	Acrivastine	8.2890
Vitamin K2	8.2581	Lapatinib ditosylate monohydrate	7.7965
Cetylpyridinium chloride monohydrate	8.2440	Otilonium bromide	7.7900
Propafenone	8.2364	Dofetilide	7.7876
Amlodipine	8.2266	gamma-Linolenic acid	7.7805
Vitamin E	8.2161	Lercanidipine hydrochloride	7.7800
Ibutilide Fumarate	8.2124	Oxytocin acetate	7.7756
Lercanidipine	8.1933	Manidipine dihydrochloride	7.7664
Mupirocin	8.1786	Vardenafil hydrochloride trihydrate	7.7560
Montelukast sodium	8.1648	Suplatast tosilate	7.7522
Osimertinib mesylate	8.1647	mbelin	7.7438

Supplementary Table 1 **Potential drugs obtained through high-throughput screening** (continued)

Name	Score	Name	Score
Sivelestat	8.1632	Lisinopril dehydrate	7.7287
Dyclonine hydrochloride	8.1300	(±)-Bisoprolol hemifumarate	7.7273
palovarotene	8.1290	Docusate sodium	7.7250
Fluprostenol isopropyl ester	8.0621	Prostaglandin E2	7.7008
Citicoline	8.0589	LCZ696	7.6718
Nadolol	8.0536	Indacaterol	7.6697
Zolmitriptan	8.0204	L-Arginine	7.6623
Diminazene Aceturate	8.0058	Pramoxine hydrochloride	7.6531
Amikacin	7.9969	Heptaminol hydrochloride	7.6518
Tamsulosin hydrochloride	7.9640	Mebeverine hydrochloride	7.6452
Dabigatran	7.9172	L-(-)-α-Methyldopa	7.6406
Plerixafor 8HCl	7.9115	Chidamide	7.6273
Lapatinib	7.8904	Flunixin meglumin	7.6261
Cetrimonium bromide	7.8824	Tandutinib	7.6155
Dibucaine	7.8780	D-Pantethine	7.6145
Pretomanid	7.8576	Erlotinib	7.6059
Dapagliflozin	7.8537	Cetilistat	7.6035
Nifekalant hydrochloride	7.8447	Deferasirox	7.5987
Etilefrine hydrochloride	7.5891	Nimodipine	7.4707
Iloperidone	7.5832	Zinc undecylenate	7.4347
Efonidipine	7.5794	Cilastatin	7.4163
Bambuterol hydrochloride	7.5761	MLN9708	7.4107
Benserazide hydrochloride	7.5721	Benactyzine hydrochloride	7.3977
Sumatriptan succinate	7.5497	Gastrodin	7.3975
Betaxolol hydrochloride	7.5422	Euquinine	7.3956
Menadione	7.5321	Spiramycin	7.3938
Procainamide hydrochloride	7.5212	Quinapril hydrochloride	7.3825
Fluvastatin sodium salt	7.5208	Proadifen hydrochloride	7.3821
Lumefantrine	7.5192	Manidipine	7.3672
Alprenolol	7.5171	Nefazodone hydrochloride	7.3635
Glafenine	7.5130	Flavin mononucleotide	7.3628
Sulfadimethoxine	7.5038	Pemetrexed disodium	7.3591
Sodium cromoglycate	7.4999	Folic acid	7.3528
Demecarium bromide	7.4875	Dequalinium chloride	7.3513
Piperonyl butoxide	7.4850	Adrenalone hydrochloride	7.3391
Tranilast	7.4830	Cefminox Sodium	7.3256
Nimodipine	7.4707	Lafutidine	7.3195
Procainamide hydrochloride	7.5212	Macitentan	7.3158
Fluvastatin sodium salt	7.5208	Drofenine hydrochloride	7.3145

Supplementary Table 1 **Potential drugs obtained through high-throughput screening** (continued)

Name	Score	Name	Score
Lumefantrine	7.5192	Azilsartan Medoxomil	7.3105
Alprenolol	7.5171	Lobeline hydrochloride	7.2963
Glafenine	7.5130	Procaterol hydrochloride	7.2944
Sulfadimethoxine	7.5038	ABT530	7.2939
Sodium cromoglycate	7.4999	Cilostazo	7.2857
Demecarium bromide	7.4875	Pemetrexed acid	7.2839
Piperonyl butoxide	7.4850	Lovastatin	7.2627
Tranilast	7.4830	Erdafitinib	7.2585
Beta-Carotene	7.2469	Torezolid	7.1083
Indacaterol maleate	7.2405	Sunitinib	7.1049
Revefenacin	7.2374	Eliglustat	7.0971
Atosiban acetate	7.2316	Paromomycin Sulfate	7.0955
Candesartan Cilexetil	7.2311	Metoclopramide hydrochloride	7.0907
Cefpiramide acid	7.2226	Tannic acid	7.0870
Verteporfin	7.2222	Ritodrine hydrochloride	7.0813
Troxerutin	7.2038	Hydroxychloroquine sulfate	7.0813
Pemetrexed Disodium Hydrate	7.1984	Cimetidine	7.0729
Acecainide	7.1941	ABT199	7.0678
Phthalylsulfacetamide	7.1843	Xylitol	7.0648
Neratinib	7.1802	Safinamide mesylate	7.0647
Oxaprozin	7.1727	Pacritinib	7.0602
Sparfloxacin	7.1694	Telmisartan	7.0599
Propitocaine hydrochloride	7.1635	Nebivolol hydrochloride	7.0593
Jaceosidin	7.1613	Siponimod	7.0582
Carazolol	7.1592	Teniposide	7.0546
Ramatroban	7.1567	Benazepril hydrochloride	7.0539
Sodium gluconate	7.1536	Eletriptan HBr	7.0487
Atracurium besylate	7.1484	Methocarbamol	7.0482
Valbenazine	7.1457	Pravastatin sodium	7.0438
Tilorone dihydrochloride	7.1447	Vemurafenib	7.0314
Treprostinil Sodium	7.1396	Mycophenolate Mofetil	7.0290
Formoterol	7.1373	Imatinib Mesylate	7.0231
Cefdinir	7.1274	Lubiprostone	7.0227
Brinzolamide	7.1264	Azelaic acid	7.0209
Brexpiprazole	7.1233	Olodaterol	7.0168
Vitamin E Acetate	7.1201	Ebastine	7.0052
Fenofibrate	7.1185	Ospemifene	7.0027

[a].Antiviral drugs. [b].Has not been approved by FDA and was screened by molecular docking.